รายงานวิจัยฉบับสมบูรณ์

โครงการสนับสนุนกลุ่มวิจัยระบาดวิทยา

โดย วีระศักดิ์ จงสู่วิวัฒน์วงศ์ และ คณะ

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กิตติกรรมประกาศ

โครงการสนับสนุนกลุ่มวิจัยระบาดวิทยา (โครงการเมธีวิจัยอาวุโส วีระศักดิ์ จงสู่วิวัฒน์วงศ์) ได้รับการสนับสนุนทางการเงินจากสำนักงานกองทุนสนับสนุนการวิจัย (สกว.) และทางด้านการบริหารจัดการจากคณะแพทยศาสตร์และคณะต่าง ๆ ในมหาวิทยาลัยสงขลานครินทร์

งานวิจัยในโครงการนี้ ส่วนใหญ่เป็นการใช้ทรัพยากรร่วมกับแหล่งทุนอื่น ๆ ทั้งในและต่างประเทศ เช่น องค์การอนามัยโลกซึ่งหน่วยระบาดวิทยาเป็นสถาบันฝึกอบรมให้กับผู้ได้รับทุน รวมทั้งเป็นผู้รับทุนวิจัยบางโครงการ, สำนักงานกองทุนสนับสนุนการสร้างเสริมสุขภาพ และสถาบันวิจัยระบบสาธารณสุข

Abstract

Project Code: RTA/09/2543

Project title: Enhancement of Epidemiological Research Group, Prince of Songkla University (Phase II)

Investigators:

Virasakdi Chongsuvivatwong* Alan Geater* Than Winn*

Silom Jamulitrat* Ladda Mo-suwan* Hutcha Sriplung*

Petchwa Pungrassami** Tippawan Liabsuetrakul* Shoko Oshikawa*

Chaveewan Ratanajamit* Nualta Arpakappakul* Mapaosis Duerawee*

Apiradee Lim* Edward McNeil*

*Faculty of Medicine, Prince of Songkla University

**Zonal TB Centre 12 Yala

Email Address: cvirasak@ratree.psu.ac.th

Project Period: 20 September 1999 – 30 September 2003

Objectives:

1. To produce high quality epidemiological research for the purposes of planning and evaluation of health care.
2. To increase the number of high quality epidemiological researchers

Methodology: various methods e.g. survey, case-control study, cohort study, randomized control trial and diagnostic test.

Results:

Twenty-five publications in international indexed journals were supported by this Senior Research Scholar Program during the funded period. Eight are presented in this report. Eight Thai and five international Ph.D. students are enrolled in the program

Discussion and conclusion

This program has contributed remarkably to scientific development in Thailand and Asia.

Suggestion:

The program needs further funding to ensure continuation of success in the development.

Keywords

Health systems research, international training program, Epidemiology.

บทคัดย่อ

รหัสโครงการ: RTA/09/2543

ชื่อโครงการ: โครงการส่งเสริมกลุ่มวิจัยระบาดวิทยา มหาวิทยาลัยสงขลานครินทร์

รายชื่อคณะทำงาน:

วีระศักดิ์ จงสู่วิวัฒน์วงศ์*	Alan Geater*	Than Winn*
สีลม แจ่มอุลิตรัตน์*	ลัดดา เหมาะสุวรรณ*	หัชชา ศรีปลั่ง*
เพชรวรรณ พึ่งรัศมี**	ทิพวรรณ เลียบสื่อตระกูล*	Shoko Oshikawa*
ฉวีวรรณ รัตนจามิตร*	นวลตา อาภาคัพภะกุล*	มะเพาซิส ดือราวี*
อภิรดี แซ่ลิ้ม*	Edward McNeil*	

Email Address: cvirasak@ratree.psu.ac.th

ระยะเวลา: 20 กันยายน 2542 – 19 กันยายน 2546

วัตถุประสงค์:

1. ผลิตผลงานการวิจัยทางระบาดวิทยาที่ช่วยการวางแผนและประเมินผลการให้บริการสาธารณสุข
2. ผลิตนักวิจัยทางระบาดวิทยาที่มีคุณภาพสูง

วิธีการ ใช้ระเบียบวิธีวิจัยต่าง ๆ เช่น survey, case-control study, cohort study, randomized control trial and diagnostic test.

ผลลัพธ์:

โครงการได้มีส่วนสนับสนุนงานตีพิมพ์ในวารสารนานาชาติใน Index Medicus รวม 25 รายการ

มีนักศึกษาระดับปริญญาเอกไทย 6 คน ต่างประเทศ 3 คน

อภิปราย

โครงการนี้ได้พัฒนาศักยภาพทางด้านการวิจัยของประเทศไทยและของเอเชีย

ข้อเสนอแนะ:

ควรสนับสนุนการพัฒนาแบบนี้ต่อไป

Executive Summary

This program is based at the Epidemiology Unit, Faculty of Medicine, Prince of Songkla University, in order to strengthen research capabilities of the epidemiological research group. Several research projects were initiated. Six Thai and three International Ph.D. students enrolled in the program and were involved in the research. Twenty-nine articles were published in international journals. The following paragraphs summarize the publications. Details of each article are in the annexed reprints and manuscripts.

เนื้อหางานวิจัย

เรียงตามผลงานวิจัยดังนี้

1. Sungthong R, Mo-suwan L, Chongsuvivatwong V, Junjana C. Secular increases in weight, height and body mass index among school children of Hat Yai, Thailand: a 5 years follow-up study. Southeast Asian J Trop Med Public Health 1999;30:532-8.

Abstract: Upward trend of growth and overweight has been reported from developed countries. As Thailand has been undergoing rapid economic transition over the previous decade, we conducted an analysis to demonstrate the secular changes of growth over five years follow-up. Subjects were a cohort of 2,252 primary school children recruited in 1992 for the Hat Yai childhood obesity study. Baseline demographic and family data were collected by a questionnaire completed by parents. To quantify the cohort effect, a generalized estimating equations analysis for a cross sectional time series data was undertaken with weight, height, and body mass index (BMI, kg/m2) as a dependent variable and containing a quadratic term of age, sex, year of birth and family variables. One thousand and ninety-four (48.5%) children completed 6 anthropometric measurements. Graphs of median weight, height, BMI and overweight prevalence of each birth cohort against age showed secular increases of growth and overweight, and an age effect. For each one-year younger cohort, the median weight, median height and median BMI increased by 1.22 kg, 1.25 cm and 0.23 kg/m2, respectively. An increasing trend of childhood overweight reported here may signify a need for preventing overweight and reducing weight in childhood adolescence in the future.

2. Thapa N, Chongsuvivatwong V, Geater AF, Ulstein M. High-risk childbirth practices in remote Nepal and their determinants. Women Health 2000;31:83-97.

Abstract: This study describes birth-related practices and their determinants among women in the Jumla district of Nepal. Data were derived from a household survey in 1996. Of 939 married women of reproductive age, 657 who had given birth to their last child during the previous five years were included in the analysis. Qualitative information was further obtained from traditional birth attendants (TBAs), mothers-in-law, community leaders and pregnant women. High-risk practices were common and related to local custom and lack of knowledge on the importance of cleanliness. Husband's level of education greater than fifth grade significantly reduced the high-risk practices in all stages of childbirth, independent of other socio-economic, biological and village variables.

3. Thongsuksai P, Chongsuvivatwong V, Sriplung H. Delay in breast cancer care: a study in Thai women. Med Care 2000;38:108-14.

Abstract: BACKGROUND: Breast cancer is the second most common cause of cancer death in Thai women. Cancer registry data reveal a high prevalence of late-stage disease at diagnosis. The factors resulting in delay in Thailand have not yet been investigated. OBJECTIVES: To determine the extent of, and the factors contributing to, delay in breast cancer care. DESIGN: Women with breast cancer who were first treated at Songklanagarind Hospital between June 1994 and June 1996 were interviewed with retrospective chart audits of care. MEASURES: Dependent variables included patient delay (symptom recognition to first care) and system delay (first care to treatment). Independent variables tested included demographic factors, help-seeking behavior, and cancer knowledge. Nonparametric rank sum tests were used for univariate analysis, and Cox regression was used for multivariate analysis. RESULTS: Ninety-four cases were included in the study. The median patient and system delays were 4 weeks; 26.6% and 24.4% of patients, respectively, experienced patient and system delay >12 weeks. Only marital status (unmarried compared with married women) was significantly associated with patient delay (hazard ratio [HR] 2.78, 95% CI 1.23-6.25). Contacting a provincial hospital instead of a university hospital as first medical care (hazard ratio 2.50, 1.23-5.26), being given a diagnosis rather than being told nothing (HR 2.04, 1.14-3.57) and being given treatment rather than being immediately referred (HR 4.55, 2.22-9.09) were associated with system delay. CONCLUSIONS: Patient delay and system delay in breast cancer care are important weaknesses of disease control in Thailand. Educational programs should target unmarried women, who are at higher risk of delay. System delay in hospitals outside the university needs to be improved by a good referral system.

4. Nguyen TM, Chongsuvivatwong V, Geater A, Prateepchaikul L. Characteristics of repeat aborters in Vietnam. Southeast Asian J Trop Med Public Health 2000;31:167-72.

Abstract: Two hundred and sixty married women seeking induced abortion service in Hanoi, Vietnam were interviewed to determine the magnitude of repeat induced abortion and explore selected characteristics of the repeat aborters. Seventy-one percent of the sample reported having had at least one previous induced abortion. After adjustment for age and number of living children, poor attitudes toward contraception, low use of modern contraceptives and failure of contraception were shown to be significantly associated with repeat induced abortion. Woman's age, number of living children, contraceptive knowledge and experience and desire for no more children were positively related to repeat induced abortion. Socio-demographic characteristics were not related to repeat induced abortion. Improvement of attitudes toward

contraception, persuasion to use modern contraception and promotion of contraceptive effectiveness are recommended strategies to prevent repeat induced abortion.

5. Tran TS, Jamulitrat S, Chongsuvivatwong V, Geater A. Risk factors for postcesarean surgical site infection. Obstet Gynecol 2000;95:367-71.

Abstract: OBJECTIVE: To determine postcesarean complications and identify independent risk factors for surgical site infection. METHODS: We studied a cohort of 969 women delivered by cesarean between May and August 1997. Infections were determined by examinations during ward rounds, reviews of laboratory results, and follow-up for 30 days after discharge. Risk factors were identified by multiple logistic regression. RESULTS: Surgical complications were rare. There were febrile morbidity and infection complications in 16.2% and 12.4% of subjects, respectively. Eighty-five subjects had 95 surgical site infections (9.8%), and seven risk factors were independently associated with infection. Risk factors included preoperative remote infection (adjusted odd ratio [OR] 16.5, 95% confidence interval [CI] 2.1, 128.3); chorioamnionitis (OR 10.6, 95% CI 2.1, 54.2); maternal preoperative condition (OR 5.3 for those with severe systemic disease [American Society of Anesthesiologists score > or =31, 95% CI 1.2, 24.0); preeclampsia (OR 2.3, 95% CI 1.1, 4.9); higher body mass index (OR 2.0 for every five-unit increment, 95% CI 1.3, 3.0); nulliparity (OR 1.8, 95% CI 1.1, 3.2); and increased surgical blood loss (OR 1.3 for every 100-mL increment, 95% CI 1.1, 1.5). CONCLUSION: Host susceptibility and existing infections were important predictors of surgical site infection after cesarean delivery. Further intervention should target this high-risk group to reduce the clinical effect of surgical site infection.

6. Teanpaisan R, Nittayananta W, Chongsuvivatwong V. Biotypes of oral Candida albicans isolated from AIDS patients and HIV-free subjects in Thailand. J Oral Pathol Med 2000;29:193-9.

Abstract: This study was conducted to examine biotypes and antifungal susceptibility patterns of oral Candida albicans isolated from HIV-infected patients, HIV-free patients with candidiasis and healthy subjects. All isolates were biotyped using a typing system based on enzyme profiles, carbohydrate assimilation patterns and boric acid resistance. Thirty-eight biotypes were found amongst 218 oral C. albicans isolates. The major biotype found was A1S, which accounted for 32.6% of all isolates, and this biotype was the most common in all groups. There was a greater variety of biotypes of C. albicans in the HIV-infected group than in the other groups; however, there was no statistically significant difference between the groups. The minimum inhibitory concentrations (MICs) of a total of 118 isolates were determined for

amphotericin B and for ketoconazole using the National Committee for Clinical Laboratory Standards (NCCLS) broth macrodilution method and the E-test. When the antifungal susceptibility patterns among the groups were compared, a statistically significant difference was found only with amphotericin B. The median MIC of amphotericin B in the HIV-infected group was higher than in the healthy group (P=0.013, NCCLS method; P=0.002, E-test). However, this difference in sensitivity was not restricted to any sub-type investigated. Our results showed that the biotype patterns of C. albicans isolates that colonize HIV-infected patients are similar to those of HIV-free subjects, and there is no relationship between antifungal susceptibility patterns and the biotypes.

7. Chowdhury ME, Akhter HH, Chongsuvivatwong V. Community-based self-reported symptoms of antepartum morbidities; the health burden and care-seeking patterns of rural Bangladeshi women. Southeast Asian J Trop Med Public Health 2000;31:598-605.

Abstract: In Bangladesh there is a dearth on information relating to complications during pregnancy. We followed up 1,019 pregnant women in rural Bangladesh sampled from all the 4 old administrative divisions of the country. Trained female interviewers visited households of the pregnant women at four-week intervals and interviewed them for their current pregnancy-related complications. Out of a total of 3,812 antepartum visits the percentage of reported symptoms of bleeding, fits and convulsions, excessive vomiting, fever >3 days, urinary problems, palpitations and symptomatic anemia were 0.3, 0.7, 1.4, 4.0, 26.8, 46.5 and 78.3 respectively. Morbidities were considered to cause a health burden if they imposed constraints in daily activities of the pregnant women and they were weighted according to intensity of the constraint. For each morbidity, the mean intensity of burden per episode and the population burden per 1,000 person months of observation of all the women were calculated. For common sustaining morbidities like symptomatic anemia and urinary problems the population burden was much heavier than that for more serious but rare morbidities like bleeding and convulsions. Among the visits in which the women had any symptoms, the percentages of care-seeking for less frequently reported morbidities such as fits and convulsions, bleeding, fever >3 days, excessive vomiting were about 74, 50, 34 and 33% respectively, whereas those for more commonly reported complications such as urinary problems, symptomatic anemia and palpitations were less than 20%. Care for these morbidities was mostly sought from untrained providers.

8. Thapa N, Chongsuvivatwong V, Geater AF, Ulstein M, Bechtel GA. Infant death rates and animal-shed delivery in remote rural areas of Nepal. Soc Sci Med 2000;51:1447-56.

Abstract: This article outlines a community-based retrospective study in a remote area of Nepal and describes local birth practices and their impact on infant mortality. Data collection was carried out in two steps, a household survey from September to October 1996 and a qualitative research phase. Data collected include socio-economic background, reproductive history, birth practices and child survival. Among 3007 live-born children, 660 (22%) died before their first birthday. In keeping with local customs, approximately half of the children were delivered in an animal shed and the other half in the home. Children born in an animal shed were at significantly higher risk of dying than were those born in the home even after adjusting for socio-economic status and biological variables. The association was stronger in the neonatal period (OR = 2.8, 95% CI 1.9-4.1) than during the post-neonatal period (OR= 1.3, 95% CI 1.02-1.6). The preparation of the delivery place was inadequate and thereby facilitated infection of both the newborn and the mother. Traditional norms and animal-shed delivery practices are common in the Jumla community. The reasons addressed for giving birth in the animal shed included (1) Household Deity's anger if delivery takes place in the home and (2) easy to clean the shed following the birth.

9. Chongsuvivatwong V, Lim A, Dueravee M, Geater A, Ritsamitchai S, Oshikawa S. Follow up of water use in a tin mining area affected with arsenic poisoning. Southeast Asian J Trop Med Public Health 2000;31:769-74.

Abstract: Ron Phibun district in southern Thailand has been known as an endemic area for arsenic contamination. The government has been trying to improve the situation by encouraging the use of rainwater and piped water. This study aimed to document the change of water use and to identify factors associated with safe water use in 1997 compared to that in 1994. Home visits and face-to-face questionnaire interviews were undertaken. Information on water use for drinking, cooking, washing food and washing utensils in 1994 and 1997 was obtained. Among 3,849 households from which data could be obtained (estimated 79% of total households), the percentages of using safe water (including water from bottled rain water, piped and artesian well water) for drinking and cooking rose from 72.5 and 57.9 in 1994 to 93.6 and 80.9 in 1997, respectively. The percentages for washing foods and for washing utensils rose from 28.6 and 20.5 to 59.1 and 53.8, respectively. In 1997, percentage of households using piped water for drinking and cooking was still low (3.6 and 12.3) compared to those using piped water for washing food and utensils (39.1 and 43.6). Multivariate analysis shows that independent factors of the household predicting safe water use are: high arsenic area, near main road and having piped water installed. The influence of these factors (as judged by the level of odds ratio) operates more or less equally on water use for all purposes,

except that installation of piped water has more influence on washing water than drinking and cooking water. We conclude that safe water supply in the area is still inadequate. Even if piped water is installed, it is often not used for drinking and cooking. The reasons for not using piped water for drinking and cooking need to be identified.

10. Ratanajamit C, Chongsuvivatwong V. Survey of knowledge and practice on oral contraceptive and emergency contraceptive pills of drugstore personnel in Hat Yai, Thailand. Pharmacoepidemiol Drug Saf 2001;10:149-56.

Abstract: In Thailand, oral contraceptive (OC) and emergency contraceptive pill (ECP) are available as over-the-counter (OTC) drugs, and drugstores share 30% of services. While the rate of dispensing contraceptive pills has increased, the knowledge and awareness of ECP use is limited among users and providers. The objective of this study was to assess knowledge and practice of drugstore personnel on providing OC and ECP, in order to improve the quality of services. Drugstores located in Hat Yai District, Songkhla Province, Southern Thailand, were the accessible population. There were 109 drugstores, half of them owned by pharmacists. The population was stratified by owner (pharmacist or non-pharmacist) and randomly selected to obtain a sample size of 30 drugstores for each class. Two study methods, questionnaire interview and secret shopping, were used to measure knowledge, and practice, respectively. History-taking, drug-choosing, and advice-giving were the domains measured. The results demonstrated that knowledge on OC was fair, but that on ECP was poor. Pharmacists had better knowledge of proper history taking and ECP indication than non-pharmacists. OC and ECP provision were inappropriately practised in drugstores in the study area. A majority of drugstores were mainly owned by non-pharmacists. For OC practice, drug-choosing was good, but history-taking and advice-giving were poor in both groups. Although both groups dispensed ECP poorly, pharmacists dispensed significantly better than non-pharmacists. Among non-pharmacist staff, the average scores of OC advice-giving, and ECP dispensing, were statistically significantly better among those working in pharmacist-owned drugstores. Both knowledge and practice on OC and ECP should be improved in both types of drugstores in the study area.

11. Huong NT, Chongsuvivatwong V, Geater A, Prateepchaikul L. Cost-benefit analysis of urine pregnancy tests prior to menstrual regulation in Vietnam. Am J Public Health 2001;91:825-6.

12. Leesmidt V, Pannarunothai S, Chongsuvivatwong V. Implementing the universal health coverage: which source of information is more reliable? Southeast Asian J Trop Med Public Health 2001;32:674-81.

Abstract: The implementation of universal health coverage needs accurate data on the distribution of health benefit coverage, particularly the uninsured. The national surveys and routine reports are two important sources of information ready for use. This study shows the validation of data from two sources. The data from national household surveys on the medical welfare, the health card and the social security schemes were validated with the routine report data of the Ministry of Public Health (MOPH) and the Social Security Office (SSO) by provinces. There were considerable differences between these data sets. The national survey data gave a 1.5 times higher estimate than the report data of the MOPH and the SSO. Financial implications of using inaccurate data to implement the universal health coverage could be huge, depending on the capitation rate.

13. Sungthong R, Mo-suwan L, Chongsuvivatwong V. Effects of haemoglobin and serum ferritin on cognitive function in school children. Asia Pac J Clin Nutr 2002;11:117-22.

Abstract: The association between iron deficiency anaemia and cognitive function impairment has been widely reported in young children, but whether the impairment is a result of iron deficiency per se or a combination of iron deficiency and anaemia, and how these conditions interact, is still questionable. Four hundred and twenty-seven school children from two schools in socioeconomically deprived communities were selected in southern Thailand. Iron status was determined by haemoglobin and serum ferritin concentrations. Cognitive function in this study was measured by IQ test and school performance, including Thai language and mathematics scores, using z-scores based on distributions within the same grade and school. Data on demography and socioeconomic status were collected by questionnaire answered by the parents. Linear regression models were used to investigate the effect of anaemia and iron deficiency, reflected by haemoglobin and serum ferritin concentration, on cognitive function and school performance. We found that cognitive function increased with increased haemoglobin concentration in children with iron deficiency, but did not change with haemoglobin concentration in children with normal serum ferritin level. Children with iron deficiency anaemia had consistently the poorest cognitive function (IQ, 74.6 points; Thai language score, 0.3 SD below average; and mathematics score, 0.5 SD below average). Children with non-anaemic iron deficiency but with high haemoglobin levels had significantly high cognitive function (IQ, 86.5 points; Thai language score, 0.8 SD above average; and mathematics score, 1.1 SD above average). This study found a dose-response relationship between haemoglobin and

cognitive function in children with iron deficiency, whereas no similar evidence was found in iron sufficient children.

14. Chowdhury ME, Chongsuvivatwong V, Geater AF, Akhter HH, Winn T. Taking a medical history and using a colour scale during clinical examination of pallor improves detection of anaemia. Trop Med Int Health 2002;7:133-9.

Abstract: We developed a colour tint scale to use as an aid in the clinical assessment of anaemia by measuring conjunctival pallor. The objectives of this study were to evaluate the accuracy and agreement among observers in detecting anaemia in three sequential phases with incremental information using clinical pallor of different anatomical sites, subsequently adding subjects' medical history for physical symptoms and the colour scale. After training in the application of these three sequential assessments, 12 primary health workers were assigned to independently examine 198 anaemic and 254 non-anaemic pregnant women while blind to the true anaemic status. Their assessments in each phase were then compared with the anaemic status based on haemoglobin level, measured using HemoCue, taken as the gold standard, to determine sensitivity and specificity, and agreements among observers in detecting anaemia were calculated. In the three sequential phases of assessment the sensitivities were 73.8, 78.3, 82.9% and specificities 76.0, 84.7 and 90.9%, respectively. In each subsequent step, the improvements in both the sensitivity and specificity were statistically significant [P(chi2(McNemar)) < 0.01]. Kappa statistics for agreement among 12 observers for assessing anaemia in the sequential phases were 0.50, 0.71 and 0.82, respectively. The Spearman rank correlation coefficient between haemoglobin level and the colour scale reading was 0.68 (P < 0.001). Taking medical history and incorporating a simple colour tint scale with examination of pallor improved the sensitivity, specificity and agreement for detection of anaemia by health workers.

15. Pungrassami P, Johnsen SP, Chongsuvivatwong V, Olsen J. Has directly observed treatment improved outcomes for patients with tuberculosis in southern Thailand? Trop Med Int Health 2002;7:271-9.

Abstract: OBJECTIVE: To validate the practice of directly observed treatment (DOT) and evaluate its effect on treatment outcomes. METHODS: This follow-up study conducted in 24 districts in southern Thailand included 411 new, smear-positive, pulmonary tuberculosis (TB) patients who started treatment between February and September 1999. Patients and/or their observers were interviewed about their actual DOT practice during the first 2 months of treatment. Treatment outcomes were evaluated at the end of the second month and at the end

of treatment. RESULTS: Of 411 patients, 379 were assigned to DOT but only 68 practised strict DOT for every dose during the first 2 months. Adjusted odds ratios (ORs) for 'no sputum conversion' and 'unsuccessful treatment' were 1.1 (95% CI 0.6-2.1) and 1.3 (95% CI 0.6-2.8), respectively, for those who practised strict DOT vs. the rest. CONCLUSIONS: Actual practice of DOT was quite different from what was intended at the assignment. Practice of strict DOT during the first 2 months was not associated with sputum conversion or treatment success in this study area.

16. Sungthong R, Mo-Suwan L, Chongsuvivatwong V, Geater AF. Once weekly is superior to daily iron supplementation on height gain but not on hematological improvement among schoolchildren in Thailand. J Nutr 2002;132:418-22.

Abstract: Intermittent iron supplementation has been suggested as a replacement for daily iron supplements for reducing anemia in developing countries. The effects of once weekly and daily iron supplementation on hemoglobin (Hb), serum ferritin (SF), prevalence of anemia, weight and height are compared in this study. Primary schoolchildren (n = 397) from two selected schools in the Hat Yai rural area, southern Thailand, were recruited in 1999. All children received Albendazole and then randomly received ferrous sulfate (300 mg/tablet) either daily or weekly, or a placebo for 16 wk. The average increase in Hb was not significantly different between the daily (mean +/- SD; 6.5 +/- 6.0 g/L) and weekly (5.7 +/- 6.3 g/L) groups. However, the average increase in SF was greater ($P < 0.01$) in the daily (mean +/- SD; 39.8 +/- 30.3 microg/L) than the weekly (13.4 +/- 17.3 microg/L) group. All cases of iron deficiency anemia were abolished in both daily and weekly groups, whereas no reduction in prevalence occurred in the placebo group. Height gain was greater in children who received weekly (mean +/- SD; 2.6 +/- 0.9 cm) than in those who received daily iron (mean +/- SD; 2.3 +/- 0.8 cm), ($P < 0.01$). Weight gain, weight-for-age and height-for-age were not significantly different among the intervention groups. It is concluded that a weekly iron dose is more effective than a daily dose in height gain but not in hematological improvement over 16 wk of supplementation.

17. Pungrassami P, Johnsen SP, Chongsuvivatwong V, Olsen J, Sorensen HT. Practice of directly observed treatment (DOT) for tuberculosis in southern Thailand: comparison between different types of DOT observers. Int J Tuberc Lung Dis 2002;6:389-95.

Abstract: SETTING: A government health system in southern Thailand where the directly observed treatment, short-course (DOTS) strategy has been implemented. OBJECTIVE: To compare the practice of actual directly observed treatment (DOT) and the observer sustainability for different types of observer. METHODS: During 1999-2000, 411 patients with

new smear-positive pulmonary tuberculosis were followed up. The patients and/or their observers were interviewed about the presence of any person with the patient during drug intake and the practice of watching the patient swallowing the medicine (actual DOT). Data were recorded monthly and analysed by Cox and logistic regression models. RESULTS: For health personnel (HP), community member (CM), and family member (FM) observers, the proportions who did not practise actual DOT were respectively 11%, 23%, and 35%, and the proportions who changed to no observer or self administration were respectively 11%, 1%, and 2%, during the first 9 months of treatment. Health personnel had the lowest risk of not practising actual DOT (odds ratio HP/FM 0.1, 95%CI 0.1-0.2; CM/FM 0.9, 95%CI 0.5-1.6) but the highest risk for change to self administration. CONCLUSION: To increase the coverage of actual DOT, strategies are needed to maintain health personnel as the DOT observers and to promote actual DOT among family member observers.

18. Ratanajamit C, Chongsuvivatwong V, Geater AF. A randomized controlled educational intervention on emergency contraception among drugstore personnel in southern Thailand. J Am Med Womens Assoc 2002;57:196-9, 207.

Abstract: OBJECTIVE: to document the effectiveness of an educational intervention in improving knowledge of and practice in dispensing emergency contraception (EC) among drugstore personnel in Thailand. METHODS: Sixty of 120 drugstores in Hat Yai, a city in Southern Thailand, were randomly selected, and half of them were randomly assigned to participate in an educational program. Well-trained "secret" shoppers went into each store before the intervention and at 1 and 3 months after the program to assess the knowledge of and practice in dispensing EC among the drugstore personnel. RESULTS: Dispensing practices at baseline were poor to fair and knowledge was fair in both groups. Sellers in the intervention group improved significantly in choice of drug, advice provided, and knowledge of the time limit for initiating EC, but those in the control group did not. However, proper history taking on the time of intercourse and menstrual cycle was poor in both groups at all study periods. CONCLUSION: All drugstore personnel should be educated on the importance of history taking and on the time limit for initiating EC.

19. Chuajedong P, Kedjarune-Leggat U, Kertpon V, Chongsuvivatwong V, Benjakul P. Associated factors of tooth wear in southern Thailand. J Oral Rehabil 2002;29:997-1002.

Abstract: The purpose of this study was to evaluate the possible risk factors connected with tooth wear. Using the Tooth Wear Index (TWI) and the charting of pre-disposing factors tooth surface loss was recorded in 506 patients, of the Dental Hospital, Prince of Songkla University.

We found that age, sex, number of tooth loss, frequency of alcohol, sour fruit and carbonate intake were significant risk factors. Regarding the tooth position, the first molar showed the greatest degree of wear, while the canine and premolar showed the least, respectively. The occlusal surface showed the greatest wear and the cervical, lingual and buccal surfaces showed the least, respectively.

20. Liabsuetrakul T, Lumbiganon P, Chongsuvivatwong V, Boonsom K, Wannaro P. Current status of prophylactic use of antimicrobial agents for cesarean section in Thailand. J Obstet Gynaecol Res 2002;28:262-8.

Abstract: AIMS: To evaluate actual practices and physician reasons for variation in prophylactic use of antimicrobial agents for cesarean section (CS). METHODS: The study combined a survey of 2726 medical records and an interview of 50 practicing physicians at the obstetric departments of a university, a regional and a general hospital in Songkhla Province, Southern Thailand. RESULTS: Practices that were consistent with systematic reviews were use in 94%, prescription after cord clamping in 86%, and choosing ampicillin in 91%, because physicians believed in the advantages of these practices. Indications for prophylactic use ranged from routine use for all cases to selective use for indicated cases such as ruptured membranes, vaginal examinations, labor, maternal obesity, or unplanned CS. Single-dose practice was varied greatly across hospitals, from 9% to 84%. The reasons given by physicians for a multiple-dose regimen were personal experience in this regimen and belief in its superiority under their local conditions. This practice was less common where the hospital had practice recommendations. CONCLUSIONS: Not all evidence-based knowledge is adopted in practice. The prophylactic use of antimicrobial agents for CS varies among physicians. Past experience and personal beliefs in the limitation of research generalizability are the barriers to such adoption.

21. Pungrassami P, Chongsuvivatwong V. Are health personnel the best choice for directly observed treatment in southern Thailand? A comparison of treatment outcomes among different types of observers. Trans R Soc Trop Med Hyg 2002;96:695-9.

Abstract: A prospective study was conducted in 24 districts in southern Thailand in 1999 with directly observed treatment, short-course strategy (DOTS) implemented to determine treatment outcomes in relation to the practical observer among 455 enrolled patients with tuberculosis. Health personnel (HP), community members (CM), family members (FM) and self-administration (SA) were initially assigned to be DOT observers in 43%, 5%, 44% and 8% of 411 analysed patients, respectively. In practice, 56% of the 379 patients with assigned

observers changed their observers. The practical observer was the assigned observer among 17% of patients assigned to HP, 57% to CM, 75% to FM, and 34% to SA, respectively. There were no significant differences in treatment success between different types of main observers. Adjusted odds ratios (95% confidence interval) of treatment non-success were 1.1 (0.3-4.7), 0.7 (0.2-3.3), and 0.5 (0.2-1.1) for HP, CM, and FM, over SA groups, respectively. HP may not be the best choice in our setting due to poor sustainability and the availability of another promising choice (CM).

22. Liabsuetrakul T, Lumbiganon P, Chongsuvivatwong V. Prophylactic antibiotic prescription for cesarean section. Int J Qual Health Care 2002;14:503-8.

Abstract: OBJECTIVES: To assess the use of prophylactic antibiotics for cesarean section, and to identify factors associated with a doctor's intraoperative prescription. DESIGN: A hospital-based, cross-sectional study. STUDY PARTICIPANTS: All 967 medical records of women undergoing cesarean section from January 1998 to February 1999 in a university hospital, Southern Thailand. MAIN MEASURES: Independent variables consisted of patient and doctor factors. The outcome variable was whether any antibiotics were given intraoperatively. Multivariate logistic regression with random effects was used to identify factors associated with the doctor's prescription. RESULTS: Prophylactic antibiotics were prescribed in 82% of all patients. One hundred and eighty-eight patients (21%) received antibiotics postoperatively. Of the patients receiving intraoperative antibiotics after cord clamping, 8% received only a single dose and 53% received an additional postoperative prescription. The most commonly used antibiotic was ampicillin. Intraoperative prescription was significantly associated with longer duration of ruptured membranes, higher number of vaginal examinations and doctors' age. Doctors aged 30-39 years had three and seven times the likelihood of prescribing intraoperative antibiotics compared with their younger and older colleagues, respectively. CONCLUSIONS: Administration of single-dose prescriptions was still an uncommon practice. Prophylaxis was given more commonly to patients with well known risks for infection, and was given by doctors aged 30-39 years.

23. Ratanajamit C, Vinther Skriver M, Jepsen P, Chongsuvivatwong V, Olsen J, Sorensen HT. Adverse pregnancy outcome in women exposed to acyclovir during pregnancy: a population-based observational study. Scand J Infect Dis 2003;35:255-9.

Abstract: This study aimed to examine the risk of adverse pregnancy outcomes in children born to mothers who redeemed a prescription for systemic or topical acyclovir during pregnancy. Data on prescriptions of acyclovir were obtained from the Danish North Jutland

Prescription Database and data on pregnancy outcomes from the Danish Medical Birth Registry and the County Hospital Discharge Registry. The risk of malformations, low birth weight, preterm birth and stillbirth in users of acyclovir were compared with non-exposed women using a follow-up design, while the risk of spontaneous abortion was examined using a case-control design. 90 pregnant women had redeemed a prescription for systemic acyclovir, and 995 women for topical acyclovir, during 30 d before conception, or during their pregnancies from 1 January 1990 to 31 December 2001. The odds ratios (95% confidence intervals) of the exposed relative to the non-exposed for the systemic and topical acyclovir were: malformations, 0.69 (0.17-2.82) and 0.84 (0.51, 1.39); low birth weight, 2.03 (0.50-8.35) and 0.48 (0.21-1.07); preterm birth, 1.04 (0.38-2.85) and 0.95 (0.70-1.28); stillbirth (for topical acyclovir), 1.70 (0.80-3.60); and spontaneous abortion, 2.16 (0.60-7.80) and 1.29 (0.80-3.60). There is increasing evidence that the use of systemic acyclovir is not associated with an increased prevalence of malformations at birth and preterm delivery. The data for low birth weight and spontaneous abortion are still inconclusive, although the risk of spontaneous abortion is increased in women exposed to acyclovir during the first month of pregnancy. The use of topical acyclovir does not seem to be associated with any adverse pregnancy outcome, although data on stillbirth are inconclusive.

24. Kuning M, McNeil D, Chongsuvivatwong V. Pregnancy loss in the Philippines. Southeast Asian J Trop Med Public Health 2003;34:433-42.

Abstract: In this cross-sectional study, 8,481 women aged 15-49 who had at least one pregnancy outcome were considered. This study aimed to examine the characteristics of Filipino women having had a pregnancy loss, and to test the association between domestic violence and pregnancy loss. To control for the confounding effect of the number of pregnancies, the sample was divided into seven groups classified by the number of pregnancies. The risk factors considered were demographic characters (age and partner's age, marital status, and place of residence), socioeconomic status (education and partner's education, having a paid helper at home, having a say in how income was spent), domestic violence (physical abuse and forced sex), sexual behavior of partner, whether the pregnancy was wanted, and disease history (tuberculosis, diabetes, hypertension, malaria, hepatitis, kidney disease, heart disease, anemia, goiter and other medical problems). The major risk factors were found to be physical abuse, region, faithfulness of partners, hypertension, hepatitis, kidney disease, anemia, and the other medical problems, respectively. The risk of pregnancy loss for the women suffering domestic violence was 1.59 (95% CI 1.28-1.97) times higher than for the women who did not. Women aged 15-19 years had a much higher risk of

pregnancy loss than the other age groups (OR = 1.49, 95% CI 1.22-1.82). There were similar risk for women aged 20-24 years (OR = 1.08, 95% CI 0.94-1.25) and 35-39 years (OR = 1.05, 95% CI 0.92-1.19). No association emerged with marital status, socioeconomic status, forced sex, the number of partners, unwanted pregnancy, tuberculosis, diabetes, malaria, heart disease, and goiter. Although women's age, partner's age, residence, women's education, partner's education, and paid helper at home were significantly associated with pregnancy loss, they were likely to be confounders rather than risk factors.

25. Aekplakorn W, Stolk RP, Neal B, Suriyawongpaisal P, Chongsuvivatwong V, Cheepudomwit S et al. The prevalence and management of diabetes in Thai adults: the international collaborative study of cardiovascular disease in Asia. Diabetes Care 2003;26:2758-63.

Abstract: OBJECTIVE: The aim of this study was to determine in Thai adults aged >or=35 years the prevalence and management of diabetes and the associations of diabetes with cardiovascular risk factors. RESEARCH DESIGN AND METHODS: The International Collaborative Study of Cardiovascular Disease in Asia was a complex sample survey. Data from a structured questionnaire, brief physical examination, and blood sample were collected from 5,105 individuals aged >or=35 years (response rate 68%). Population estimates were calculated by applying sampling weights derived from the 2000 Thai census. RESULTS: The estimated national prevalence of diabetes in Thai adults was 9.6% (2.4 million people), which included 4.8% previously diagnosed and 4.8% newly diagnosed. The prevalence of impaired fasting glucose was 5.4% (1.4 million people). Diagnosed diabetes, undiagnosed diabetes, and impaired fasting glucose were associated with greater age, BMI, waist-to-hip ratio, systolic blood pressure, total cholesterol, and serum creatinine levels. The majority of individuals with diagnosed diabetes had received dietary or other behavioral advice, and 82% were taking oral hypoglycemic therapy. Blood pressure-lowering therapy was provided to 67% of diagnosed diabetic patients with concomitant hypertension. CONCLUSIONS: Diabetes is common in Thailand, but one-half of all cases are undiagnosed. Because diagnosed diabetes is likely to be treated with proven, low-cost, preventive therapies such as glucose lowering and blood pressure lowering, initiatives that increased diagnosis rates would be expected to produce substantial health benefits in Thailand.

26. Liabsuetrakul T, Chongsuvivatwong V, Lumbiganon P, Lindmark G. Obstetricians' attitudes, subjective norms, perceived controls, and intentions on antibiotic prophylaxis in caesarean section. Soc Sci Med 2003;57:1665-74.

Abstract: Over 10% of current births in all countries of the world are delivered by caesarean section. Single-dose ampicillin or cefazolin administered after cord clamping has been proven to be effective for the prevention of post-caesarean infections as indicated in many randomised trials and reviews in the Cochrane Library. This study aimed to determine three determinants of behavioural intention using the theory of planned behaviour: attitudes, subjective norms, and perceived controls. Intentions were examined for five aspects of the use of antibiotic prophylaxis, namely whether or not antibiotics were used, used in all caesarean sections, after rather than before cord clamping, whether ampicillin/cefazolin or broader-spectrum antibiotics were used, and whether single or multiple doses were given. Fifty obstetricians selected from university, regional, and general hospitals in southern Thailand, were surveyed using a questionnaire and in-depth interview. Their intentions to use a single dose and to use in all cases were low, and this was related to negative attitudes and reference groups who did not approve of the single dose. The negative attitude was based on scepticism concerning the applicability of well-equipped trials from the developed world and fear of consequences of post-caesarean infections. Norms carried over from residency training had more long-term influence in their practice than newer information from books or journals. Perceived external controls on their practice were less predictive of intentions. Intentions were only partly predictive of behaviour. Changing attitudes, introducing evidence-based information into residency training and strengthening control systems in the hospital are essential to improve intentions.

รายชื่อผู้ทำงานในโครงการ

ชื่อ-นามสกุล	ตำแหน่งวิชาการ		ต้นสังกัด			ตำแหน่งในโครงการ	สถานภาพในปัจจุบัน
	เมื่อเข้าร่วมโครงการ	ปัจจุบัน	ภาควิชา	คณะ	มหาวิทยาลัย		
1. วีระศักดิ์ จงสูวิวัฒน์วงศ์	รศ.	ศ.	ระบาดวิทยา	แพทยศาสตร์	สงขลานครินทร์	หัวหน้าโครงการ*@	ยังอยู่
2. ธาดา ยิบอินชอย	ศ.	ศ.	-	แพทยศาสตร์	สงขลานครินทร์	ที่ปรึกษาโครงการ	ยังอยู่
3. Alan Geater	Dr	Dr	ระบาดวิทยา	แพทยศาสตร์	สงขลานครินทร์	นักวิจัย*	ยังอยู่
4. Than Winn	ศ.	ศ.	ระบาดวิทยา	แพทยศาสตร์	สงขลานครินทร์	นักวิจัย*	ย้ายไปทำงานมาเลเซีย
5. สลม แจ่มอุลิตรัตน์	รศ.	รศ.	เวชศาสตร์ชุมชน	แพทยศาสตร์	สงขลานครินทร์	นักวิจัย@	ยังอยู่
6. ลัดดา เหมาะสุวรรณ	รศ.	รศ.	กุมารเวชศาสตร์	แพทยศาสตร์	สงขลานครินทร์	นักวิจัย@	ยังอยู่
7. หัชชา ศรีปลั่ง	รศ.	รศ.	พยาธิวิทยา	แพทยศาสตร์	สงขลานครินทร์	นักวิจัย	ยังอยู่
8. ปารมี ทองสุกใส	ผศ.	รศ.	พยาธิวิทยา	แพทยศาสตร์	สงขลานครินทร์	นักวิจัย	ยังอยู่
9. นวลตา อาภาคัพภะกุล	-	ชำนาญการ	ระบาดวิทยา	แพทยศาสตร์	สงขลานครินทร์	นักวิจัย*	ยังอยู่
10. มะเพาซิส ดือราวี	-	-	ระบาดวิทยา	แพทยศาสตร์	สงขลานครินทร์	นักวิจัย*	ยังอยู่
11. อภิรดี แซ่ลิ่ม	-	-	ระบาดวิทยา	แพทยศาสตร์	สงขลานครินทร์	นักวิจัย*	ยังอยู่
12. ภัทราภรณ์ สาวิชชโก	-	-	ระบาดวิทยา	แพทยศาสตร์	สงขลานครินทร์	ฝ่ายการศึกษา	ยังอยู่

ชื่อ-นามสกุล	ตำแหน่งวิชาการ		ต้นสังกัด			ตำแหน่งในโครงการ	สถานภาพในปัจจุบัน
	เมื่อเข้าร่วมโครงการ	ปัจจุบัน	ภาควิชา	คณะ	มหาวิทยาลัย		
13. จิรา เหมือนพิทักษ์	-	-	ระบาดวิทยา	แพทยศาสตร์	สงขลานครินทร์	การเงิน*	ยังอยู่
14. รวีวรรณ สุขเกษม	-	-	ระบาดวิทยา	แพทยศาสตร์	สงขลานครินทร์	ธุรการ*	ยังอยู่
15. เพชรวรรณ พึ่งรัศมี	พญ	พญ	ศูนย์วัณโรคเขต 12			นศ. ป.เอก*@	จบแล้ว
16. รัศมี สังข์ทอง	พญ.	พญ.	-	-	-	นศ. ป.เอก*@	จบแล้ว
17. วินัย ลีสมิทธิ์	นพ.	นพ.	สสจ. กำแพงเพชร			นศ. ป.เอก@	ยังอยู่
18. ฉวีวรรณ รัตนจามิตร	อจ.	อจ.	เภสัชกรรมคลินิก	เภสัชศาสตร์	สงขลานครินทร์	นศ. ป.เอก	จบแล้ว
19. นิภา มหารัชพงศ์	-	-	-	-	-	นศ. ป.เอก*	ยังอยู่
20. ทิพวรรณ เลียบสื่อระกูล	ผศ.	ผศ.	สูตินรีเวช	แพทยศาสตร์	สงขลานครินทร์	นศ. ป.เอก*@	จบแล้ว
21. Ngueyen Thi My Huong	Dr.	Dr.	ประเทศเวียดนาม			นศ. ป.เอก	จบแล้ว
22. Shoko Oshikawa	Ms.	Ms.	ประเทศญี่ปุ่น			นศ. ป.เอก	ยังอยู่
23. Mahbub-E-Elahi Khan Chowdhury	Mr.	Mr.	ประเทศบังคลาเทศ			นศ. ป.เอก	จบแล้ว
24. ภาสุรี แสงศุภวานิช	อจ.	อจ.	กุมารเวชศาสตร์	แพทยศาสตร์	สงขลานครินทร์	นศ. ป.เอก@	ยังอยู่
25. บุญสิน บูรณะพาณิชย์กิจ	รศ.	รศ.	ออโธพิดิกส์	แพทยศาสตร์	สงขลานครินทร์	นศ. ป.เอก@	ยังอยู่

* หมายถึงได้รับทุนยังชีพจากโครงการกลุ่มวิจัยระบาดวิทยา @ หมายถึงได้รับทุนจากโครงการปริญญาเอกกาญจนาภิเษก

Research Output ซึ่งได้รับการสนับสนุนจากทุนเมธีวิจัยอาวุโส (ส่วนมีดอกจันทน์ได้แสดงไว้ในภาคผนวกเป็นรายงานที่ได้ระบุ สกว. ไว้กิตติกรรมประกาศในวารสาร)

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3.Thongsuksai P, Chongsuvivatwong V. Delay in treatment of breast cancer in southern Thailand. Medical Care. 2000; 38(1): 1-7 *(Impact factor = 2.552)

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20.Liabsuetrakul T, Lumbiganon P, Chongsuvivatwong V. Prophylactic antibiotic prescription for cesarean section. Int J Qual Health Care 2002;14:503-8.*

21.Ratanajamit C, Vinther Skriver M, Jepsen P, Chongsuvivatwong V, Olsen J, Sorensen HT. Adverse pregnancy outcome in women exposed to acyclovir during pregnancy:

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ชื่อที่ขีดเส้นใต้คือนักศึกษาปริญญาเอกที่ได้รับทุนจากสกว.

ผลงานดีพิมพ์ในวารสารวิชาการในประเทศไทย

ไม่มี

หนังสือ

"กราฟ ตาราง และ สมการ สำหรับการวิจัยทางสุขภาพ" โอเอส พริ้นติ้งเฮ้าส์ กรุงเทพ พ.ศ. 2545 (ตำราเล่มนี้ได้รับคัดเลือกเป็นผลงานดีเด่นของมหาวิทยาลัยสงขลานครินทร์ สาขาการแต่งตำรา ประจำปี 2546)

การจดทะเบียนสิทธิบัตร

- ไม่มี

การนำเสนอผลงานในที่ประชุมวิชาการนานาชาติ

- ไม่มี

ผลงานอื่น ๆ

- ปี 2545 ได้รับรางวัลศิษย์เก่าดีเด่นของคณะแพทยศาสตร์รามาธิบดี

- ปี 2545 ได้รับรางวัลเป็นอาจารย์ควบคุมวิทยานิพนธ์ดีเด่นสาขาวิทยาศาสตร์สุขภาพ มหาวิทยาลัยสงขลานครินทร์

- ปี 2545 ได้รับรางวัลงานวิจัยยอดเยี่ยมด้านการสร้างงานวิจัยที่เป็นประโยชน์ต่อภาคใต้จาก มหาวิทยาลัยสงขลานครินทร์

- ปี 2546 ได้รับรางวัลผลงานวิชาการดีเด่นประเภทตำราเรื่อง"กราฟ ตาราง และ สมการ สำหรับการวิจัยทางสุขภาพ"

- ปี 2546 ได้รับรางวัลประกาศเกียรติคุณที่ได้ใช้ความพยายามและสติปัญญาในการวางแผน ควบคุมโรคซาร์สจากมหาวิทยาลัยสงขลานครินทร์

- ตลอดระยะเวลา 3 ปีในการรับทุนรอบที่สอง เป็นที่ปรึกษาองค์การอนามัยโลก ช่วยพัฒนา งานวิจัยในประเทศอินโดนีเซีย, มองโกเลีย, บังคลาเทศและลาวปีละ 3-4 ครั้ง

- เป็นหัวหน้าโครงการประเมินผลงานวิจัยท้องถิ่น สกว. ระดับประเทศ

ภาคผนวก

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SECULAR INCREASES IN WEIGHT, HEIGHT AND BODY MASS INDEX AMONG SCHOOL CHILDREN OF HAT YAI, THAILAND: A 5 YEARS FOLLOW-UP STUDY

Rassamee Sungthong[1], Ladda Mo-suwan [2], Virasakdi Chongsuvivatwong[1] and Chaon Junjana [2]

[1]Epidemiology Unit and [2] Department of Pediatrics, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla 90110, Thailand

Abstract. Upward trend of growth and overweight has been reported from developed countries. As Thailand has been undergoing rapid economic transition over the previous decade, we conducted an analysis to demonstrate the secular changes of growth over five years follow-up. Subjects were a cohort of 2,252 primary school children recruited in 1992 for the Hat Yai childhood obesity study. Baseline demographic and family data were collected by a questionnaire completed by parents. To quantify the cohort effect, a generalized estimating equations analysis for a cross sectional time series data was undertaken with weight, height, and body mass index (BMI, kg/m^2) as a dependent variable and containing a quadratic term of age, sex, year of birth and family variables. One thousand and ninety-four (48.5%) children completed 6 anthropometric measurements. Graphs of median weight, height, BMI and overweight prevalence of each birth cohort against age showed secular increases of growth and overweight, and an age effect. For each one-year younger cohort, the median weight, median height and median BMI increased by 1.22 kg, 1.25 cm and 0.23 kg/m^2, respectively. An increasing trend of childhood overweight reported here may signify a need for preventing overweight and reducing weight in childhood adolescence in the future.

INTRODUCTION

Child growth and nutrition has been suggested as a good indicator of health as well as socioeconomic well being of a country. Over the previous decades, upward change in growth and increasing prevalence of obesity have been observed in developed countries. Hughes *et al* (1997) reported an average increase of 1 to 3 cm in English and Scottish primary school children from 1972 to 1994. During the same period, the adjusted increase in height of children aged 5 to 14 years old of the Bogalusa heart study was 1.6 cm (Freedman *et al*, 1997). Among inner city children and ethnic minorities of Britain, height increased approximately 1.5 cm over the period from 1983-1993 (Chinn *et al*, 1998). While growing taller, these children were getting fatter too. The US national health and nutritional surveys showed that the prevalence of overweight based on the 85th percentile cutoff point for body mass index increased from 15% to 22% during 1963 to 1991 (Troiano *et al*, 1995). This trend of increasing prevalence of obesity found in developed countries was also documented in lower income countries, *eg* China, Brazil, Cuba, Vietnam and Thailand (Popkin *et al*, 1998). From a longitudinal study of school children in Hat Yai, Thailand, obesity prevalence was reported to increase from 12% to 15.6% in two years (Mo-suwan *et al*, 1994). Among school children in China, obesity rates, associated with stunting, were reaching a level comparable to those in the United States (Popkin *et al*, 1996).

Most growth studies, however, were carried out in cross-sectional samples. Investigations of birth cohort or secular trend effects on growth and obesity are limited in such design. With the longitudinal data from a cohort of school children residing in Hat Yai in the southern part of Thailand, we conducted the analysis to demonstrate the secular changes of weight, height and body mass index over the five years.

MATERIALS AND METHODS

Study site

Hat Yai, a city in Songkhla Province, is the center of economy of the southernmost part of Thailand. It is about 1,000 km from Bangkok the capital city, and 100 km from the Malaysian border. Rubber, sea-food, wood furniture and tourism industry are its main business. Population was about 290,000 in 1997, 53.5% residing in the municipality.

Correspondence: Dr Rassamee Sungthong, Epidemiology Unit, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla 90110, Thailand.
E-mail: mladda@ratree.psu.ac.th

Subjects

A cohort of 2,252 primary school children was recruited in 1992 for the Hat Yai childhood obesity study using two stage sampling. Six schools (two municipality-operated and four private) were randomly selected from 13 primary schools in the Hat Yai municipality area, then one or two classes of each grade were randomly selected from each school. The study was approved by the Committee for Research in Humans, Faculty of Medicine, Prince of Songkla University and parental consent was obtained.

Collection of data

Subjects were weighed wearing school uniforms without belts and shoes and with empty pockets. Weight and height were measured annually (in January) from 1992-1997 with a beam balance Detecto scale and stadiometer (Detecto Scales, Inc, Brooklyn, NY, USA) to the nearest 0.1 kg and 0.5 cm, respectively. We used the same and careful quality control of measurement techniques over time. Incomplete data was due to either children move to other schools or to other places where we could not follow them. Baseline demographic and family data were collected by a questionnaire completed by parents as described in the previous report (Mo-suwan and Geater, 1996).

Data analysis

Only subjects with complete 6 anthropometric measurements were included in the analysis. To

Table 1
Baseline characteristics of the selected and non-selected subjects.

Variables	Selected (%)	Non-selected (%)	Chi-square *
Overweight at entry	1,094 (18.1)	1,155 (14.6)	11.7
Sex = male	456 (41.7)	643 (55.7)	44.0
Father's education	887	892	17.7
no	16 (1.8)	26 (2.9)	
primary	195 (22.0)	263 (29.5)	
secondary	278 (31.3)	265 (29.7)	
higher than secondary	398 (44.9)	338 (37.9)	
Mother's education	916	926	19.0
no	29 (3.2)	52 (5.6)	
primary	332 (36.2)	398 (43.0)	
secondary	193 (21.1)	176 (19.0)	
higher than secondary	362 (39.5)	300 (32.4)	
Father's occupation	889	905	28.2
no	4 (0.5)	6 (0.7)	
casual	191 (21.5)	230 (25.4)	
farmer	12 (1.4)	43 (4.8)	
trader	405 (45.6)	348 (38.5)	
government officer	201 (22.6)	218 (24.1)	
office worker	76 (8.6)	60 (6.6)	
Mother's occupation	918	933	23.5
no	176 (19.2)	161 (17.3)	
casual	129 (14.1)	161 (17.3)	
farmer	10 (1.1)	33 (3.5)	
trader	402 (43.8)	390 (42.0)	
government officer	158 (17.2)	166 (17.8)	
office worker	43 (4.68)	22 (2.4)	
Parent monthly income *	936	930	24.8
<5,000 baht	141 (15.1)	211 (22.7)	
5-10,000 baht	319 (34.1)	337 (36.2)	
1-<30,000 baht	360 (38.5)	293 (31.5)	
≥30,000 baht	116 (12.4)	89 (9.6)	

* All were significant at p level less than 0.05.
* Parental monthly income, 1 baht = 0.04 US dollar at the time of data collection.

Table 2
Birth cohort effect on weight, height and BMI by generalized estimation equations analysis.

Variables	Weight (kg)		Height (cm)		Body mass index (kg/m²)	
	Coefficient	p	Coefficient	p	Coefficient	p
Age*	6.16	<0.001	10.93	<0.001	1.20	<0.001
Age²	-0.09	<0.001	-0.26	<0.001	-0.03	<0.001
Birth year	1.22	<0.001	1.25	<0.001	0.23	0.001
Sex = female	-0.35	0.023	-0.53	<0.001	-0.002	NS †
Parental income	2.69	0.001	1.41	0.019	0.92	0.001

* Age = age in year at the time of data collection.
† NS = non significant

examine for possibility of selection bias, a chi-square test was used to detect differences between selected and non-selected groups. Due to its high correlation with total body fat (Roche *et al*, 1981), we used the body mass index [BMI, body weight (kg) divided by height (m) squared] to define obesity in our study. A child with a BMI value above the US First National Health and Nutrition Examination Survey (NHANES-I) 85th percentile for age and sex was considered overweighted (Must *et al*, 1991).

Secular changes of growth and overweight and age effect were demonstrated by plotting median weight, median height, median BMI and overweight prevalence of each birth cohort against age. To quantify the cohort effect, a generalized estimating equations analysis for a cross sectional time series data was undertaken with weight, height, or BMI as a dependent variable and containing sex, year of birth, and quadratic term of age (age and age²). Quadratic term of age is used instead of linear term because we expected that the age effect on weight, height and BMI will decrease as children grow into adolescence and adulthood. Family variables including parental education and occupation, and parental income was retained in the models only if it was statistically significant at the 5% level. All analysis were done using the STATA statistical software version 5 (StataCorp, 1997).

RESULTS

Of 2,252 subjects followed from 1992 to 1997, 1,094 (48.5%) had 6 complete anthropometric measurements and hence were included in this report. Comparison of characteristics of the selected group and the rest is presented in Table 1. The selected group contained more females and had higher socioeconomic status.

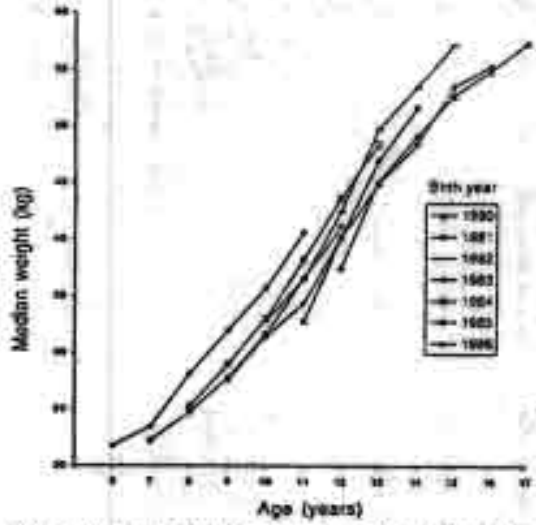

Fig 1–Median weight for age of male birth cohorts from 1992-1997.

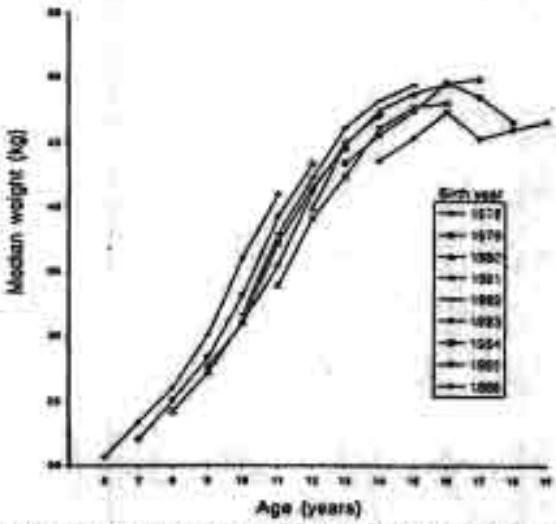

Fig 2–Median weight for age of female birth cohorts from 1992-1997.

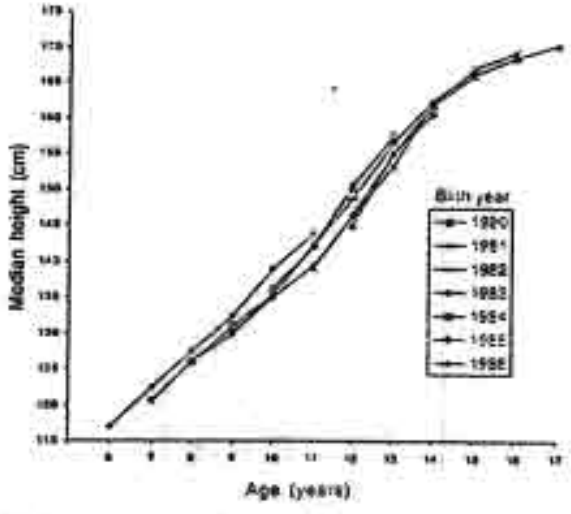

Fig 3–Median height for age of male birth cohorts from 1992-1997.

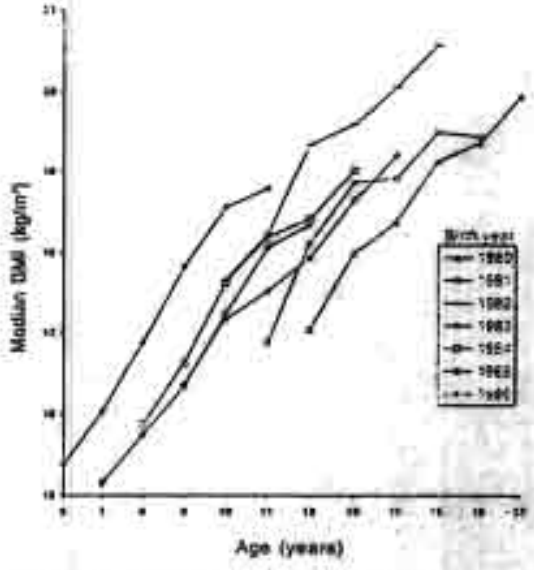

Fig 5–Median BMI for age of male birth cohorts from 1992-1997.

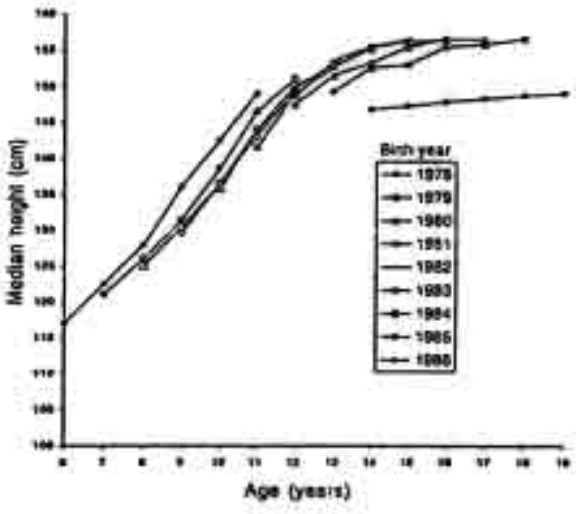

Fig 4–Median height for age of female birth cohorts from 1992-1997.

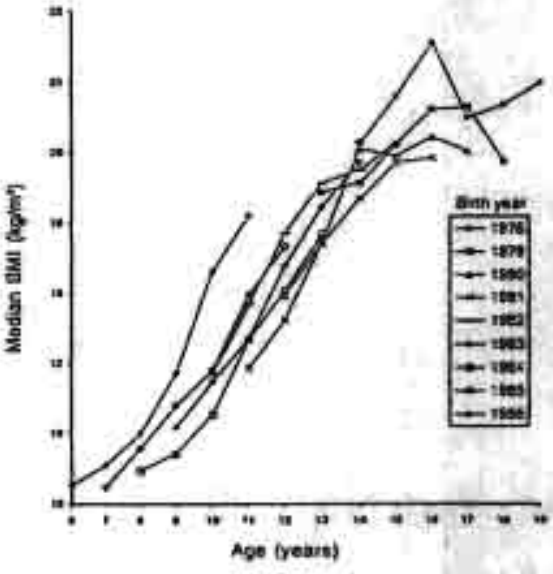

Fig 6–Median BMI for age of female birth cohorts from 1992-1997

Figs 1 and 2 show median weight for age of each cohort of males and females, respectively. For males, at each age point, latter cohort was heavier than the former ones with the youngest cohort being the heaviest. A similar trend was observed for females. The youngest cohort had a median weight higher than the elder cohorts. In contrast to males, median weights of females appeared to be stable at mid adolescence.

Median height for age of female cohorts stabilized earlier than those of males (Figs 3, 4). Similar to weight aspect, younger cohort was taller than the elder ones. At the mid and late adolescence, girls born in 1978 were approximately 6-10 cm shorter than those born 1-5 years later.

Similar to weight and height, median BMI of the younger cohort of both sexes was greater than those of the elders (Figs 5, 6). Because they were

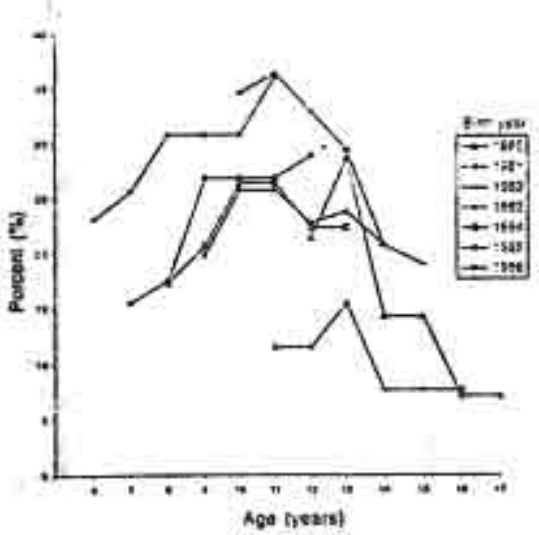

Fig 7–Percent overweight for age of male birth cohorts from 1992-1997.

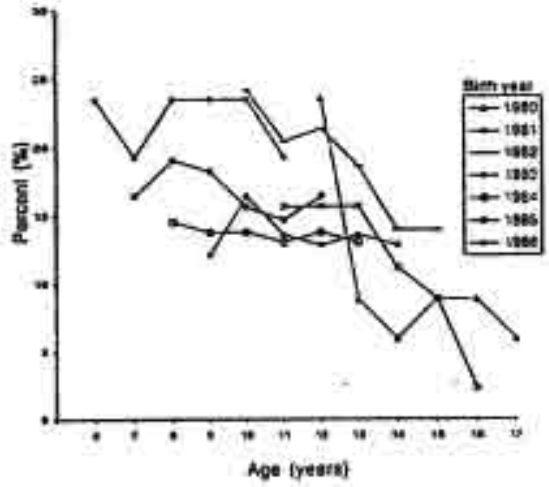

Fig 8–Percent overweight for age of female birth cohorts from 1992-1997.

6-10 cm shorter but only 2-5 kg lighter than other cohorts, the eldest female cohort exceptionally had the highest BMI. While BMI of males increased linearly with age from 6 to 17 years old, BMI increment in females appeared to slow down after thirteen years of age.

Figs 7, 8 depicted prevalence of overweight for age for males and females, respectively. Females had a lower prevalence than males. With exception of some birth cohorts, the younger cohort tended to have a greater prevalence of overweight than the older ones. However, a decreasing prevalence of overweight was observed in females entering adolescence.

Result of the generalized estimating equations analysis is shown in Table 2. Each model was adjusted with age, sex and a quadratic term of age. Birth cohort effect on weight, height and BMI was significant. Children who were born one year younger weighed 1.22 kg heavier, were 1.25 cm taller, and had a BMI of 0.23 kg/m^2 greater than those being born earlier. Similar findings of a greater value of weight, height and BMI were observed in children of the high income family.

DISCUSSION

The present longitudinal study of school children demonstrated significant birth cohort effect and age effect on growth and overweight prevalence. The new birth cohort had a greater value of weight, height and BMI than the elder cohorts. The difference was mostly noticeable in the youngest group. Prevalence of overweight was also increased with age up to early adolescence then had a downward trend. Males and females had a different pattern of age effect. Anthropometric parameters of females reached plateau earlier than those of males. Prevalence of overweight of females was lower than that of males and decreased when reaching adolescence.

Our findings of secular increases of growth and overweight support previous reports from developed countries (Chinn *et al*,1998; Freedman *et al*, 1997; Hughes *et al*, 1997; Starks *et al*, 1981; Troiano *et al*, 1995). These studies (Chinn *et al*,1998; Freedman *et al*, 1997; Hughes *et al*, 1997) reported height increments of 0.1 to 3.3 cm over the period of 10 to 22 years. Using birth cohort analysis, we demonstrated much greater increase, 1.25 cm per birth year. This enlarged effect probably reflected a wide gap between the actual growth and the growth potential among children of a country undergoing an economic transition like Thailand (Kachondham *et al*, 1993). For children of high-income countries who almost grew to their fullest potential, economic effect on height would then take a longer time to be noticed. Use of different anthropometric index to define obesity renders a direct comparison of prevalence of obesity across studies infeasible. However, no matter which index was utilized, an increasing trend of obesity was documented. BMI was recommended as a screening index of obesity for adolescents (Himes and Dietz, 1994). From the Bogalusa

heart study, BMI increased by 1.5 kg/m^2 over the twenty years or 0.075 kg/m^2/y (Freedman *et al*, 1997). Again, we found a greater increase of 0.23 kg/m^2/ birth year. From our previous report, a significant trend of increased risk for childhood obesity was associated with higher family income (Mo-suwan and Geater, 1996). The bias of subjects included in our analysis towards upper income groups may partly explain this observation.

Different patterns of overweight by sex were observed. From 9 US surveys (a mix of cross-sectional and cohort studies) including 66,772 children aged 5 to 17 years, mean BMI increased with age and was slightly higher for girls than for boys (Rosner *et al*, 1998). Mean BMI of white female cohort of Bogalusa heart study leveled off around 15 years of age, whereas those of white males did a little later at 20s (Freedman *et al*, 1997). On the contrary, mean BMIs of black cohorts of both sexes showed rather steady increase up to 25 years of age. BMI pattern of our female subjects was similar to that of Bogalusa white female cohort, while that of our male cohorts behaved like Bogalusa black subjects. Consequently we found a higher percentage of overweight for boys than for girls.

The use of NHANES-I BMI data to classify our subjects may need justification. Lack of local BMI reference and upper height limit of 170 cm of the local weight-for-height curves restrict the use of local standard for overweight categorization in our study. Due to notable ethnic difference (Rosner *et al*, 1998), utilization of NHANES-I reference may underestimate overweight prevalence of our prepubertal children.

Concern of overweight in children comes from its long term effects on morbidity and mortality. From the Harvard growth study of 508 lean (BMI value below 25th percentile of the NHANES-I reference for age and sex) or overweight (BMI value above 75th percentile of the NHANES-I reference) adolescents 13 to 18 years old, after 55 years of follow-up overweight was associated with an increased risk of mortality among men (Must *et al*, 1992). The relative risks were 1.8 [95% confidence interval (CI), 1.2 - 2.7] for mortality from all causes and 2.3 (95% CI, 1.4 to 4.1) for mortality from coronary heart disease. Another report of 57 years follow-up of the Boyd Orr cohort of children aged 2 years to 14 years 9 months (Gunnell *et al*, 1998), the hazard ratio for all cause mortality in those with BMIs above the 75th percentile for age and sex was 1.5 (95% CI, 1.1 -2.2) and for ischemic heart disease it was 2.0 (95% CI, 1.0-3.9). Providing an observed increasing trend of childhood overweight, there is an immediate need of intervention aiming at preventing overweight and reducing weight in childhood and adolescence.

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High-Risk Childbirth Practices in Remote Nepal and Their Determinants

Narbada Thapa, PhD
Virasakdi Chongsuvivatwong, MD, PhD
Alan F. Geater, PhD
Magnar Ulstein, MD, PhD

ABSTRACT. This study describes birth-related practices and their determinants among women in the Jumla district of Nepal. Data were derived from a household survey in 1996. Of 939 married women of reproductive age, 657 who had given birth to their last child during the previous five years were included in the analysis. Qualitative information was further obtained from traditional birth attendants (TBAs), mothers-in-law, community leaders and pregnant women. High-risk practices were common and related to local custom and lack of knowledge on the importance of cleanliness. Husband's level of education greater than fifth grade significantly reduced the high-risk practices in all stages of childbirth, independent of other socio-economic, biological and village variables. *[Article copies available for a fee from The Haworth Document Delivery Service: 1-800-342-9678. E-mail address: <getinfo@haworthpressinc.com> Website: <http://www.HaworthPress.com>*

Narbada Thapa is in Epidemiology, Medical Division, Birendra Hospital, Kathmandu, Nepal. Virasakdi Chongsuvivatwong is with the Epidemiology Unit, Faculty of Medicine, Prince of Songkla University, Hat-Yai, Thailand. Alan F. Geater is with the Epidemiology Unit, Faculty of Medicine, Prince of Songkla University, Hat-Yai, Thailand. Magnar Ulstein is with the Department of Obstetrics and Gynecology, Bergen University, Norway.

Address correspondence to: Narbada Thapa, PhD, G.P.O. 7605, Kathmandu, Nepal (E-mail: narbada@mail.com.np).

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KEYWORDS. High-risk birth practice, childbirth, postpartum care

INTRODUCTION

It is estimated that globally every year about half a million women die as a result of pregnancy and childbirth; almost 99% of these deaths occur in the developing world (WHO, 1998). The most common causes are obstetric hemorrhage and puerperal infections, which can lead to death rapidly in the absence of prompt life-saving care and are often the consequence of poor hygiene during delivery (WHO, 1998: Cunningham et al., 1997).

In Nepal, the latest reported maternal mortality rate was 515 deaths per 100,000 live births (Ministry of Health, 1993), infant mortality was 96 per 1000 live births (Central Bureau of Statistics, 1993) and perinatal mortality was 138/1000 live births (Pradhan et al., 1997). It has been estimated that at least 4,400 Nepali women die each year because of pregnancy or delivery. Even though delivery is a crucial period for the health and well-being of both mother and child, it is evident that most women in Nepal do not have access to basic maternity services. More than 80% of the deliveries are assisted by a relative or an untrained person, 90% of all deliveries occur at home and only 24% receive antenatal care (ANC) (Ministry of Health, 1993).

The current study was conducted in Jumla, one of the remote districts of Nepal. The reported local maternal death rate is 2000/100,000 live births (Ministry of Health, 1993) and the infant mortality rate is 130 per 1000 live births (Central Bureau of Statistics, 1993). More than 95% of all deliveries take place outside the hospital. Our previous analysis found that an animal shed is the most common place for delivery, with an associated high infant death rate (Thapa et al., 2000). The present study aimed to gain insights into the traditional birth practices, which may contribute to high maternal and infant death rates in this area.

METHODS

Setting

Jumla is one of the least accessible hilly districts, reached either by foot, which takes 5-6 days from the nearest municipality, or by air. The population of the district in the 1991 census was 75,964, with a population density of 30 per km^2. The district is divided into 278 administrative wards (village level political unit). The adult literacy rate in this area is 25.4% (for women, 8.5%). Most people live in mud and stone houses and are economically dependent on a combination of subsistence agriculture and animal husbandry. The villages are 3-6 hours' walk from one another and 6-12 hours from the centre, and are usually situated on a mountain slope. The main sources of drinking water are rivers and springs. The general level of sanitation is poor, and the majority of people do not have a toilet. A 15-bed governmental hospital and 17 health posts or sub-health posts serve the district. There is practically no hospital delivery and no facility for caesarian section or blood transfusion.

Study Population

This study incorporates both survey data and qualitative information.

A *household survey* was carried out from September to October 1996. Out of 270 administrative wards in the district, 20 were randomly selected. All married women of reproductive age (MWRA) residing in the study area were included as potential subjects for interview. Of the 939 MWRA so identified, 657 women who had given birth to their last child during the previous five years were included in the analysis. Mothers were interviewed using a pre-tested open- and closed-ended questionnaire by trained female interviewers. Data on socio-economic status, reproductive history, birth practices and child survival were obtained.

For more detail on childbirth practices, *focus group discussions and in-depth interviews* were undertaken following the survey. A total of 6 wards were randomly selected from the 20 surveyed wards. The sample comprised 29 participants in four focus group sessions. Four separate groups were arranged: (1) traditional birth attendants (TBAs); (2) mothers-in-law who were not pregnant; (3) currently pregnant women; and (4) household heads (men). Participants were in the age range 37-59 years, 45-60 years, 20-35 years and 40-57 years, respectively. Among 8 TBAs, 4 were trained and 4 untrained. Each group had between 4 and 9 participants. The session was held only one time for each group and lasted a maximum of 2-3 hours. The facilitator introduced each topic or question for general discussion and then

probed when necessary. Each focus group session was audiotaped and summary notes of the participants' responses to each question kept.

For in-depth interviews, a total of 14 key informants were selected from different wards, based on the impression from the survey that they would give valuable information. They were elder women, TBAs, community leaders and mothers with a child aged less than 5 years. Each interview lasted 1-2 hours and was recorded in field notes. All discussions and interviews were conducted by two experienced female research assistants.

The following key points were included in the in-depth interview and focus group guide.

1. *Beliefs and practice during pregnancy:* Food and rest, health-seeking and other beliefs
2. *Delivery practice and experiences:* Delivery place and their reasons, birth attendant, conduct of labor and delivery, postpartum care and practice
3. *Management of obstetric problems:* Prolonged and obstructed labor, placenta retention, immediate postpartum hemorrhage

Verbal informed consent was sought from the village heads and interviewees. No one refused to participate. Permission to conduct the study was provided by the Nepal Health Research Council.

Data Analysis

Qualitative data were transcribed from tape to paper in the same dialect and cross-checked with field notes. The transcripts were translated into English and analyzed using Ethnograph Version 4 computer software. The quantitative data were entered and processed using Epi-Info Version 6 software, and analyzed using STATA Version 5 statistical software. Unconditional logistic regression was used to examine factors associated with the following outcomes: antenatal care, delivery place, birth attendant and disinfection of the cord-cutting instruments. To control for clustering, village was specified as a cluster variable using the robust command in STATA.

RESULTS

Qualitative Information

Beliefs and Practice During Pregnancy

It was clear from discussion that even though women know the importance of diet and rest during pregnancy, they had very little control over it. A young woman moves to the home of her in-laws upon marriage, where she immediately assumes the burden of labor. She is supposed to continue to work both in the field and at home throughout pregnancy until labor pain begins. Limited food resources, a low priority accorded to daughters-in-law, and pregnancy being considered as a normal condition are the main reasons for not placing any emphasis on food and care during pregnancy.

Regarding antenatal care, trained TBAs claim that even though women were advised to go for ANC, only a few who reside near the hospital did so. Pregnant women feel that it is not worth sacrificing a whole day's work in order to go for ANC, while ANC in the absence of any problem was considered to be unnecessary by mothers-in-law.

Delivery Practices and Experiences

Selection of Delivery Place and Reasons

Participants from different groups expressed similar ideas and perceptions regarding delivery places. The ground floor of the house, used to shelter the livestock, is the same place used by many women for childbirth. Women preferred to give birth in an animal shed for three expressed reasons: deities; cleanliness; and sin.

Reasons based on deities: "The household deity will get angry if delivery takes place in the home." If the deity becomes angry, health problems may result. For example, the child may get sick, breast milk secretion may be reduced, or maternal uterine infection may occur. Delivery in the home has been prohibited by Jhankri (conjuror, wizard) for the past several generations. "If delivery takes place in the home we need to perform some rituals to ask forgiveness from the deity." a community leader revealed. Though animal-shed delivery is not related to caste, the practice is more common among the lower-

caste Hindus. "Though our caste is small, our god is stronger and big," a low-caste TBA stated with pride.

Reasons based on cleanliness: "It is easier to clean the shed before and after delivery than the home. The animal shed is on the ground floor without any artificial flooring, so even if it is blood-soaked, we can dig up and throw out blood-contaminated soil/mud after the delivery procedure."

Reasons based on avoiding sin: The periods of menstruation and childbirth are considered to be polluted days. If the woman touches earth during this period, there will be less sin. The animal shed is the only suitable place for this purpose. In the market area, where there are no animal sheds, they give birth in a separate room.

None of the women interviewed agreed to go to hospital for the delivery unless there was a serious problem. The reasons expressed were: "The hospital is cold and has no warming system," "We are not acquainted," "No relatives are allowed to stay with the mother during delivery," "It is not convenient" and "TBAs are more experienced." According to a TBA, "last year one woman died due to placenta retention. The placenta was not expelled even after 5 hours of childbirth and there was excessive bleeding. They took her to the hospital but doctors couldn't manage and she was referred to the Nepalgunj (referral hospital). The flight had already gone that day. They had to wait for the flight the next day, but the mother died after a few hours. All three of her children became orphans. This hospital could not save her life."

Birth Attendance

Some women give birth alone and some are attended. The main reasons for unattended deliveries were natural process, polluted period and self-confidence. (1) Child delivery is considered a *natural process*. Women often say "Jun Bela Bela Unhi Bela Chela," meaning the childbirth will occur on its own time, hence no attendance is needed. (2) *Polluted period*. The common belief is that their "deity will get angry if they touch the polluted woman." This polluting period commences at a different point in time. For some it begins at membrane rupture and for others from separation of the child. For all polluting period stops after performing Nuaran, which is the end of 6-15 days of seclusion. In an illustrating case of fear of pollution, a TBA told how she helped a woman with placenta retention. "The placenta was not expelled even after two hours of childbirth. The mother was nearly in shock. Though there were many women around nobody touched her for help. If I hadn't helped her, she might have died." She changed her clothes and performed some ritual before and after touching the "polluted" woman, and luckily the woman survived. (3) *Self-confidence* in giving birth alone. Confidence was strong among multi-parous and ethnic Sherpa. "I gave birth to all my three children alone. Why do we need anyone to help?" one woman in her fourth pregnancy stated.

The decision to seek help from an attendant depends on the woman herself or on the mother-in-law. TBAs often complained that the mothers who do not encounter a problem have never called them. The problems include "pollution," according to one TBA: "they do call sometimes because no one wants to touch the women during and after delivery." Further questioning of TBAs revealed dissatisfaction because they are not paid for attending the deliveries.

Conduct of Normal Labor and Delivery by TBA

Preparation of the place and cleaning: If delivery is to take place in an animal shed, the animals are moved to another place; the dung and dirt are swept away; clean dry grass or hay are laid down. A plastic sheet or blanket is used to cover the dry grass. Generally, hand washing is not considered to be important. One mother reported: "TBAs rarely wash their hands. They smoke and gossip in between procedures and start again without washing and insert their hand into the vagina if needed."

Delivery position and procedure: There was no specific position preferred for the first stage of labor. To facilitate a smooth and comfortable delivery, *in the first stage of labor*, the birth-attendant starts with mustard-oil massage on the woman's abdomen, feet and hands, and puts oil on her head. To keep strong during the labor, mothers used to drink cumin seed soup and glucose water. The usual position the woman adopts during the *second stage* of labor is prone on the hands and knees. From the TBA's perspective, this position is best because she can provide pressure on the woman's rectum with her thumb when the woman pushes. This procedure results in easier childbirth and prevents perineal tearing. One untrained TBA revealed, "This support also prevents the child coming through the anus." From the mother's perspective, "This position is easy for pushing, accumulates more

strength, and is quick." "I delivered all my children in this position without any assistant. This position is good when we are alone," a 24-year-old mother stated.

Umbilical cord cutting: Most commonly used instruments for cord cutting include sickle, knife, bamboo and razor. One TBA said, "For the cord cutting they gave me a sickle at first but it was not sharp, then a knife but it was also not sharp. Finally I cut it with a bamboo stick." A metal coin is placed under the cord during cutting as a base. No one mentioned that they disinfect the cord-cutting instrument before use. Even trained TBAs said it is not practical to follow what they have been taught in training because usually they are called in an urgent case. They do not have a ready-made delivery kit. When mothers deliver alone they also do not prepare the things beforehand.

Postpartum-Care and Practice

Seclusion period: The formal period of seclusion starts at delivery and in most cases lasts for 30 days. Even though mothers are purified by 6-15 days, they take rest during seclusion. If delivery took place in an animal shed they move to the house after purification. A woman goes into seclusion because this practice prevents her from polluting other people and protects her from the attentions of evil spirits. However, this is not practiced by the poor who do not have a helping hand in the family.

Food practices: Immediately after delivery all women are provided with 100-500 ml of raw mustard oil to drink in order to gain energy, make the womb strong and relieve post-partum pain. Sometimes turmeric and egg are added to the oil. Women reduce salt intake for 6-10 days to prevent swelling and infection. Green vegetables, pumpkins and apples are restricted for 2-3 months after delivery. They are considered to be cold food and believed to cause diarrhoea for the child through the mother's milk. Buffalo butter is also restricted because it may cause itching and vaginal infection. Food restriction is not practiced among the ethnic Sherpa.

Management of Obstetrical Problems

Prolonged or obstructed labor: Management of prolonged labor is generally beyond the skills of both mothers and TBAs. Helping procedures include abdominal massage, putting oil on the head, giving soup to drink and performing rituals to worship the god, etc. Many of the TBAs reported attempting internal manipulation without proper cleaning and without wearing a glove.

Placenta retention: Most attendants wait for spontaneous expulsion of the placenta. If the period is considered delayed (more than 1-2 hours) various measures such as abdominal massage, induction of vomiting, fundal pressure, cord traction and manual removal are then attempted. To induce vomiting, either the mother's hair or a finger is forced down her throat. Sometimes water used for washing clothes or a soup of bitter herbs is given to the mother to drink.

Immediate postpartum hemorrhage: Here as in other Asian studies (Goodburn et al., 1995; Bhatia, 1981), "bleeding like a river" or bleeding "as much as fills a water jar" were common descriptions for the excessive bleeding. Some TBAs said, "There is a hard mass in the lower abdomen following delivery so we massage and squeeze the mass." Other TBAs, however, are not ready to take the risk so they refer the case without delay. At the same time foods such as millet puwa (a confection prepared with millet flour, cumin seed, pepper, clove, cinnamon and coriander) and mustard oil mixed with turmeric are provided. One mother-in-law stated that keeping the mother in complete rest could control the bleeding automatically.

Results from Survey Data

Table 1 shows the different stages of childbirth practices and their relationship with delivery places. Almost half of the deliveries occurred in an animal shed (46.9%). Ninety percent of the women did not receive antenatal care; 48% of the deliveries were unattended, 74% of the women used a sickle as the cord-cutting instrument and 95% did not disinfect the instrument before use. The women who gave birth in the home were more likely to have had antenatal care and to have used a razor blade to cut the umbilical cord than those who delivered in an animal shed.

Childbirth practices by socio-demographic chawomen are summarized in Table 2. Women of Chhetri or Thakuri ethnicity, and those who were illiterate, older and of higher parity were more likely to follow high-risk birth practices such as no antenatal care, giving birth

TABLE 1. Distribution of Birth Practices by Delivery Place

Variables	Place of delivery: Animal shed N (%)	Home N (%)	Total N (%)	Chi² P-value
Antenatal care				
Yes	18 (5.8)	49 (14.0)	67 (10.2)	0.001
No	290 (94.2)	300 (86.0)	590 (89.8)	
Birth attendant				
TBAs/nurses*	76 (24.7)	91 (26.1)	167 (25.4)	0.102
Relatives	92 (29.9)	79 (22.6)	171 (26.0)	
Not attended	140 (45.5)	179 (51.3)	319 (48.6)	
Cord cutting instrument**				
Razor blade	66 (22.1)	103 (30.4)	169 (26.5)	0.019
Sickle/others***	232 (77.9)	236 (69.6)	468 (73.5)	
Disinfect the instrument				
Yes	10 (3.4)	19 (5.6)	29 (4.6)	0.179
No/don't know	288 (96.6)	320 (94.4)	608 (95.4)	

* Three percent were nurses. ** Twenty stillbirths are not included.
*** Includes wood, bamboo bark, and stone

in an animal shed, having unattended delivery and not disinfecting the cord-cutting instrument before use. The women whose husbands were illiterate were more likely to be exposed to these risks.

Table 3 shows the adjusted odds ratios for the association between selected birth practices and potential risk factors. Compared to the Brahmin, ethnic Chhetri/Thakuri were significantly more likely to have no antenatal care and to give birth without an attendant. The ethnic Kami/Sharki had more attended delivery. Husband's education > 5 grades significantly reduced high-risk birth practices in all stages of delivery. Women's education was, however, significantly associated with antenatal care and boiling the cord-cutting instrument. Women with increased parity were more likely to give birth without an attendant. Other factors, such as distance from health service, pregnancy morbidity and other socio-economic factors, were not associated with birth practices and did not contribute to the fit of the model.

TABLE 2. Distribution of Selected Birth Practices by Socio-Economic and Biological Factors

Variables	Total No (col %)	No ANC %	Animal shed delivery %	Unattended delivery %	Instrument not boiled %
Ethnic group					
Brahmin	98 (14.9)	77.6	34.7	35.7	34.4
Chhetri/Thakuri	414 (63.1)	97.3	47.8	58.2	87.5
Kami/Sharki	121 (18.4)	73.6	55.4	26.5	64.1
Others	24 (3.6)	91.7	37.5	45.8	41.7
Mother's education					
Illiterate	620 (94.4)	90.9	48.2	49.1	74.1
Literate	37 (5.6)	70.3	24.3	40.5	62.9
Mother's age					
Below 20	24 (3.7)	79.2	29.2	29.2	71.4
20-29 years	364 (55.4)	87.6	46.1	40.4	69.1
30-34 years	125 (19.1)	91.2	44.0	60.0	78.1
35+	144 (21.9)	95.8	49.3	62.5	80.7
Parity					
1	126 (19.2)	85.7	43.6	30.2	68.9
2-3	208 (31.7)	87.9	47.1	43.3	70.9
4-5	166 (25.3)	92.3	51.2	59.6	78.4
5 +	157 (23.9)	92.9	44.6	58.6	75.2
Husband's education					
Illiterate	347 (52.8)	91.6	53.1	53.1	79.3
1-5 grade	191 (29.1)	95.8	44.5	49.7	76.5
6 + grade	119 (18.1)	74.8	32.8	33.6	50.9
Husband's occupation					
Farming	460 (70.0)	89.8	44.6	51.1	76.7
Trade/office	137 (20.9)	90.5	45.9	40.9	62.6
Laborer/others	60 (9.1)	88.3	66.8	46.7	73.2

% row percents for each variable.

DISCUSSION

Compared to other studies on childbirth in Nepal and in other countries (Goodburn et al., 1995; Binka et al., 1995; Hoque et al., 1996; National Planning Commission Secretariat, 1998; Bhatia, 1981) our study is unique in revealing the animal shed as an choice for child birthplace. Other practices such as inadequate ANC, unhygienic um-

TABLE 3. Adjusted Odds Ratios for Factors Associated with Selected Childbirth Practices

Variables	No ANC OR (95%CI)	Animal shed OR (95%CI)	Unattended OR (95% CI)	Inst. not boiled OR (95%CI)
Ethnic group	*		*	*
Brahmin[a]	1.0	1.0	1.0	1.0
Chhetri/Thakuri[b]	**7.8(2.2–28.5)**	1.6(0.5–5.1)	**2.1(1.0–4.3)**	2.4(0.9–6.2)
Kami/Sharki[c]	0.4(0.1–3.3)	1.7(0.7–4.1)	**0.5(0.2–0.9)**	0.8(0.3–2.5)
Others[ab]	2.5(0.3–22.4)	0.9(0.2–3.9)	1.2(0.5–2.9)	0.4(0.2–1.1)
Mother's education	*	*	*	*
Illiterate	1.0	1.0	1.0	1.0
Literate	**0.2(0.1–0.3)**	0.4(0.2–1.1)	0.9(0.5–1.5)	**0.3(0.1–0.8)**
Father's education	*	*	*	*
Illiterate	1.0	1.0	1.0	1.0
1-5 grade	2.4(0.9–6.7)	0.7(0.5–1.1)	0.9(0.6–1.3)	0.8(0.3–1.7)
6+ grade	**0.2(0.1–0.5)**	**0.5(0.2–0.9)**	**0.5(0.3–0.9)**	**0.3(0.1–0.6)**
Parity			*	
1	1.0	1.0	1.0	1.0
2-3	1.3(0.8–2.2)	1.3(0.6–2.4)	1.8(1.1–2.9)	1.2(0.6–2.6)
4-6	1.2(0.7–2.2)	1.3(0.6–2.5)	**3.1(2.0–4.8)**	2.0(0.5–8.0)
>6	1.5(0.8–3.2)	0.9(0.4–1.7)	**2.9(1.7–5.0)**	4.3(0.7–25.9)

Adjusted for village and occupation. Mother's age is not included as it was highly correlated with parity (Spearman correlation coefficient $p < 0.0005$)
* Significant changes in loglikelihood at < 0.05.
** Test for trend across the parity by birth attendant was $p < 0.0005$
[a b c] Ethnic groups not having a superscript letter in common differ significantly ($p < 0.05$) for unattended delivery.

bilical cord cutting and dressing, and local management for complicated delivery are similar to those found in other studies from South Asia (Marta, 1993; Goodburn et al., 1995; Hoque et al., 1996; Bhatia, 1981).

The reasons for giving birth in an animal shed were mostly related to superstition and lack of knowledge regarding hygiene. In addition, poor transportation and inadequate facilities in the hospital add to the existing fear of loneliness and lack of acquaintance preventing these women from contact with modern obstetrics. Though it was not mentioned in focus group discussion, the husband's level of education was found to be a strong determinant for the delivery practices in the quantitative analysis. Relatively few mothers in the study area had had any formal education (5.6%), and thus there was not enough variability to demonstrate a significant effect. After all, it is consistent with

previous reports that child survival rates and health behaviors are associated with parental education (Hemminki et al., 1992; Panta, 1991; Baker et al., 1998).

Among several problems, the custom of polluted period is most strict in the Jumla community. Because of this custom a woman must care for herself when actually she is at high risk of pregnancy-related problems (Cunningham et al., 1997), although in the present study unhappiness among the participants was not noticed. In an earlier report (Thapa, 1996) a feeling of hatred, isolation, and dissatisfaction among the women was revealed: "At the time of giving birth and for quite some time afterwards, we are treated even by our jati (women) worse than dead animals; no one touches us." Unattended deliveries were more common among ethnic Chhetri and Thakuri. Maybe these ethnic groups adhered to tradition more strictly than the others. A previous study in Nepal (Choe et al., 1989) revealed the ethnic Chhetri and Thakuri ranked third highest in infant mortality rate among all eight categories studied.

Delivery procedures in Jumla did not follow aseptic technique. Animal sheds are favorable for the growth of micro-organisms (Park, 1997). This, combined with poor or no disinfection, may explain the association with increased mortality among infants born in animal sheds (Thapa et al., 2000). Mustard oil and turmeric are often used for cord dressing; no one mentioned using ash or cow dung as has been reported in Bangladesh and in Nepal (Marta, 1993; National Planning Commission Secretariat, 1998).

In common with previous studies (Goodburn et al., 1995; Bhatia, 1981), some of the delivery procedures described herein are potentially harmful and likely to contribute to the development of postpartum morbidity. Such procedures include internal manipulation, pulling on the umbilical cord and choking or inducing vomiting in the mother to expedite placental delivery. However, some traditional practices seem likely to be not harmful. These include adopting an upright position and walking during labor, adopting a prone position on hands and knees for delivery (Gardosi et al., 1989), giving gentle oil massage which may give psychological support, and giving soup or glucose water during labor.

The practice of seclusion in the postpartum period is an important and beneficial custom in this community. From this custom, a woman gets rest and nutritious food particularly during the recovery period.

Food restriction during pregnancy and the postpartum period was not prominent in Jumla, which differed markedly from the long list of food taboos in Bangladesh (Goodburn et al., 1995).

In conclusion, while there are tremendous contrasts between modern obstetrical practice and birth practices in Jumla, underlying both is the wish for safe delivery. The modern world benefits from knowledge and technology of which Jumli people are ignorant and to which they have no access. High rates of animal shed delivery and delivery without an assistant strongly reflect a definition of safe motherhood that differs from the WHO definition. Safe delivery in Jumla means "delivery which does not pollute other people or the community." These divergent definitions must be reconsidered. Emphasis should be placed on exploring beliefs and providing both culturally accepted and feasible education and health care programs for all women, adolescents to elderly. Training for TBAs alone is not enough, as it does not substantially alter either beliefs or practices. Finally, emergency obstetric care facilities should be established at the community level.

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Brief Report

Delay in Breast Cancer Care: A Study in Thai Women

PARAMEE THONGSUKSAI, MD,* VIRASAKDI CHONGSUVIVATWONG, MD, PHD,† AND HUTCHA SRIPLUNG, MD*

BACKGROUND. Breast cancer is the second most common cause of cancer death in Thai women. Cancer registry data reveal a high prevalence of late-stage disease at diagnosis. The factors resulting in delay in Thailand have not yet been investigated.

OBJECTIVES. To determine the extent of, and the factors contributing to, delay in breast cancer care.

DESIGN. Women with breast cancer who were first treated at Songklanagarind Hospital between June 1994 and June 1996 were interviewed with retrospective chart audits of care.

MEASURES. Dependent variables included patient delay (symptom recognition to first care) and system delay (first care to treatment). Independent variables tested included demographic factors, help-seeking behavior, and cancer knowledge. Nonparametric rank sum tests were used for univariate analysis, and Cox regression was used for multivariate analysis.

RESULTS. Ninety-four cases were included in the study. The median patient and system delays were 4 weeks; 26.6% and 24.4% of patients, respectively, experienced patient and system delay >12 weeks. Only marital status (unmarried compared with married women) was significantly associated with patient delay (hazard ratio [HR] 2.78, 95% CI 1.23–6.25). Contacting a provincial hospital instead of a university hospital as first medical care (hazard ratio 2.50, 1.23–5.26), being given a diagnosis rather than being told nothing (HR 2.04, 1.14–3.57) and being given treatment rather than being immediately referred (HR 4.53, 2.22–9.09) were associated with system delay.

CONCLUSIONS. Patient delay and system delay in breast cancer care are important weaknesses of disease control in Thailand. Educational programs should target unmarried women, who are at higher risk of delay. System delay in hospitals outside the university needs to be improved by a good referral system.

Key words: breast cancer; patient delay; system delay, help-seeking behavior. (Med Care 2000;38:108–114)

Delay in diagnosis and treatment of breast cancer leads to progression of disease to a late stage and is associated with high mortality.[1–3] Furthermore, smaller tumors are more likely to be treated successfully with limited breast surgery.[4–6] Understanding the nature of delay in each society

*From the Department of Pathology, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand.

†From the Epidemiology Unit, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand.

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Address correspondence to: Paramee Thongsuksai, MD, Department of Pathology, Faculty of Medicine, Prince of Songkla University, Hat-Yai, Songkhla, Thailand 90110.

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should lead to earlier diagnosis and treatment, thus improving the outcome.

In Thailand, breast cancer is the second most common cancer in women. The data from our Cancer Registry reveal that most patients receive treatment at a late stage (56% at Stages III and IV). These figures suggest delay in breast cancer care, which needs to be investigated.

Delay in breast cancer care can be divided into patient delay (time from symptom recognition to initial medical consultation) and system delay (time from first medical consultation to treatment).[7] Several studies concerning delay in breast cancer care have been reported.[7-14] Factors that have been found to be associated are age, economic status, education, history of chronic disease, symptom perception, cancer knowledge, and previous health care experience. However, most of these studies are from developed countries or high-incidence areas. It is appropriate to gain insight into the nature of delay and the association of delay with these factors in Thailand. This is true because sociocultural aspects of care or help-seeking behavior particular to Thailand are unknown and because cancer education is not well developed.

Health services in Thailand are mainly provided by public hospitals run by the Ministry of Public Health, university hospitals, and the private sector. Public health services include small health centers covering 3,000 to 5,000 people, 10- to 60-bed community hospitals covering 20,000 to 40,000 people and 100- to 400-bed provincial hospitals covering more than 200,000 people. A patient can visit any of these health services and be referred to a larger hospital. The services are free for civil servants and the poor who have registered and received a government health card.

Cancer has been recognized as an important health problem for Thai people only since 1994. University hospitals are the main providers of cancer care, especially radiation and chemotherapy. There are fewer than 10 university hospitals in Bangkok, the capital city, and 1 or 2 in each region of the country. Songklanagarind hospital, the study site, has 700 beds and is the only university hospital in the southern region of Thailand, serving 14 provinces with a population of 8 million people.

Materials and Methods

Subject Selection

Eligible subjects included patients with histologically confirmed primary invasive carcinoma of the breast who were admitted to Songklanagarind Hospital for initial treatment between June 1994 and June 1996. Subjects were excluded if they did not cooperate or data concerning delay were unreliable.

The number of subjects was determined by sample size calculation, based on testing a null hypothesis of no difference between the incidence rates in two (or more) groups,[15] and assuming the presence of an independent factor with two levels, with approximate median survival times of 3 to 5 weeks and 5 to 8 weeks, and ~50% of the subjects in each level. At a 5% level of significance and with 80% power, 44 to 130 subjects were required.

Data Collection

Data on personal and health care behavior were obtained by interview by a trained ward nurse using a structured questionnaire. Clinicopathologic data—for example, type of surgery, laboratory results, and pathology results—were abstracted from hospital and pathology records. Duration of delay was also determined from hospital records and compared with interview data. If a large discrepancy existed, the case was excluded because of possible unreliability of the data.

Study Variables

The independent variables included sociodemographic background, patient assessment of first symptom and date on which it was recognized, source and date of first care, diagnosis and treatment by first doctor, previous health care practice, and cancer knowledge. Pathologic tumor/nodes/metastasis staging was based on the staging system of the American Joint Committee on Cancer.[16]

The dependent variables were patient delay and system delay. Patient delay was calculated in weeks from the date on which a patient first noticed the symptom to the date of first medical consultation. System delay was the interval from first medical consultation to the date of admission for treatment at the study hospital.

Statistical Analysis

Nonparametric statistics using Kruskal-Wallis and Wilcoxon rank sum tests were initially used to explore the association between delay and inde-

pendent variables. Cox regression for survival time data was used in multivariate analysis. Hazard ratios for each level of a factor were reciprocated to denote the ratio of the natural logarithm of the probability of delay among subjects at that level to that among subjects at the reference level at any given time. Thus, a ratio >1 indicates a greater probability of delay, and a ratio <1 a lower probability of delay, compared with the reference level. The best fitted models were obtained by backward elimination guided by the change in log likelihood, using a P value > 0.05 as the criterion for removal.

Results

There were a total of 101 eligible subjects during the study period. Seven subjects were excluded because of noncooperation and unreliability of delay data. These subjects were not different from the included subjects regarding to stage of disease. Four of them had Stage II disease, two had Stage III and one had Stage IV. The final number of subjects used in the analysis was 94.

Patient delay ranged from 1 to 207 weeks, with a median of 4 weeks. Patient delay >12 weeks was experienced by 26.6% of patients. A breakdown of duration of patient delay by demographic characteristics, symptom-related factors, and tumor stage is shown in Table 1. Unmarried women had remarkably long patient delay compared with married women. However, the difference is not significant in univariate analysis. Tumor stage was also not significant if separated into four stages but appeared significant when grouped into Stages I + II and Stages III + IV (P value = 0.038, Wilcoxon rank sum test). In multivariate analysis, only marital status was statistically significant: HR 2.78 (95% CI 1.23–6.25).

The system delay ranged from <1 week to 104 weeks, with a median of 4 weeks. System delay >12 weeks was experienced by 24.4% of patients. Diagnosis and management by first physician were statistically significant in univariate analysis. These two variables and source of first care were assessed separately in Cox regression because they were correlated. All these three variables gave statistically significant hazard ratios (Table 2). Because no other factor was significant, the results in Table 2 are given without adjustment.

None of the factors related to past health care utilization was associated with patient or system delay (Table 3).

Discussion

This study demonstrates a high proportion of patient and system delay in breast cancer care. Being unmarried was the only significant predictor for patient delay, whereas sources of first care and diagnosis and treatment of first contacting physician were associated with system delay.

In our study, the proportion of study subjects who experienced delays of ≥3 months is comparable with other studies, but the median delay is longer. In the literature, the proportion of delay >3 months has been reported mainly for patient delay. In a large review of this topic in 1974 by Antonousky et al, patient delay of ≥3 months ranged from 35% to 50%.[17] The results of a meta-analysis of 12 publications during 1975 through 1992 found a 3-month delay of 34.2% (range 9%–50%),[18] and other recent individual studies reported a range of 19% to 27%.[7,10–12,19] However, our median patient and system delay were 2 weeks longer than in other studies.[7,8,12,19] These results indicate the existence of delay in diagnosis and treatment of breast cancer in our country. However, the comparison of delay duration with other studies has to be interpreted with caution because different definitions and terms were used.

Sociodemographic background has long been found to be associated with delay in breast cancer care,[9,17,20,21] although conflicting results exist.[7,13,22] The fact that unmarried women had a significantly longer patient delay in this study contrasts with other studies.[7,12,13,23] We have no data to show why these unmarried women had such a long delay. It may be due to shyness concerning consultation and exposure of the breast to another person, or to lack of psychosocial networks and support.[18] Because this delay is quite significant, and the incidence of breast cancer is expected to rise because of an increasingly Westernized lifestyle, this issue should be considered in attempts to improve breast cancer care. Further study to gain insight into causes of the delay, which might lead to intervention, is necessary.

Our data suggest that the first doctor plays a very important role in determining the duration of system delay. The subjects who had their first consultation at

TABLE 1. Duration of Patient Delay by Demography, Symptom-Related Factors, and Tumor Stage

Study Variables	Number of Cases	Median Duration (interquartile range in weeks)
Age (y)		
≤40	31	2 (1–8)
41–50	36	8 (1–22)
>50	27	2 (1–12)
Marital status		
Unmarried	9	29 (2–104)
Married	85	3 (1–10)
Education level		
≤Primary school	66	3 (1–12)
Secondary-high	14	3 (1–32)
>High school	14	4.5 (2–9)
Family monthly income (Baht)		
≤5000	50	2.5 (1–12)
5001–10000	17	2 (1–7)
>10000	27	8 (2–24)
Type of symptom		
Mass	80	4 (1–12)
Pain or other	13	2 (1–7)
Patient symptom assessment at first recognition		
Benign	77	5 (1–12)
Tumor/cancer	15	2 (1–5)
Tumor stage		
Stage I	6	3 (1–6)
Stage II	66	2.5 (1–12)
Stage III	15	8 (2–27)
Stage IV	4	28 (3.5–67.5)

a provincial hospital experienced longer system delay than those who contacted the university hospital. Referred patients without previous treatment had shorter system delay. Thus, the development of a good referral system may shorten delay. Most patients did not have access to the university hospital for first care, and ~20% of cases were given medical treatment by their first doctor. This resulted in a median system delay of 13 weeks. Thus, these doctors need feedback and perhaps a refresher course to improve case management.

However, the fact that not being informed of the diagnosis by the first doctor was associated with shorter delay is problematic. We have no data to show whether in fact the doctor did use verbal communication to encourage the patient to go to the referral center quickly, or whether not being informed of the diagnosis increased the patient's anxiety and thus led the patient to go to the referral center more quickly, or, by contrast, whether being informed of the diagnosis of possible cancer frightened the woman and made her avoid further treatment.

Health beliefs,[21–25] health education exposure,[26] and family factors[27] have been shown to be associated with help-seeking behavior. However, the present study could not demonstrate the relationship of these factors to the delay. Although unmarried women had a higher risk of delay, unfortunately other detailed reasons, such as a woman's shyness or the physician's gender, were not explored. Further study aimed to elucidate these relationships should be considered so that public education health efforts can be better directed.

TABLE 2. Relationship Between Current Health Care Utilization and System Delay

Study Variables	Number of Cases	Median Duration (interquartile range in weeks)	Hazard Ratio (95% CI)
Source of first medical care			
Private clinic	22	3.5 (1–12)	1.85 (0.91–3.85)
Community hospital	22	4 (3–6)	1.69 (0.81–3.45)
Provincial hospital	28	4 (2–21)	2.50 (1.23–5.26)
Private hospital	10	4 (2–11)	1.79 (0.77–4.17)
University hospital	12	2 (1–3.5)	1
Diagnosis of first physician			
Benign	23	7 (2–17)	2.04 (1.14–3.57)
Tumor/possible cancer	42	4 (1–12)	1.69 (1.02–2.70)
Not informed of diagnosis	28	2 (1–4)	1
Management of first physician			
Medicine	20	13 (3–28)	4.55 (2.22–9.09)
Biopsy	49	4 (2–9)	5.56 (2.04–1.56)
Others	6	3 (1–4)	2.00 (0.76–5.26)
No treatment	6	6 (3–7)	3.70 (1.34–11.11)
Refer	13	1 (0–1)	1
Transportation condition to study hospital			
Easy	35	3 (2–6)	1
Fair	35	4 (1–11)	0.99 (0.62–1.58)
Difficult	24	7 (2.5–19)	0.67 (0.96–2.86)

Our study has some limitations, including sampling bias. Our hospital is a referral center, and patients with advanced disease may be less likely to seek treatment. This was shown by the very few patients with stage IV disease in our sample. In fact, therefore, the extent of delay may be more severe than we observed. This sampling bias could also be responsible for the nonassociation of many variables tested. Another limitation is the reliability of the data as a result of recall bias. The patients were asked to recall such times as when they first recognized the lump and when they first went for medical consultation. Reliability should be more questionable in those with longer delay before data collection. The last major limitation was an inability of the study to give in detail the associated reason for the observed association. However, because this is an exploratory study, and because no other data concerning this problem are available in our country, our results will serve as a guide for further investigation.

The study, however, had some strengths. Most previous studies have used simple statistical tests by dividing the time into two or more intervals. By using this method, significant factors may appear insignificant. In contrast, if Cox regression is used for the continuous timing data, even a small difference will be detected.[7] A few recent studies have used Cox regression analysis.[8,9] The final strength of this study is that the study explored many potential variables that allowed us to identify factors independently associated with delay.

In summary, patient and system delay in breast cancer care are important weaknesses of breast cancer control in Thailand. Unmarried women are more vulnerable to prolonged patient delay, but the reason for this remains unknown. Educational programs should address this expanding high-risk group. System delay in hospitals outside the university needs to be minimized by a good referral system. General practitioners in this country may need a refresher course to improve case management, avoid unnecessary medical treatment, and properly refer patients.

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TABLE 3. Relationship of Patient and System Delay With Past Health Care Practices and Cancer Knowledge

Study Variables	Number of Cases	Patient Delay		System Delay	
		Median	HR (95% CI)	Median	HR (95% CI)
Cancer history in family					
No	79	3	1	4	1
Yes	14	4	1.14 (0.63–2.00)	3	1.00 (0.55–1.82)
History of chronic disease					
No	68	4.5	1	4	1
Yes	25	1	0.73 (0.46–1.18)	4	0.84 (0.52–1.33)
Usual help-seeking behavior					
Non-professional	19	5	1	3	1
Professional	75	2	1.01 (0.61–1.69)	4	1.19 (0.72–2.00)
Past experience with hospital admission					
No	41	5	1	4	1
Yes	45	3	0.76 (0.49–1.18)	4	1.39 (0.76–1.82)
Ever heard of breast disease					
No	47	5	1	3	1
Yes	45	2	0.79 (0.51–1.25)	3	1.04 (0.66–1.67)
Ever practiced breast self-examination					
No	50	3	1	4	
Yes	30	3	0.78 (0.49–1.23)	2.5	0.79 (0.50–1.27)
Think cancer is curable					
No	15	1	0.94 (0.51–1.75)	3	1.23 (0.65–2.33)
Don't know	35	6	1.28 (0.84–2.04)	3	1.04 (0.66–1.63)
Yes	43	4	1	4	1

Note: HR = hazard ratio.

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CHARACTERISTICS OF REPEAT ABORTERS IN VIETNAM

Nguyen Thi My Huong[1], Virasakdi Chongsuvivatwong[2], Alan Geater[2] and Ladawan Prateepchaikul[3]

[1]Scientific Research Department, Institute for the Protection of the Mother and Newborn, Hanoi, Vietnam; [2]Epidemiology Unit, Faculty of Medicine, Prince of Songkla University, Hat Yai, Thailand; [3]Department of Pediatric Nursing, Faculty of Nursing, Prince of Songkla University, Hat Yai, Thailand

Abstract. Two hundred and sixty married women seeking induced abortion service in Hanoi, Vietnam were interviewed to determine the magnitude of repeat induced abortion and explore selected characteristics of the repeat aborters. Seventy-one percent of the sample reported having had at least one previous induced abortion. After adjustment for age and number of living children, poor attitudes toward contraception, low use of modern contraceptives and failure of contraception were shown to be significantly associated with repeat induced abortion. Woman's age, number of living children, contraceptive knowledge and experience and desire for no more children were positively related to repeat induced abortion. Socio-demographic characteristics were not related to repeat induced abortion. Improvement of attitudes toward contraception, persuasion to use modern contraception and promotion of contraceptive effectiveness are recommended strategies to prevent repeat induced abortion.

INTRODUCTION

Induced abortion occurs in great numbers throughout the world (Henshaw *et al*, 1999). Repeat induced abortion accounts for a substantial proportion of all induced abortion in many countries, with reports ranging from 34% to 77% (Vach *et al*, 1998; Westfall and Kallail, 1995; Heinrich and Bobrowsky, 1984). The risks on subsequent pregnancies of repeat induced abortion are reported to be higher than those of the first induced abortion (Levin *et al*, 1980). Along with the high rate of induced abortion, public health services have been faced with serious health problems and severe financial costs (Singh *et al*, 1997).

Although repeat induced abortion status has been addressed in many previous reports, most studies have focused only on determinants of women having an induced abortion (Okonofua *et al*, 1999; Gorbach *et al*, 1998). Studies on repeat induced abortion in the existing literature were almost all conducted in developed countries. The results of these studies varied greatly. Characteristics of women who have repeat induced abortion are unclear.

In Vietnam, induced abortion is legal and provided without charge at all levels of the public health system. Data for 1995 showed an annual induced abortion number of nearly 1.4 million, a rate of 83 induced abortions per 1,000 women of reproductive age and an average of 2.5 abortions during the lifetime of a woman. These rates were documented as the highest among countries where abortion is legal (Henshaw *et al*, 1999; Goodkind, 1994). Contraceptive prevalence rate in 1996 was 68.3%. Intrauterine devices were used predominantly (54.8%) followed by traditional methods such as periodic abstinence and withdrawal (23.9%) (NCPFP, 1997). Prevention of induced abortion was considered as a high priority in the National Family Planning Program (Ministry of Health, Vietnam, 1997).

Repeat induced abortion is common in Vietnam (Vach *et al*, 1998; Hieu *et al*, 1993) but characteristics of women having repeat induced abortion have not been fully explored. Therefore, this study aimed to determine the magnitude of repeat induced abortion among the aborters and to identify their characteristics with an emphasis on socio-demographic and contraceptive knowledge, attitude and practice in order to gain better insight into the repeat aborters. Information from this study would be helpful for program planners and policy makers to orient future interventions to prevent repeat induced abortion.

MATERIALS AND METHODS

A cross-sectional study was conducted at the Institute for the Protection of the Mother and

Correspondence: Dr Nguyen Thi My Huong, Epidemiology Unit, Faculty of Medicine, Prince of Songkla University, Hat Yai, 90110, Thailand.
Fax: 66 74 212 900; E-mail: huongly94@hotmail.com

Institute for the Protection of the Mother and Newborn 43 Trang Thi street, Hoan Kiem District,Hanoi, Vietnam Fax: 84 48 254638 or 84 48 245811

Newborn, Hanoi, Vietnam. This is the leading research institute for Obstetrics, Gynecology, Neonatology and Family Planning in Vietnam with 300 in-patient beds. This study was approved by the Scientific and Ethical Review Group of the Institute.

A consecutive sample of 260 married women seeking induced abortion services between April and June 1997 was recruited and interviewed by trained interviewers before performing induced an abortion procedure. The main instrument for collecting data was a structured questionnaire. It covered socio-demographic information, reproductive history, contraceptive and induced abortion experience, and knowledge and attitudes toward contraception and induced abortion.

Economic status was measured based on 4 questions concerning monthly income per person of the aborter's family (score 1-4) and the ownership (score 1-2), architecture (score 1-4) and area (score 1-4) of the aborter's living house. The economic status was defined as the sum of scores for all 4 questions (theoretical range 0-14). Knowledge of the aborter was evaluated by knowledge of modern contraceptives (13 questions) and traditional contraceptives (2 questions) that showed awareness of contraceptives, understanding about the correct use and side-effects of methods. The general knowledge of the aborter was determined by combining knowledge of modern and traditional methods with awareness of fertile period and knowledge about supply sources of family planning (total of 17 questions). Each question on knowledge was scored 0 for an incorrect and 1 for a correct answer (theoretical range 0-17). Attitudes toward contraception and induced abortion were measured by 9 questions on beliefs and perceptions of the aborter regarding contraception and induced abortion. The attitude questions were scored based on the Thurstone scale divided into three degrees, namely disagree, not sure and agree. For positive questions, the scores of 1, 2 and 3 were given to the answers "disagree", "not sure" and "agree", respectively. In contrast, the scores of 1, 2 and 3 were given to the answers "agree", "not sure" and "disagree" respectively, in the negative questions (theoretical range 9-27). The questionnaire was pretested and modified accordingly. Final reliability coefficient (Cronbach alpha) was 0.78 for knowledge scores and 0.83 for attitude scores.

All questionnaire data were double-entered into the computer using Epi-Info software. Statistical analysis was performed using STATA software. Characteristics of the aborters were summarized according to repeat aborter and first aborter groups. Continuous variables were explored using mean and standard deviation (SD) and the difference between the two groups tested using Student's *t*-test. Categorical variables were stated as percentages and the differences in proportions between the two groups was tested using Chi-squared test. Multivariate logistic regression was applied to measure association between characteristics of the aborters and the repeat induced abortion with emphasis on knowledge, attitudes and practice of contraception and socio-economic status. In order to adjust for confounding, age and number of living children were included in the model.

RESULTS

One hundred and eighty-five (71%) among 260 women seeking induced abortion reported having at least one previous induced abortion. Of the repeat aborters, 52% had had one previous induced abortion and 48% had had at least two previous induced abortions.

Socio-demographic and reproductive characteristics of the aborters

The average ages were 31.8 (SD: 5.5) and 28.5 (SD: 4.9) years ($p < 0.05$), respectively, for the repeat aborters and the first aborters (Table 1). Age groups 30-34 and 35-40 were more common among repeat aborters than among first aborters. The education, occupation and economic status of the aborters were similar in the two groups.

The repeat aborters had significantly higher mean numbers of pregnancies and living children than the first aborters, 4.5 versus 2.2 pregnancies and 1.5 versus 1.1 living children (Table 2). In addition, significantly more repeat aborters than first aborters stated that they desired no more children. A larger proportion of repeat aborters sought abortion service at low gestational age (under 6 weeks) than did first aborters, 82.7% *vs* 62.7% ($p < 0.05$).

Contraceptive knowledge, attitudes and practice of the aborters

The repeat aborters reported significantly more experience of any contraception in the past than the first aborters, 91.9% *vs* 74.7% (Table 3). Nearly 80% of the repeat aborters stated that they had become pregnant while they were using a contraception compared to 50% of the first aborters.

Table 1
Socio-demographic characteristics of repeat aborters and first aborters.

Characteristic	Repeat aborter (N=185)	First aborter (N=75)
Age (years)* (%)		
19-24	10.3	21.3
25-29	28.1	42.7
30-34	24.3	17.3
35-40	37.3	18.7
Mean age** (SD)	31.8 (5.5)	28.5 (4.9)
Education (%)		
Secondary school	6.6	2.7
High school	50.3	49.3
College	15.7	14.7
University or higher	27.5	33.3
Mean economic score (SD)	8.2 (2.0)	8.0 (2.0)

SD = Standard deviation.
* Significant at $p < 0.05$ by chi-squared test
** Significant at $p < 0.05$ by Student's *t*-test

Table 2
Reproductive history of repeat aborters and first aborters.

Characteristics	Repeat aborter (N=185)	First aborter (N=75)
Mean age at first marriage - years (SD)	23.3 (3.0)	23.8 (3.0)
Mean number of pregnancies** (SD)	4.5 (1.6)	2.2 (0.7)
Mean number of living children** (SD)	1.5 (0.7)	1.1 (0.6)
Number of living children* (%)		
None	6.0	12.0
one child	40.5	62.7
two or three children	53.5	25.3
Desire for more children* (%)		
no	58.4	32.0
yes	41.6	68.0
Gestational age at induced abortion* (%)		
under 6 weeks	82.7	62.7
6 - 12 weeks	17.3	37.3

SD = Standard deviation.
* Significant at $p < 0.05$ by chi-squared test.
** Significant at $p < 0.05$ by Student's *t*-test.

However, the traditional methods were more commonly used than the modern methods.

The repeat aborters had better knowledge of both traditional and modern contraception than the first aborters. Mean score of the general knowledge of the repeaters was significantly higher than that of the first aborters, 9.0 (SD: 3.4) *vs* 7.2 (SD: 3.5). The repeat aborters stated less worry about induced abortion and less concern about contraception than the first aborters. The general attitude of the repeat aborters was significantly more likely to be in favor of induced abortion and not in favor of contraception than the first aborters, mean scores of 19.7 (SD: 3.2) and 22.0 (SD: 2.6), respectively.

Table 3
Knowledge, attitudes and practice of contraception of repeat aborters and first aborters.

Characteristics	Repeat aborter (N=185)	First aborter (N=75)
Experience of contraception in the past* (%)		
never	8.1	25.3
ever	91.9	74.7
Contraceptive use at the time of conception* (%)		
no method	21.6	49.3
traditional method	63.3	42.7
modern method	15.1	8.0
Mean score of knowledge of traditional methods** (SD)	1.0 (0.5)	0.8 (0.5)
Mean score of knowledge of modern methods** (SD)	6.9 (2.7)	5.5 (2.9)
Mean score of general knowledge** (SD)	9.0 (3.4)	7.2 (3.5)
Mean score of perceived worry about induced abortion** (SD)	2.7 (0.5)	2.9 (0.3)
Mean score of belief that induced abortion is harmful** (SD)	2.6 (0.6)	2.9 (0.3)
Mean score of perception that induced abortion cannot be used as contraception** (SD)	2.7 (0.5)	2.9 (0.3)
Mean score of belief that contraception is necessary** (SD)	2.6 (0.5)	2.9 (0.3)
Mean score of general attitude** (SD)	19.7 (3.2)	22.0 (2.6)

SD = Standard deviation.
* Significant at $p < 0.05$ by chi-squared test.
** Significant at $p < 0.05$ by Student's *t*-test.

Table 4
Crude and adjusted* odds ratios for selected characteristics of repeat aborters.

Characteristics	Crude odds ratio	Adjusted odds ratio (95% CI)
Experience of contraception in the past		
never	1	1
ever	3.85	3.36 (0.90-12.61)
Contraceptive use at the time of conception		
no method	1	1
traditional method	3.38	2.57 (1.08-6.16)
modern method	4.32	4.11 (1.18-14.32)
General knowledge scores	1.15	1.32 (1.15-1.52)
General attitude scores	0.76	0.63 (0.54-0.74)
Desire more children		
yes	1	1
no	2.98	1.70 (0.45-6.37)
Education		
Secondary school	1	1
High school	0.42	0.41 (0.07-2.43)
College	0.44	0.30 (0.04-2.31)
University or higher	0.34	0.28 (0.04-2.04)
Economic score	1.10	1.03 (0.86-1.23)

* Adjusted for age and number of living children.

Association between selected characteristics and repeat induced abortion

Multivariate logistic regression adjusted for age and number of living children revealed that contraceptive use at the time of conception as well as knowledge and attitudes toward contraception were significantly associated with the repeat induced abortion (Table 4). Repeat aborters who were significantly more likely to have better knowledge of contraception and report that they became pregnant while using a contraception than were first aborters. By contrast, the repeat aborters were less likely to express positive attitudes (*ie* in favor of contraception and less in favor of induced abortion) than were first aborters (adjusted odds ratio = 0.63; 95% CI: 0.54-0.74).

Experience of any contraception in the past and desire for no more children were not associated with repeat induced abortion when controlling for the other characteristics. Educational and economic status showed no relationship with repeat induced abortion.

DISCUSSION

This study revealed that more than 70% of women seeking induced abortion services had had at least one previous induced abortion. The repeat aborters tended to be older women with high parity and have had all their desired children. They were more likely to have had contraceptive experience in the past and more likely to have used a method at the time they became pregnant than the first aborters. The repeaters also tended to have better knowledge of contraception than the first aborters. In contrast, they more commonly had an unfavorable attitude toward contraception and a favorable attitude toward induced abortion.

The proportion of repeat induced abortion in this study is consistent with that of a recent study (Vach *et al*, 1998) showing nearly 77% repeat induced abortions among aborters. However, it is substantially higher than that of an earlier report (Hieu *et al*, 1993).

Repeat aborters were more likely to report both previous and current use of contraception. A possible explanation is that the repeaters were more active in controlling their fertility than the first aborters so they tended to seek both contraception and induced abortion to achieve their goal. In addition, the previous induced abortion experience might urge them to use a contraception to avoid subsequent induced abortion. In turn, the more common use of contraception among repeat aborters was a possible explanation for their better knowledge of contraceptive methods. On the other hand, it also reflected poor practice of contraception such as incorrect and inconsistent use leading to contraceptive failures. More favorable attitudes toward induced abortion and unfavorable attitudes toward contraception among repeat aborters is consistent with the fact that they practice more traditional methods. The characteristics of repeat aborters identified in this study are mostly consistent with those reported in studies in other settings.

A similar study among 580 induced abortion women in Canada (Berger *et al*, 1984) showed a lower proportion of repeat induced abortion (22%). The repeat aborters were older with higher number of living children and their attitude was more tolerant to induced abortion than the first aborters. No association between socio-demographic characteristics and repeat induced abortion was found, implying that the socio-demography might have little effect on the repeat induced abortion.

An Australian study (Callan, 1983) indicated that women seeking repeat induced abortion had better knowledge of contraception and were more likely to use a contraception than first abortion seekers. They also had more favorable attitudes to induced abortion than the first aborters. However, similar age between the first and the repeat aborters in this study might result from different pattern of subjects between the two studies. This study investigated only single women while our study included only married women.

The results of a Singapore study (Tsoi *et al*, 1984) also revealed that repeat aborters had more pregnancies and more living children than first aborters. A higher proportion of traditional methods was found among the repeat than among first aborters which is comparable to the findings of our study. No relationship between repeat induced abortion and educational and socio-economic status was recorded.

However, several findings inconsistent with those of the current study have been documented, namely, a higher proportion of repeat aborters not using any contraception at the time of conception (Osler *et al*, 1997) and a significant relationship between repeat induced abortion and socio-economic status (Osler *et al*, 1992).

In conclusion, poor attitudes toward contraception, low use of modern contraceptives and failures of contraception were shown to be significantly associated with repeat induced abortion. Woman' s age, number of living children, contraceptive knowledge and experience and desire for no more children were positively related to repeat induced abortion. By contrast, socio-demographic characteristics were not related to the repeat induced abortion. The findings of this study suggest a need for improving attitudes toward the use of modern contraception and promoting contraceptive effectiveness in order to prevent repeat induced abortion. It is recommended that the family planning program should pay more attention to the contraceptive users to ensure that they can apply the method correctly in order to reach the goal of avoiding unintended pregnancy. However, this study was conducted at a hospital in the capital city so its results may not be representative of aborters in other settings. Further study on a larger scale including various groups of aborters will be necessary to better understand repeat aborters in Vietnam.

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Risk Factors for Postcesarean Surgical Site Infection

THACH SON TRAN, MD, PhD, SILOM JAMULITRAT, MD, VIRASAKDI CHONGSUVIVATWONG, MD, PhD, AND ALAN GEATER, PhD

Objective: To determine postcesarean complications and identify independent risk factors for surgical site infection.

Methods: We studied a cohort of 969 women delivered by cesarean between May and August 1997. Infections were determined by examinations during ward rounds, reviews of laboratory results, and follow-up for 30 days after discharge. Risk factors were identified by multiple logistic regression.

Results: Surgical complications were rare. There were febrile morbidity and infection complications in 16.2% and 12.4% of subjects, respectively. Eighty-five subjects had 95 surgical site infections (9.8%), and seven risk factors were independently associated with infection. Risk factors included preoperative remote infection (adjusted odd ratio [OR] 16.5, 95% confidence interval [CI] 2.1, 128.3); chorioamnionitis (OR 10.6, 95% CI 2.1, 54.2); maternal preoperative condition (OR 5.3 for those with severe systemic disease [American Society of Anesthesiologists score ≥3], 95% CI 1.2, 24.0); preeclampsia (OR 2.3, 95% CI 1.1, 4.9); higher body mass index (OR 2.0 for every five-unit increment, 95% CI 1.3, 3.0); nulliparity (OR 1.8, 95% CI 1.1, 3.2); and increased surgical blood loss (OR 1.3 for every 100-mL increment, 95% CI 1.1, 1.5).

Conclusion: Host susceptibility and existing infections were important predictors of surgical site infection after cesarean delivery. Further intervention should target this high-risk group to reduce the clinical effect of surgical site infection. (Obstet Gynecol 2000;95:367–71. © 2000 by The American College of Obstetricians and Gynecologists.)

Maternal morbidity related to infections after cesarean was eight-fold higher than after vaginal delivery.[1] Surgical site infection is defined operationally as infection involving the abdominal incision or the uterus.[2,3] Total cost in the United States, including indirect expenses related to this morbidity, could exceed $10 billion annually.[4]

Reported rates of postcesarean surgical site infection vary greatly, from 0.3% in Turkey,[5] 11.6% in Brazil,[6] to 18.3% in Saudi Arabia.[7] Despite numerous investigations, there is disagreement about risk factors of surgical site infection after cesarean delivery. Many factors affect infection rates in different settings. Confounding variables were not sufficiently controlled in many of those studies. Therefore, we conducted this prospective study to determine postoperative complications and to identify risk factors for surgical site infection after cesarean, by multivariate analysis. A better understanding of predictors might improve infection control by reducing clinical effects of postcesarean infections.

Materials and Methods

We prospectively studied a cohort of 969 women who had cesareans at Hungvuong Hospital in Ho Chi Minh City, Vietnam. It is a 450-bed, tertiary care obstetric and gynecologic hospital with an average of 1300 deliveries and 350 major operations per month. It serves the population of 2.5 million women in Ho Chi Minh City and is a referral center for 18 district hospitals and the obstetrics and gynecology departments of other hospitals in the city.

From May to August 1997, all women who had cesareans were recruited. The principal investigator visited each postoperative ward twice weekly and collected all pertinent data. Demographic information, putative factors, and surgical indications were recorded. Host-related variables included age, residence, parity, body mass index (BMI), preoperative stay, existing comorbidities, prior amniocentesis, labor induction, rupture of membrane duration, and preoperative condition. Surgery-related variables included emergency nature of the operation, cesarean hysterectomy, surgical

From the Hungvuong Obstetric and Gynecological Hospital, Ho Chi Minh City, Vietnam.

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luration, wound class, type of anesthesia, type of ibdominal incision, experience of surgeon, volume of lood loss, and timing of prophylactic antibiotics. The ariable "residence" was specified as urban or rural. lody mass index was calculated using postpartum veight and height, which were determined on postop- rative day 3 by research assistants. Preoperative stay vas the interval in days between hospital admission nd surgery. Existing comorbidities investigated were liabetes mellitus, remote infection, preeclampsia, ane- nia, and chorioamnionitis. Preoperative condition was ssessed by the American Society of Anesthesiologists reoperative assessment score.[8] A woman with mild ystemic disease was classified as class 2, whereas lasses 3 and 4 were associated with severe systemic lisease. We applied the modified wound classification o cope with difficulties in obstetric wound classifica- ion. Cesareans were classified class I if there was no upture of membranes or labor, class II if there was less han 2 hours of rupture of membranes without labor or abor of any length with no rupture of membranes, class II for rupture of membranes greater than 2 hours, and lass IV for purulent amniotic fluid.[9] Rupture of mem- ranes duration was the interval, in hours, between ecorded timing of rupture of membranes and surgical ncision. An emergency cesarean delivery was defined s an operation for compelling reasons that had not een planned, and an elective cesarean was defined as n operation planned and done when scheduled or ooner if labor accelerated the delivery time.[10] We lassified surgeon experience into three levels, supervi- or, attending physician, and resident. Volume of blood oss was calculated by subtracting total irrigation fluid sed and amount of amniotic fluid from the total olume of fluid in the suction container at the end of urgery, then adding the amount of blood on sponges, letermined by weight. The true volume of blood loss vas recorded after subtracting the volume of possible lood replacement. Timing of antibiotic prophylaxis vas classified as early (2–24 hours before surgical ncision), preoperative (0–2 hours before incision), peri- perative (within 3 hours after incision), or postopera- ive (more than 3 hours after the incision).

Postoperatively women were monitored for signs of nfection. Temperature was measured orally every 4, 6, nd 12 hours for the first, second, and following post- perative days, respectively. In women who had fever temperature 38.0C or greater) the temperature was aken every 4 hours until it was less than 37.5C on two consecutive measurements. Leukocyte count was done routinely when a woman's temperature was over 38.5C. Further tests such as urine analysis, urine culture, and chest x-ray or wound culture were not done routinely unless infection was suspected. Surgical sites were re-examined by research assistants when women returned to the outpatient clinic as scheduled after discharge.

Surgical complications included intraoperative hemorrhage necessitating transfusion, postoperative hemorrhage, and injury to adjacent organs. Any bleeding event requiring postoperative intervention was called postoperative hemorrhage complication. The standard criterion of postoperative febrile morbidity was an oral temperature of at least 38.0C on any two of the first 10 days postpartum, excluding the first 24 hours.[11] Postoperative infections were diagnosed by using the Centers for Disease Control and Prevention (CDC) definitions.[2,3] Surgical site infection included superficial, deep, and space-organ infection. Endometritis and vaginal cuff infections constituted organ surgical site infections.[3] Surgical site infection was operationally identified by purulent discharge, positive culture, deliberate reopening of surgical wounds, evidence of abscess, or diagnosis by the attending physician.[3]

Data management and analysis were done with the statistical software Epi Info version 6.04b (CDC, Atlanta, GA) and STATA version 5.0 (StataCorp, College Station, TX). χ^2, Fisher exact test, and Student t test or Mann-Whitney test were used for discrete and continuous variables, when appropriate. Multiple logistic regression analysis was done to obtain adjusted estimates of odds ratios (ORs) and to identify independent risk factors. Variables that were likely to be associated with outcome ($P \leq .2$ in univariate analysis) or considered potential confounders were included in the multiple logistic regression model. $P < .05$ was considered statistically significant.

Results

During the 4-month study, there were 969 cesareans among 5181 deliveries, a rate of 18.7%. There were five obstetric hysterectomies, two of which were selectively indicated for different extents of placenta increta. More than four fifths of the women were free from comorbidity (Table 1). Ovarian carcinoma was confirmed histologically in one cesarean with oophorectomy; radical hysterectomy was done 1 month later. Although 19.4% of subjects had repeat cesareans, only 15.4% had previous operation as the only indication for the current cesarean (Table 2). Placenta previa, rather than previous cesarean, was recorded as the indication if this placental abnormality resulted in the current operation. External fetal heart rate monitoring was used for fetal assessment.

The rate of surgical complications was low. Estimated volume of blood loss over 1 L occurred in 15 cases, 12 associated with abnormal implantation of placenta.

Table 1. Demographic Characteristics and Comorbidities

Characteristic	% (*n* = 969)
Age (y) (mean ± standard deviation)	29.7 ± 5.7
Nulliparous	44.7
Body mass index (mean ± standard deviation)	22.6 ± 2.9
Residence (% rural)	31.4
Repeated cesarean (%)	19.4
Patients with comorbidities (%)*	
None	85.2
Preeclampsia	6.0
Hypertension	3.5
Preoperative fever	2.3
Chorioamnionitis	0.8
Anemia	0.6
Diabetes mellitus	0.6
Preoperative infection	0.5
Heart diseases	0.3
Others†	0.4

* Total might exceed 100% because a patient could have had more than one disease.
† One ovarian carcinoma, two asthma, and one hyperthyroidism.

Blood replacement was indicated for 27 cases (2.8%). There was only one postoperative hemorrhage, diagnosed 4 hours after surgery. Partial bladder injury occurred in two cases of repeat cesarean; one was complicated by placenta increta.

There were 157 women (16.2%) with febrile morbidity and 95 (9.8%) with surgical site infections, 19 with urinary tract infections, two with pneumonia, and three cases of gastroenteritis. Superficial and organ-space surgical site infection accounted for 52.9% and 24.4% of all postoperative infections, respectively. Infection of deep soft tissues was diagnosed in three cesareans. One vaginal cuff infection was identified after a cesarean hysterectomy. Ten infected wounds were documented after discharge.

We identified ten factors that were associated with surgical site infections by univariate analysis ($P < .05$), including nulliparity, BMI, preeclampsia, remote infection, chorioamnionitis, preoperative hospitalization, rupture of membranes–operation interval, American Society of Anesthesiologists score, cesarean hysterectomy, and volume of blood loss. Other variables likely related to outcomes ($P < .20$) were residence, experience of surgeon, kinds of abdominal incisions, wound contamination level, and surgical duration. Labor induction ($P = .96$) and indication for dystocia ($P = .32$) were not likely to be associated with postcesarean infection. All cesarean deliveries received parenteral antibiotics for prophylaxis, and timing of administration appeared not to be closely associated with subsequent infections ($P = .28$). Those variables were included in the initial multiple logistic regression model. Multiple logistic regression found seven predictors independently associated with postcesarean surgical site infection (Table 3). Host susceptibility had an essential effect on prediction of that complication.

Table 2. Indications for Cesarean

Surgical indication	%
Dystocia	35.2
Repeat cesarean*	15.4
Breech and malpresentation	13.8
Cephalopelvic disproportion	13.3
Fetal condition†	9.8
Umbilical cord compression	4.5
Placenta previa	4.9
Placental abruption	1.4
Placenta increta	0.2
Others‡	1.5

* Indicated because of previous operation.
† Included acute fetal heart rate abnormality and fetal growth restriction.
‡ Included maternal diseases, failed forceps trial, failed labor induction, twin pregnancy, and malformation of reproductive tract.

Discussion

The short duration and CDC definitions of the present study allowed uniformity in diagnoses of various sources of postcesarean infections, highlighting the importance of complications and risk factors for surgical site infection. Surgical complications were rare in the present study. Our blood transfusion rate was within the limits of other reports, which varied from 1.2%[12] to 6.3%.[13] Incidence of reoperation because of intra-abdominal hemorrhage in the study by Nielsen and Hokegard[14] (0.3%) was triple that in ours. The likelihood of bladder injury in our data was identical to findings of Nielsen and Hokegard[12] and Eisenkop et al.[15] There was no ureter injury in our study, whereas Eisenkop et al reported a rate of 0.09%.[15]

Our postcesarean infection rate compared favorably with those of other settings. Febrile morbidity was reported from 15.3%[16] to 23.3%[13] of abdominal deliveries. The overall rate of postoperative infection in the present study was 12.4%, which is consistent with the rate of 13.9% reported in a prospective study of 1319 cesareans in Denmark.[14] Our rate of surgical site infection, contributing four fifths of all postoperative infections, was within the range reported by others who also used CDC definitions.[5–7,17] Neither the rate of Yalcin et al[5] nor Eltahawy et al[7] was determined from a large-scale study, so it might be distorted. Rates comparable to ours were reported from Canada (8.8%[17] and 9.6%[13]) and Brazil (11.6%).[6]

Multiple logistic regression showed seven variables independently associated with postcesarean surgical site infection. Preoperative remote infection and chorioamnionitis, although they occurred in only a few of our

Table 3. Multiple Logistic Regression Analysis and Independent Risk Factors for Surgical Site Infection After Cesarean Delivery

Variables	Coefficient	OR	95% CI	P
Constant	−7.5			
Preoperative remote infection	2.8	16.5	2.1, 128.3	.007
Chorioamnionitis	2.2	10.6	2.1, 54.2	.004
American Society of Anesthesiologists score ≥3	1.7	5.3	1.1, 24.0	.029
Preeclampsia	0.8	2.3	1.1, 4.9	.037
Body mass index (every five-unit increment)	0.7	2.0	1.3, 3.0	.001
Nulliparity	0.6	1.8	1.1, 3.2	.03
Blood loss (every 100-mL increment)	0.2	1.3	1.1, 1.5	.005

OR = odds ratio; CI = confidence interval.

subjects, appeared strongly to predispose women to postcesarean surgical site infection. Remote infection not only compromises the immune status of the patient but can increase the innoculum of microorganisms contaminating the surgical site. A remote infection indicates heavy abnormal bacterial colonization that can readily contaminate the surgical site. Garibaldi et al[18] found that distant infections independently carried risks 2.8 times higher. Intrauterine,[10] pathologic,[19] and clinical intra-amniotic infections[20,21] were found to be risk factors for subsequent endometritis. Prompt and aggressive antibiotic therapy should be started as soon as suspected infection is confirmed, to reduce subsequent postoperative infections.[10]

The American Society of Anesthesiologists physical status classification is a standardized, reproducible numeric determination that is used routinely to stratify severity of illness for surgical patients and is known to be a good indicator of host susceptibility to infection.[5,18] A concept of antepartum risk factors, a complex proxy of host susceptibility, was proved closely correlated with postcesarean endometritis,[1] but the association was not examined by multivariate analysis. Our data supported the finding of Garibaldi et al[18] that the association between preoperative health status and postoperative wound infection remained valid even after multivariate modeling analysis. Severe systemic disease (American Society of Anesthesiologists class of 3 or more) can increase risk of infection by five times.

Preeclampsia increases risk of postcesarean infection by a factor of two. Asymptomatic bacteriuria was documented more frequently among preeclamptic women (19%) compared with controls (4.5%) ($P < .005$).[22] That remote infection was not intentionally identified or included in analysis, so its contribution to the risk of postoperative infection could not be specified, but it could partially explain the association between preeclampsia and surgical site infection after cesarean.

Obesity as a risk of postcesarean wound infection has been known for years.[9,14,23,24] Unlike general patients, it is usually difficult to measure precisely the weight of obstetric patients. Neither prepregnancy[24] nor delivery data[14] reflect the current condition of postpartum subjects. Patients' weight measured at postoperative day 3 would be a better indicator because it was not yet substantially affected by diuresis.[25] We attempted to identify the association between increments of BMI, rather than an arbitrarily dichotomous variable of obesity, and postcesarean infection. The risk of infection doubled for every five-unit increment of BMI. That risk could be due to the relative avascularity of adipose tissue or technical difficulties of handling adipose tissue that can result in more traumas to the abdominal wall or difficulties to obliterate dead space in the fat abdominal wall.

Regardless of other risk factors, we found nulliparity and high volume of blood loss as determinants of postcesarean surgical site infection. Nulliparity was reported to be independently associated with increased risk of postcesarean endometritis.[26] The precise mechanism by which nulliparity increases the risk of infection is not fully understood. The present data showed the risk of surgical site infection reduced by 39% and 60% when women had one or more children, respectively. Likewise, risk of postoperative infection has been shown to be proportional to volume of blood loss during cesarean.[1,10] Risk of surgical site infection increased 30% for every 100-mL increment of blood loss. Precise measurement of blood loss during cesarean is almost impossible because of difficulties quantifying amniotic fluid. Blood loss volume was recorded without knowledge of outcome, so potential measurement bias would be minimal in our study. The association between each 100-mL increment of blood loss, instead of its precise volume, and postcesarean infection was examined, increasing the accuracy of the analysis. A high volume of blood loss is usually associated with poor control of bleeding, increased tissue damage from prolonged retraction and manipulation, and more sutures. Suture, a foreign body, can promote contamination and reduce local resistance mechanisms.

We could not confirm some variables that had been predictors of postcesarean wound infection, namely duration of rupture of membranes,[1,9,14,23,24] and surgical duration.[10,20,26] Confounding effects were controlled sufficiently by multiple logistic regression in only two studies.[20,23] Prolonged rupture of membranes increased the likelihood of an infection ascending from vagina into uterine cavity. However, chorioamnionitis was closely related to prolonged rupture of membranes ($P < .001$). In a multivariate model this strong predictor would have masked the hypothesized association between prolonged rupture of membranes and postcesarean infection.

Although the cesareans that lasted longer than 1 hour had 2.4 times the risk of postoperative infection, by univariate analysis, a larger sample is needed to confirm its independent predictive role. Assuming an α of .05, power of .80, and assumed infection rate in controls of 8.5%, at least 264 subjects would be needed for each study arm.

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Address reprint requests to:
Thach Son Tran, MD, PhD
Postoperative Department
Hungvuong Obstetric and Gynecological Hospital
128 Hungvuong Street, District 05
Ho Chi Minh City
Vietnam
E-mail: transon_thach@hotmail.com

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Biotypes of oral *Candida albicans* isolated from AIDS patients and HIV-free subjects in Thailand

R. Teanpaisan[1]
W. Nittayananta[2]
V. Chongsuvivatwong[2]

[1]Department of Stomatology, Faculty of Dentistry and
[2]Epidemiology Unit, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla, Thailand

Abstract: This study was conducted to examine biotypes and antifungal susceptibility patterns of oral *Candida albicans* isolated from HIV-infected patients, HIV-free patients with candidiasis and healthy subjects. All isolates were biotyped using a typing system based on enzyme profiles, carbohydrate assimilation patterns and boric acid resistance. Thirty-eight biotypes were found amongst 218 oral *C. albicans* isolates. The major biotype found was A1S, which accounted for 32.6% of all isolates, and this biotype was the most common in all groups. There was a greater variety of biotypes of *C. albicans* in the HIV-infected group than in the other groups; however, there was no statistically significant difference between the groups. The minimum inhibitory concentrations (MICs) of a total of 118 isolates were determined for amphotericin B and for ketoconazole using the National Committee for Clinical Laboratory Standards (NCCLS) broth macrodilution method and the E-test. When the antifungal susceptibility patterns among the groups were compared, a statistically significant difference was found only with amphotericin B. The median MIC of amphotericin B in the HIV-infected group was higher than in the healthy group ($P=0.013$, NCCLS method; $P=0.002$, E-test). However, this difference in sensitivity was not restricted to any sub-type investigated. Our results showed that the biotype patterns of *C. albicans* isolates that colonize HIV-infected patients are similar to those of HIV-free subjects, and there is no relationship between antifungal susceptibility patterns and the biotypes.

Key words: biotypes; *Candida albicans*; HIV infection; Thailand

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A number of reports have revealed that the frequency of isolation of *Candida* and clinical signs of oral candidiasis increase with advancing HIV infection (1–4). Although *C. albicans* is the most common of the *Candida* species isolated in these studies, relatively few details of the pathogenic features of this organism and AIDS-associated oral candidiasis are known. In healthy humans, *C. albicans* is present as part of the normal flora of the oral cavity and gastrointestinal tract; however, in immunosuppressed patients it can cause severe mucosal or invasive disease (5). The high incidence of mu-

Correspondence to:
R. Teanpaisan
Department of Stomatology, Faculty of Dentistry, Prince of Songkla University, Hat Yai, P.O. Box 17 Khor Hong, Songkhla 90112, Thailand

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oral candidiasis in patients with AIDS may be due to infection with the same strains that are non-pathogenic in healthy subjects but that become pathogenic in AIDS patients due to impaired host defence mechanisms. Alternatively, it may be due to infection with unique or more virulent strains. In addition, the significance of oral candidiasis as a disease entity in HIV-related immunosuppression is its frequent recurrence (6, 7). The mechanism behind the ability of this fungus to cause recurrent disease is unknown. It is postulated that one factor that may influence this is a decrease in susceptibility to antifungal agents (7, 8), and this may be related to certain types of *C. albicans* (9). Because of this, many attempts have been made to search for particularly virulent types of *C. albicans* using a number of techniques, such as serotyping (10), biotyping (11), morphotyping (12, 13) and genotyping (14, 15). On account of the difficulties with some of these techniques, a standardised, simple and highly specific biotyping system developed by Williamson et al. (11), which is technically undemanding and utilises relatively inexpensive commercially available quality controlled media, has been increasingly used in recent years (16–19).

In a previous paper (4) we showed that there is an association between candidal load and HIV infection. The aims of the present study were to determine whether any sub-strains of *C. albicans* isolated from HIV patients, HIV-free subjects with candidiasis and healthy subjects are particularly associated with health or disease using the biotyping method of Williamson et al. (11), and to compare isolates for their susceptibility to two commonly used antifungal agents (amphotericin B and ketoconazole).

Material and methods

Sources of *C. albicans*

A total of 218 isolates of *C. albicans* were included in this study, which comprised 82 isolates from salivary samples of 15 HIV-infected patients, 76 isolates from 15 HIV-free patients with oral candidiasis and 60 isolates from 16 healthy subjects. The specimen collection and methods used for fungal cultivation and identification have been described previously (4). Briefly, an oral rinse specimen was obtained from each subject using 10 ml sterile phosphate buffered saline according to the method of Samaranayake et al. (20). Colonies showing yeast-like morphology within the 48–72 h incubation period were selected for study. All colonies showing variation in morphology, as well as identical colonies, were selected from the same isolation plate. The number of colonies chosen depended on the density of growth recovered on the primary culture plate. For example, usually 10–20 colonies from 20–40 colonies on the same plate were selected for identification and biotyping, but when recovery was lower (e.g., from healthy subjects) fewer colonies could be sampled. All isolates were identified by using production of chlamydospores, production of germ tubes and carbohydrate assimilation with API 20 C AUX (Bio Merieux, France).

Biotyping of *C. albicans* isolates

All isolates of *C. albicans* were biotyped using the method of Williamson et al. (11), which employs two commercially available kits, [API ZYM and API 20 C AUX (Bio Merieux)], and a boric acid resistance test. In brief, the API ZYM system evaluates the enzyme activity of the isolates by means of a set of 19 enzyme substrates contained in a tray of miniaturised plastic cupules. After inoculation of a standard suspension of the organism and incubation for 4 h at 37°C, the colour reactions in each cupule were read according to the manufacturer's instructions. The API 20 C AUX system utilises the ability of *C. albicans* isolates to assimilate 19 different carbohydrates as sole sources of carbon. The results were determined by comparison of the opacity in the test and control cupules. Finally, the boric acid resistance test assesses the sensitivity of the isolates to 1.8 mg/ml of boric acid incorporated into an agar medium.

Antifungal susceptibility testing

A total of 118 isolates of *C. albicans* were chosen to represent strains with either different or the same colony morphology and biotype. These included 52 isolates from the HIV-infected group, 33 isolates from the HIV-free candidiasis group and 33 isolates from the healthy group. For each isolate, minimal inhibitory concentrations (MICs) for amphotericin B and ketoconazole were determined using the NCCLS macrodilution method (21) and the E-test strip (AB Biodisk, Sweden).

The NCCLS broth dilution method was performed according to NCCLS document M27-P (21). A working suspension of the inoculum was made by a 1:100 dilution of the 0.5 McFarland standard yeast suspension in 0.85% saline followed by a 1:20 dilution in RPMI broth. Two-fold dilutions of the antifungal agents from 64 to 0.015 μg/ml were prepared and inoculated with the working suspension. The tubes were incubated at 37°C for 48 h. The MIC was read as the concentration that inhibited growth (amphotericin B) or produced an 80% reduction of turbidity in comparison with a drug-free control (ketoconazole). For the E-test, colonies of each yeast were suspended in saline to produce a turbidity equivalent to a 0.5 McFarland standard. The inoculum was swabbed on to Sabouraud's dextrose agar and allowed to dry for 10–15 min before each of the antifungal E-test strips was applied. Plates were read at 24 h and

Table 1. Biotype profiles of oral *Candida albicans* isolated from HIV infected patients, HIV-free patients with candidiasis and healthy subjects

Biotypes	HIV-infected group No. (%)	HIV-free with candidiasis No. (%)	Healthy subjects No. (%)	Total
A1R	3 (3.6)	0	1 (1.7)	4 (1.8)
A1S	26 (31.7)	25 (32.8)	20 (33.3)	71 (32.6)
A4R	1 (1.2)	0	1 (1.7)	2 (0.9)
A4S	6 (7.3)	6 (7.8)	5 (8.3)	17 (7.8)
A65*	0	0	1 (1.7)	1 (0.5)
A7S*	1 (1.2)	0	0	1 (0.5)
A8S	4 (4.9)	2 (2.6)	0	6 (2.6)
A14R	1 (1.2)	0	0	1 (0.5)
A17S	0	1 (1.3)	1 (1.7)	2 (0.9)
A18S	0	2 (2.6)	3 (5.0)	5 (2.3)
A19S*	1 (1.2)	0	0	1 (0.5)
A20S*	1 (1.2)	0	0	1 (0.5)
A23S*	0	1 (1.3)	1 (1.7)	2 (0.9)
A24S*	0	0	1 (1.7)	1 (0.5)
B1R	0	6 (7.9)	5 (8.3)	11 (5.0)
B1S	4 (4.9)	6 (7.9)	7 (11.7)	17 (7.8)
B2S*	0	0	1 (1.7)	1 (0.5)
B4R*	1 (1.2)	2 (2.6)	0	3 (1.4)
B4S*	13 (15.9)	12 (15.8)	7 (11.7)	32 (14.7)
B6S*	2 (2.4)	1 (1.3)	0	3 (1.4)
B15S*	0	0	1 (1.7)	1 (0.5)
B16S*	0	0	1 (1.7)	1 (0.5)
B16R*	0	2 (2.6)	0	2 (0.9)
B15S*	1 (1.2)	0	0	1 (0.5)
B19S*	1 (1.2)	0	0	1 (0.5)
B20S*	2 (2.4)	0	0	2 (0.9)
B21S*	1 (1.2)	1 (1.3)	0	2 (0.9)
B22S*	1 (1.2)	0	0	1 (0.5)
B24S*	1 (1.2)	0	0	1 (0.5)
C1S	1 (1.2)	2 (2.6)	0	3 (1.4)
D1R	1 (1.2)	1 (1.3)	0	2 (0.9)
D1S	6 (7.3)	2 (2.6)	0	8 (3.7)
D6S*	0	2 (2.6)	1 (1.7)	3 (1.4)
D8S	3 (3.6)	0	0	3 (1.6)
D24S*	0	0	1 (1.7)	1 (0.5)
F1R	0	0	1 (1.7)	1 (0.5)
F4S*	0	0	1 (1.7)	1 (0.5)
H4S*	0	2 (2.6)	0	2 (0.9)
Total	82 (100)	76 (100)	60 (100)	218 (100)
*New biotypes	26 (31.7)	23 (30.3)	16 (26.7)	65 (29.8)

48 h according to the E-test technical guide for antifungal susceptibility testing.

Results

The biotyping system employed in this study utilized three tests: the API ZYM test (the first letter of the code), the API 20 C system (the middle digit of the code), and resistance or sensitivity to boric acid, denoted as either R or S (the last letter of the code). The reproducibility of the results obtained by these methods has not been tested on a broad scale, but some isolates chosen at random were tested on multiple occasions and have shown clearly reproducible results. A total of 38 biotypes was found among the 218 oral *C. albicans* isolates (Table 1). The major biotype, A1S, accounted for 32.6% of the isolates, and this biotype was commonly found in HIV-infected patients, HIV-free candidiasis subjects and healthy subjects (31.7%, 32.8%, and 33.3%, respectively). The second most common biotype was B4S, which represented 14.7% of total isolates. The other biotypes found were A4S, B1S and B1R (7.8%, 7.8% and 5.0%, respectively). When the number of different biotypes in each of the HIV-infected patients, HIV-free with candidiasis and healthy subjects was compared, the first group had a higher number of biotypes than the others (Fig. 1); however, this difference was not statistically significant (Kruskal-Wallis test).

A total of 118 strains of *C. albicans* obtained from HIV-infected patients, HIV-free candidiasis subjects and healthy subjects were compared for their MICs against amphotericin B and ketoconazole using the NCCLS macrodilution method and the E-test, and the results are shown in Table 2. Generally, results obtained by the NCCLS broth method were largely in agreement with those obtained by the E-test. Pearson correlation coefficients of both methods for amphotericin B and ketoconazole were 0.89 and 0.57, respectively. The median MIC for amphotericin B in isolates from the HIV-infected group was statistically significantly higher than that of isolates from the healthy subjects ($P=0.013$, NCCLS method; $P=0.002$, E-test). Also, there were statistically significant differences in the mean MIC for amphotericin B between the HIV-infected group and the HIV-free subjects with candidiasis ($P=0.01$, NCCLS method) and between the HIV-free candidiasis group and the healthy group ($P<0.03$, E-test). When the patients' history of antifungal therapy was taken into account, it showed that there was no significant difference between the MIC and whether or not a patient had taken amphotericin B previously. The mean MICs of ketoconazole among

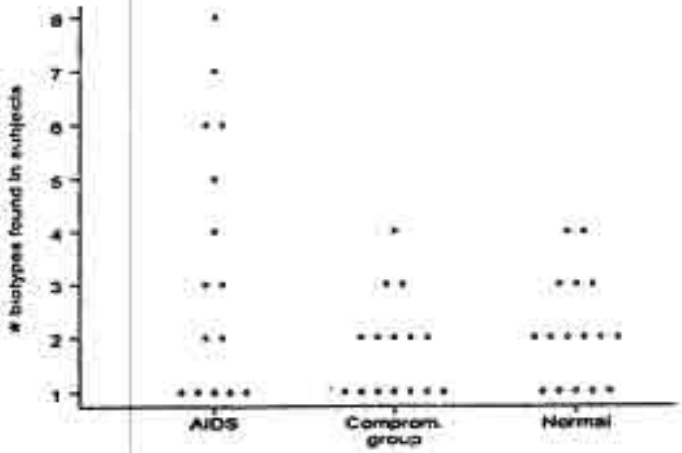

Fig. 1. Number of biotypes identified in the AIDS group, HIV-free patients with candidiasis (compom.) group and normal subjects.

Table 2. Median of MICs (μg/ml) of amphotericin B and ketoconazole

Group	Amphotericin B				Ketoconazole	
	NCCLS	*P*-value	E-test	*P*-value	NCCLS	E-test
HIV-infection:	0.500 (0.062–4.0)	0.013*	0.315 (0.032–>32)	0.002*	0.062 (0.015–16.0)	0.094 (0.012–>32)
Taking antifungals	0.500 (0.250–1.0)		0.380 (0.032–>32)		0.062 (0.031–1.0)	0.094 (0.012–>32)
No antifungals	0.500 (0.125–0.500)		0.250 (0.190–0.500)		0.062 (0.015–4.0)	0.125 (0.032–0.500)
HIV-free candidiasis:	0.250 (0.562–1.0)	0.01[a]	0.250 (0.038–0.500)	0.49*	0.062 (0.015–8.0)	0.094 (0.032–>32)
Taking antifungals	0.310 (0.125–0.500)	"	0.380 (0.125–0.500)		0.062 (0.062–0.125)	0.079 (0.032–0.094)
No antifungals	0.250 (0.062–1.0)		0.250 (0.038–0.500)		0.062 (0.015–8.0)	0.125 (0.032–>32)
Healthy subjects	0.250 (0.031–1.0)	0.96*	0.190 (0.032–0.500)	0.03*	0.062 (0.015–8.0)	0.064 (0.047–>32)

* Median MICs of HIV group vs healthy subjects.
[a] Median MICs of HIV group vs HIV-free candidiasis group.
* Median MICs of HIV-free candidiasis patients vs healthy subjects.

isolates from the three groups showed no significant differences using either the NCCLS method or the E-test.

Discussion

Among the numerous AIDS-associated oral diseases, oral candidiasis is the most frequent, with up to 90% of HIV-infected patients being affected (22, 23). The clinical syndrome is not life-threatening but it is painful and its recurrent nature makes it of importance. Oral candidiasis is caused mainly by *C. albicans* but its pathogenesis is still unclear. The condition of the patient is probably the major factor governing the development of clinical candidiasis and this is often associated with immunodeficiencies (24). However, as recently shown for many other microbial pathogens, the possibility that certain strains or groups of strains are more likely to be involved in clinical disorders cannot be excluded (25). Whether or not HIV patients are colonized with selected strains of *C. albicans* has been a matter of debate. Using DNA fingerprinting, the results of two studies showed that no particular strain was associated with HIV-infected patients and that *C. albicans* populations from the oral cavities of HIV-infected and HIV-negative people have a similarly disparate clonal origin (26, 27). Some researchers have used a DNA probe to track the *C. albicans* isolates from oral lesions in HIV-seropositive individuals, and their data suggest that each patient carries a unique strain of *C. albicans*. Furthermore, it was shown that the strains present during both symptomatic and asymptomatic states of candidiasis were the same (28, 29). However, others have produced evidence that there is increased genetic variation of *C. albicans* isolates in HIV-infection compared to controls (30, 31). These differences were noted when the appropriate molecular technique coupled with appropriate analyses were used (31). Also, Sweet et al. (32, 33) showed that more biotypes of *C. albicans* were present in HIV/AIDS groups than in control subjects, and that almost all *Candida* species isolated from HIV subjects adhered to buccal epithelial cells in higher numbers than did those strains isolated from controls.

Here, we have used the biotyping method of Williamson et al. (11) to evaluate the biotypes of isolates from a range of patient groups. It is known that genetic typing methods provide more sensitive and specific means to discriminate among isolates. However, biotyping has the advantages of being simple to perform, technically undemanding and inexpensive compared to molecular techniques. In addition, it also has the advantage of allowing more meaningful comparison of the present studies with those of previous studies of a similar nature. The first study of *C. albicans* biotypes in HIV-infected patients was conducted by Korting et al. (34) and employed the API 20 C (carbohydrate assimilation) system. Their results showed that from a total of 61 oral *C. albicans* strains isolated from HIV-infected individuals, with or without signs of candidiasis, the majority (64%) of isolates belonged to group 1. However, there was no detail given of the incidence and proportions of each of the biotypes between the groups with and without signs of clinical candidiasis, and no HIV-negative subjects were included in the study. Since the API 20 C carbohydrate assimilation system has a relatively poor discriminatory power, API ZYM and boric acid sensitivity tests were added to complement the API 20 C profiles (11). Results from previous studies of others (16–19) have demonstrated that this system serves to further differentiate the biotypes into smaller sub-groups. Using this biotyping system, Tsang et al. (17) showed that there are many different sub-strains of oral *C. albicans* in HIV-infected patients. However, no data on healthy subjects were provided. Our present results showed that there were 38 biotypes among 216 strains. When the results were compared among the groups, HIV-infected patients had more sub-types (1–8) than HIV-free candidiasis patients (1–4) or healthy subjects (1–4), and there were no

significant differences in the biotypes between the three groups. The results of statistical analysis suggested that this is maybe affected by the small sample size in this study. Thus, larger numbers of patients will need to be studied for further confirmation.

With regard to the geographic distribution of the different biotypes, it has been shown that some biotypes are globally prevalent. However, almost one-third of the biotypes reported here have not been previously described and may reflect geographical exclusivity. Tsang et al. (17) has reported that A1R (18%) and A1S (11%) are the most common biotypes among the oral *C. albicans* isolates derived from HIV-infected patients in Hong-Kong, Australia, England and Germany. Another previous study in healthy individuals in Britain found that A1R and A1S were also the commonest biotypes, accounting for 23% and 26% of the total isolates, respectively (11). The biotypes A1S and J1S have been found to predominate in China (18) and in Tanzania (19). Our results concur with the findings in China and Tanzania that the most common biotype is A1S, accounting for 32.6% in all groups investigated. It is noted that in previous studies (17–19), only a single representative isolate was selected from each culture plate, whereas multiple colonies from each plate were collected in the present study. It is assumed that the colonies examined represent the predominant strains present on the plate. No clear explanation for the widespread over-representation of such biotypes has been given. It may be hypothesized that they are better adapted than other sub-types to life on or in the human body. They may also be more easily transmitted between humans than are other sub-types. When compared with previous data of new biotypes from the foregoing countries, our results showed that almost one-third (65 of 218) of isolates were previously undescribed new biotypes. As the previous reports were from Scotland (11), Germany, Australia, England and Hong-Kong (17), China (18) and Tanzania (19), it is likely that there are geographical variations in *C. albicans* biotypes.

Up to now, there has been no general agreement about a standardized method of *in vitro* antifungal susceptibility testing, since results have shown great inter- and intra-laboratory variations. The NCCLS has established a broth macrodilution method as a reference method for antifungal susceptibility testing; however, it is labour-intensive and time-consuming. We are in agreement with the previous studies that the E-test appears to be equivalent to the NCCLS reference macrobroth method for testing susceptibility of *Candida* species to azole antifungal agents (35, 36). Wanger et al. (37) has concluded that the E-test is comparable to the NCCLS method for testing of susceptibility to amphotericin B and fluconazole; in addition, the E-test appears to be superior for the detection of resistance to amphotericin B. Our results have shown that the NCCLS reference macrodilution method and the E-test gave very similar results for amphotericin B and showed moderate agreement for ketoconazole. Generally, the endpoints obtained were identical or different by no more than two two-fold dilutions. However, when the MIC level is high, the results of both methods show a greater difference; if the MICs given by the NCCLS method are more than 1–4 μg/ml, they would be >32 μg/ml by the E-test. This may be due to the problem of diffusion of the agent through the agar medium necessary for the E-test. In the present study, we have shown that susceptibility of our isolates to amphotericin B was significantly different between the patient groups but that there was no difference in sensitivity to ketoconazole. It was found that isolates from the AIDS group were more resistant to amphotericin B than were isolates from the HIV-free candidiasis group and the healthy group. This resistance is not associated with a history of amphotericin B therapy or restricted to any sub-type investigated (data not shown). Gallagher et al. (38) have shown that phenotypically switched variants of *C. albicans* can develop decreased azole susceptibility even though these strains remained genetically identical. The results of McCullough et al. (39) showed that the same *C. albicans* genotypes tended to persist during the course of disease progression, but that the colonial morphologies of the isolates changed. Also, Soll et al. (40) found that despite a high frequency of phenotypic switching by *C. albicans*, nucleic acid hybridization of DNA from multiple phenotypes from a single culture site consistently yielded identical genotypes. These observations have shown that it is not necessary to have alterations in the type of strain present for there to be changes in the drug susceptibility of *C. albicans*. This may explain our finding of increased resistance to amphotericin B among *C. albicans* strains isolated from HIV-infected patients but no difference in biotypes. However, further work on genetic analysis is required to clarify this.

To conclude, it is worth emphasizing here that the present data are the first base-line information for studies of oral candidal infection in different cohorts (AIDS patients, HIV-free healthy subjects and HIV-free patients with candidiasis) of the Thai population. Our results show that the biotype patterns of *C. albicans* that colonize AIDS patients are similar to those in normal Thai subjects. This suggests that there may be no particular biotypes of *C. albicans* linked with specific clinical characteristics. Similarly, the oral *C. albicans* isolates showing *in vitro* susceptibility to amphotericin B and ketoconazole were not restricted to any sub-group investigated. However, the concept of phenotypic switching of *C. albicans* among HIV-infected patients could not be excluded, and the resistance of these isolates to amphotericin B needs further explanation.

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COMMUNITY-BASED SELF-REPORTED SYMPTOMS OF ANTEPARTUM MORBIDITIES; THE HEALTH BURDEN AND CARE-SEEKING PATTERNS OF RURAL BANGLADESHI WOMEN

Mahbub-E-Elahi Khan Chowdhury[1], Halida Hanum Akhter[1] and Virasakdi Chongsuvivatwong[2]

[1]Bangladesh Institute of Research for Promotion of Essential and Reproductive Health and Technologies (BIRPERHT); [2]Epidemiology Unit, Faculty of Medicine, Prince of Songkla University (PSU), Hat Yai, Thailand

Abstract. In Bangladesh there is a dearth on information relating to complications during pregnancy. We followed up 1,019 pregnant women in rural Bangladesh sampled from all the 4 old administrative divisions of the country. Trained female interviewers visited households of the pregnant women at four-week intervals and interviewed them for their current pregnancy-related complications. Out of a total of 3,812 antepartum visits the percentage of reported symptoms of bleeding, fits and convulsions, excessive vomiting, fever >3 days, urinary problems, palpitations and symptomatic anemia were 0.3, 0.7, 1.4, 4.0, 26.8, 46.5 and 78.3 respectively. Morbidities were considered to cause a health burden if they imposed constraints in daily activities of the pregnant women and they were weighted according to intensity of the constraint. For each morbidity, the mean intensity of burden per episode and the population burden per 1,000 person months of observation of all the women were calculated. For common sustaining morbidities like symptomatic anemia and urinary problems the population burden was much heavier than that for more serious but rare morbidities like bleeding and convulsions. Among the visits in which the women had any symptoms, the percentages of care-seeking for less frequently reported morbidities such as fits and convulsions, bleeding, fever >3 days, excessive vomiting were about 74, 50, 34 and 33% respectively, whereas those for more commonly reported complications such as urinary problems, symptomatic anemia and palpitations were less than 20%. Care for these morbidities was mostly sought from untrained providers.

INTRODUCTION

More than half a million women die every year due to pregnancy complications or childbirth and about 99% of these deaths occur in the developing countries (WHO, 1991). Women in the developing countries bear about 200 times greater risk of dying from pregnancy related complications than those in the developed world (Mahler, 1987). Behind the death of each woman resulting from pregnancy complications there are many more women who suffer from serious, even long-term non-fatal pregnancy complications and in many situations without taking any appropriate measures for them. The earliest study (Datta *et al*, 1980), conducted on maternal morbidity in rural India, reported that for every maternal death 16.5 complications taking place related to pregnancy or puerperium. Based on this estimate Walsh *et al* (1989) estimated about 8 million pregnancy complications occur every year in the world. In 1993 Koblinsky *et al*, after evaluating several population-based studies in developing countries, assessed 40% of the pregnancies as complicated which revealed a several fold higher estimated total number of maternal morbidities than the earlier estimate, arising every year globally.

In Bangladesh since 1967-1968 several well designed maternal mortality studies (Chen *et al*, 1974; Khan *et al*, 1986; Alauddin, 1986; Koenig *et al*, 1988) have suggested that there has been a decline in maternal mortality in Bangladesh from 7.7 in 1967-1968 to 5.5 in 1976-1985 per 1,000 live births. In 1996 the maternal mortality ratio was estimated as 4.3 per 1,000 live births in Bangladesh (Islam and Hossain, 1997) which is still among the highest in the world. The severity of the problem of maternal morbidity in Bangladesh is also well conceived from these high maternal mortality ratios.

In 1992 a multinational collaborative retrospective study (Fortney and Smith 1996; Akhter *et al*, 1996) on maternal morbidity was conducted in four developing countries - Bangladesh, India, Egypt and Indonesia. We joined that study and

Correspondence: Mahbub-E-Elahi Khan Chowdhury, Epidemiology Unit, Faculty of Medicine, Prince of Songkla University, Hat Yai 90110, Thailand.
E-mail: g4228005@maliwan.psu.ac.th

added a follow-up component with currently pregnant women to assess the level of their pregnancy-related complications throughout the course of pregnancy. Duration of identification of pregnant women from the community for this study was September-October 1992 and admission of subjects into the follow-up process was from October to December 1992.

The objectives of this study were (1) to estimate the occurrence of symptoms of various antepartum morbidities during different trimesters of pregnancy, (2) to assess the health burden of the pregnant women due to those morbidities, (3) to find out the care-seeking behavior of the pregnant women for their reported symptoms of morbidities among a representative sample of rural Bangladeshi population.

METHODS

Study design and sampling

This was a community-based cohort study. The sample was collected from rural areas of all the four old administrative divisions, Dhaka, Chittagong, Rajshahi and Khulan, of Bangladesh. In Bangladesh the administrative hierarchy is division, district, thana and union. We selected one district randomly from each division and from each of the selected districts one thana was selected randomly. From each of the selected thanas two unions were randomly selected. We included all the villages of the selected eight unions to identify married women who were within 24 weeks of gestation to enroll into this study.

Training of interviewers and quality control of data

A total of 12 female interviewers, 3 for each division, was recruited. A male supervisor supervised each of the teams. All of the interviewers and supervisors were graduates in social science or related subjects from local universities. A two-week intensive training course was given to them by the experienced researchers. In addition to training on basic interview techniques the training also emphasized maternal morbidity. The interviewers were also trained to minimize the inter-observer variation. Research physicians visited data collection spots at biweekly intervals and gave necessary guidelines to supervisors and interviewers to assure the quality of the collected data.

Identification of subjects and admission into the study

At first, the interviewers visited all the households in the selected unions to come up with a master list of currently pregnant women within 24 weeks of gestation among the currently married. The gestational age of the women were calculated by the interviewers from the first day of their last menstrual period. Later on they filled-out an admission form for each of the subjects and enrolled them into this study. At admission women were interviewed for their socio-demographic and reproductive characteristics. This form also included data for their morbidities such as hypertension, diabetes, pulmonary tuberculosis and jaundice during the current pregnancy.

Antenatal follow-up

The interviewers visited the subjects at home at every 4 weeks and obtained the symptoms of their current pregnancy-related morbidities. Women who reported symptoms of any morbidity were asked whether they had problems in their daily activities due to that morbidity and the types of problems they had. Women were also asked whether they sought care for their reported health problems and in case of seeking care, the person who provided care, was also recorded.

We defined the 1st trimester of pregnancy as completion of 14 weeks of gestation, the 2nd trimester as over 14 weeks to completion of 28 weeks of gestation, and the 3rd trimester as over 28 weeks of gestation. We defined bleeding as hemorrhage from the genital tract occurring after first trimester but before childbirth, fits and convulsions as a state in which the woman's body was affected by convulsion and eventually passed into coma. We defined excessive vomiting as persistent vomiting perceived serious by the pregnant woman, fever > 3 days as fever accompanying any infectious illness like burning urination or vaginal discharge, headache as intense pain felt deep in the skull. Symptomatic anemia was defined as pallor of conjunctivae and palm, palpitation was defined as awareness of the heart beat. Urinary problem was defined as irritation in the urinary tract or in mucous membrane of the genital tract during urination. Health burden was defined as constraints in daily activities of the pregnant women due to morbidities. Weights were applied to each report of morbidity according to intensity of constraints to estimate the summary measures of health burden. Constraints in activities were

categorized as follows - bed ridden for at least 3 days due to a morbidity and inability to do any work was defined as heavy health burden, daily activities hampered was defined as moderate burden, ability to continue daily activities despite difficulties as minimum burden, reported no problem in daily activities as no health burden. The mean intensity of burden for each episode of a morbidity was the weighted mean of burden over all the episodes of that morbidity. The population burden per 1,000 person months of a morbidity was the weighted mean of burden per 1,000 person months of observation of all the women in this study.

Statistical analysis

Descriptive analysis was used for percentages of symptoms of antepartum morbidities and percentages of types of burden in different trimesters of pregnancy. The health burden weighting scheme was as follows - bed-ridden and could not do any work:heavy=3, normal activities hampered : moderate=2, continued activities despite difficulties : minimum=1, no problem in activities : none=0.

RESULTS

Characteristics of sampled women (Table 1)

The sampled women had a low mean age at marriage (14.8 years) but at the time of interview (at mean age of 23 years) their parity was still relatively low (mean of 2.1). Their level of education and monthly per capita household expenditure were somewhat low. These characteristics were almost homogeneous except for parity, which was high in Chittagong (mean of 3.1) and low (mean of 1.4) in Rajshahi.

Dynamic cohort of the sampled women (Table 2)

Among 1,019 pregnant women 777 (76.3%) women were admitted into the study within 24 weeks of gestation as planned. The remaining 242 (23.7%) women entered after 24 weeks of gestation because there was a time lag between getting the master list and the time of first interview. During follow-up, some of the women were not at home and number of missed visits increased with increased gestation. Ten women were lost to follow-up - all of them due to a change of their usual residence. During the follow-up period, 37 (3.6%) reported having miscarriage and only 8 (0.8%) women admitted having induced abortion. We interviewed 964 women regarding their delivery. There was a total of 934 live births and 41 still births. We recorded 3 maternal deaths, occurring within 42 days of delivery, which gave an estimate of maternal mortality ratio of 3.2 per 1,000 live births.

Baseline morbidity from the admission records

Nearly 2% of the pregnant women reported having been diagnosed of having hypertension, more than 1% diabetes, nearly 4% jaundice, less than 1% (0.3%) pulmonary tuberculosis.

Occurrence of symptoms of antepartum morbidities (Table 3)

The percentages of visits in any trimester at which symptoms of morbidities were reported ranged

Table 1
Characteristics of the sampled women in 4 administrative divisions of Bangladesh

Characteristics	Dhaka n=214	Chittagong n=262	Rajshahi n=274	Khulna n=269	Total n=1,019
Mean age of respondents in years (SD)	23.8 (5.7)	25.6 (6.7)	21.4 (5.4)	21.5 (5.3)	23.0 (6.1)
Mean age at marriage in years (SD)	15.7 (2.3)	14.8 (2.2)	14.7 (2.1)	14.1 (2.5)	14.8 (2.3)
Mean no. of parity (SD)	2.3 (2.3)	3.1 (2.6)	1.4 (1.7)	1.6 (1.9)	2.1 (2.2)
Percentage never attended school	55.1	46.9	56.2	62.5	55.3
Median monthly per capita expenditure (in Taka)	333.00	364.00	384.00	375.00	333.00

Table 2
Dynamic cohort of the sampled women.

Gestational weeks	Number of women						No. of antepartum visits
	Admitted	Miscarriage	Induced abortion	Delivered	Lost to follow-up	Continued pregnancy	
05-08	7	3	0	-	-	4	4
09-12	55	2	3	-	-	54	54
13-16	170	6	4	-	1	213	202
17-20	309	10	0	-	2	510	490
21-24	236	4	0	-	1	741	680
25-28	173	8	1	3	2	900	802
29-32	59	4	0	23	3	929	793
33-36	8	-		98	0	839	578
37-40	2	-		455	1	385	184
40+	-	-		385	-	-	25

Table 3
Symptoms of various antepartum morbidities among rural Bangladeshi women.

Symptoms of morbidity*	%(number) of visits in trimesters				%(number) of women
	1st n=134	2nd n=2098	3rd n=1580	All n=3812	n=1019
Bleeding		0.3 (6)	0.3 (4)	0.3 (10)	1.0 (10)
Fits and convulsions		0.5 (10)	1.1 (17)	0.7 (27)	2.3 (23)
Swelling of hands and legs		2.0 (43)	5.4 (86)	3.4 (129)	9.1 (93)
Excessive vomiting	4.5 (6)	1.4 (30)	1.2 (19)	1.4 (55)	4.4 (45)
Fever > 3 days	5.3 (7)	3.6 (75)	4.5 (71)	4.0 (153)	12.4 (126)
Headache	30.3 (40)	22.6 (474)	19.6 (309)	21.6 (823)	43.7 (445)
Urinary problem	23.5 (31)	26.3 (552)	27.5 (434)	26.8 (1,021)	48.2 (491)
Palpitation	37.9 (50)	44.9 (942)	49.5 (782)	46.5 (1,774)	69.0 (703)
Symptomatic anemia	65.2 (86)	74.5 (1,564)	84.4 (1,334)	78.3 (2,984)	91.7 (934)
None of the above	25.0 (33)	18.4 (386)	10.3 (162)	15.2 (581)	6.1 (62)

*Multiple responses.

Table 4
Percentage (number) of visits in each trimester in which women in rural Bangladesh experienced types of health burden for symptoms of any antepartum morbidity.

Type of burden	%(number) of visits in trimesters			
	1st n=101	2nd n=1,712	3rd n=1,418	All n=3,231
Bedridden - could not do any work	1.0 (1)	1.1 (19)	1.3 (18)	1.2 (38)
Normal activities hampered	11.9 (12)	7.2 (123)	7.6 (108)	7.5 (243)
Continued activity with difficulty	62.4 (63)	61.2 (1,048)	58.6 (831)	60.1 (1,942)
No problem in activity	24.8 (25)	30.5 (522)	32.5 (461)	31.2 (1,008)

Table 5
Health burden for different antepartum morbidities of the pregnant women in rural Bangladesh.

Symptoms of morbidity	No. of visits with types of burden				Weighted burden	
	Heavy n=38	Moderate n=243	Minimum n=1,942	None n=1,008	Mean intensity of burden	Population burden /1,000 person months
Bleeding	1	1	6	2	1.10	3.63
Fits and convulsions	8	8	10	1	1.85	16.52
Swelling of hands and legs	7	13	98	11	1.12	47.90
Excessive vomiting	3	10	32	10	1.11	20.15
Fever > 3 days	4	22	87	40	0.93	47.24
Headache	16	97	562	148	0.98	265.61
Urinary problems	11	105	616	289	0.84	283.78
Palpitation	20	169	1,092	493	0.84	492.24
Symptomatic anemia	29	216	1,810	929	0.78	769.41

Total time observed 1,019 women for antepartum morbidities = 3,027 person months.

form 0.3% for bleeding to 78.3% for symptomatic anemia. The majority of the symptoms were more common in the second and third trimesters except excessive vomiting, headache and fever. The percentages of women who reported symptoms of morbidity at any time during pregnancy were 1% for antepartum bleeding and above 2% for fits and convulsions.

Health burden due to morbidity (Tables 4 and 5)

Most of symptoms of morbidity led to difficulty in daily activity in one way or another. Symptoms in the 1st trimester gave more health burden (75.2%) than those in the 2nd (69.5%) and 3rd (67.5%) trimesters. There was a inverse relationship between mean intensity of burden and population burden for most of the morbidities. For example, for fits and convulsions mean intensity of burden per episode of this morbidity was 1.85 and for symptomatic anemia it was only 0.78 whereas the population burden per 1,000 person months for fits and convulsions was about 4 but that for anemia was more than 700.

Care-seeking pattern for symptoms of morbidities (Table 6)

The percentage of visits in which women did not seek care from any provider for experiencing symptoms of different antepartum morbidities ranged from 25.9% for fits and convulsions to 87.4% for symptomatic anemia. For any episodes of convulsion and bleeding more than half of the attacks resulted in care seeking, in which majority of the care providers were either quack doctors or traditional healers.

DISCUSSION

Women in rural Bangladesh in our study were at a low socio-economic status and the symptoms of antepartum morbidities were very common. Health burden associated with their reported symptoms of morbidities was very heavy. Almost all of the women who had any symptom of morbidity had difficulty in one way or another in doing their daily activities. On the other hand, care-seeking behavior of the women having those symptoms was very poor. For most morbidities the majority of the times women did not seek care from any provider.

The number of women lost to follow-up from this study was quite low. The percentage of visits at which the woman was absent was low in 1st and 2nd trimesters but increased in the 3rd trimester because by tradition rural Bangladeshi women prefer to go to their father's home to deliver the baby and return to their husband's home afterwards.

Our finding of early marriage at the mean age of 14.2 years is consistent with the national statistic of median age at first marriage of the rural Bangladeshi women 14.0 years (Mitra *et al*, 1997). The majority of our study subjects (55.3%) never

Table 6
Percentage (number) of visits in which women in rural Bangladesh sought care from various types of providers for symptoms of different antepartum morbidities.

Care provider	Fits and convulsions n=27	Bleeding n=10	Fever>3days n=153	Excessive vomiting n=55	Headache n=823	Swelling of hands and face n=129	Symptomatic anemia n=2,984	Urinary problem n=1,021	Palpitation n=1,774
Physician	33.3 (9)	10.0 (1)	7.8 (12)	12.7 (7)	6.8 (56)	7.8 (10)	7.9 (235)	4.4 (45)	5.9 (105)
FWV/FWA/TBA/paramedic*	-	-	1.3 (2)	1.8 (1)	0.1 (1)	0.8 (1)	1.2 (36)	0.8 (8)	0.5 (9)
Homeopath	3.7 (1)	-	4.6 (7)	1.8 (1)	2.3 (19)	2.3 (3)	0.8 (24)	2.3 (23)	1.0 (18)
Quack*	33.3 (9)	10.0 (1)	19.0 (29)	14.5 (8)	13.5 (111)	6.2 (8)	7.6 (226)	5.9 (60)	4.3 (76)
Traditional*	3.7 (1)	30.0 (3)	1.3 (2)	-	2.4 (20)	0.8 (1)	1.0 (29)	2.4 (25)	0.8 (15)
Relative/neighbor	-	-	-	1.8 (1)	0.2 (2)	3.1 (4)	0.7 (20)	1.6 (16)	-
Sought no care	25.9 (7)	50.0 (5)	66.0 (101)	67.3 (37)	74.6 (614)	79.1 (102)	80.9 (2,412)	82.7 (844)	87.4 (1,551)

*FWV/FWA/TBA/paramedic - Family Welfare Visitor/Family Welfare Assistant/Trained Traditional Birth Attendant/Medical Assistant.
*Quack - Unqualified village doctor, *Traditional - Herbal medicine from traditional provider called Kabiraj

attended school, which is also consistent with the national data (of 57.1 %) of ever married rural women never having attended school (Mitra *et al*, 1997). This early marriage combined with the hardship of poverty and low education may easily make these women vulnerable to various complications during pregnancy. Differences in parity between two sampled areas, Chittagong and Rajshahi in our study is ineversely related with the contraceptive prevalence rate (CPR) in those two divisions of Bangladesh. CPR is low in Chittagong and high in Rajshahi; for example in 1993-1994 CPR in these two divisions were 29.3% and 54.8%, respectively (Mitra *et al*, 1997).

We can compare the 3.7% miscarriage among 1,019 women of our study with that of 5.0% among 33,473 pregnancies during 1982-1991 in Matlab, Bangladesh (Ahmed *et al*, 1998). However, our finding for induced abortion ratio of 8.6/1,000 live births was much lower than 20.0/1,000 live births in Matlab of the same study. The reasonable explanation for underestimation of our these two statistics in our study is that majority of our sampled women entered into the follow-up process after the first trimester. The still birth ratio of 43.9/1,000 live births of our study is somewhat higher than the estimate of 35.3/1,000 live births of the same study in Matlab, which is an intervention area of ICDDR,B (International Center for Diarrheal Diseases and Research, Bangladesh) for family planning and maternal and child health care. Our estimated maternal mortality ratio of 3.2/1,000 live births can be compared with the 1996 estimate of 4.3/1,000 live births (Islam and Hossain, 1997) and the slight difference may be due to chance for observation of rare events like maternal death.

Among baseline morbidities our findings on jaundice (4.0%) and pulmonary tuberculosis (0.3%) can be compared with 5.9 and 0.3%, respectively, of the retrospective study (Fortney and Smith, 1996). The same study found 3.6% of the women had hypertension during pregnancy whereas nearly 2% of our subjects reported diagnosed hypertension at the time of admission.

One percent of women in our study experienced antepartum bleeding either in 2nd or 3rd trimester. Among the other studies conducted in Bangladesh the Maternal Care Project in Matlab also found 1% antepartum hemorrhage (Stewart and Maxine, 1991). The retrospective study conducted among Indian women (Bhatia, 1995) found 0.9% women experiencing antepartum bleeding.

Fits and convulsions were reported 4 times more commonly in the 3rd trimester than in the 2nd trimester. More than 2% of the pregnant women in our study had fits and convulsions which can be compared with the findings of 3% fits/convulsion (Fortney and Smith, 1996) and 6% severe eclampsia found in Maternal Care Project in Matlab (Stewart *et al*, 1991).

The fact that fever >3 days and urinary problems were common may be due to high incidence of urinary tract infections. This suggests a need to study to confirm the clinical nature of these two problems. Palpitation and symptomatic anemia (as judged by the trained home visitors) were very common and increased with increased gestational age. Iron deficiency anemia is known to be very common in rural areas of South Asian countries due to poverty and undernourishment (Stewart and Maxine, 1991; Krishnaswami, 1998; DeMaeyer *et al*, 1985). This may be the explanation for the commonness of these symptoms in our population.

Despite the problem of clinical uncertainties over the precise medical diagnosis of the symptoms of antepartum morbidities, our study has shed some light on the extent of the burden on the pregnant women's daily life activities. The measures of burden are likely to be valid measures of the problem in such an area where medical facilities are not available. Looking at the seriousness of the symptoms alone might not be enough to reflect the magnitude of burden. Our study show that mild symptoms (such as palpitation and urinary problems) are very common. Each of these brings a little bit of burden every day but its commonness and long lasting nature lead to a large magnitude of population burden compared to those more serious symptoms such as bleeding and fits.

Poor care-seeking behavior has been observed among the pregnant women for their antepartum morbidities. Except for fits and convulsions, the majority of the times women sought no care for their health problems. For about three fourth of the episodes of having fits and convulsions, women sought care from a provider. If we consider physicians and family planning workers like family welfare visitors (FWV) and family welfare assistant (FWA) including trained traditional birth attendants (TTBA) and paramedics as trained providers and the rest as untrained providers for management of pregnancy complications, then the village women had a tendency to visit untrained providers, especially the quack, more frequently than their trained counterparts.

CONCLUSION

Since the symptoms of antepartum morbidities were very commonly reported by rural Bangladeshi women there is a need for further investigation to explore the underlying reasons for this immense problem. Further studies with appropriate clinical facilities are recommended. Care-seeking behavior of the pregnant women of rural Bangladesh was very poor whereas trained health care providers like FWVs, FWAs, TTBAs and paramedics were grossly underutilized. There is a need to conduct a research project to find out the reasons for this problem. Further understanding of the nature of these morbidities and the health care-seeking behavior will assist the implementation of a more appropriate prevention and treatment program for poor pregnant women of rural Bangladesh

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FOLLOW UP OF WATER USE IN A TIN MINING AREA AFFECTED WITH ARSENIC POISONING

Virasakdi Chongsuvivatwong, Apiradee Lim, Mafaosis Dueravee, Alan Geater, Skulrat Ritsamitchai and Shoko Oshikawa

Epidemiology Unit, Faculty of Medicine, Prince of Songkla University, Hat Yai 90112, Thailand

Abstract. Ron Phibun district in southern Thailand has been known as an endemic area for arsenic contamination. The government has been trying to improve the situation by encouraging the use of rainwater and piped water. This study aimed to document the change of water use and to identify factors associated with safe water use in 1997 compared to that in 1994. Home visits and face-to-face questionnaire interviews were undertaken. Information on water use for drinking, cooking, washing food and washing utensils in 1994 and 1997 was obtained. Among 3,849 households from which data could be obtained (estimated 79% of total households), the percentages of using safe water (including water from bottled rain water, piped and artesian well water) for drinking and cooking rose from 72.5 and 57.9 in 1994 to 93.6 and 80.9 in 1997, respectively. The percentages for washing foods and for washing utensils rose from 28.6 and 20.5 to 59.1 and 53.8, respectively. In 1997, percentage of households using piped water for drinking and cooking was still low (3.6 and 12.3) compared to those using piped water for washing food and utensils (39.1 and 43.6). Multivariate analysis shows that independent factors of the household predicting safe water use are: high arsenic area, near main road and having piped water installed. The influence of these factors (as judged by the level of odds ratio) operates more or less equally on water use for all purposes, except that installation of piped water has more influence on washing water than drinking and cooking water. We conclude that safe water supply in the area is still inadequate. Even if piped water is installed, it is often not used for drinking and cooking. The reasons for not using piped water for drinking and cooking need to be identified.

INTRODUCTION

Problems of arsenic contamination in water leading to arsenosis are not uncommon. Endemic arsenosis has been documented in Japan (Tsuda *et al*, 1995), Taiwan (Smith *et al*, 1992), India (Chakraborty and Saha, 1987; Guha Mazumder *et al*, 1988; 1992; Saha, 1995), Bangladesh (Nickson *et al*, 1998; Tondel, 1998; Tondel *et al*, 1999), China (Wu, 1993; Zhang and Chen, 1997), Mongolia (Luo *et al*, 1995), Mexico (Cebrian *et al*, 1983), Argentina (Astofi *et al*, 1981) and Chile (Borgono *et al*, 1977). This problem also occurs in Thailand.

In addition to development of skin lesions and skin cancer, arsenic contamination has been demonstrated to be associated with increased risk for hypertension (Rahman *et al*, 1999), diabetes mellitus (Rahman *et al*, 1998) and internal cancers (Ferreccio *et al*, 1998; Karagas *et al*, 1998). There is a need to improve the situation by the supply of safe water supply to the affected communities. The current article illustrates an evaluation of water supply program in a contaminated area in Thailand.

In 1987, more than 1,000 cases of skin arsenosis were reported from Ron Phibun Sub-district, Nakhon Si Thamarat Province, southern Thailand (Arrykul *et al*, 1996). This area has been the site of tin mining activities for almost a century. Although most of the mines ceased operation in the late 1980s, the release of arsenopyrite (FeAsS) from the tin ore has left a legacy of extensive arsenic contamination in many areas of Ron Phibun District. Groundwater and many shallow wells are contaminated by arsenic (Boriboon, 1996) above the acceptable level for drinking water set by WHO (0.01 ppm) (WHO, 1993) expecially in villages 2, 12 and 13 (Paijitprapaporn, 1997).

Since arsenic contamination of shallow well water, surface water and soil was detected in 1987, various governmental departments have tried to solve this problem. Water jars for storing rainwater were distributed and piped water systems were expanded. However, the effect of such intervention has never been evaluated and changing water use among the villagers had not been investigated. This study aimed to investigate the change of water use between 1994 and 1997 and to identify

Correspondence: Virasakdi Chongsuvivatwong, Epidemiology Unit, Faculty of Medicine, Prince of Songkla University, Hat Yai 90112, Thailand.
E-mail: cvirasak@ratree.psu.ac.th

the factors associated with safe water use in 1997. Experience from this program may be useful in further planning of intervention in this community as well as in other affected areas in developing countries.

MATERIAL AND METHODS

Study sites

The study area consists of 16 villages with a population of approximately 15,095 and 4,900 households three of these villages (2, 12 and 13) are known to have high prevalence of shallow well water found contaminated with arsenic (Table 1).

Data collection

Following a survey in April-November 1996, a map of each village was drawn showing location of households, roads, key sites and distribution of pipelines of water supply. Home visits were made between April and May 1997 by a group of researchers and medical students. A structured questionnaire was tested and used to collect data by face-to-face interview with the head of the family or other available member. Variables collected consisted of household and family head characteristics, and water use (including source of water for drinking, cooking, washing food and washing utensils) in 1994 and 1997.

Data management and statistical analysis

Data collected with the questionnaire were computerized using Epi Info software. The map was digitized using Arc-Info software for geographical query. Stata version 6 program package was used for statistical analysis. Descriptive statistics were computed. Types of water use were bottled, piped, artesian well, rain, shallow well, and stream water. The first four were classified as safe and the latter two as unsafe. Factors associated with safe water use in 1997 were identified using logistic regression.

RESULTS

Data were obtained from 3,849 households out of 4,900 (an availability proportion of 79%). Incomplete data collection was due to the fact that many houses were closed during the home visit. This was common in the suburban area of village 12 where people went out to work in the city. Breakdown by village is shown in Table 1.

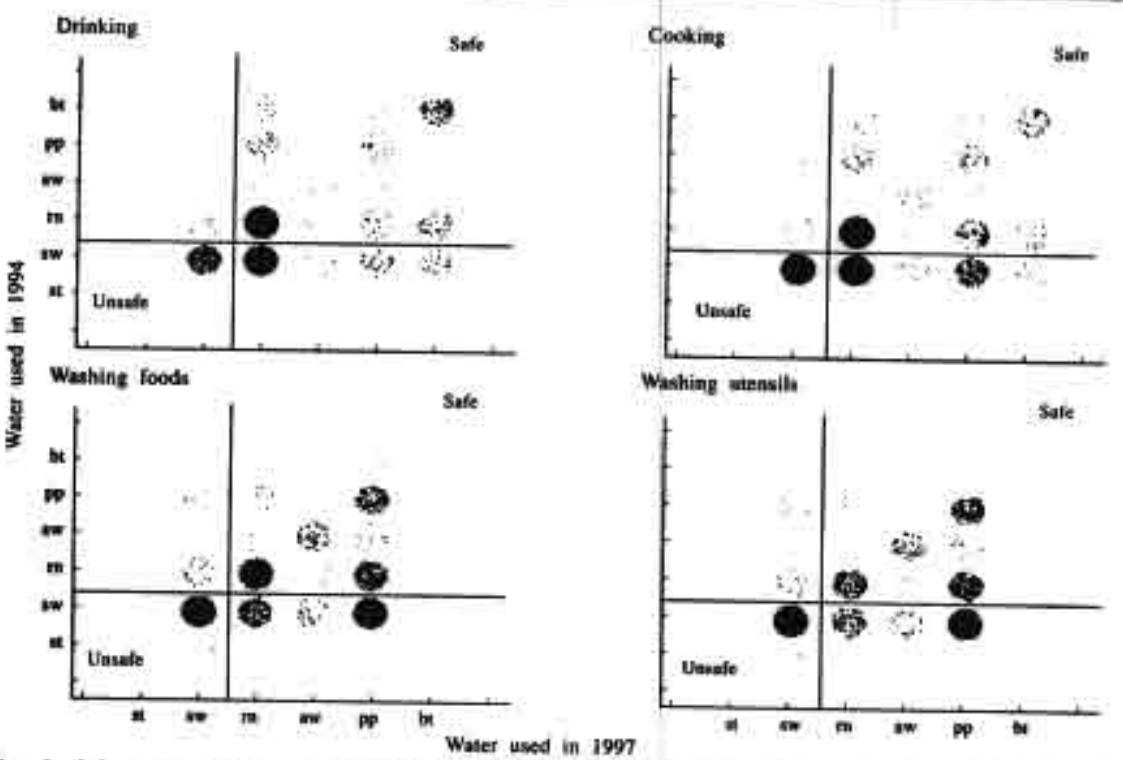
Table 1
Characteristics of study villages sorted by proportion of shallow wells with arsenic contaminated water.

Village	Total number of visited households	Number of household with data	Population in households with data	% of wells with As>0.05 (ppm[a])
2	378	329	1,145	35.4
12	672	404	1,502	30.4
13	525	290	1,099	25.5
5	282	246	1,064	10.0
1	131	116	497	9.2
8	309	240	981	4.5
10	306	229	924	4.2
14	172	144	690	2.6
9	214	193	859	2.2
3	330	272	1,013	1.6
4	279	256	1,260	1.5
7	643	484	1,514	0.9
6	231	207	965	0.6
11	147	133	497	0.0
15[b]	80	65	242	-
16[b]	201	177	834	-
Total	4,900	3,849	15,095	

[a]Reported in 1994 (Choprapawon, 1994).
[b]Village 15 was previously part of village 1 and village 16 part of village 9.

Table 2
Water used in 1994 and 1997.

Type of water	Number (%) of household using water for			
	Drinking	Cooking	Washing food	Washing utensils
Water used in 1994	n = 3,255	n = 3,209	n = 3,147	n = 3,134
Bottled	118 (3.6)	61 (1.9)	2 (0.1)	1 (0.0)
Piped	47 (1.4)	66 (2.1)	174 (5.5)	186 (5.9)
Artesian well	6 (0.2)	23 (0.7)	79 (2.5)	91 (2.9)
Rain	2,189 (67.3)	1,706 (53.2)	646 (20.5)	365 (11.7)
Shallow well	895 (27.5)	1,353 (42.2)	2,245 (71.3)	2,490 (79.5)
Stream			1 (0.0)	1 (0.0)
Water used in 1997	n = 3,785	n = 3,783	n = 3,783	n = 3,784
Bottled	257 (6.8)	136 (3.6)	3 (0.1)	
Piped	137 (3.6)	466 (12.3	1,479 (39.1)	1,650 (43.6)
Artesian well	9 (0.2)	34 (0.9)	108 (2.9)	114 (3.0)
Rain	3,143 (83.0)	2,424 (64.1)	643 (17.0)	275 (7.3)
Shallow well	239 (6.3)	722 (19.1)	1,550 (41.0)	1,745 (46.1)
Stream		1 (0.0)		



bt = bottled water; pp = piped water; aw = artesian well water; rn = rainwater; sw = shallow well water; st = stream water

Fig 1–Scatter plot of type water used in 1994 against type of water used in 1997.

Table 2 shows that the situation of water use in 1997 was improved compared to that in 1994. Of various types of water source for drinking and cooking, there was a noticeable increase in rainwater and slight absolute increase in percentage in bottled and piped water. Shallow well water use for these purposes decreased. For washing purposes, use of piped water was remarkably increased whereas use of rainwater was decreased. For more detail, a scatter plot is shown in Fig 1.

Table 3
Factor associated with using safe water in 1997 for various purposes.

Household Characteristics	No. (%) of households using safe water use			
	Drinking (n=3,785)	Cooking (n=3,783)	Washing food (n=3,783)	Washing utensils (n=3,784)
High contamination area				
No (ref)	2,540 (92.0)	2,080 (75.3)	1,415 (51.3)	1,277 (46.2)
Yes	1,006 (98.3)	980 (95.9)	818 (80.0)	762 (74.5)
cOR (95% CI)	5.2 (3.1-8.5)	7.6 (5.5-10.5)	3.8 (3.2-4.5)	3.4 (2.9-4.0)
aOR (95%CI)	3.1 (1.9-5.2)	4.1 (2.9-5.8)	1.9 (1.5-2.4)	1.4 (1.1-1.9)
Distance from main road (<200 m)				
No (ref)	2,260 (92.7)	1,857 (76.1)	1,285 (52.7)	1,151 (47.2)
Yes	1,286 (95.5)	1,203 (89.5)	948 (70.5)	888 (66.0)
cOR (95%CI)	1.7 (1.3-2.3)	2.7 (2.2-3.3)	2.1 (1.9-2.5)	2.2 (1.9-2.5)
aOR (95%CI)	1.1 (0.8-1.5)	1.7 (1.3-2.1)	1.4 (1.1-1.7)	1.5 (1.2-1.9)
Access to piped water				
No (ref)	1,869 (89.8)	1,409 (67.7)	577 (27.7)	376 (18.1)
Yes	1,677 (98.5)	1,651 (97.1)	1,656 (97.4)	1,663 (97.7)
cOR (95% CI)	7.4 (4.9-11.1)	15.8 (11.7-21.2)	96.0 (70.3-131)	194 (138-271)
aOR (95% CI)	5.8 (3.8-8.8)	12.6 (9.3-17.0)	89.4 (64.8-123)	183 (129-158)
Education of family head				
≤ Primary (ref)	835 (94.8)	761 (86.4)	574 (65.2)	527 (59.8)
> Primary	2,657 (93.3	2,255 (79.2)	1,629 (57.2)	1,482 (52.1)
cOR (95% CI)	1.3 (0.9-1.8)	1.7 (1.3-2.1)	1.4 (1.2-1.6)	1.4 (1.2-1.6)
aOR (95% CI)	1.0 (0.7-1.3)	0.8 (0.6-1.0)	0.9 (0.7-1.1)	0.9 (0.7-1.2)

Fig 1 is a "jittered" scatter plot, in which source of water in 1994 (Y axis) is plotted against that in 1997 (X axis). The vertical lines divide water use in 1997 into "safe"on the left side and "unsafe" on the right. Horizontal lines divide water use in 1994 into "safe" above the line and "unsafe" underneath. Dots in the central diagonal represent households not changing water source. As expected, the major changes in drinking and cooking (upper two graphs) were from shallow well to rain water, whereas changes in washing (lower two graphs) were from various types to piped water.

Fig 2 shows percent of households using safe water in 1994 (base part of the arrows) and 1997 (point of the arrow) of villages sorted into ascending order along the X-axis by percent of safe water use in 1994. Bold arrows indicate villages with high levels of contamination. Drinking water has the highest overall percentages of being safe, both in the baseline (1994) and after the change (1997). Water for cooking and washing was not as safe. Most households in the heavily contaminated villages with high contamination turned to use safe water for all purposes in 1997.

Table 3 displays the percentage of safe water use for different purposes broken down by various independent variables. Living in an area with high level of arsenic contamination, living closer to main road (except for drinking purpose), and having access to piped water are positively associated with use of safe water. However, it should be noticed that among these variables, access to piped water is the most powerful determinant as the odds ratios are very high. Again, it is shown that the effect of this variable is stronger for washing purposes than for drinking or cooking.

DISCUSSION

It is clear that water use pattern in the study area has improved as more households turned to use rainwater and piped water, which has been shown to be relatively arsenic-free (Oshikawa, 1997). However, there are still some important pitfalls in the program. First, at the time of evaluation, there

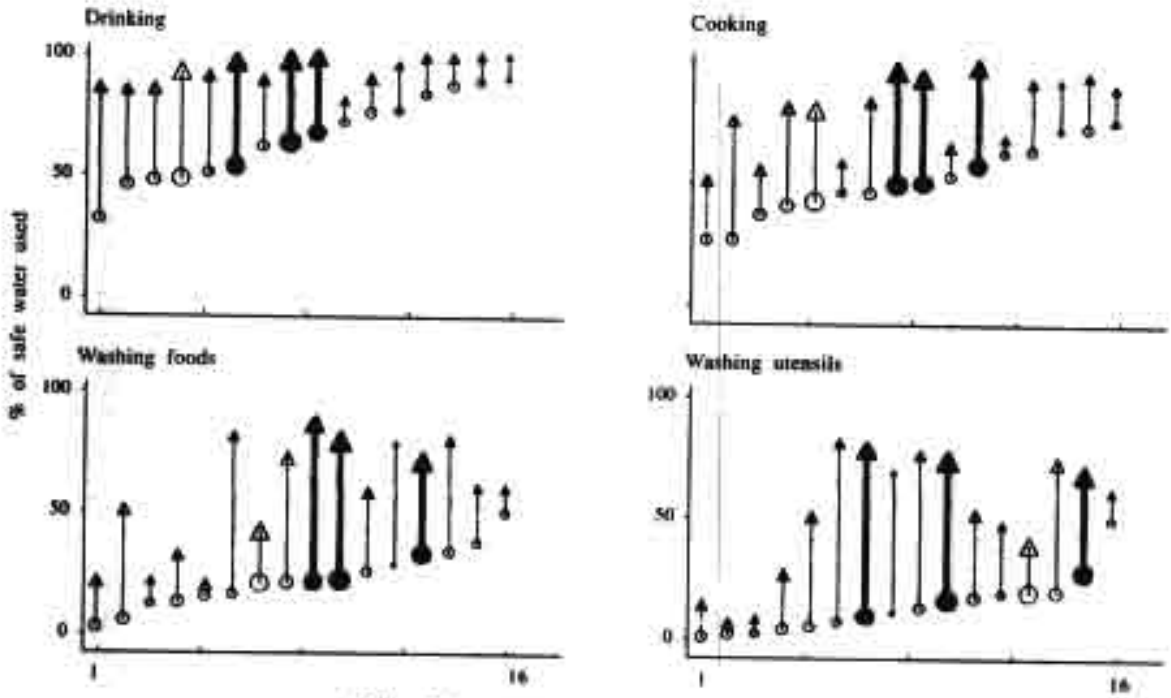


Fig 2–Sorted percent of households using safe water for drinking, cooking, washing food and washing utensils in 1994 in each of 16 villages.

were still 6 to 19% of the population using unsafe water for drinking and cooking and over 40% using it for washing food and utensils. Moreover, piped water was not popular for drinking and cooking but was used for mainly for washing. Thus the investment on provision of piped water did not reach its goal.

The use of rainwater should be encouraged with proper instruction regarding the collection process. Dusts in this area may contain arsenic and it can be accumulated on the roof of the house. The rainwater jar provided by the government was also difficult to clean (Adjimangkul, 1992). Therefore, it is strongly advised that rainwater should be collected only in high rainy season. One should let initial heavy rains wash away the dusts on the roof and gutters several days before the rainwater is collected.

The availability proportion in our study was 79%. We still lack data from more than one-fifth of the total households. The non-responders tended to go to work in nearby cities where arsenic contamination was not shown to be an important problem. Their lifestyles are likely to be more urbanized than the responder households. As our multivariate analysis demonstrated that households with higher level of urbanization (nearer to main road and access to piped water) are more likely to use safe water, the non-responders are therefore likely to have less serious problems.

In conclusions, the situation of water supply has been improved but still requires further effort to increase the coverage. Research on sociological aspects to explain low level of use of piped water for drinking and cooking should be initiated.

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ORIGINAL REPORT

Survey of knowledge and practice on oral contraceptive and emergency contraceptive pills of drugstore personnel in Hat Yai, Thailand

Chaveewan Ratanajamit*[1] MSc(Pharm) and Virasakdi Chongsuvivatwong[2] MD, PhD

[1]*Department of Clinical Pharmacy, Faculty of Pharmaceutical Sciences, Prince of Songkla University, Thailand*
[2]*Epidemiology Unit, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand*

SUMMARY

In Thailand, oral contraceptive (OC) and emergency contraceptive pill (ECP) are available as over-the-counter (OTC) drugs, and drugstores share 30% of services. While the rate of dispensing contraceptive pills has increased, the knowledge and awareness of ECP use is limited among users and providers. The objective of this study was to assess knowledge and practice of drugstore personnel on providing OC and ECP, in order to improve the quality of services. Drugstores located in Hat Yai District, Songkhla Province, Southern Thailand, were the accessible population. There were 109 drugstores, half of them owned by pharmacists. The population was stratified by owner (pharmacist or non-pharmacist) and randomly selected to obtain a sample size of 30 drugstores for each class. Two study methods, questionnaire interview and secret shopping, were used to measure knowledge, and practice, respectively. History-taking, drug-choosing, and advice-giving were the domains measured. The results demonstrated that knowledge on OC was fair, but that on ECP was poor. Pharmacists had better knowledge of proper history taking and ECP indication than non-pharmacists. OC and ECP provision were inappropriately practised in drugstores in the study area. A majority of drugstores were mainly owned by non-pharmacists. For OC practice, drug-choosing was good, but history-taking and advice-giving were poor in both groups. Although both groups dispensed ECP poorly, pharmacists dispensed significantly better than non-pharmacists. Among non-pharmacist staff, the average scores of OC advice-giving, and ECP dispensing, were statistically significantly better among those working in pharmacist-owned drugstores. Both knowledge and practice on OC and ECP should be improved in both types of drugstores in the study area. Copyright © 2001 John Wiley & Sons, Ltd.

KEY WORDS — ECP; OC; drugstore; pharmacist; emergency contraception

INTRODUCTION

Oral contraception (OC) is the most popular fertility regulating method worldwide,[1,2] both in developed and in developing countries.[1,3] The status of OC in most developed countries is prescription-only,[1,4,5] while it is available as an over-the-counter (OTC) drug in most developing countries.[6,7] The emergency contraceptive pill (ECP) is available as a prescription drug in developed countries with intensive campaigns launched to promote its availability and use.[8,9] In most developing countries, there is no policy to promote the use of ECP.[10] In the countries where OC and ECP are available as prescription-only drugs, the need for OC[4,5] and ECP[11–13] availability OTC are increasing. In addition, a pilot project making ECP available OTC is being run in the US.[11,14]

In Thailand, drugstores share approximately 30% of the OC service.[3] The rates of ECP use are not available, but a study on the guidance for the use of

*Correspondence to: Chaveewan Ratanajamit, Department of Clinical Pharmacy, Faculty of Pharmaceutical Sciences, Prince of Songkla University, Songkhla Province, 90110 Thailand. Tel: 66-074-429754. Fax: 66-074-212900.
E-mail: rchaveew@ratree.psu.ac.th

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levonorgestrel (the available ECP product in Thailand) among drugstore personnel, reported that this drug has been used widely and inappropriately among teenagers (N. Matananpun *et al*., unpublished data). Therefore, it is necessary to conduct a survey of the knowledge of and practice regarding OC and ECP provision by drugstore personnel since they play an important role in providing OC and ECP to teenagers and other users.

The aim of this study was to measure the knowledge and practice of OC and ECP provision by drugstore personnel, to compare the quality of service given by drugstores owned by a pharmacist and by a non-pharmacist and to measure the association between knowledge and practices on OC and ECP services.

STUDY METHODS

Setting

In Thailand, there are approximately 10,000 drugstores. Of these, approximately 45% are registered as being run by pharmacists [15] who may or may not be the owner. In practice, very often drug dispensing is carried out by a non-pharmacist employee.

The study was carried out in 1999 in Hat Yai, the largest city in southern Thailand with a population of 150,000 and 109 drugstores, 55 of which were pharmacist-owned.

Sampling

The drugstores were classified according to whether or not the owner was a pharmacist (for the pharmacist-owned drugstores, the pharmacist is assumed to spend more time with the client and closer supervision of other personnel than a (usually part-time) pharmacist employee in the non-pharmacist owned drugstores). Thirty pharmacist-owned and 30 non-pharmacist-owned drugstores were randomly selected from each class.

Ethical clearance

The study protocol was approved by the ethical committee of the Faculty of Medicine, Prince of Songkla University.

Development of instrument

For OC, a checklist for good practice guidelines was produced by the Ministry of Public Health. This includes the need to interview for contraindications and physical examination including blood pressure measurement, but does not include PAP smear. For ECP, there is no such a guideline. The checklist for ECP was developed based on the fact that it should be used within defined time constraints to prevent pregnancy when no contraceptive had previously been used or when the method failed. The questionnaire for interviewing the dispenser was devised using the checklist. Questions were devised to obtain the answers which reflected each item on the checklist. A weighting scheme was set up by the research team. The questionnaire and the weighting scheme were then discussed with a panel of pharmaceutical experts in the university and further modification to the weighting scheme was made as deemed appropriate.

Data collection

Drugstore visit and interview: Formal visit to and interview of drugstore personnel were carried out by the research team. A pre-tested questionnaire, including closed-ended and open-ended questions, was used to measure the knowledge, regarding both OCs and on ECPs, of volunteer drugstore personnel. It recorded the sociodemographic data of the interviewee, the most common OC dispensed to a new user, whether history taking was routinely carried out (and if so the details such as contraindications, menstrual cycle history, contraceptive use and concurrent drug use), the major concern about the content (type and amount of estrogen and progestin) of the OC chosen, the frequency and content of advice given (such as OC dosing and continuation, common side-effects and problem solving, danger signs of OC). Regarding knowledge about ECP, the questionnaire sought to assess whether sufficient details of the index coitus were taken from the client, the ability to evaluate risk of pregnancy from the unprotected intercourse, the type of ECP dispensed and related advice, and the ECP regimens available in the drugstore for different indications.

Secret shopping. Secret shopping study was conducted after finishing the formal interview by a group of well-trained and validated research assistants (two females and two males) who were pharmacy students. In each drugstore, both OC and ECP were bought by one male shopper and one female shopper on different occasions at least 1 day apart using the scenarios given in Appendix.[1] During shopping, the main variables related to the behaviour of the seller were noticed and

memorized by the shopper. The data were then immediately recorded into the checklist form after the shopper left the drugstore.

Data management and analysis

The data were coded after checking for completeness and accuracy and then computerized using Epi Info version 6.03 and analysed using Stata version 6.0. Data from the questionnaire interview and from secret shopping were handled in the same manner. Variables were grouped into four categories; history taking, drug-choosing and advice-giving for both OC and ECP and another category that was different between OC and ECP (see Table 3). The items on history-taking, drug-choosing and advice-giving were similar in both OC and ECP, while items related to OC choosing, which were of most concern (to examine their knowledge about the differences between high-dose versus low-dose pills, especially in terms of composition, drug of choice for OC initiator and adverse effects) and that on ECP indication were different and not related. The knowledge about what history (e.g. medical, menstrual, concurrent drug use) should be asked, what drug should be chosen and on the basis of what, what and how advice should be given to the new client was asked in the questionnaire interview. In secret shopping, it measured whether these components were actually practiced or not. Each item was scored 1 for a correct answer or practice and 0 for an incorrect answer or practice. The score was then multiplied by a weighting factor (shown in Table 1) whose value was based on its relative importance. For example, in the interview, history taking on disease contraindication was considered to be the most important and was given a weighting of 20, whereas menstrual cycle history was believed to be relatively less important and was weighted at 15, etc. From secret shopping, the weighting scheme was slightly different from the questionnaire. History taking on previous use of OC was considered important because more intensive counselling is needed among new OC users. Disease contraindication had a lower weighting because in our scenario, the client was healthy. Knowledge and practice composite scores were derived from the summation of the weighted score of each item that belonged to the composite. The internal consistency of the items in each category from the questionnaire study were checked using Cronbach's alpha which ranged from 0.47 and 0.94.

Student's *t*-test was used to test for statistically significant differences between groups of sample i.e. owner or interviewee (or seller for secret shopping study). Each composite score was rated on the basis of the average composite score (pharmacist-owned and non-pharmacist-owned drugstore). Multiple linear regression was used to test the independent influence of owner and seller on the score of practice from secret shopping.

History-taking and advice-giving practice in each drugstore in the secret shopping situation were cross-tabulated against corresponding answers in the questionnaire to check the discrepancy between actual and reported practice.

RESULTS

In most pharmacist-owned drugstores, the questionnaires were answered by the owner, but in only half of them did the owners act as sellers in the secret shopping study (Table 2). In non-pharmacist-owned drugstores which were supposed to be run by pharmacists, both questionnaire answering and secret shopping were almost exclusively carried out by non-pharmacists. This indicated that the actual service in a majority of drugstores was mainly provided by non-pharmacists. As expected, informants for the pharmacist-owned drugstore generally had a higher education than those in non-pharmacist-owned drugstores.

From the OC questionnaire study, the only statistically significant difference in composite scores between groups was on advice-giving (pharmacist-owned drugstores did better) (Table 3). The knowledge about OC was acceptable in all groups. The average composite scores for ECP were poor in all groups. Pharmacists had better knowledge of proper history-taking (especially in details of time and frequency of intercourse–not shown in the table) and indications for ECP than the non-pharmacist group. There were no statistically significant differences on ECP choosing and advice giving.

Data from secret shopping of OC and ECP were stratified by both owner and seller (Table 4). Pharmacist sellers in non-pharmacist-owned drugstores had significantly higher scores (mean $\pm$ SD) in OC history-taking (16.2 ± 3.2 vs. 10.0 ± 7.6) and advice-giving (18.0 ± 1.4 vs. 13.7 ± 5.3). There was no problem with OC choosing because most of the available OC in local market were standard low-dose pills at the time of this study. Of several items of quality of service on OC and ECP from secret shopping, only drug dispensing was rated good for OC and fair for ECP. The remaining items were all poor or very poor. Pharmacist sellers generally gave better service than non-pharmacist sellers, except in OC dispensing.

Table 1. Scheme for weighting of items of knowledge and practice

Variable	Questionnaire interview		Secret shopping	
	OC	ECP	OC	ECP
1. History-taking of OC and ECP				
History of use of OC or other methods of contraception	-	-	8	-
The two most important issues on OC history taking		-	-	-
• disease history (contraindication for OC user)	20	-	8	-
• Cycle history	15	-		
• last menstrual period	-	-	3	4
• regularity of cycle	-	-	1.5	1.5
• cycle length	-	-	1.5	1.5
• menstrual duration	-	-	1.5	-
• menstrual related symptoms	-	-	1.5	-
History of concurrent drug use	10	-	6	-
Assessment of hormonal type	5	-		
History of sexual intercourse	-		-	
• Time of intercourse	-	10	-	10
• Time related to menstrual cycle	-	5	-	-
• Frequency of intercourse	-	5	-	-
• Prevention	-	-	-	5
ECP indication	-	-	-	5
2. Drug-choosing				
Popular brand of OC dispensed in drugstore	10	-	-	-
Brand of OC most frequently dispensed to initiator	10	-	-	-
Most concern on pill choosing	10	-	-	-
First OC pill dispensed in secret shopping	-	-	10	-
Actual pills dispensed	-	-	10	-
ECP dispensed	-	-	-	25
Availability of pills within	-		-	
• 1 h of intercourse	-	5	-	-
• 24 h of intercourse	-	5	-	-
• 72 h of intercourse	-	5	-	-
Effectiveness of ECP	-	5	-	-
3. Advice-giving				
Drug dosing for				
• 21/22 tablets package	3.5	-	5	-
• 28 tablets package	3.5	-	5	-
• how to continue the new package	-	-	2	-
• ECP within 1 h of intercourse	-	5	-	-
• ECP within 24 h of intercourse	-	5	-	8
• ECP within 72 h of intercourse	-	5	-	-
Advice on pill missing	5	-	5	-
Side-effects	7	-	7	6
Solving of common side-effects	-	-	4	2
Warning signs for pill stopping	7	-	10	-
Follow advice strictly	-	-	-	2
Evaluation of the effectiveness of ECP	-	-	-	10
ECP indication and limitation	-	-	-	10

Table 5 cross tabulates answers in the questionnaire with data from secret shopping. The strikingly discordant numbers were in ECP history-taking and advice-giving. Among those shops where these practices were claimed in the questionnaire, more than a half did not provide such service during the secret shopping. No statistically significant predictors were found by multiple linear regression.

Table 2. Characteristics of drugstore personnel

Characteristics	Questionnaire		OC shopping		ECP shopping	
	Pharmacist owner $N=30$	Non-pharmacist owner $N=30$	Pharmacist owner $N=60$*	Non-pharmacist owner $N=60$*	Pharmacist owner $N=60$*	Non-pharmacist owner $N=60$*
Provider status						
Pharmacist	26	0	35	2	32	0
Non-pharmacist	4	30	25	58	28	60
Interviewee's education			–	–	–	–
Primary school	0	1				
Secondary school	1	15				
Undergraduate	1	4				
Graduate	22	9				
Postgraduate	6	0				
Average duration of experience (mean ± SD) (years)	5.9 ± 4.0	12.6 ± 10.0	–	–	–	–

*N is twice that in the questionnaire study because each drugstore was visited by one male and one female shopper.

Table 3. Summary of the composite and total scores (mean ± SD) from the OC and ECP questionnaire interview stratified by owner and by interviewee

Variable (maximum score)	Owner		Interviewee		Overall assessment
	Pharmacist ($N=30$)	Non-pharmacist ($N=30$)	Pharmacist ($N=26$)	Non-pharmacist ($N=34$)	
OC					
History taking (20)	15.5 ± 6.1	15.2 ± 5.7	16.3 ± 5.4	14.6 ± 6.2	Good
Most concern on OC choosing (10)	7.0 ± 3.0	5.8 ± 4.4	6.7 ± 3.1	6.2 ± 4.3	Fair
OC choosing (20)	19.2 ± 2.3	18.0 ± 3.8	19.2 ± 2.3	18.1 ± 3.7	Good
Advice giving (26)	17.0 ± 4.5*	13.5 ± 5.6*	17.7 ± 4.3†	13.4 ± 5.4†	Fair
Total score (76)	58.7 ± 9.5*	52.6 ± 13.1*	60.0 ± 8.8*	52.3 ± 11.8*	Fair
ECP					
History taking (20)	11.5 ± 4.9*	8.0 ± 7.0*	12.1 ± 4.9†	7.9 ± 6.6†	Poor
ECP indication (5)	4.5 ± 1.5**	2.0 ± 2.5†	4.8 ± 1.0†	2.1 ± 2.5†	Fair
ECP choosing (20)	11.0 ± 3.3	9.2 ± 2.3	11.2 ± 3.6	9.3 ± 2.2	Poor
Advice giving (15)	4.2 ± 3.7	3.7 ± 2.2	4.2 ± 3.9	3.7 ± 2.2	Poor
Total score (60)	35.7 ± 10.0†	24.8 ± 11.6†	37.1 ± 9.6†	25.0 ± 11.2†	Poor

*$p < 0.05$; †$p < 0.01$, the level of statistically significant difference between different owner and between different interviewee.

DISCUSSION

The results demonstrate that knowledge of OC was good or fair, but knowledge of ECP was poor in all groups. In pharmacist-owned drugstores, very few sellers were pharmacists indicating that these drugstores had only pharmacists' licenses that were required by law. Practice on OC and ECP dispensing were inappropriately undertaken in drugstores in the study area. Both kinds of pills were sold without or with very little history-taking and advice-giving. Failure to practice proper history-taking before OC dispensing might do harm to those who have some contraindications for OC use. Statistically significant higher composite scores on ECP practice such as history-taking, drug-dispensing and advice-giving including OC advice-giving practice in pharmacist-owned drugstores indicated that irrespective of who provided the service, the quality of service was better in pharmacist-owned drugstores. It is very important to counsel clients about pill dosing, common or possible side-effects, pill-by continuation, and drug interaction, otherwise it might result in pill discontinuation, and failure. It has been found that very few

Table 4. Summary of the composite and total scores (mean ± SD) from the OC and ECP secret shopping study stratified by owner and by seller

Variable (maximum score)	Owner						Overall assessment
	Pharmacist seller			Non-pharmacist seller			
	Pharmacist	Non-pharmacist	Total	Pharmacist	Non-pharmacist	Total	
OC	$N=35$	$N=25$	$N=60$	$N=2$	N=58	$N=60$	
History taking (31)	10.0 ± 7.6	8.1 ± 4.8	9.2 ± 6.6	16.2 ± 3.2	7.7 ± 4.5	8.0 ± 4.7	Very poor
Drug dispensing (20)	17.1 ± 6.2	17.2 ± 6.1	17.2 ± 6.1	20.0 ± 0	16.9 ± 6.5	17.0 ± 6.5	Good
Advice giving (32)	13.7 ± 5.3	12.0 ± 4.5	13.0 ± 5.0	18.0 ± 1.4	9.4 ± 4.5	9.7 ± 4.7†	Poor
Total score (83)	40.8 ± 14.5	37.3 ± 9.6	39.3 ± 12.7*	54.2 ± 4.6	34.0 ± 10.4	34.7 ± 10.9*	Very poor
ECP	$N=32$	$N=28$	$N=60$	$N=0$	$N=60$		
History taking (22)	4.3 ± 7.2	2.0 ± 5.4	3.2 ± 6.5*	–	1.2 ± 3.3*		Very poor
Drug dispensing (25)	11.7 ± 10.6	10.7 ± 8.7	11.2 ± 9.7†	–	6.8 ± 6.9†		Poor
Advice giving (28)	7.4 ± 8.3	5.1 ± 5.5	6.3 ± 7.2†	–	3.3 ± 4.7†		Very poor
ECP indication and limitation (10)	6.2 ± 4.9	5.7 ± 5.0	6.0 ± 4.9	–	4.7 ± 5.0		Poor
Total score (85)	29.7 ± 23.6	23.5 ± 14.3	26.8 ± 19.9†	–	16.0 ± 12.4†		Very poor

*$p < 0.05$; †$p < 0.01$, the level of statistically significant difference between different owners.

Table 5. Cross tabulation of answers from questionnaire interview against actual practice in the secret shopping study

Answer in the questionnaire	Actual practice (number of shoppers who received these services)			
	0	1	2	Total
OC				
Advice giving				
Take	1	4	51	56
Not take	0	1	3	4
ECP				
History taking				
Take	37	12	3	52
Not take	8	0	0	8
Advice giving				
Take	33	24	0	57
Not take	3	0	0	3
ECP available (Yuzpe regimen)				
Yes	1	3	0	4
No	52	4	0	56
ECP available (levonorgestrel alone)				
Yes	4	0	0	4
No	40	16	0	56

OC users know the basic pill rules.[16] For ECP practice, history-taking about unprotected intercourse is very important to evaluate the risk of becoming pregnant. ECP counselling (which emphasizes ECP dosage administration, side-effects, and limitations) is still important even though noncompliance may not be a problem.[17]

The knowledge and practice of ECP provision were consistently poor, whereas sellers knew these details of OC well, but practised its administration improperly. Although knowledge and practice in pharmacist-owned drugstores were better than those in non-pharmacist-owned drugstores, both kinds of drugstores should be improved. The knowledge of OC was good, but the selling practice was poor indicating that knowledge was not appropriately applied in practice. It has been documented that the major causes of OC failure (and unwanted pregnancy) were lack of knowledge,[18] noncompliance,[19] and OC discontinuation.[20] These might result from the provider's lack of awareness about the need for counselling. We did not have data on these variables among our clients, but a national contraceptive prevalence survey reported that the 6-month OC discontinuation rate was 27.3%.[3] That might be significantly reduced by proper counselling.

Discrepancies exist between knowledge and actual practice. For example, among the 52 drugstores in which the interviewee answered that history-taking was done before ECP was dispensed, only 15 actually enquired about history-taking in practice and 12 of those did so only in the case of one of the two secret shoppers. In addition, 16 out of 56 drugstores where levonorgestrel-only emergency contraception was reportedly not available (in the questionnaire

interview) sold this drug to our shoppers. In Thailand, the drug company leaflet states that one tablet of levonorgestrel-only emergency contraception should be used within 1 h after unprotected intercourse. This is contrary to the dosing recommendation established by WHO which states that it can be used up to 72 h after unprotected sexual intercourse to prevent pregnancy (either when no method was used or the method failed at intercourse).[21,22] From interview, dispensers' knowledge was based on the leaflet, but they still gave this ECP after 24 h of unprotected intercourse. This discrepancy of knowledge (which was incorrect) and practice (which was against their belief) was also found among obstetrician–gynecologists in a study in Brazil.[23] Answering that this drug was not available in a drugstore did not imply that it would not be sold. High-dose combined contraceptive pills such as the Yuzpe regimen was used as an off-labeling, so that it was not popular among drugstore providers, especially those who were not pharmacists.

The fact that ECP provision practice was poor was not surprising because knowledge was poor. A study conducted by Rojpibulsatit in the same region of Thailand found that knowledge regarding the treatment of common diseases (such as gonorrhoea) was good, but that of uncommon disease (i.e. chancroid) was poor.[24] The poor knowledge and poor practice relating to ECP might be partly explained by this reason. Although knowledge on ECP pharmacology has been available and it has been proved to be safe[25] and effective,[26] it has not reached those who need it throughout the world.[10,27] In addition, it was found that health providers in South Africa were not aware of the dispensing of ECP even though the policy about ECP use in unprotected intercourse was clear.[10]

The higher scores regarding OC advice-giving and ECP dispensing among non-pharmacist sellers working in the pharmacist-owned drugstores than among those working in the non-pharmacist-owned drugstores, reflected the role of pharmacists in training their assistants.

Without adequate counselling on both the advantages and limitations of each type of oral hormonal pill to new clients, unwanted pregnancies will result.

KEY POINTS

(1) Acceptable OC knowledge, but improper practice
(2) Poor ECP knowledge and practice
(3) Pharmacist dispensed ECP better than non-pharmacist

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APPENDIX 1

Scenario

Oral contraceptive (OC). A recently married woman aged 23 years who plans to have a child in the next 2 or 3 years comes into a drugstore. She has never used any methods of contraception. She is healthy, her medical history is negative for contraindication of combined oral contraceptive(COC) use. Her menstrual history is normal and regular except moderate dysmenorrhea. Is she a good candidate for COC? If yes, what COC should be selected for this client and what instructions/advice should this woman receive regarding use of COC?

Emergency oral contraceptive Pill (ECP). A college student experienced unprotected mid-cycle intercourse, 24 h ago. What is the role of the drugstore in the prevention of an unwanted pregnancy at this time?

IMPLEMENTING THE UNIVERSAL HEALTH COVERAGE: WHICH SOURCE OF INFORMATION IS MORE RELIABLE?

Vinai Leesmidt[1], Supasit Pannarunothai[2] and Virasakdi Chongsuvivatwong[3]

[1]Khlongkhlung Hospital, Khlong Khlung District, Kamphaeng Phet 62120; [2]Center for Health Equity Monitoring, Faculty of Medicine, Naresuan University, Phitsanulok 65000; [3]Epidemiology Unit, Faculty of Medicine, Prince of Songkla University, Songkhla 90110, Thailand

Abstract. The implementation of universal health coverage needs accurate data on the distribution of health benefit coverage, particularly the uninsured. The national surveys and routine reports are two important sources of information ready for use. This study shows the validation of data from two sources. The data from national household surveys on the medical welfare, the health card and the social security schemes were validated with the routine report data of the Ministry of Public Health (MOPH) and the Social Security Office (SSO) by provinces. There were considerable differences between these data sets. The national survey data gave a 1.5 times higher estimate than the report data of the MOPH and the SSO. Financial implications of using inaccurate data to implement the universal health coverage could be huge, depending on the capitation rate.

INTRODUCTION

Universal health coverage has become one of the most important health policies in Thailand since the victory of the new government early 2001. The first near-majority victory was the result of a brave election campaign to cover all Thai citizens. The government has to merge the existing scattered, fragmented health coverage scheme in order to cover the uninsured population (see appendix). The most crucial questions for policy implementation were: how many were the uninsured, and how much money the government had to raise in order to achieve universal coverage. These questions need basic information on the coverage of various existing insurance schemes. Unfortunately, the existing information on insurance coverage and its relevant information such as the distribution of the coverage was insufficient, inaccurate and, often, inconsistent.

Basically, information used for health planning can be obtained from either survey or routine report, or both. Particularly, the survey data have become more important if the routine reports are inadequate. This problem is very prevalent in the developing and the least-developed countries (Oyoo *et al*, 1991; Indrayan, 1995). In the same vein, the information about the insurance coverage depends much on the survey data because the data from the report is not complete. However, the survey data are still inconsistent with the report data. So there is a necessity that the data from these two different sources be validated in order to know how much they differ from each other. It is hoped that the result of the data validation will be beneficial for data improvement for future health insurance planning and implementation. This paper aimed to present the methods of data validation and the implications on policy implementation for effective universal health coverage planning and development. These experiences may be learned by other countries attempting the universal coverage policy.

This data validation aimed at identifying the differences between the survey data of the National Statistical Office and the report data of the Ministry of Public Health and the Social Security Office about the insurance coverage under the public medical welfare, health card and social security schemes. Financial implications were estimated if inaccurate data were used for policy implementation.

Correspondence: Dr Supasit Pannarunothai.
Fax: +66 55 261198; E-mail: supasitp@nu.ac.th,

MATERIALS AND METHODS

Sources of data

There were two major sources of data for validation. The first data set was the National Statistical Office survey on household health and welfare 1999. The second data set was the report data to the Ministry of Public Health (MOPH) and the Social Security Office (SSO), Ministry of Labor and Social Welfare.

The survey was the cross-sectional national data obtained from the 32,724 households in May 1999. Sample households were taken from all provinces in the country as the National Statistical Office (NSO) aimed to represent situation of each province. These households accounted for 94,971 individual members (National Statistical Office, 2000).

The routine reports were also the 1999 data on the entitlement to health coverage of the medical welfare and the voluntary health card schemes under the MOPH (Ministry of Public Health, 1999), and the social security scheme under the SSO. The MOPH reports were compiled from the registration system of individual members in 76 provinces including the Bangkok Metropolitan. This data set has been used by the MOPH to allocate the medical welfare and the health card budget according to the number of cards issued to the target populations in each province since 1999. The SSO report was compiled from the database on the insured workers choosing their main contractors at the annual matching process that the insured exercising their choices. The provider choice data have been used to pay main contractors (hospital with 100 beds or higher) on a capitation basis since 1994. Unfortunately, study could not be carried out for the civil servant medical benefit scheme because database for the scheme was non-existent, even though it was the most expensive scheme compared with others (Tangcharoensathien *et al*, 2001).

Data structure and data handling

The unit of analysis of this study was province. Data handling to support provincial analysis had to be accomplished. The format of the survey data differed from those of report data. The structure of the survey data was an individual record of each member in a household (Table 1) while the report data (at MOPH and SSO) were readily available by province (Table 2). Steps were undertaken to make analysis by province possible:

Firstly, all data sources needed to have the same provincial codes in order to link all data to the same province.

Secondly, collapsed the survey data (94,971 individuals) into 76 provincial data according to provincial code. Created new variables to each individual record according to the insurance status. To get the estimates of how many people were under the existing schemes in each province, the sampling fraction (or weight in Table 1) of each individual record was used to blow up to represent the whole population, then sum the blow up by province (Fig 1).

Thirdly, merged data from different sources according to provincial code.Finally, validated the report and the survey data using double log graph (plotting the report data on the X-axis and the survey data on the Y-axis) in STATA (1999). Presented the discrepancy by descriptive statistics such as means and standard deviation.

RESULTS

The results will be presented in 2 parts. First, the same data from two different sources were validated to establish the discrepancy index. Financial implications were then estimated to flag the warning if inaccurate data were used for implementation.

Data validation

The matched data were validated respectively according to the insurance schemes. The first data validation started with the distribution of insurance coverage under the medical welfare scheme. Fig 2 showed that in most provinces the coverage of the medical welfare lied below the line of identity (if both sources of data had the same value, the scatter plots

Table 1
Data structure of the survey data.

Record	Cwd*	Insurance*	Weight*
1	10	4	911.73
2	10	3	1,057.71
3	10	1	993.53
4	10	8	112.01
:	:	:	:
30675	71	6	123.94
30676	71	4	106.73
:	:	:	:
94971	76	5	55.22

* Cwd = Provincial code
* 1 = Civil servant medical benefit scheme
3 = Social security scheme
4 = Medical welfare scheme
5 = Voluntary health card scheme
6 = Private insurance
8 = Uninsured
*The sampling fraction or weight was the figure given by the National Statistical Office according to different sampling proportions in urban, semi-urban and rural areas.
Source: National Statistical Office, 1999.

Table 2
Data structure of the report data.

Record	Cwd	WC	HC	SSS
1	10	780,794	5,427	174,533
2	11	202,435	26,379	636,056
3	12	155,700	97,144	162,991
4	13	116,682	25,242	248,757
:	:	:	:	:
62	77	136,154	21,875	41,431
63	80	637,826	30,597	41,508
:	:	:	:	:
75	95	194,435	18,608	19,160
76	96	328,555	6,158	10,916

Cwd = Provincial code; WC = Welfare card; HC = Health card; SSS = Social security scheme.
Source: Ministry of Public Health, 1999, and the Social Security Office, 1999

would lie along this line). The mean of the medical welfare coverage in all provinces was 2.4 below the identity line. It could be either the routine data were over-reported, or the survey data under-reported. However it indicated that the data from the national survey and the report of the MOPH differed from each other.

Table 3 summarized the differences between the survey and report data by type of health benefit schemes. In contrast to the medical welfare scheme, the survey data gave a 5.4 times higher than the MOPH report data for the voluntary health card scheme. Since respondents of the NSO survey may be confused between the medical welfare and the health card schemes, the two schemes were then combined and analysed on the log graph. By this time, the differences became narrower. The survey under-reported about 1.6 times lower than the MOPH data.

The closest variation between two sources of data was the social security scheme. However, the survey gave the lower estimate, average at 1.5 times lower than the SSO data (Fig 3).

When subcategories of the medical welfare scheme were analysed according to age (0-12, 13-59 and 60 years and above), the elderly gave the narrowest variation (1.4 times) while the working age had the widest variation (10 times). When analysed the variations by region (76 provinces were collapsed to 5 regions, namely: Bangkok, the North, Northeast, Central and South), it was surprising that the disagreement became wider, *eg* the disagreement of the medical welfare rose from 2.4 to 3.2. On the contrary, the disagreement of the social security scheme when analysed by region gave the opposite direction as when analysed by province. The survey data gave higher estimate than the SSO data. However, if looked at the scatter graph in Fig 4, it was more surprising that the respondents in Bangkok produced a higher disagreement (between the survey and the report) than respondents of other regions.

Financial implications

Financial implications of using inaccurate data for implementation of the universal cov-

Rec	Cwd	Ins	Wt
1	10	8	911.73
2	10	4	1,057.71
:	:	:	:
2,000	32	5	1,218.18
:	:	:	:
94,971	96	3	912.85

Create new variables from ins

Rec	Cwd	WC	HC	SSS	Un	Wt
1	10	0	0	0	1	911.73
2	10	1	0	0	0	1,057.71
:	:	:	:	:	:	:
2,000	32	0	1	0	0	1,218.18
:	:	:	:	:	:	:
94,971	96	0	0	1	0	912.85

Blow up data (insurance type x wt)

Rec	Cwd	WC	HC	SSS	Un	Wt
1	10	0	0	0	911.73	911.73
2	10	1,057.71	0	0	0	1,057.71
:	:	:	:	:	:	:
2,000	32	0	1,218.18	0	0	1,218.18
:	:	:	:	:	:	:
94,971	96	0	0	912.85	0	912.85

Data processing

Sum by Cwd

Rec	Cwd	WC	HC	SSS	Un
1	10	103,200	35,835	1,463,910	4,546,725
2	11	26,566	8,594	418,319	648,479
3	12	13,618	2,618	123,420	432,315
:	:	:	:	:	:
62	77	61,645	41,789	7,302	199,869
63	80	431,466	176,318	45,849	725,635
:	:	:	:	:	:
75	95	153,085	129,538	10,898	88,488
76	96	289,377	164,192	6,193	323,506

Fig 1–Handling of data from the National Statistical Office for validation.

erage were illustrated. To achieve universal coverage, the uninsured population was the target to be brought under the umbrella of the universal health insurance. Therefore the degree of financial implication varied according to the number of the uninsured and the capitation rate for health benefit coverage.

The number and percentage coverage of the insurance schemes estimated from the national survey and the routine reports were shown in Table 4. It was assumed that the number of the uninsured was also 1.5 times higher in the survey data than in the reports (since the survey produced lower coverage of benefit schemes, the uninsured therefore tended to be overestimated, 1.5 times was used for the least difference). If 24.8 million uninsured was used to estimate the additional budget to achieve universal coverage, the budgets would vary from 6.8 billion baht to 37.2 billion depending on the capitation rate (Table 5). However, if the number of the uninsured was 1.5 times lower than the survey figure, the range of the additional budget was narrower (from 4.5 billion to 24.8 billion baht).

Table 3
Summary results of the validation of insurance schemes.

	No.	Direction	Mean	SD	Min-Max
By schemes					
Medical welfare	76	Low*	2.37	1.84	0.82-13.32
Health card	76	High	5.40	2.95	0.30-14.10
Medical welfare + health card	76	Low	1.58	1.73	0.27-11.56
Social security	76	Low	1.54	1.17	0.12-6.71
Medical welfare by age group					
0-12	76	Low	3.19	4.86	0.80-30.30
13-59	76	Low	9.95	23.07	0.60-179.0
60+	76	Low	1.36	0.81	0.62-6.43
By region					
Medical welfare	5	Low	3.21	2.87	1.53-8.28
Social security	5	High	2.33	3.43	0.68-8.46

*The survey was lower than the routine report.

Table 4
Insurance coverage distribution 1999.

Type of insurance	Survey		Report	
	Population	Percentage	Population	Percentage
Social security scheme	4,319,083	7.00	4,079,128	6.61
Medical welfare	13,990,560	22.67	23,181,057	37.57
Health card	11,094,440	17.98	2,305,154	3.76
CSMBS	5,485,784	8.89		
Private insurance	834,806	1.35	32,139,342 (CSMBS+Private Insurance+Other +Uninsured)	52.09 (CSMBS+Private Insurance+Other+ Uninsured)
Other	1,057,858	1.71		
Uninsured	24,808,433	40.21		
Blank	113,616	0.18		
Total	61,704,581	100	61,704,581	100

Source: National Statistical Office 1999, Ministry of Public Health 1999, Social Security Office, 1999.

Table 5
Scenarios of financial implication for universal health insurance financing.

Per capitation (Baht)	Survey		Expected*		Discrepancy	
	Uninsured (million)	Budget (million)	Uninsured (million)	Budget (million)	Uninsured (million)	Budget (million)
273[b]	24.8	6,770	16.5	4,505	8.3	2,266
1,197[c]	24.8	29,686	16.5	19,751	8.3	9,935
1,500[d]	24.8	37,200	16.5	24,750	8.3	12,450

* = uninsured of expected numbers is 1.5 lower than the survey data.
[b] = per capitation of medical welfare scheme.
[c] = per capitation agreed by the Bureau of Budget.
[d] = per capitation of the universal coverage proposed by the working group.

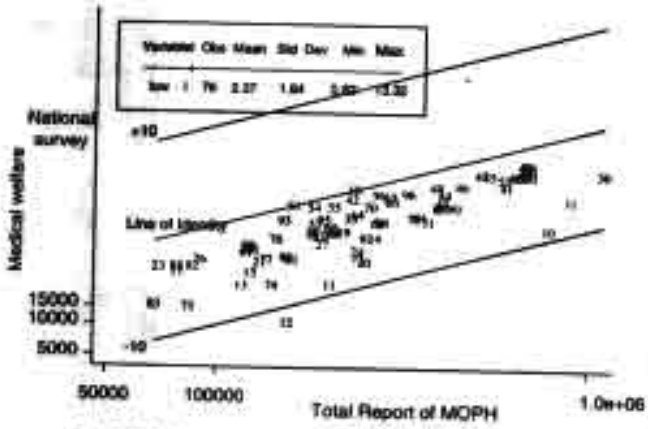

Fig 2–Validation of log of total insurance coverage of the medical welfare scheme.

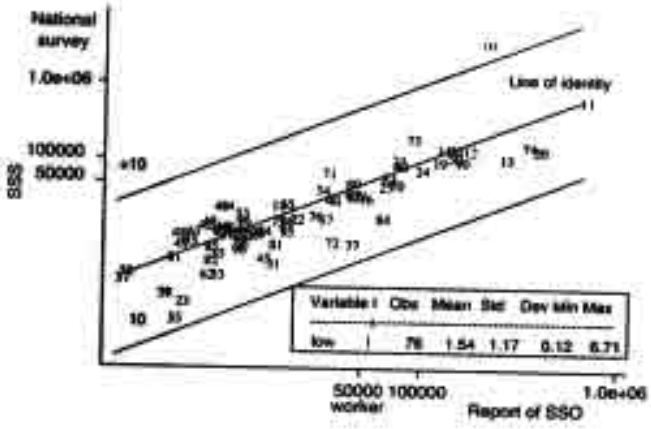

Fig 3–Validation of log of total insurance coverage of the social security scheme.

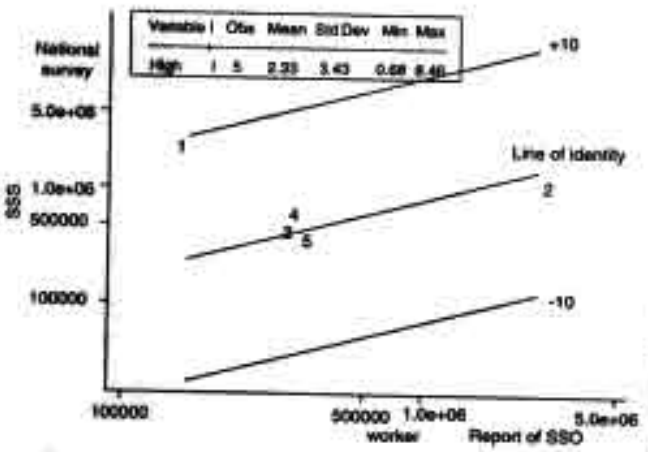

Fig 4–Validation of log of insurance coverage of the social security scheme by region.

Three scenarios of different per capitation rates were used. The lowest capitation rate (273 baht as for the medical welfare scheme in 2001) produced a discrepancy of 2.3 billion baht between the survey and the expected figures. If the capitation rate increased to 1,197 baht as agreed by the Bureau of Budget at the meeting chaired by the Prime Minister on 17 March 2001 (Ministry of Public Health, 2001), the discrepancy would be 9.9 billion baht. If the capitation rate was 1,500 baht as recommended by the Working Group of the Health Systems Research Institute (2001), the additional budget varied from 24.8 billion to 37.2 billion, or with the discrepancy of 12.5 billion baht.

Inaccuracies of the target population affected the financing of both health care providers and the government. If the expected data was used for universal health insurance implementation, it may create financial problem to the services facilities and hospitals, because there would be some degree of under-reporting leading to financial inadequacy. But if the survey data were used, it would be the great burden for the government to raise the subsidy. Therefore, it was important for the government to obtain more accurate data on the population coverage before implementing the universal health insurance policy. Moreover, it was as well important to justify the optimal level for per capitation rate that would bring about the most efficient resource use in order to meet the real health needs.

DISCUSSION

To consider the data validation of the medical welfare scheme in Fig 2, it was found that most of the insurance coverage distribution was below the identity line. It might be either the result of under-report of the national survey or over-report of the MOPH. It was more likely to be under-reported because the respondents who responded to the questionnaires did not know exactly what types of insurance their household members were entitled to. In addition, misclassification was very likely between the medical welfare and the

voluntary health card as both respondents and interviewer had little knowledge on the rapidly changing policy of the MOPH. The reason to support the over-reporting of MOPH system because the numbers of the coverage of the medical welfare were used for budget allocation of the scheme, therefore, most provinces tended to report the maximum number of the target group to maximize the budget allocation. While the process of issuing the welfare card was slow, therefore the reported data were higher and people who had received the welfare cards were lower than the target.

The pattern for the health card coverage was the opposite of the medical welfare scheme. It might be the effect of over-report of the national survey because of misclassification between the health card and the medical welfare card. In other way, it might be the under-report of the MOPH. But the under-report was unlikely because the process of health card issuance was checked by the report of the banking system. The transactions through the bank account were used for allocating budget subsidy. Therefore, the national survey was more likely to be over-reported.

Two reasons to explain why the routine report of social security insurance was very close to the survey were as follows. The routine data were derived from the pay role system. The contributions paid by employees, employers and the government were collected monthly to the social security fund. Furthermore, all social security members had to register with the main contractor for their entitlement, therefore the report of the SSO was more accurate and more reliable than the MOPH's medical and health card schemes.

When the medical welfare distribution was combined with the health card scheme, the pattern of the coverage shifted, and came closer to the identity line. It could be that the effect of misclassification between the health card and the medical welfare card had cancelled each other. The mean of the difference changed from 2.2 lower for the medical welfare and 4.9 higher for the health card to be 1.6 lower the identity line, very close to the social security scheme.

Within the medical welfare insurance, there were several sub-groups from age-related (children and the elderly), income-related (the low income), social characteristics (the veteran, community and religious leaders) and disability-related (the handicapped). If re-categorized the medical welfare into three main groups according to their age (0-12 years, 13-59 years and 60 years and over), children and the elderly were straightforward for their eligibility, therefore the disagreement of both information sources was narrow. The working age group produced the highest variation between the survey and report data. Issuance of the medical welfare card for the working age had to rely on income means testing, which was more difficult than calculating the age.

Comparing the distributions of medical welfare, and social security schemes by region and by province, the medical welfare by region produced a higher discrepancy but with the same directions as those of provincial distribution. However, the social security scheme produced results with different directions when analysed by province and by region. This was because the analysis by region gave equal weight to the 5 regions, while analysis by province gave equal weight for 76 provinces. So the result by region was biased in favor of Bangkok but not for the result by province.

Conclusions and recommendations

From the results of the data validation above, some conclusions could be drawn as follows:

- It is evident that there were considerable differences between the survey data of the National Statistical Office and the report data of the Ministry of Public Health and the Social Security Office.

- The differences varied according to the insurance types of which the medical welfare and voluntary health card had higher variations than the social security insurance.

- The national survey data had a tendency to be over-reported, on average 1.5 times over

the report data.

- Misclassification between medical welfare and voluntary health card led to the variation of the distributions in different age groups and regions of the country.

The followings were recommendations for the implementation of universal health coverage policy:

- It would be dangerous if the universal health coverage policy would be set up and implemented by using single source of data either the survey or the report data.

- It would be crucial that the data from various sources and be validated before finally used.

- It would be necessary to improve the data quality before using them for the implementation of universal coverage policy to reduce errors and weaknesses of the existing data.

- Routine data are a necessity for the proper monitoring system such as financial audit of the policy, however survey data are also helpful for confirmation of the reliability of the data.

Appendix

In 1999, the Health and Welfare survey of the National Statistical Office showed that the civil servant medical benefit scheme which was financed by taxation as a fringe benefit for government employees covered about 9% of the total population. The compulsory social security scheme for employees in formal private sectors covered about 7% of the total population. The MOPH had introduced the low income card scheme to cover the poor, the elderly, children under 12 years old, the handicapped, community and religious leaders about 23% of the total population. The voluntary health card scheme of the MOPH covered family who purchased the health card annually about 18% of the total population. Because 40% of the population were left uncovered, therefore the new government proposed the universal coverage policy. This policy aimed to cover all populations in informal sectors by consolidating previous MOPH's schemes (see Table).

Schemes before 2001	% of total population	From 2001 onwards
Civil servant medical benefit scheme	9	Same target
Social security scheme	7	Same target
Formal sector employees	16	Same
Low income card scheme	23	
Voluntary health card scheme	18	The new universal coverage scheme
Private health insurance	1	
Others	2	
Uncovered	40	
The informal sectors	84	
Grand total (61,704,581 pop)	100	Totally covered

Source: Analysis on the Health and Welfare Survey, 1999.

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Original Article

Effects of haemoglobin and serum ferritin on cognitive function in school children

Rassamee Sungthong[1] MD, Ladda Mo-suwan[2] MD and Virasakdi Chongsuvivatwong[1] MD, PhD

[1]*Epidemiology Unit, Faculty of Medicine, Prince of Songkla University Songkhla, Thailand*
[2]*Enterology and Nutrition Division, Department of Pediatrics, Prince of Songkla University, Songkhla, Thailand*

The association between iron deficiency anaemia and cognitive function impairment has been widely reported in young children, but whether the impairment is a result of iron deficiency per se or a combination of iron deficiency and anaemia, and how these conditions interact, is still questionable. Four hundred and twenty-seven school children from two schools in socioeconomically deprived communities were selected in southern Thailand. Iron status was determined by haemoglobin and serum ferritin concentrations. Cognitive function in this study was measured by IQ test and school performance, including Thai language and mathematics scores, using z-scores based on distributions within the same grade and school. Data on demography and socio-economic status were collected by questionnaire answered by the parents. Linear regression models were used to investigate the effect of anaemia and iron deficiency, reflected by haemoglobin and serum ferritin concentration, on cognitive function and school performance. We found that cognitive function increased with increased haemoglobin concentration in children with iron deficiency, but did not change with haemoglobin concentration in children with normal serum ferritin level. Children with iron deficiency anaemia had consistently the poorest cognitive function (IQ, 74.6 points; Thai language score, 0.3 SD below average; and mathematics score, 0.5 SD below average). Children with non-anaemic iron deficiency but with high haemoglobin levels had significantly high cognitive function (IQ, 86.5 points; Thai language score, 0.8 SD above average; and mathematics score, 1.1 SD above average). This study found a dose–response relationship between haemoglobin and cognitive function in children with iron deficiency, whereas no similar evidence was found in iron sufficient children.

Key words: cognitive function, educational achievement, Hat Yai, IQ, iron deficiency, iron status, school performance, Songkhla, Thailand.

Introduction

Iron deficiency and iron deficiency anaemia (IDA) are common in young children. Cognitive function impairment, the consequence of greatest concern, is well established in school children with late stage iron deficiency once anaemia is recognized,[1–5] but it is still controversial in non-anemic iron deficient children.[2,3,6–8] It has been suggested that tissue iron deficiency may develop early by means of a decrease in iron storage without anaemia that may have non-haematological consequences, for example, cognitive function or physical performance impairment.[6,7] However, previous studies have not demonstrated clearly whether the cognitive function impairment found in children with IDA is due to iron deficiency or a combination of iron deficiency and anaemic status, or how these two conditions interact.

The National Anemia Surveillance Program[9] showed that the prevalence of anaemia has been declining in Thailand. A careful re-evaluation of existing iron supplementation in school children is therefore needed. In this study the baseline data of an intervention study were analysed in order to elucidate the relationships between iron deficiency, reflected by serum ferritin (SF), and anaemia, reflected by haemoglobin (Hb), and their effects on cognitive function in school children. We attempted to separate the effect of iron storage from that of haemoglobin level.

Materials and methods

Study site

From the records of primary schools outside Hat Yai municipality, two primary schools were selected as our study site as they were considered to have a high risk of anaemia, comprised at least 150 students, was accessible by automobile and teachers were willing to co-operate in the study.

These two schools, located approximately 35 km from the research centre, had a mixture of Buddhist and Muslim

Correspondence address: Dr Rassamee Sungthong, Epidemiology Unit, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla 90110, Thailand.
Tel: +66 74 4511657; Fax: +66 74 212900
Email: sburapat@medicine.psu.ac.th
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students. Thai-Buddhists speak Thai whereas Thai-Muslims speak both the Thai and Melayu languages. Family incomes were derived mainly from selling plantation products, particularly the rubber latex. The area is free from malaria and no iron supplementation program had been implemented previously at this study site.

Study subjects

An invitation letter providing information about the research project and requesting consent was sent to the parents of children who were in the first to sixth grades. Only children with written informed parental consent were recruited for the study.

Cognitive function assessment

The cognitive function of each subject was measured using the Test of Nonverbal Intelligence (TONI II)[10] and school performance without knowing the child's iron status. TONI II is easy to administer in the field. It is a standardized and culturally fair test for measuring abstract and figural problem solving, a major aspect of intelligence, in 5–80 years-olds.[10,11] Its high test–retest reliability (R^2 = 0.86) and its high correlation (R^2 = 0.7) with a standard intelligence test (i.e., Wechsler's Intelligence Scale for Children (WISC)) in Thai children was its justification for use in this study.[12]

Each of three trained testers established a rapport with each child and demonstrated how to complete the TONI II (form A). Items are arranged in order of difficulty and each consists of one picture question and four or five available responses, but only one correct response. Each child began with the item indicated in the manual (depending on age) and continued until he/she made three incorrect responses in five consecutive items. Total raw scores were computed and then converted to the corresponding IQ using the table provided within the manual. School performance included the average Thai language and mathematics scores collected from the two latest examinations in the previous academic year.

Determination of iron status

Haemoglobin and SF were used to determine iron status from a single venipuncture. A 2 mL sample of blood was placed into an ethylenediaminetetraacetic acid (EDTA) prepared tube for Hb, and 3 mL was kept in a plastic sealed test tube at ambient temperature (approximately 25°C) for serum ferritin measurement. Within three hours, all blood samples were transferred to the laboratory at Songklanagarind Hospital.

Haemoglobin content was measured using an automated machine (Technicon H*1E™ system; Technicon, Tarrytown, NY, USA) using the cyanmethemoglobin method.[13] Serum ferritin concentration (SF) was assessed by the IMx® assay (Abbott Laboratories, Abbot Park, IL, USA) using the Microparticle Enzyme Immunoassay (MEIA) method.[14]

Collection of other independent variables

Demographic variables, including school, class, sex, age, ethnic group, number of siblings and child ordinal position, and socioeconomic variables, including parents' education in years, father's and mother's occupations (none, casual/farmer/trader, or government officer/private), family monthly income (≤ 5000 baht or > 5000 baht) were collected by a questionnaire answered by parents.

Body weight and height of children wearing school uniforms, without belts or shoes and with empty pockets, were measured using a beam balance Detecto scale and stadiometer (Detecto Scales, Brooklyn, NY, USA) to the nearest 0.1 kg and 0.5 cm, respectively. The weight-to-height ratio of each child was then compared with the weight-to-height data from the Nutrition Division, Ministry of Public Health, in 1996–97.[15] Using cut-off points at the 10th, 90th and 97th percentiles for weight-to-height, the children were classified as underweight (< 10th percentile), normal (10th – 90th percentile), overweight (> 90th – 97th percentile) and obese (> 97th percentile). Physical examination was performed by the first author to detect serious illness or infection.

Ethical consideration

This research was approved by the Ethical Review Committee of the Faculty of Medicine, Prince of Songkla University, Thailand.

Data analysis

Scatter plots were constructed between each cognitive function and Hb, broken down by SF into low SF group (≤ 20 µg/L) and normal SF group (SF > 20 µg/L).[16] On the horizontal axis, the points were grouped into three equal bands. The median values of each band were used to fit a cubic spline smoothing function curve.[17]

For modelling, Hb concentration was classified into three groups at the cut-off points of 11.5 and 12.5 g/dL. Mean IQ, Thai language score and mathematics score converted to z-scores, based on the distribution within the same grade and school were compared across each subgroup of Hb and SF, with adjustment for potential confounders. Test for trend was carried out to examine the dose–response relationship between Hb and cognitive function for each group of SF. All analyses were carried out using STATA statistical software version 6 (StataCorp, College Station, TX, USA).[18]

Results

Out of 427 eligible children, the ratio of male to female subjects was 1:1, the average age was 9.6 years and the percentage of underweight and normal weight were 15 and 80%, respectively. Two-thirds of the children were Muslim and slightly more than one half had three siblings or more. Almost all parents were farmers whose formal education averaged 6 years and whose monthly income was less than 5000 baht or US$125.00, compared to the Thai national average of 12 729 baht or $US318.00, reported by the Household Socioeconomic Survey, National Statistical Office. None of the children had overt manifestation of thalassemia disease.

Of the total number of subjects, one-eighth had SF ≤ 20 µg/L and 22% were classified as anaemic (Hb < 11.5 g/dL for 5–11 years old; Hb < 12.0 g/dL for 12–13 years old).[19] The prevalence of IDA in these subjects

was 4.2% of all of the children and 19.4% among the anaemic children. A screening test showed that two-thirds were positive for thalassemia traits.

As seen in Table 1, age, height, parents' education and family monthly income were associated significantly with IQ. Sex, parents' education and family monthly income were associated with Thai language scores whereas only sex and parents' education were associated with mathematics scores. The overall average IQ was 78 ± 12 points (mean ± SD); higher IQ scores were found among children who were older and taller and whose parents had higher education levels and whose families had higher monthly incomes. Better school performance was found among children who were female and whose parents had a higher level education.

Figure 1a,c,e shows that IQ, Thai language and mathematics scores increased with increasing Hb in the low SF group with a significant dose–response relationship, while these cognitive function scores barely changed with Hb concentration in the normal SF group (Fig. 1b,d,f). The group with the highest scores were children with high Hb but low SF. This pattern was verified after adjustment for potential confounders (Table 2).

Using a group of exclusively SF > 20 μg/L subjects as the reference, significantly poorer mathematics score were found in children with low Hb and low SF concentrations, whereas significantly higher of IQ, Thai language and mathematics scores were found in children with high Hb but low SF.

Discussion

There was a significant different pattern of association between cognitive function and Hb in the different iron status groups, as reflected by SF level. IQ, Thai language scores and mathematics scores in children with low SF increased with increasing of Hb with a significant dose–response relationship. In contrast, these measures of cognitive function in children with SF above 20 μg/L was not affected by Hb concentration. Unexpectedly, the highest scores for cognitive

Table 1. Characteristics of children in the study

Variables	n	IQ (point)	Thai language (Z-score)	Mathematics (Z-score)
Categorical variables†				
Sex	427			
Male	199	79 ± 11	−0.4 ± 1.0	−0.2 ± 1.0
Female	228	78 ± 13	0.4 ± 1.0¶	0.2 ± 1.0¶
Weight for height	427			
Underweight	66	78 ± 12	−0.01 ± 1.0	−0.03 ± 1.1
Normal	341	78 ± 12	0.03 ± 1.0	0.02 ± 1.0
Overweight	11	79 ± 8	0.2 ± 1.2	0.24 ± 1.1
Obese	9	77 ± 11	−0.1 ± 0.8	−0.3 ± 0.8
Ethnic group	427			
Thai-Buddhist	133	78 ± 11	−0.01 ± 1.0	−0.1 ± 0.9
Thai-Muslim	294	79 ± 13	0.04 ± 1.0	0.04 ± 1.0
Child ordinal position	426			
≤3	308	78 ± 11	−0.1 ± 1.0	−0.04 ± 1.0
>3	118	79 ± 14	0.2 ± 1.0	0.2 ± 1.0
Siblings	426			
≤3	203	79 ± 12	0.1 ± 1.0	0.1 ± 1.0
>3	223	78 ± 12	−0.02 ± 1.0	−0.1 ± 1.0
Mother's occupation	424			
None	14	81 ± 13	0.3 ± 1.0	0.6 ± 1.0
Casual/farmer/seller	401	78 ± 12	0.01 ± 1.0	−0.01 ± 1.0
Government/officer/private	9	80 ± 10	0.5 ± 1.0	0.6 ± 1.0
Father's occupation	423			
None	4	72 ± 5	−1.0 ± 1.0	0.2 ± 1.0
Casual/farmer/seller	393	78 ± 12	−0.02 ± 1.0	−0.03 ± 1.0
Government/officer/private	26	84 ± 9	0.6 ± 1.0	1.0 ± 1.0
Family monthly income§	418			
≤5000 baht	338	78 ± 12¶	−0.03 ± 1.0¶	−0.03 ± 1.0
>5000 baht	80	82 ± 12	0.2 ± 1.0	0.2 ± 1.0
Continuous variables‡				
Age (years)	427	0.8 ± 0.3¶	−0.1 ± 0.03	−0.05 ± 0.03
Weight (kg)	427	0.2 ± 0.1	−0.004 ± 0.01	−0.01 ± 0.01
Height (cm)	427	0.2 ± 0.1¶	0.001 ± 0.01	−0.001 ± 0.01
Parents' education (years)	418	0.9 ± 0.2¶	0.1 ± 0.2¶	0.1 ± 0.02¶

†Mean ± SD; ‡Coefficient ± SE; §Family monthly income, 1 baht = US$0.025 at the time of data collection; ¶Statistically significant association ($P < 0.05$).

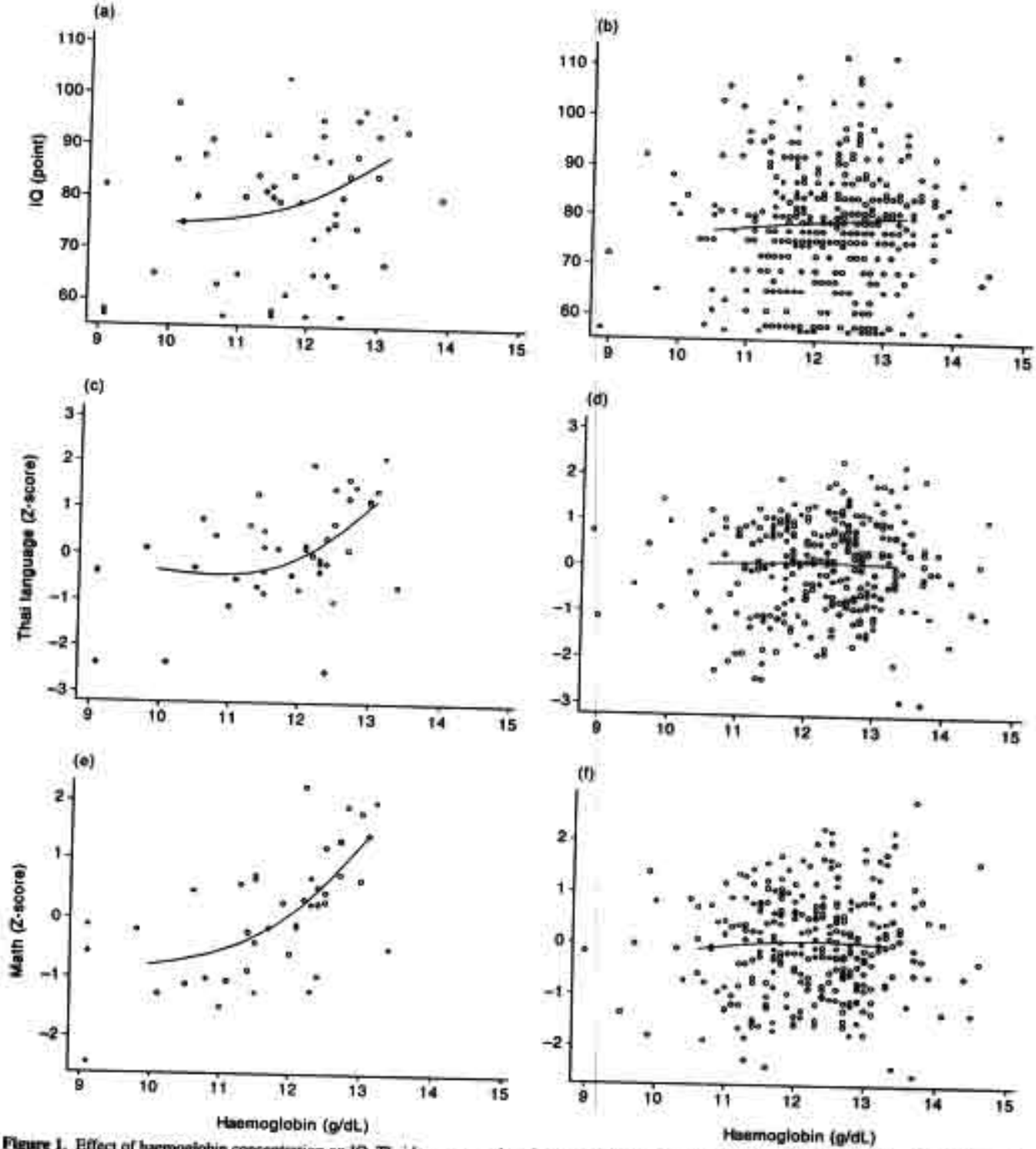

Figure 1. Effect of haemoglobin concentration on IQ, Thai language and mathematics scores in children with (a, c, e) low serum ferritin (≤ 20 μg/L) and (b, d, f) normal serum ferritin (> 20 μg/L) concentrations.

function were in children with high Hb but low SF, whereas the lowest levels were found in those with both low Hb and low SF.

High prevalence of anaemia with relatively low prevalence of iron deficiency (SF ≤ 20 μg/L) suggests that IDA might not be the most common cause of anaemia in this area. Linpisarn *et al.*[20] also found that only 19% of anaemia cases in preschool-age children was IDA, and no IDA was found among anaemic school-age children in Northern Thailand. An SF concentration of ≤ 20 μg/L may not be a gold standard for iron deficiency as it can be elevated with infection or inflammation.[21,22] However, we did not find such infection

Table 2. Mean ± SE of IQ, Thai language and mathematics scores by serum ferritin and haemoglobin categories

Serum ferritin (μg/L)	Hb (g/dL)			P
	<11.5 (n)	11.5–12.5 (n)	>12.5 (n)	
Adjusted mean IQ points†				
≤20	75.0 ± 2.6 (20)	76.2 ± 2.6 (20)	86.5 ± 3.6* (11)	0.03
>20	78.5 ± 1.3 (80)	78.2 ± 1.0 (149)	78.7 ± 1.0 (135)	0.41
Adjusted mean Thai language score (z-score)‡				
≤20	−0.3 ± 0.2 (17)	−0.1 ± 0.2 (15)	0.8 ± 0.3* (9)	<0.01
>20	−0.1 ± 0.1 (64)	0.1 ± 0.1 (119)	0.03 ± 0.1 (125)	0.57
Adjusted mean Mathematics score (z-score)				
≤20	−0.5 ± 0.2* (17)	0.2 ± 0.2 (15)	1.1 ± 0.3* (9)	<0.01
>20	−0.1 ± 0.1 (64)	0.1 ± 0.1 (119)	−0.01 ± 0.1 (125)	0.67

*Significantly different from serum ferritin concentration > 20 μg/L; †Adjusted for family monthly income and parents' education; ‡Adjusted for sex and parents' education. Statistical significance (test for trend): *P*-values < 0.05 were considered statistically significant.

among our subjects. Nopparatana *et al.* found that 24 and 30% of pregnant women and their spouses who attended the antenatal clinic at the teaching hospital near the study area in 1994–95 had thalassemia traits.[23] In addition, β-thalassemia trait, a local common variant, can protect the carrier from iron deficiency.[24] Thus, the thalassemia trait may be an important contributor to non-iron deficiency anaemia. However, due to budget limitations, Hb typing was not undertaken in this study.

Average IQ on figural problem solving, measured by TONI II in this study (mean, 78; SD, 12 point), was relatively low compared with the average IQ in Southern rural Thai children reported by The National Health Survey (mean, 92; SD, 13 point) using similar measurements.[12] This may be influenced by socioeconomic deprivation in the study area.

Although cognitive function tended to be lower in children with iron deficiency anaemia, only mathematics scores were significantly lower than in the normal SF group. Previous studies reported both significantly and non-significantly different lower IQ scores in children with IDA.[2–4,25,26] The variability may be due to using different measurements, in which different aspects of IQ may be assessed. In contrast to our study, Pollitt *et al.*[2] found that Thai language scores were significantly lower while mathematics scores showed no significant difference in IDA children. This inconsistent finding may be explained by differences in assessment systems at different schools. Owing to the use of different measurements of IQ and assessments of school achievement, we may conclude only that IDA has a significant adverse effect at least in some areas of cognitive function.

The adverse effect of iron deficiency on cognitive function may be explained by diminished synthesis, packaging, uptake and degradation of neurotransmitters.[27] The most prominent feature of iron deficiency on cognitive function is the significant and selective diminution of central dopamine neurotransmission.[28] Electroencephalogram power spectrum also showed a slower activity in children with iron deficiency than in iron replete children, suggesting a developmental lag or central nervous system dysfunction among the former group.[29]

Most studies have reported that children with iron depletion did not differ significantly in cognitive function from their peers,[2,3,8,30] whereas a few studies have reported significantly poorer cognitive function.[6,7] Our study unexpectedly found that children with iron depletion accompanying high Hb had the best cognitive function. When Hb is high enough, increasing iron levels may have some adverse effect on cognitive function. Studies in rats and mice reveal that iron overload may cause oxidative stress and has been related to carcinogenesis of the oesophagus and liver.[31–35] In children, iron supplementation does not always result in improvement of cognition.[2,25] This evidence and the findings of our study suggest a need to carefully review the strategy of the iron supplementation program in Thailand.

Bias, chance and confounders can distort the results of epidemiological studies. Measurement bias in this study was overcome by blinding and a standardized process. The investigation of Hb and SF in this study was performed in a standard laboratory using standardized techniques (coefficient of variation = 0.5–5.3%). Low SF has 95–100% specificity in determining low iron stores.[21,36] This study allowed only a 5% chance of type I error, which is acceptably low, and we also found similar associations in different cognitive function tests. It is therefore unlikely to happen by chance. Potential confounders in this study (including socioeconomic status) were adjusted for.

Although bias was minimised and confounders were adjusted for, these results should be interpreted with caution because of the cross-sectional nature of the study. Further randomised control trials should investigate whether an increase in Hb can increase cognitive function in children with iron depletion.

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Taking a medical history and using a colour scale during clinical examination of pallor improves detection of anaemia

Mahbub-E-Elahi K. Chowdhury[1], Virasakdi Chongsuvivatwong[2], Alan F. Geater[2], Halida H. Akhter[1] and Than Winn[2]

1 *Bangladesh Institute of Research for Promotion of Essential and Reproductive Health and Technologies (BIRPERHT), Dhaka, Bangladesh*

2 *Epidemiology Unit, Faculty of Medicine, Prince of Songkla University, Hat-Yai, Thailand*

Summary We developed a colour tint scale to use as an aid in the clinical assessment of anaemia by measuring conjunctival pallor. The objectives of this study were to evaluate the accuracy and agreement among observers in detecting anaemia in three sequential phases with incremental information using clinical pallor of different anatomical sites, subsequently adding subjects' medical history for physical symptoms and the colour scale. After training in the application of these three sequential assessments, 12 primary health workers were assigned to independently examine 198 anaemic and 254 non-anaemic pregnant women while blind to the true anaemic status. Their assessments in each phase were then compared with the anaemic status based on haemoglobin level, measured using HemoCue, taken as the gold standard, to determine sensitivity and specificity, and agreements among observers in detecting anaemia were calculated. In the three sequential phases of assessment the sensitivities were 73.8, 78.3, 82.9% and specificities 76.0, 84.7 and 90.9%, respectively. In each subsequent step, the improvements in both the sensitivity and specificity were statistically significant [$P(\chi^2_{McNemar}) < 0.01$]. Kappa statistics for agreement among 12 observers for assessing anaemia in the sequential phases were 0.50, 0.71 and 0.82, respectively. The Spearman rank correlation coefficient between haemoglobin level and the colour scale reading was 0.68 ($P < 0.001$). Taking medical history and incorporating a simple colour tint scale with examination of pallor improved the sensitivity, specificity and agreement for detection of anaemia by health workers.

keywords validation, anaemia, colour scale, medical history, pallor, health worker, Bangladesh

correspondence Mahbub-E-Elahi K. Chowdhury, Epidemiology Unit, Faculty of Medicine, Prince of Songkla University (PSU), Hat-Yai 90110, Thailand. E-mail: birperht@citechco.net

Introduction

High prevalence of anaemia during pregnancy (40–60%) is a major problem in many developing countries (WHO 1992). To assist diagnosis of anaemia in rural areas where laboratory facilities are limited, we need a test which is cheap, convenient to use, less dependent on equipment or reagents, reasonably accurate and which requires no invasive procedure. Among simple reliable methods the copper sulphate method (Pistorius *et al.* 1996) and the Lovibond-undiluted method (van Lerberghe *et al.* 1983) have been recommended by several studies for rural settings. However, both depend either on standard solutions or equipment and often are difficult to use. The WHO haemoglobin colour scale, which requires no reagents, has been found to be unreliable in the field setting (van Lerberghe *et al.* 1983). After eliminating the possible sources of error of the haemoglobin scale, Stott and Lewis (1995) developed a new colour scale that proved reliable in laboratory conditions, but in the field had low specificity (47%) at Hb < = 11 g/dl (Van den Broek *et al.* 1999). All of the above methods require either finger blood pricking or venipuncture, which also may be harmful when the supply of instruments and sterilization are not reliable.

Previous studies have shown that the clinical pallor of an individual anatomical site has either low sensitivity or low specificity for diagnosis of anaemia (Nardone *et al.* 1990; Stoltzfus *et al.* 1999). Using the presence of pallor at several sites with an 'or' option could improve the sensitivity; however, the results are still poor (Gjorup *et al.* 1986; Nardone *et al.* 1990). Strobach *et al.* (1988), after measuring the conjunctival pallor with a colour tint scale, found a high correlation (Spearman rank correlation coefficient = 0.84) between the colour scale reading and blood haemoglobin level. However, in that study the observers were not blinded to subjects' haemoglobin level and the authors did not assess how much improvement they could achieve in detecting anaemia after use of the colour scale. These studies have demonstrated that sensitivity for clinical diagnosis of severe anaemia (Hb < 7 g/dl) is high, although traded-off with a high proportion of false positives. However, as the majority of anaemic women have moderate (Hb = 7–10 g/dl) or mild (Hb > 10 & < 11 g/dl) anaemia (WHO 1993), there is a need to improve the sensitivity in these two groups while maintaining an acceptable specificity.

Beside the presence of pallor, many other physical symptoms result from anaemia, among which fatigue, dizziness and palpitation are common. Decreased work capacity and reduced productivity because of anaemia also have been reported by several studies (Scholz *et al.* 1997; Chowdhury *et al.* 2000). To our knowledge no study has explored the usefulness of these physical symptoms in improving the accuracy of diagnosis of anaemia.

Using the simple PC colour technology we developed a new colour tint scale to evaluate conjunctival pallor for clinical assessment of anaemia for use by health workers. We hypothesized that the incorporation of this colour scale and medical history for symptoms related to anaemia with the physical examination of pallor could improve the accuracy and agreement among observers in detecting anaemia. We also estimated the correlation of this colour scale reading with actual blood haemoglobin level and agreement among observers in reading the scale.

Materials and methods

Study design and setting

We evaluated the accuracy and agreement among trained health workers in clinical diagnosis of anaemia in three sequential phases of assessment with incremental information by (1) examining clinical pallor of different anatomical sites, (2) adding medical history of physical symptoms related to anaemia and (3) incorporating the colour scale for assessing conjunctival pallor. During assessment the health workers were blinded to the true haemoglobin level of each subject. Their assessments were subsequently compared with the subject's true anaemia status according to measured haemoglobin level. Prior to this evaluation study, the health workers were trained to clinically assess anaemia over a 4-day training session. The study took place among outpatient pregnant women at two urban health care facilities in Dhaka, Bangladesh, which served the surrounding middle and lower middle class communities, where prevalence of anaemia among pregnant women was 53–60% (Jahan & Hossain 1998). The study protocol was approved by the technical subcommittee and the human subjects subcommittee of the Bangladesh Institute of Research for Promotion of Essential and Reproductive Health & Technologies (BIRPERHT).

Development of colour scale

Our colour scale contained 13 ordinal shades of pink coded 1–13 with an increment of red tint from nearly paper white to deep pink. We made this colour scale by mixing specific proportions of three basic colours – red, green and blue – using the custom colour feature of Microsoft Power Point 97. For shade 01 of the colour scale we mixed 255 units of red with 245 units of each of green and blue. For each of the subsequent shades we kept red fixed at 255 units and subtracted 10 units of each of green and blue from the preceding shade. As the proportion of green and blue decreased the red tinge on the colour scale increased gradually. We printed out the colour scale on white photo paper using an Epson Stylus Photo 700 Inkjet printer at a resolution of 1440 × 720 dpi. We chose this colour scale among eight different scales, with variant shades of red tint, upon agreement among three senior medical students by matching with the natural colour tint of conjunctiva among 20 patients with different haemoglobin levels at the Hematology Department of Songklanagarind Hospital, Thailand.

Gold standard

The measurement of haemoglobin concentration from finger-tip blood using HemoCue (HemoCue AB, Angelholm, Sweden), which employs the modified azide methaemoglobin method of Vanzetti (1966), was taken as gold standard in our study. For calibration of HemoCue we conducted a small pilot study among 20 outpatients at the Hematology Department of Songklanagarind Hospital in Thailand, comparing the results of HemoCue with those of a Coulter Counter. Pearson's correlation coefficient was 0.98. The mean value of difference (Coulter Counter readings – HemoCue readings) was –0.21 g/dl with standard

deviation (SD) of 0.64 g/dl. An experienced laboratory technician collected blood and operated HemoCue.

Phases of clinical assessment

After each of the three phases of clinical assessment each of the observers made her own judgement on the subject's anaemia status in four categories, viz. severe, moderate, mild and non-anaemia. In phase I, each observer independently examined every subject for presence or absence of pallor on nine different anatomical sites, viz. nail-beds, nail-bed blanching, palm, palmar creases, face, lips, tongue, oral mucosa and conjunctiva. In Phase II, in addition to knowledge of clinical pallor, the assessment was based on the subject's medical history which was recorded by a nurse by asking questions of current experience of fatigue, dizziness, palpitation, physical constraints in performing usual daily activities and the burden of workload. The interviewer was blinded from the haemoglobin level and the interview was conducted in a room separately from the observers. The interview results were disclosed to the observers after completion of their assessments in Phase I. In Phase III, the observers assessed the conjunctival pallor by selecting the particular shade of the colour tint that most closely matched the palpable conjunctivae after placing the colour scale adjacent to the everted lower eyelid. The examinations were held in a spacious room at the selected facilities in broad daylight with as much natural light as possible. Examinations were conducted without knowledge of the true haemoglobin level of subjects except during the latter part of the training program. Each observer used a separate observation checklist for every subject.

Selection and training of the observers

We recruited and trained 12 observers, four government and eight non-government organization primary health care providers in Bangladesh. On the first day of a 4-day hands-on training, M-E-E. K. Chowdhury, who was present throughout the study period, familiarized observers with the aetiology and management of anaemia. On the following 3 days each of the observers examined 60 pregnant women from three trimesters covering a range of haemoglobin levels. During training each observer clinically examined every subject in two rounds. In the first round, without having any knowledge of the actual haemoglobin level, the observers independently judged anaemia of one subject through the three sequential phases of assessment. In the second round, the true haemoglobin level of the subject was revealed and the observers were allowed to reexamine the patient through the three sequential phases and reassess their judgement. Through this process the observers could correlate the pallor of different anatomical sites, the physical symptoms and the colour scale with the actual haemoglobin level.

Sample sizes

We estimated sample sizes for anaemic and non-anaemic subjects for each trimester separately using the sample size formula for precision of estimation of proportion. Using the commonly taken cut-off of Hb < 11 g/dl (WHO 1972) for anaemic subjects, we considered the desired sensitivity in first, second and third trimesters as 0.80, 0.85 and 0.80, respectively, and for the non-anaemic the desired specificity as 0.75, 0.80 and 0.75, respectively. Seeking 10% absolute precision with 95% CI for each estimate, the minimum required numbers of anaemic subjects for first, second and third trimesters were 61, 49 and 61 and those for non-anaemics were 72, 61 and 72, respectively.

Subject selection

Pregnant women attending each selected facility were recruited consecutively within each trimester. Gestational age was calculated from the date of last menstrual period (LMP) recorded during monthly visits. The exclusion criteria were: unable to recall the LMP date, unwilling to provide fingertip blood, had inflammation in eyes, had jaundice diagnosed symptomatically by yellow eyes or attending the facility with haemorrhage. A nurse screened the subjects for eligibility criteria and asked the patients to participate. Only women who provided free and informed written consent were finally recruited. Every subject was examined independently by each of the observers for clinical detection of anaemia through the three sequential phases of assessment.

Statistical analysis

In analysis we regrouped the clinical assessment of anaemia status by the observers into two levels, anaemic and non-anaemic, where the anaemic group was formed by combining three subgroups of anaemia, viz. severe, moderate and mild. As each subject was examined by 12 observers, we employed the generalized estimating equations approach to logistic regression, which takes into account the repeated measures, to estimate sensitivity, specificity and 95% CI. For agreement among 12 observers in detecting anaemia at each phase of clinical assessment we used kappa for multiple observers (Fleiss 1981). For testing the hypothesis that incremental introduction of methods improved the sensitivity and specificity we divided the dataset into anaemic and non-anaemic groups according to actual haemoglobin level and in each group analysed the discordant pairs between two

sequential phases of assessment using McNemar's χ^2 with 1 d.f. for paired sample. To compare the improvement in sensitivity in subsequent phases of assessment between mildly and moderately anaemic subgroups, we used the Z-test to compare the McNemar χ^2-values. We used the Spearman rank correlation coefficient (Conover 1980) to summarize the relationship between actual haemoglobin level of the subjects and the colour scale reading. For agreement in reading the colour scale we used weighted kappa between pairs of observers. Weighted kappa was used in order to accommodate different degrees of disagreement of reading the ordinal colour scale by the observers. We applied a weight of 1 for perfect agreement, 0.5 for disagreement of one unit and 0 otherwise. Stata Software 6.0 (Statacorp, 1999, Stata Statistical Software: release 6.0, College Station, Texas, USA) was used in analysis.

Results

In the first, second and third trimester we included 36, 101, 61 anaemic and 90, 86, and 78 non-anaemic subjects, respectively. The smaller than planned number of anaemic subjects in the first trimester theoretically reduced our planned precision from 10% to 13% in that group. We excluded five subjects for an eye inflammation, three diagnosed for jaundice and two for unwillingness to have their finger pricked. Twelve observers made a total of 5165 independent assessments for anaemia among 452 subjects. The maximum number of subjects examined by an observer was 452 and the minimum was 343.

Characteristics of the subjects

The mean age of all the subjects was 23.2 years. The mean haemoglobin level of 198 anaemic subjects was 10.0 g/dl (range = 7.7–10.9 g/dl) and that of 254 non-anaemic subjects was 12.1 g/dl (range = 11.0–15.0 g/dl). Of the anaemic subjects 45.4% were moderately and 54.6% were mildly anaemic.

Improvements in sensitivity, specificity and agreements

Sensitivities, specificities and agreements improved consistently over the three sequential phases of clinical assessment based on pallor, medical history and the colour scale in each category of anaemia as seen in Table 1. Details of tabulation for statistical test of significance are shown in Table 2, where the numbers in the cells are the numbers of matched pair observations.

At each phase of clinical assessment the observers could detect a higher proportion of anaemia among the moderate anaemic subgroup than among the mild anaemic subgroup (Table 1). Comparison of these improvements in sensitivity in subsequent phases of assessment between moderately and mildly anaemic subgroups revealed no significant difference in the improvements from phase I to II, but a significantly greater improvement from phase II to III in mildly anaemic subjects [$P(z) < 0.05$].

Association of anaemia status with physical symptoms

Among the anaemic subjects fatigue, dizziness and palpitation were reported by 90.4, 31.8 and 28.8%, respectively, as compared with 52.4, 13.0 and 4.7% among the non-anaemic. Each of these symptoms was significantly associated with anaemic status [$P(\chi^2_{1df}) < 0.001$]. Fifty per cent of the anaemic women said they had constraints in daily activities compared with less than one in 10 (9.3%) among non-anaemic women; this relationship remained

	(I) Clinical pallor	(II) I + Medical history	(III) II + Colour scale
Sensitivity percentage (95% CI)			
Anaemia Hb < 11 g/dl	73.8 (71.4–76.1)	78.3 (75.8–80.6)	82.9 (81.3–84.4)
Moderate anaemia Hb = 7–10 g/dl	83.3 (80.7–85.6)	90.8 (88.9–92.4)	93.0 (91.2–94.4)
Mild anaemia Hb > 10 & < 11 g/dl	62.8 (59.6–66.0)	67.7 (64.3–70.9)	74.6 (72.1–76.9)
Specificity percentage (95% CI)			
Non-anaemic Hb > = 11 g/gl	76.0 (73.9–78.0)	84.7 (82.8–86.4)	90.9 (89.8–91.9)
Kappa	0.50	0.71	0.82

Table 1 Sensitivity, specificity with 95% CI and agreement (kappa) for detecting anaemia at three sequential phases of assessment using clinical pallor, medical history and the colour scale

Table 2 Matched pair analysis results for test of significance for improvement in diagnosing true anaemics (sensitivity) and true non-anaemics (specificity), from (a) Phase I to Phase II and (b) Phase II to Phase III

a. Improvement from Phase I* to Phase II†

	True anaemics		True non-anaemics	
	Dx in Phase II		Dx in Phase II	
Dx in Phase I	Anaemic	Non-anaemic	Anaemic	Non-anaemic
Anaemic	1466	125	310	392
Non-anaemic	293	367	140	2072
P (McNemar χ^2)	< 0.01		< 0.01	

b. Improvement from Phase II† to Phase III‡

	True anaemics		True non-anaemics	
	Dx in Phase III		Dx in Phase III	
Dx in Phase II	Anaemic	Non-anaemic	Anaemic	Non-anaemic
Anaemic	1701	58	207	243
Non-anaemic	166	326	58	2406
P (McNemar χ^2)	< 0.01		< 0.01	

* Dx based on clinical pallor; †Dx based on clinical pallor and medical history; ‡Dx based on clinical pallor, medical history and color scale

significant [$P(\chi^2_{1df}) < 0.001$] after controlling for burden of daily household activities.

Correlation between Hb level and colour scale reading

The Spearman rank correlation coefficient between haemoglobin level and the colour scale reading for conjunctival pallor was 0.68 ($P < 0.001$). For haemoglobin levels < 11 g/dl most assessors had colour scale readings of 9 or below and for Hb > = 11 g/dl most read 10 or above (Table 3).

Agreement among observers for reading the colour scale

Weighted kappa between pairs of observers for agreement in reading the ordinal colour scale ranged between 0.46 and 0.83. For 52 of 66 possible pairs among 12 observers this kappa value lay between 0.61 and 0.80.

Discussion

In this study, augmenting clinical assessment of pallor successively with medical history and the colour scale improved both the sensitivity and specificity in detecting anaemia among pregnant women. The agreement among observers in assessing anaemia also improved successively. Both the correlation of the colour scale measurements with the actual haemoglobin concentration and the agreement among observers for reading the scale were moderately high.

Examining pallor at nine anatomical sites for detection of anaemia, our observers achieved a sensitivity of 74% and a specificity of 76% among pregnant women, which are higher than those reported by Nardone *et al.* (1990) of 65% sensitivity and 71% specificity for the presence of pallor at any one of conjunctiva, face or palm among older hospitalized whites. The improved accuracy in our study

Table 3 Percentage distribution of ordinal colour scale reading among pregnant women with various levels of haemoglobin

	Ordinal colour scale reading						
Hb (g/dl)	*n*	≤ 6	7	8	9	10	≥ 11
≤ 9.9	884	28.1	42.1	16.0	7.0	5.0	1.9
10.0–10.9	1366	0.8	13.3	36.0	25.6	22.2	2.1
11.0–11.9	1444	0.9	1.0	5.8	19.5	62.3	10.5
12.0–12.9	906	0.8	1.6	4.0	12.0	55.7	25.9
≥ 13	562	–	–	4.3	10.1	52.7	32.9

may be a result of the inclusion of more anatomical sites and an overall judgement of anaemia status based on examination of different sites.

Combining the presence of physical symptoms from medical history with the results of examination of pallor improved the sensitivity to 78% and specificity to 85%. In general, symptoms of morbidities reported by patients during history taking are as valuable as those noted from examinations of professionals (DeGowin 1994). Incorporating medical history also augmented agreement among observers in detecting anaemia. Using the printed colour scale in assessing conjunctival pallor appeared to add an objective element in clinical detection of anaemia that helped further improve both sensitivity and specificity to 83 and 91%, respectively. The colour scale was also useful in raising agreement among observers. An important point to note is that in each subsequent phase of clinical assessment relatively greater improvement occurred in specificity than in sensitivity. This reflects the improved ability of each successive phase to correctly diagnose non-anaemic subjects who were inaccurately diagnosed in the preceding phase of assessment.

In our study, at each phase of clinical assessment the observers could better detect moderate anaemia than mild anaemia, which confirms other study findings (Strobach *et al.* 1988; Stoltzfus *et al.* 1999) that clinical examination is more sensitive in identifying severe or moderate anaemia than mild anaemia. However, we could also demonstrate that incorporating the colour scale gave a relatively greater improvement in identifying mild anaemia than moderate anaemia compared with assessment based on pallor and medical history together. This finding may have a public health implication of using our colour scale for its ability in detecting anaemia at early stages when timely treatment may prevent further reduction of haemoglobin level.

The production of our colour tint scale is simple, inexpensive and, after lamination, convenient to use in the field. This colour scale can be reproduced locally at a health facility with a personal computer and a photo-quality colour printer and thus is less dependent on a central supply. One of the difficulties that may arise in the development of this colour scale is that there may be a variation in printed output depending on the type of printer and its colour technology. Further studies should be carried out to investigate the extent of such differences and the effect of different colour scales on sensitivity and specificity. For the above reasons, we recommend that every time upon arrival of a new batch of colour scales, training of the health workers should take place for 'calibration' of the new scale in the community population. Standardized mass production may simplify the application of the colour scale, even though this would mean some dependence on a central supply. Because of the associated problem of fading of the printed colours in the course of time, especially when used in the field, the user should carefully protect the scale from direct sunlight. Moreover, regular replacement of scales may be required.

We selected anaemic and non-anaemic women in all three trimesters and thus covered a full span of gestational age for validation of clinical diagnosis of anaemia. The proportion of excluded subjects was low (about 2%) and they were distributed across all three trimesters. We included a large number of observers for clinical assessment of every subject whereby the likelihood of observer bias was reduced. Examinations performed by paramedics who work in the field is also an advantage in that these results may be applicable to the setting of Bangladesh. On the other hand, in our study the observers performed the test having fresh knowledge immediately after training, which might have improved the results. In real situations the accuracy of clinical assessment by the paramedics may decrease over time, especially in the absence of regular examination of patients; thus, occasional training may be necessary to maintain their level of skills.

The implication of this study is that physical symptoms are useful in improving the accuracy of diagnosis of anaemia and should be included in the training program of the health workers. The colour tint can also improve the accuracy although training in its use will be required. Assimilating this training with the refresher-training course of the health workers may help implement our method of clinical diagnosis of anaemia along with the existing health care program. In countries where resources are limited, this simple technique may provide an effective means of diagnosis of anaemia particularly suited to use in the field.

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Has directly observed treatment improved outcomes for patients with tuberculosis in southern Thailand?

Petchawan Pungrassami[1], Søren P. Johnsen[2], Virasakdi Chongsuvivatwong[3] and Jørn Olsen[4]

1 *Zonal Tuberculosis Centre, Yala, Thailand*
2 *Department of Clinical Epidemiology, Aarhus University Hospital and Aalborg Hospital, Aarhus, Denmark*
3 *Epidemiology Unit, Faculty of Medicine, Prince of Songkla University, Hatyai, Songkhla, Thailand*
4 *The Danish Epidemiology Science Centre, University of Aarhus, Aarhus, Denmark*

Summary

OBJECTIVE To validate the practice of directly observed treatment (DOT) and evaluate its effect on treatment outcomes.

METHODS This follow-up study conducted in 24 districts in southern Thailand included 411 new, smear-positive, pulmonary tuberculosis (TB) patients who started treatment between February and September 1999. Patients and/or their observers were interviewed about their actual DOT practice during the first 2 months of treatment. Treatment outcomes were evaluated at the end of the second month and at the end of treatment.

RESULTS Of 411 patients, 379 were assigned to DOT but only 68 practised strict DOT for every dose during the first 2 months. Adjusted odds ratios (ORs) for 'no sputum conversion' and 'unsuccessful treatment' were 1.1 (95% CI 0.6–2.1) and 1.3 (95% CI 0.6–2.8), respectively, for those who practised strict DOT *vs.* the rest.

CONCLUSIONS Actual practice of DOT was quite different from what was intended at the assignment. Practice of strict DOT during the first 2 months was not associated with sputum conversion or treatment success in this study area.

keywords tuberculosis, directly observed treatment, compliance, treatment outcome, Thailand

correspondence Petchawan Pungrassami, Zonal Tuberculosis Centre 12, Amphur Muang, Yala 95000, Thailand. E-mail: ppetch@cscoms.com

Introduction

Thailand is among the 23 countries which host 80% of the estimated incident cases of tuberculosis (TB) in the world (World Health Organization 2001a), and Thailand is among the 10 countries with the highest prevalence of primary multidrug resistance (The WHO/IUATLD Global Project 1997). The World Health Organization (WHO) reviewed Thailand's National TB Programme in 1995 and found low cure rates of 17–68% (Ministry of Public Health 1995). WHO (1999) thus recommended a Directly Observed Treatment, Short-course (DOTS) strategy, which involves the following five elements: (1) government commitment, (2) case detection by sputum smear microscopy, (3) standardized short course regimen with DOT for at least the initial 2 months, (4) uninterrupted supply of qualified drug, and (5) standardized recording and reporting system. As an element of DOTS, DOT implies that an observer watches the patient swallow the medicine with the aim of improving patient compliance, which is considered the most serious problem in TB control (Addington 1979).

The National TB Programme has adopted the WHO proposals and planned to cover all 810 districts by the year 2001 (Payanandana *et al.* 1999). Since the implementation of DOTS in 1996, cure rates have apparently improved, but they are still below the WHO target of 85% (Ministry of Public Health 1999).

In spite of worldwide implementation, the efficacy of DOT remains questionable (Volmink *et al.* 2000). Randomized controlled trials have given opposite results, and compliance to the DOT principle has not been reported in these studies (Zwarenstein *et al.* 1998; Kamolratanakul *et al.* 1999; Zwarenstein *et al.* 2000; Walley *et al.* 2001). It is expected to be difficult to maintain the initial allocation

of DOT over several months, and analysis according to the 'intention-to-treat' principle may leave a too limited exposure contrast to produce meaningful results.

Because the use of DOT observers takes away resources from other tasks, it is important to know if DOT works. The aim of this study is to quantify DOT in practice and to estimate the effect of actual DOT practice on treatment outcomes.

Methods

Study design and population

We selected a group of patients currently diagnosed with TB and followed them to document their actual practice of DOT and treatment outcomes. The study area covered a population of about 1.2 million in 24 districts in southern Thailand.

Through the TB registers at the 22 governmental TB clinics (one zonal TB centre, one regional hospital, three general hospitals and 17 community hospitals), we identified all 455 patients who were compatible with WHO definition of new, smear-positive, pulmonary TB (Maher *et al.* 1997), and who started treatment between 1 February and 30 September 1999.

Treatment

All the patients started the treatment with either daily or intermittent short-course drug regimens. The daily regimen combined a 2-month initial phase of four drugs (isoniazid, rifampicin, pyrazinamide and ethambutol) and a 4-month continuation phase of two drugs (isoniazid and rifampicin). A three-times per week treatment with the same drug combination was used only for 21 patients who agreed to take the medicine at the zonal TB centre. According to national guidelines, the treatment was evaluated by sputum examinations at the end of the second, fifth and sixth months. If sputum still contained acid fast bacilli (AFB) at the end of the second month, the initial phase was extended for 1 or 2 more month(s). For patients who could not tolerate the standard treatment, the drug regimen was changed to a 9-month regimen without pyrazinamide or to an 18-month regimen without rifampicin and pyrazinamide.

Initial assignment of DOT observer

The TB clinic staff chose a DOT observer with the patient's agreement and recorded the information on the patient's treatment card. The initially assigned observers were divided into three groups (Ministry of Public Health 1998): health personnel (including staff members of TB clinics, hospital wards and health centres); community members (including village health volunteers, community leaders and friends); and family members (including both close and distant relatives).

Sources of information

Data on exposure, outcomes and potential confounders were obtained from interviews using structured questionnaires and from medical records. The questionnaires were pilot-tested twice before starting the data collection and participants were interviewed at least once and up to four times during the treatment, and/or after the end of the treatment. The interviewers were 24 health professionals working at the TB clinics involved in the study and the first author (P.P.), who selected and trained all interviewers and supervised the interview process. We informed the patients and/or their observers about the aim of our study, confirmed their verbal consent to be interviewed, and emphasized the importance of their answers before interviewing them during the clinic attendance or the ad hoc home visit. Two cases were interviewed solely by telephone because of misappointment and patient migration.

Exposure variables

Two types of DOT were defined, DOT by the initial assignment (assigned DOT) and DOT in actual practice (actual DOT). The patients initially assigned to have any types of observer were grouped as 'assigned DOT', and those without observer assigned as 'assigned no DOT'.

The patients and/or their observers were asked whether the observers actually watched the patients swallow the medicine during the first 2 months (strict DOT). The less strict practices, such as just staying with the patient during drug intake without watching, preparing medicine for patients, and reminding patients about the drug intake were considered as 'not strict DOT'. Three cut-off points were used to define the actual practice of strict DOT: (1) every dose *vs.* some doses or never, (2) more than 50% of the expected doses *vs.* 50% or less, and (3) every dose or some doses *vs.* never. We defined the former group in each cut-off point as 'actual DOT' and the latter group as 'actual no DOT'. All definitions were analysed, however, we only present results according to the first cut-off point.

Outcome variables

We measured the effect of DOT using the following two endpoints: sputum negative conversion at the end of the

second month, and treatment success at the end of the treatment. The WHO definitions of treatment outcomes (Maher *et al.* 1997) were applied to both endpoints. Accordingly, we classified treatment outcomes into six mutually exclusive categories: (1) AFB-negative sputum at time of evaluation; (2) no AFB result at time of evaluation; (3) AFB-positive sputum at time of evaluation; (4) death (died of any cause before time of evaluation); (5) treatment interruption for at least two consecutive months; and (6) transferred out to another TB clinic with unknown sputum result.

At the end of the second month, patients who had AFB-negative sputum were classified as 'sputum conversion', the rest as 'no sputum conversion'. Similarly, patients who received the full course of treatment and had AFB-negative sputum or had no sputum result at the end of the treatment were classified as 'treatment success', the rest as 'unsuccessful treatment'.

Potential confounders

Several potential confounders were considered and divided into three groups: (1) demographic and socio-economic status (gender, age, marital status, ethnic group, formal education, understanding Thai language, occupation, income, feasibility to be free from work or study, independence in travel and number of living places); (2) health services provided (type of TB clinic, drug regimen, and use of fixed dose combination); and (3) disease condition (initial weight, initial AFB result, initial drug resistance, adverse drug effect, HIV/AIDS status, and associated diseases/conditions including diabetes mellitus, cardiovascular disease, cerebrovascular disease, liver cirrhosis, psychosis, alcoholic consumption, drug abuse and imprisonment). The patients without information on income or susceptibility tests were treated as separate groups.

Variable selection and statistical analysis

Univariate analyses were performed by Pearson's chi-square test. Only covariates with at least marginal association with the outcome (sputum conversion *vs.* no sputum conversion and successful treatment *vs.* unsuccessful treatment) (P-value < 0.2) were selected to be tested in the models, as described in the following paragraph.

Four logistic regression models with increasing numbers of covariates were applied to determine the association between the exposure and the outcome (1) without covariates, (2) with inclusion of the first group of covariates, (3) with inclusion of the first and second groups of covariates, and (4) with inclusion of all three groups of covariates. For each step of adding the group of covariates, only covariates with the following criteria were retained in the model: (1) having significant association with the outcome ($P < 0.05$) or (2) having marginal association with the outcome ($P < 0.1$) plus leading to a change of more than 15% of OR for any DOT comparison in the larger model, if removed. Once a variable was included, it was also included in the following model to ensure comparability of the log likelihood.

The confounders for the effect of each type of DOT on each outcome were controlled by multivariate analysis. The results were presented as odds ratios (OR) with 95% confidence intervals (CIs). We performed the likelihood ratio test to check the significance of each covariate group in the models (Kleinbaum 1994), and used the Hosmer–Lemeshow statistic to check the fit of the logistic regression models (Hosmer & Lemeshow 2000). A P-value of less than 0.05 was considered statistically significant in interpreting the resulting models. All analyses were carried out using STATA (StataCorp. 1999).

Results

Of the 455 patients who started treatment, 44 were excluded because the interviewers were unable to establish contact with them or their DOT observers. Compared with the remaining patients, the excluded patients were younger (median age 31 *vs.* 42 years), were more often HIV positive or suffered from AIDS (27 *vs.* 11%), and had poorer treatment outcomes (sputum conversion rate 57 *vs.* 78%; cure rate 30 *vs.* 75%).

The remaining 411 patients were from 6 to 86 years of age (mean 44 years, 95% CI 42–46); and 75% were male. Of the 323 patients who provided information on income, 76% earned less than the official 'minimal daily wage' in the study area (3–3.5 US$). Among the 104 tested, 2% (95% CI 1–3%) had multidrug resistance (resistance to at least isoniazid and rifampicin).

Initial DOT assignment

Of the 411 patients, 379 (92%) had been initially assigned to any type of observer and the remaining 32 patients were not assigned to any, because they refused to accept one (18), because no suitable observers were available (9) or both (5). DOT was more often assigned to patients who were female, who had a living partner, who were treated at the zonal TB centre, who used fixed dose combination, or who had initial drug resistance (Table 1).

Actual DOT practice

Overall, only 68 of 411 patients (17%) practised strict DOT in every dose during the first 2 months, 97 of 393 patients with available information on the following DOT duration practised for more than 50% of expected doses (25%), whereas 154 of 411 (37%) patients took the medicine without being watched by observers. Of 379 patients assigned to DOT, 65 (17%) practised strict DOT for every dose during the first 2 months, 93 of 362 patients with available information on the following DOT duration practised for more than 50% of expected doses (26%), whereas 133 of 379 patients (35%) never practised strict DOT. Practice of strict DOT for every dose during the first 2 months was found more often among the patients who had lower income, who could be free from work/study, had any drug resistance, who were HIV positive had AIDS or other comorbidity, who travelled with others, who did not use fixed-dose combination, or who were treated at the zonal TB centre (Table 1).

Treatment outcomes

Overall sputum conversion and treatment success rates were 78 and 85%, respectively. Sputum conversion rates were lower among male patients and those who were single, divorced or widowed. Treatment success rates were lower among patients who were male, Bhuddist, never travelled alone, were treated at hospitals, did not use

Table 1 Initial DOT assignment and actual DOT practice during the first 2 months by patient characteristics

Patient characteristics	*n*	Assignment at the start DOT/No DOT	Actual practice 2 months DOT/No DOT
Gender			
Male	308	280/28	53/255
Female	103	99/4	15/88
Living partner			
Not having	140	125/15	23/117
Having	271	254/17	45/226
Minimal daily income			
> Minimal daily wage	79	73/6	6/73
< Minimal daily wage	244	222/22	48/196
No information	88	84/4	14/74
Free from work/study			
Not free	307	282/25	42/265
Free	104	97/7	26/78
Dependence in travel			
Need/with other	139	131/8	42/97
Travel alone	272	248/24	26/246
TB clinic			
Community hospital	236	223/13	32/204
General/regional hospital	119	100/19	20/99
Zonal TB centre	56	56/0	16/40
Use of fixed dose combination			
No use	244	221/23	47/197
Use	167	158/9	21/146
HIV/AIDS status			
No	364	334/30	53/311
Yes	47	45/2	15/32
Co-morbidity*			
No	317	294/23	47/270
Yes	94	85/9	21/73
Initial drug resistance			
Sensitive to all four drugs	85	82/3	9/76
Any resistance	19	19/0	6/13
No test	307	278/29	53/254
All patients	411	379/32	68/343

*Co-morbidity: diabetes mellitus, cardiovascular disease, cerebrovascular accident, psychosis, liver cirrhosis, alcoholic, drug abusers, prisoners.

fixed-dose combination, with HIV/AIDS or with other comorbidity (data not shown).

Table 2 shows the proportions of all possible outcomes at the end of the second month and at the end of the treatment by type of DOT. Short- and long-term outcomes were different between 'actual DOT' and 'actual no DOT' groups, not between 'assigned DOT' and 'assigned no DOT' groups.

Multivariate analysis results

No significant differences in risk of no sputum conversion were seen between DOT and No DOT groups, regardless of DOT types or statistical models (Tables 3 and 4). Males had approximately twice the odds of no sputum conversion as female patients. Risks of no sputum conversion were reduced to about half among the patients who had no living partner or who travelled independently (Model 2).

Without the presence of covariates, DOT was positively associated with the chance of treatment success when data were analysed according to the assignment (Table 5), but DOT had opposite effects when analysed according to the actual DOT practice (Table 6). However, no association was found between DOT, either assigned or actual, and chance of treatment success after adjustment for potential confounders (Model 4 in Tables 5 and 6).

Men had an approximately four- to fivefold increased risk of unsuccessful treatment compared with women (Model 4). The risk of unsuccessful treatment was approximately eight times higher among those with HIV/

Table 2 Treatment outcomes at the end of the second month and at the end of the treatment. Results are given according to the assigned DOT at the start of treatment and the actual DOT practice during the first 2 months of the treatment

Time of evaluation	Type of DOT	Group	*n*	Outcomes (row percentage in parenthesis) AFB negative	No AFB result	AFb positive	Death	Default
At the end of the 2nd month	Assigned	No DOT	32	25 (78.1)	3 (9.4)	1 (3.1)	1 (3.1)	2 (6.3)
		DOT	379	296 (78.1)	29 (7.7)	39 (10.3)	10 (2.6)	5 (1.3)
	Actual*	No DOT	343	271 (79.0)	29 (8.5)	34 (9.9)	3 (0.9)	6 (1.8)
		DOT	68	50 (73.5)	3 (4.4)	6 (8.8)	8 (11.8)	1 (1.5)
	Total		411	321 (78.1)	32 (7.8)	40 (9.7)	11 (2.7)	7 (1.7)
At the end of the treatment	Assigned	No DOT	32	19 (59.4)	4 (12.5)	0	4 (12.5)	5 (15.6)
		DOT	379	290 (76.5)	35 (9.2)	5 (1.3)	30 (7.9)	19 (5.0)
	Actual†	No DOT	343	267 (77.8)	30 (8.8)	4 (1.2)	20 (5.8)	22 (6.4)
		DOT	68	42 (61.8)	9 (13.2)	1 (1.5)	14 (20.6)	2 (2.9)
	Total		411	309 (75.2)	39 (9.5)	5 (1.2)	34 (8.3)	24 (5.8)

*$\chi^2_{4\ d.f.} = 26.65$, $P = 0.000$. †$\chi^2_{4\ d.f.} = 19.31$, $P = 0.001$.

Table 3 Odds ratios of 'no sputum conversion' at the end of the second month for 'assigned DOT' vs. 'assigned no DOT' groups after adding various confounder groups

Included variable	Compared group	OR (95% CI) of no sputum conversion† Model 1	Model 2	Model 3
Assigned DOT	DOT/no DOT	1.00 (0.42–2.40)	0.98 (0.40–2.42)	1.08 (0.43–2.71)
Gender	Male/female	–	**2.36 (1.24–4.47)**	**2.44 (1.28–4.65)**
Living partner	No/having	–	**0.54 (0.31–0.92)**	**0.58 (0.33–0.99)**
Independence in travel	Yes/no	–	**0.55 (0.34–0.91)**	**0.54 (0.33–0.90)**
TB clinic*	CH/GH-RH	–	–	1.02 (0.59–1.75)
	ZTC/GH-RH	–	–	0.48 (0.19–1.22)
Log likelihood		−216.03	−208.00	−206.34
Degrees of freedom		1	4	6

*CH = community hospital, GH = general hospital, RH = regional hospital, ZTC = zonal TB centre.
†Model 1 = crude analysis, Model 2 = Model 1 + demographic and socio-economic covariates, Model 3 = Model 2 + covariates related to health services, Model 4 = Model 3 + covariates related to disease condition. Bold indicates $P < 0.05$.

Table 4 Odds ratios of 'no sputum conversion' at the end of the second month for 'actual DOT' *vs.* 'actual no DOT' groups after adding various confounder groups

		OR (95% CI) of no sputum conversion†		
Included variable	Compared group	Model 1	Model 2	Model 3
Actual DOT	DOT/no DOT	1.36 (0.75–2.46)	1.10 (0.58–2.07)	1.20 (0.63–2.29)
Gender	Male/female	–	**2.34 (1.23–4.44)**	**2.40 (1.26–4.57)**
Living partner	No/available	–	**0.54 (0.31–0.92)**	**0.57 (0.33–0.99)**
Independence in travel	Yes/no	–	**0.57 (0.34–0.95)**	**0.57 (0.33–0.96)**
TB clinic	CH/GH-RH	–	–	1.03 (0.60–1.77)
	ZTC/GH-RH	–	–	**0.48 (0.19–1.20)**
Log likelihood		−215.55	−207.96	−206.21
Degrees of freedom		1	4	6

*CH = community hospital, GH = general hospital, RH = regional hospital, ZTC = zonal TB centre.
†Model 1 = crude analysis, Model 2 = Model 1 + demographic and socio-economic covariates, Model 3 = Model 2 + covariates related to health services, Model 4 = Model 3 + covariates related to disease condition. Bold indicates $P < 0.05$.

AIDS, and approximately twofold for those with other comorbidity. By contrast, the risk of unsuccessful treatment was reduced among patients who travelled alone (OR = 0.2), and patients who were treated at a community hospital (OR = 0.4) or the zonal TB centre (OR = 0.1).

Discussion

We did not find a statistically significant effect of DOT on sputum conversion or on treatment success; regardless of whether DOT was analysed according to the initial assignment or according to what was reported by the patients and/or their observers. A lower chance of sputum conversion was seen among male patients, patients who had a living partner, or who never travelled alone. Furthermore, male patients, who never travelled alone, who were treated at a general/regional hospital, and patients with HIV/AIDS, or other comorbidity, had worse chances of treatment success.

The Centers for Disease Control and Prevention in the United States (US Department of Health & Human Services 1994) and WHO 1994, 1995, 1997, 1999) have recommended DOT for all TB patients because it is difficult to predict whether a patient will follow the treatment. They have done so without requesting DOT to be evaluated in practice including measurement of the adherence to the DOT principle. Our findings show that actual DOT practice could be very different from the intended assignment. The result also calls for caution when interpreting the results of the four randomized controlled trials analysed according to the 'intention-to-treat' principle and without information on actual DOT practice

Table 5 Odds ratios of 'unsuccessful treatment' for 'assigned- DOT' *vs.* 'assigned no DOT' groups after adding various confounder groups

		OR (95% CI) of unsuccessful treatment†			
Included variable	Compared group	Model 1	Model 2	Model 3	Model 4
Assigned DOT	DOT/no DOT	**0.42 (0.19–0.97)**	**0.37 (0.15–0.89)**	0.52 (0.21–1.32)	0.45 (0.17–1.17)
Gender	Male/Female	–	**4.90 (1.97–12.16)**	**5.57 (2.21–14.08)**	**4.33 (1.62–11.56)**
Ethnic group	Muslim/Buddhist	–	**0.44 (0.25–0.79)**	**0.40 (0.22–0.73)**	0.54 (0.28–1.05)
Independence in travel	Yes/no	–	**0.23 (0.13–0.42)**	**0.20 (0.11–0.37)**	**0.21 (0.11–0.40)**
TB clinic*	CH/GH-RH	–	–	**0.46 (0.24–0.88)**	**0.44 (0.22–0.88)**
	ZTC/GH-RH	–	–	**0.15 (0.04–0.56)**	**0.10 (0.02–0.40)**
HIV/AIDS	Yes/no	–	–	–	**8.11 (3.74–17.60)**
Other co-morbidity	Yes/no	–	–	–	**2.40 (1.22–4.70)**
Log likelihood		−174.19	−154.21	−148.27	−131.40
Degrees of freedom		1	4	6	8

*CH = community hospital, GH = general hospital, RH = regional hospital, ZTC = zonal TB centre.
†Model 1 = crude analysis, Model 2 = Model 1 + demographic and socio-economic covariates, Model 3 = Model 2 + covariates related to health services, Model 4 = Model 3 + covariates related to disease condition. Bold indicates $P < 0.05$.

Table 6 Odds ratios of 'unsuccessful treatment' for 'actual DOT' *vs.* 'actual no DOT' groups after adding various confounder groups

		OR (95% CI) of unsuccessful treatment†			
Included variable	Compared group	Model 1	Model 2	Model 3	Model 4
Actual DOT	DOT/no DOT	**2.15 (1.15–4.04)**	**1.39 (0.68–2.82)**	1.61 (0.77–3.35)	1.28 (0.58–2.83)
Gender	Male/female	–	**5.09 (2.05–12.66)**	**5.76 (2.28–14.58)**	**4.62 (1.73–12.33)**
Ethnic group	Muslim/Buddhist	–	**0.47 (0.27–0.84)**	**0.40 (0.22–0.74)**	**0.55 (0.29–1.06)**
Independence in travel	Yes/no	–	**0.26 (0.14–0.49)**	**0.23 (0.12–0.43)**	**0.22 (0.11–0.45)**
TB clinic*	CH/GH-RH	–	–	**0.43 (0.23–0.81)**	**0.40 (0.20–0.79)**
	ZTC/GH-RH	–	–	**0.12 (0.03–0.45)**	**0.08 (0.02–0.32)**
HIV/AIDS	Yes/no	–	–	–	**7.52 (3.46–16.34)**
Other comorbidity	Yes/no	–	–	–	**2.44 (1.25–4.77)**
Log likelihood		−173.42	−156.03	−148.39	−132.50
Degrees of freedom		1	4	6	8

*CH = community hospital, GH = general hospital, RH = regional hospital, ZTC = zonal TB centre.
†Model 1 = crude analysis, Model 2 = Model 1 + demographic and socio-economic covariates, Model 3 = Model 2 + covariates related to health services, Model 4 = Model 3 + covariates related to disease condition. Bold indicates $P < 0.05$.

(Zwarenstein *et al.* 1998; Kamolratanakul *et al.* 1999; Zwarenstein *et al.* 2000; Walley *et al.* 2001). The effect measures of these studies are likely biased by a difference between initial assignment and actual practice.

Balasubramanian *et al.* (2000) were the first to report whether patients travelled to the clinic and received the medicine, as recorded by health workers. They found that 27% of 200 patients did not receive DOT and outcomes among this group were significantly worse than those who received DOT. However, they did not provide information on whether actual DOT was practised among those who came. Accordingly, the proportion of not receiving DOT in this study may not be readily comparable with the proportion of no DOT practice among those assigned to DOT in our study (35%). As indicated in our study, many risk factors confounded the association between DOT and treatment outcomes. Hence, the trend toward worse outcomes among those who did not receive DOT or were not assigned to DOT should not be considered reliable evidence of DOT benefit.

Regardless of the cut-off point used to classify the actual practice of DOT (data not shown), the non-significant association of DOT and outcomes and the independent predictors remained the same. This finding challenges not only the policy of universal DOT (Bailey & Sbarbaro 1988; Anna 1993; Salomon *et al.* 1997; Weis 1997; Bayer *et al.* 1998; Heymann *et al.* 1998), but also the recommended period of applying DOT (World Health Organization 1999). Although the results may reflect selection bias or uncontrolled confounding, the results do not rule out that the practice of DOT during the first 2 months may be counter-productive for some and insufficient for others, particularly for the long-term outcome.

On the other hand, the failure to find significant effects of DOT supports the experience-based conclusion that 'DOT is not panacea' (Fujiwara *et al.* 1997) but DOT may be a part of good case management to support TB patients to achieve cure (World Health Organisation 2001b).

By using observational studies in settings where the DOTS programme has been implemented, we faced an expected lack of comparability between the DOT and No-DOT groups. We used logistic regression models with different number of covariate groups in attempt to determine the confounding effect of each group and finally to adjust for the lack of comparability at baseline. Without randomization, we cannot be sure that the DOT and No-DOT groups are comparable, even after adjustment for the included confounders. The study was also analysed using the confounder score approach as described by Miettinen (1976) in order to make the control of potential confounding more efficient and to examine results as a function of baseline risks. The results were virtually unchanged and the effect measure were rather similar in the different risk groups (data not shown). Randomized trials will not solve the problem of compliance to the DOT principle. Practical problems and the patients' rights to choose the treatment modality they prefer will probably limit the scientific value of a randomized trial that aims at quantifying the effect of DOT. During the course of treatment, the patients may gain insight into their own ability to manage the treatment and may move out of the DOT group that would bias the comparison in disfavour of the DOT group. One should therefore not disregard the DOT principle on the basis of our findings but take the results

as a reason for caution. Any DOT services should try to identify the patients who actually will benefit from the DOT principle and the patients who can manage the drug intake on their own.

Although several steps were taken to examine DOT practice, the study may still be subject to exposure misclassification. DOT practice could be over-stated in the interviews because patients and observers saw interviewers as part of the health personnel. We also miss DOT information on 44 cases who more often interrupted the treatment (20 *vs.* 6%) and if they mostly were No-DOT group, we may underestimate the beneficial effect of DOT.

In conclusion, we found no significant improvement in the prognosis for those who practised DOT as part of their treatment for pulmonary TB. Tuberculosis control programmes should probably not focus on DOT without strengthening other strategies of good patient management.

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Once Weekly Is Superior to Daily Iron Supplementation on Height Gain but Not on Hematological Improvement among Schoolchildren in Thailand[1]

Rassamee Sungthong,[2] Ladda Mo-suwan,* Virasakdi Chongsuvivatwong and Alan F. Geater

*Epidemiology Unit and *Enterology and Nutrition Division, Department of Pediatrics, Faculty of Medicine, Prince of Songkla University Songkhla, 90110 Thailand*

ABSTRACT Intermittent iron supplementation has been suggested as a replacement for daily iron supplements for reducing anemia in developing countries. The effects of once weekly and daily iron supplementation on hemoglobin (Hb), serum ferritin (SF), prevalence of anemia, weight and height are compared in this study. Primary schoolchildren ($n = 397$) from two selected schools in the Hat Yai rural area, southern Thailand, were recruited in 1999. All children received Albendazole and then randomly received ferrous sulfate (300 mg/tablet) either daily or weekly, or a placebo for 16 wk. The average increase in Hb was not significantly different between the daily (mean ± SD; 6.5 ± 6.0 g/L) and weekly (5.7 ± 6.3 g/L) groups. However, the average increase in SF was greater ($P < 0.01$) in the daily (mean ± SD; 39.8 ± 30.3 μg/L) than the weekly (13.4 ± 17.3 μg/L) group. All cases of iron deficiency anemia were abolished in both daily and weekly groups, whereas no reduction in prevalence occurred in the placebo group. Height gain was greater in children who received weekly (mean ± SD; 2.6 ± 0.9 cm) than in those who received daily iron (mean ± SD; 2.3 ± 0.8 cm), ($P < 0.01$). Weight gain, weight-for-age and height-for-age were not significantly different among the intervention groups. It is concluded that a weekly iron dose is more effective than a daily dose in height gain but not in hematological improvement over 16 wk of supplementation. J. Nutr. 132: 418–422, 2002.

KEY WORDS: • *iron supplementation* • *iron status* • *growth* • *schoolchildren*

In children, the seriousness of iron deficiency anemia (IDA) arises from its consequences for health, including changes in immune function, growth and cognitive development (1–3). The WHO recommends large-scale programs of daily iron supplementation to reduce the prevalence of anemia in high risk areas (4). However, IDA remains common in many parts of the world, particularly among children in developing countries (5–7). Insufficient supply of iron tablets, low coverage of the target population and poor compliance with tablet intake are among the main reasons for the ineffectiveness of supplementation programs (8,9).

Administration of weekly iron as a replacement for the existing daily iron supplement programs has been discussed widely in developing countries (10–14) due to greater iron absorption in animal studies (15–17), fewer side effects in humans (15) and potentially greater cost-effectiveness. However, field studies have yielded controversial results. Several studies have reported comparable effects between intermittent and daily iron supplementation on improvement of iron status and growth among anemic young children and adolescents (10–12); however, a subsequent comparative study (13) showed significantly greater efficacy of daily over twice weekly iron supplementation in adolescents.

In Thailand, where the nature of anemia includes not only iron deficiency but also thalassemia (18,19), a once daily iron supplementation program has been carried out among anemic children since 1988, and a once weekly dose administered through a school-based program among primary schoolchildren will soon be implemented. It is essential to conduct a randomized controlled trial to assess the efficacy of once weekly iron supplementation before the large-scale program is launched. The main objective of this study was to compare the results of once weekly and daily iron supplementation on hemoglobin (Hb), serum ferritin (SF) and physical growth among primary schoolchildren in southern Thailand.

SUBJECTS AND METHODS

Study site and study subjects. Data collection was carried out from June to December 1999 in a socioeconomically disadvantaged community in Songkhla Province, southern Thailand. The two (public) schools were selected because they had at least 150 pupils with a high prevalence of underweight children according to previous school records, were accessible by automobile and had teachers who were willing to cooperate in the study. These two schools were located ~35 km from the research center and had a mixture of Buddhist and Muslim students. Family occupation was mainly as rubber plantation workers. This area was free from malaria and no previous large-scale program of iron supplementation had been implemented.

The sample size was calculated to provide a power of 95% in

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[2] To whom correspondence should be addressed.
E-mail: sburapat@medicine.psu.ac.th.

[3] Abbreviations used: Hb, hemoglobin; IDA, iron deficiency anemia; SF, serum ferritin.

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detecting a difference at $\alpha = 0.05$ between daily and weekly supplements, and between either of these iron doses and a placebo of 1 SD in the pre- to post-treatment measurements of iron status and growth. At least 62 subjects per group were required.

An invitation letter and consent form were sent to the parents whose children were in primary school. All subjects who received parental consent had their baseline data measured. We excluded those with severe malnutrition (weight for height ≤ 3rd percentile of the Thai reference), chronic illness such as obvious thalassemia or hemolytic disease, high iron storage (SF > 100 μg/L), physical handicaps or no baseline laboratory assessment. The children were stratified by anemic status to balance the proportion of anemic and nonanemic children across the intervention groups. Anemic children were defined as Hb < 115 g/L among children 5–11 y and Hb < 120 g/L among children 12–13 y. These cut-off levels are recommended by the WHO (20). The children were then assigned by simple random allocation within each stratum using a computer to daily or once weekly iron supplemented or placebo groups.

Measurement of variables. School, class, sex, age, ethnic group and socioeconomic status (parents' education, father's and mother's occupations and family monthly income) data were collected via a questionnaire completed by parents before the intervention started.

At baseline and the end of the study, weight and height were measured with subjects wearing school uniforms without belts and shoes and with empty pockets using a beam balance Detecto scale and stadiometer (Detecto Scales, Brooklyn, NY) to the nearest 0.1 kg and 0.5 cm, respectively.

Before supplementation, well-trained nurses drew a 5-mL blood specimen from the cubital vein. A 2-mL portion of the blood was transferred to an EDTA-prepared tube and then stored in an ice box for subsequent Hb determination, blood morphology examination and screening for thalassemia. The remaining 3 mL of the blood was kept in a sealed plastic test tube at ambient temperature for SF assessment.

Hb level was assessed with an automated machine (Technicon H*1E system, Tarrytown, NY) using the cyanmethemoglobin method (CV = 0.6–3.4%). The One Tube Osmotic Fragility Test combined with the Dichlorophenol Indophenol Precipitation Test was used to screen for potential thalassemic disease (19). Children with a positive One Tube Osmotic Fragility Test < 85% or Dichlorophenol Indophenol Precipitation Test had further examination of blood cell morphology by a hematologist and were excluded from the study if there was evidence of thalassemia or hemolytic diseases such as ovalocytosis, which is common in the study area (19,21). There was no attempt to exclude the thalassemia trait in this study. SF was assessed by the IMx assay (IMx Ferritin assay, Abbot Park, IL) using The Microparticle Enzyme Immunoassay method (CV = 4.4–6.4%). SF ≤ 20 μg/L was used to define anemia due to iron deficiency. At the end of intervention, a new 3-mL specimen of blood for Hb and SF testing was taken.

Intervention. All eligible children were given a single dose of 400 mg Albendazole at the beginning of the study and again 11 wk later to eliminate hookworm infection. Ferrous sulfate 300 mg tablets (60 mg elemental iron) (Government Pharmaceutical Organization, Bangkok, Thailand) were used in this study because these will be used in the real supplementation program. Placebo tablets, produced by the Faculty of Pharmacy, Prince of Songkla University, Thailand, were similar in color, shape, size and taste to the iron tablet. The tablets were placed in bottles, which were labeled only with the subject's name. Their content was unknown to any of the project personnel. Each child received 2 bottles. The first was to be taken on Monday only. The second was to be taken for the remaining days of the week. The daily group had iron in all the bottles, whereas the once weekly group had iron in the Monday bottle and placebo in the rest. The placebo group had placebo tablets in all of the bottles. After packing, the codes were kept secret throughout the supplementation process. All oral administrations were strictly observed by either the principal investigator or the research assistant on each school day to ensure that the tablets were swallowed.

Ethical consideration. The research proposal was approved by the Ethical Review Committee of Faculty of Medicine, Prince of Songkla University, Thailand. Children with severe IDA (Hb ≤ 80 g/L and SF ≤ 20 μg/L) were excluded from the study and treated immediately to prevent unnecessary delay. Children who had hemolytic disease or relatively high iron storage (SF >100 μg/L) were also excluded to prevent the risk of iron overload. Children who continued to have IDA at the end of the study received appropriate iron supplementation.

Data analysis. The balance of baseline measurements across the interventions was examined. The effects of iron supplementation were analyzed on an intention-to-treat basis. The change of Hb from pre- to post-treatment was examined and compared across the interventions using Student's paired *t* test and ANOVA with Bonferroni's multiple comparison tests. Due to a problem of nonnormal distribution with SF, nonparametric statistics were used in the comparison. The Wilcoxon signed-rank test was used to see the change of SF from pre- to postintervention and the Kruskal-Wallis test was used to compare the effect across interventions. Mann-Whitney tests were performed for multiple pair-wise comparisons only when the Kruskal-Wallis test suggested a significant difference of SF among interventions. The reduction in prevalence of IDA was also compared across the interventions by using the Z-test applied to the McNemar's χ-squares for each intervention.

Anthropometric indices used in assessing growth were weight gain, height gain, change in weight-for-age and change in height-for-age. Z-scores of weight-for-age and height-for-age were calculated using the National Center for Health Statistics growth references for weights and heights using the EPI INFO software, version 6 (Centers for Disease Control, Atlanta, GA). These constitute the international growth reference curves recommended by WHO. Anthropometric indices were compared across interventions using ANOVA. Weight and height gain were also adjusted for age using multivariate regression analysis.

RESULTS

Overall, 61% of the parents consented to the study, resulting in 462 study subjects; 65 of these children were excluded from the study before randomization due to thalassemic disease ($n = 3$), ovalocytosis ($n = 18$), high iron storage ($n = 6$), severe malnutrition ($n = 9$), severe IDA ($n = 1$), partial blindness ($n = 1$) or no baseline laboratory investigation ($n = 27$). The excluded and the remaining children were otherwise comparable in all sociodemographic characteristics.

Eventually, 397 primary schoolchildren, aged ranging from 6 to 13 y, participated in the study; of these, 140, 134 and 123 children were allocated to daily, weekly and placebo groups, respectively. Most of the children belonged to socioeconomically deprived families as indicated by low parental education and income. Approximately 80% of family monthly incomes were ≤5000 baht (125.00 US$) per month compared with the Thai national average of 12,729 baht (318.00 US$) for the same year reported by the Household Socioeconomic Survey, National Statistical Office. The prevalence of anemia was 27% but only 21.5% of these anemic children were iron deficient. Children from the two schools had similar distribution of the above-mentioned socioeconomic variables; thus, no stratification by school was used in the analysis. Baseline measurements were similarly distributed among intervention groups as summarized in Table 1.

Over the 16 wk of intervention, 93.8 and 93.5% children in the daily and weekly groups received iron tablets as planned. Six children ($n = 1$, 4 and 1 in the daily, weekly and placebo groups, respectively) moved to other schools out of the study site during the study period and were thus excluded from the analysis of outcome. Means of Hb, SF, weight and height increased significantly from pre- to postintervention measurements except SF in the placebo group. Means of Hb change in the daily and weekly supplemented groups were similar but both were greater than that in the placebo group ($P < 0.001$ and $P = 0.026$, respectively). The mean increase in SF con-

TABLE 1

Baseline variables of primary schoolchildren among intervention groups given 300-mg tablets of ferrous sulfate (daily or weekly) or a placebo for 16 wk[1,2]

Variables	Intervention		
	Daily	Weekly	Placebo
n	140	134	123
Hemoglobin, g/L	121.3 ± 10	121.2 ± 9	121.8 ± 10
Anemic, *n*	39	40	28
Nonanemic, *n*	101	94	95
Serum ferritin, μg/L	39.9 ± 20.4	39.9 ± 19.3	38.5 ± 19.3
Sex (male:female)	69:71	64:70	52:71
Age, y	9.6 ± 1.7	9.7 ± 1.9	9.7 ± 1.7
Ethnic group, *n*			
Thai-Buddhist	41	47	34
Thai-Muslim	99	86	89
Weight, kg	25.5 ± 7.1	26.3 ± 8.0	26.4 ± 8.5
Height, cm	126.7 ± 10.7	128.5 ± 10.9	127.4 ± 10.3
Father's occupation, *n*			
None	3	1	0
Casual/farmer/seller	130	122	112
Government/private	7	8	9
Mother's occupation, *n*			
None	2	4	7
Casual/farmer/seller	134	126	111
Government/private	3	1	5
Parents' education, y	6 ± 3	6 ± 3	6 ± 3
Family monthly income, *n*			
≤5000 baht[3]	114	108	93
>5000 baht	25	21	27

[1] Values are means ± SD or numbers of children.
[2] The numbers for some variables do not equal the column totals because of missing data.
[3] 1 baht = 0.025 U.S. $ at the time of data collection.

centration in the daily group was greater than that in the weekly group ($P < 0.001$), which in turn was greater than that in the placebo group ($P < 0.001$). All IDA children in the weekly and daily groups became nonanemic ($P = 0.001$ and 0.025, respectively), whereas only one of the six IDA children in the placebo group had improved SF but were still anemic, and two children in the placebo group developed IDA by the end of the study ($P = 0.56$). These reductions of IDA in the daily and weekly groups did not differ, but each was different from the placebo group ($P = 0.006$ and $P = 0.047$, respectively, Table 2). Weight gain, change of weight-for-age and change of height-for-age among intervention groups were not significantly different across the groups. The increase in height of children in the weekly group was greater than that in the other two groups, but the only significant difference was between the daily and the weekly groups ($P = 0.02$, Table 3). This significance of height gain difference persisted after adjustment for age.

DISCUSSION

In this supplementation experiment, in which iron was given to primary schoolchildren in southern Thailand for 16 wk, comparable effects between once weekly and daily supplementation were found in both change in Hb and reduction of the prevalence of IDA. The daily group had a significantly greater SF than the other two groups, but significantly lower height gain than the weekly group. Neither supplementation regimen showed an effect on weight gain, change in weight-for-age or change in height-for-age.

During the supplementation period, the mean Hb improvement seen in the placebo group may have been due to various

TABLE 2

Change in hematological variables in each intervention group among schoolchildren given 300-mg tablets of ferrous sulfate (daily or weekly) or a placebo for 16 wk[1,2]

Variables	Intervention		
	Daily	Weekly	Placebo
n	138	130	121
Hemoglobin (Hb), g/L			
Before	121.3 ± 10	121.2 ± 9.1	121.8 ± 9.8
After	127.8 ± 9.2	126.9 ± 9.2	125.3 ± 9.3
Change	6.5 ± 6.0[a]	5.7 ± 6.3[a]	3.4 ± 5.5[b]
n	137	123	117
Serum ferritin (SF), μg/L			
Before	39.9 ± 20.5	40.6 ± 19.6	38.5 ± 19.4
After	79.7 ± 36.6	54.0 ± 24.2	37.4 ± 18.9
Change	39.8 ± 30.3[a]	13.4 ± 17.3[b]	−1.1 ± 17.1[c]
n	140	134	123
IDA,[3] *n*			
Before	11	6	6
After	0	0	7
Change	11[a]	6[a]	−1[b]

[1] Values are means ± SD. Means in a row without a common letter differ, $P < 0.05$.
[2] The numbers of children do not equal the total eligible subjects (see Table 1) because of missing data.
[3] IDA, iron deficiency anemia, is defined as Hb < 115 g/L and SF ≤ 20 μg/L for children <12 y old or Hb <120 g/L and SF ≤20 μg/L for children >12 y old.

TABLE 3

Change in growth variables in each intervention group among schoolchildren given 300-mg tablets of ferrous sulfate (daily or weekly) or a placebo for 16 wk[1,2]

Variables	Intervention		
	Daily	Weekly	Placebo
n	139	129	122
Weight, kg			
Before	25.5 ± 7.1	26.4 ± 8.0	25.4 ± 6.5
After	26.8 ± 7.8	27.8 ± 8.5	26.9 ± 7.2
Change	1.3 ± 1.6	1.4 ± 1.8	1.5 ± 1.6
Height, cm			
Before	126.6 ± 10.7	128.6 ± 10.8	127.4 ± 10.3
After	128.9 ± 10.8	131.2 ± 10.8	129.8 ± 10.2
Change	2.3 ± 0.8[b]	2.6 ± 0.9[a]	2.4 ± 0.9[ab]
Weight-for-age, *Z*-score			
Before	−1.30 ± 0.9	−1.25 ± 1.0	−1.32 ± 0.9
After	−1.32 ± 0.9	−1.27 ± 1.0	−1.34 ± 0.9
Change	−0.02 ± 0.30	−0.02 ± 0.20	−0.02 ± 0.20
Height-for-age, *Z*-score			
Before	−1.55 ± 0.9	−1.44 ± 1.0	−1.54 ± 0.9
After	−1.62 ± 0.9	−1.47 ± 1.0	−1.59 ± 0.9
Change	−0.07 ± 0.14	−0.03 ± 0.15	−0.05 ± 0.15

[1] Values are means ± SD. Means in a row without a common letter differ, $P < 0.05$.

[2] The numbers of children do not equal the total eligible subjects (see Table 1) because of missing data.

causes such as deworming, shift in age among children or some unknown effect of the follow-up. After allowing for the placebo effect, the net gain of Hb in the daily and weekly groups was 3.1 and 2.3 g/L, respectively, in 16 wk. The poor response to iron supplementation in these subjects may be attributable to the low prevalence of IDA or to the thalassemia trait, which exists in the southern Thai population (19).

Our study was confined to 16 wk of supplementation. However, the real supplementation program will be implemented year round. The findings that the daily dose yielded a higher SF than the weekly dose may simply reflect a slower increase of SF. Prolonged weekly dosing may eventually lead to adequate saturation of iron in blood and in tissue.

To our knowledge, only two previous studies (13,14) have assessed intermittent iron supplementation as a blanket supplementation, that is, including both anemic and nonanemic subjects as in our study. A study of weekly iron supplementation among Tanzanian adolescents (14) found a significantly greater increase in serum ferritin compared with a vitamin B-12 control group, but there was no significant difference in change in Hb. However, a study in Peru (13) found that a 17-wk daily supplementation led to significantly higher Hb increases than twice weekly supplementation; however, SF and free erythrocyte protoporphyrin were similar in the two groups. It is possible that the 60 mg iron/d given to adolescents whose average weight was almost 50 kg may be too small a dose to improve Hb and correct anemia in the intermittent schedule; the actual values of SF were not shown in that paper.

Our study found no significant difference in weight gain, change of weight-for-age, or change of height-for-age among weekly, daily and placebo groups, but a significantly greater height gain among children receiving once weekly iron supplementation than that in the daily group. The patterns of height gain and change of height-for-age were consistent (i.e., worst in the daily group and best in the weekly group), but a significant difference was detected only in height gain. The lack of significance in height-for-age may be due to the lower precision of this variable. Almost 50% of our subjects had a height exceeding the limit for calculation of weight-for-height; thus, we omitted this anthropometric index.

Studies regarding the effects of daily iron deficiency upon growth have shown inconsistent results. Studies in India, Kenya and Indonesia found an improvement in growth after iron supplementation (22–25). Improved appetite and decreased morbidity were the explanations given in those studies for enhanced growth after iron supplementation. Studies in Mexico, Bangladesh and Thailand, however, reported no benefit of iron supplementation on growth (26–28). One proposed explanation is that deficiency of multiple micronutrients such as zinc and vitamin A could have limited the growth response to iron (27). Furthermore, a report of the adverse effect of iron on weight gain in children with adequate iron status has raised concerns among public health researchers about giving supplemental iron to children (29).

We could find only one previous study comparing weekly iron supplementation with daily dosing on growth. This study on Indonesian primary schoolchildren (10) reported no significant differences in increases of weight-for-age, weight-for-height or height-for-age after 3 mo of weekly and daily iron supplementation among anemic schoolchildren.

Using subjects in a different age group, a study among Tanzanian adolescent girls comparing weekly iron supplementation and a vitamin B-12 control group reported a significantly greater weight gain in the weekly iron supplemented group than in the vitamin B-12 control group after 4 mo of supplementation (14).

Iron intake in our study was observed closely, and >90% of children received complete iron supplementation. Thus, the lack of significant difference in some of the outcome measurements among the groups cannot be explained by low compliance.

The immediate goal of the iron supplementation program in Thailand is to reduce the prevalence of anemia and increase tissue iron concentration, on the assumption that this will improve the health and performance of the children. Our data suggest that the goal of iron saturation is better achieved with daily rather than weekly supplementation but the potential adverse effect on growth (height gain) should be taken into consideration.

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Practice of directly observed treatment (DOT) for tuberculosis in southern Thailand: comparison between different types of DOT observers

P. Pungrassami,*†‡ S. P. Johnsen,§ V. Chongsuvivatwong,† J. Olsen,¶ H. T. Sørensen§

* Zonal Tuberculosis Centre 12, Amphur Muang, Yala, † Epidemiology Unit, Faculty of Medicine, Prince of Songkla University, Hatyai, Songkhla, Thailand; § The Danish Epidemiology Science Centre, University of Aarhus, Aarhus, ¶ Department of Epidemiology and Social Medicine, University of Aarhus, Aarhus, ‡ Department of Clinical Epidemiology at Aarhus University Hospital and Aalborg Hospital, Aarhus, Denmark

SUMMARY

SETTING: A government health system in southern Thailand where the directly observed treatment, short-course (DOTS) strategy has been implemented.

OBJECTIVE: To compare the practice of actual directly observed treatment (DOT) and the observer sustainability for different types of observer.

METHODS: During 1999–2000, 411 patients with new smear-positive pulmonary tuberculosis were followed up. The patients and/or their observers were interviewed about the presence of any person with the patient during drug intake and the practice of watching the patient swallowing the medicine (actual DOT). Data were recorded monthly and analysed by Cox and logistic regression models.

RESULTS: For health personnel (HP), community member (CM), and family member (FM) observers, the proportions who did not practise actual DOT were respectively 11%, 23%, and 35%, and the proportions who changed to no observer or self administration were respectively 11%, 1%, and 2%, during the first 9 months of treatment. Health personnel had the lowest risk of not practising actual DOT (odds ratio HP/FM 0.1, 95%CI 0.1–0.2; CM/FM 0.9, 95%CI 0.5–1.6) but the highest risk for change to self administration.

CONCLUSION: To increase the coverage of actual DOT, strategies are needed to maintain health personnel as the DOT observers and to promote actual DOT among family member observers.

KEY WORDS: tuberculosis; compliance; directly observed treatment; Thailand

THAILAND is one of the 22 countries that have 80% of the estimated incident cases of tuberculosis (TB) in the world,[1] and one of the 10 countries with the highest prevalence of primary multidrug resistance.[2] When the World Health Organization (WHO) reviewed Thailand's National Tuberculosis Programme (NTP) in 1993, low cure rates were found (17%–68%).[3] The NTP adopted the directly observed treatment, short course (DOTS) strategy in 1996, and full DOTS coverage of all 810 districts in the country was planned by the year 2001.[4] Training in the DOTS strategy follows the modified WHO modules of managing TB at district level,[5] and involves TB coordinators, doctors and staff members of TB clinics, laboratory technicians, and health centre staff members. The cure rate in Thailand has improved, but it is still below the WHO target of 85%.[6]

The use of directly observed treatment (DOT), one element of the DOTS strategy, has been recommended for improving patient adherence to TB treatment.[7,8] Most studies, however, focus on the effect of DOT without providing data on compliance with DOT,[9] and when available, data on compliance with the DOT principle have not been quantified.[10,11]

Three main types of DOT observer are used in Thailand: health personnel (HP: staff members of TB clinics, hospital wards and health centres), community members (CM: village health volunteers, community leaders and friends), and family members (FM: close and distant relatives). Before starting the patients on treatment, TB clinic staff members are responsible for informing them about the disease, the treatment and DOT, and for selecting a DOT observer. As the national guidelines recommend that the preferred choice of observer is HP, CM, and FM, in descending order,[12] they try to convince patients to take their drugs at a TB clinic or health centre during weekdays. However, the choice of DOT observers and places generally depends on negotiation, and the majority of assigned DOT observers are family members.[13,14] Comparative data on compliance with DOT for these three types of observer are not available.

Correspondence to: Petchawan Pungrassami, MD, Zonal Tuberculosis Centre 12, Amphur Muang, Yala 95000, Thailand. Tel: (+66) 073 212 332. Fax: (+66) 073 211 727. e-mail: ppetch@csconis.com

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For these reasons, we examined the practice of DOT and compared compliance with the DOT principle between the different types of observer available for monitoring TB treatment in southern Thailand. The comparison focused on the risk of not practising actual treatment observation, and the risk of changing from having an observer to having no observer.

STUDY POPULATION AND METHODS

Study population and design

The study area covered 1.2 million people in 24 districts in southern Thailand. Through the TB Registers at the 22 TB clinics (one Zonal TB Centre, one regional hospital, three general hospitals, and 17 community hospitals), we identified and followed up all 455 patients with new smear-positive pulmonary TB according to WHO criteria,[15] who started treatment between 1 February and 30 September 1999.

Treatment

As recommended by the WHO,[15] the standard daily drug regimen consisted of a 2-month initial phase of four drugs (isoniazid, rifampicin, pyrazinamide and ethambutol) and a 4-month continuation phase of two drugs (isoniazid and rifampicin). Treatment was given three times weekly for 21 patients at the Zonal TB Centre, while the other clinics used daily regimens. If the sputum still contained acid-fast bacilli (AFB) at the end of the second month, the initial phase was extended for 1 or 2 months. For patients who could not tolerate the standard treatment, the drug regimen was changed to a 9-month regimen without pyrazinamide, or to an 18-month regimen without rifampicin or pyrazinamide.

Assigned DOT observer, practical observer and actual DOT

Assigned DOT observers were chosen by the TB clinic staff members on the first day of treatment. In practice, the person who actually stays with the patient during drug intake, defined as a 'practical observer', may or may not be the same as the assigned observer. The practical observer may change over time, or may stop observing, which is equal to treatment with no observer. When more than one type of observer was involved during a given month, the one with the highest frequency of being the observer in that month was used in the analyses. For each dose of drug intake, DOT was considered to be 'actual DOT' only if the practical observer watched the patient swallow the drugs. Other practices, such as staying with the patient during drug intake, preparing the drugs for patients, or reminding patients about drug intake without watching, were classified as 'actual non-DOT'.

Data collection

The patient records and registers relevant to TB were reviewed. In addition, the patients and/or their observers were interviewed by the first author (PP) and/or one of 24 health professionals working in the study TB clinics. There were two planned interviews per patient, at least one month after starting the treatment and at the end of treatment. Data on the practical observer and actual DOT practice were recorded for each month until the end of treatment (data shown only for the first 9 months).

Data management and statistical analysis

Compliance with the DOT principle and sustainability of observer were our two outcome variables; the unit of analysis was patient-month. For the compliance with the DOT principle, an odds ratio (OR) of no practice divided by practice of actual DOT for any dose during each month was compared between the different types of practical observer. As the compliance each month varied over time in the same patient, logistic regression with population-average model and exchangeable intra-subject correlation was used to deal with the repeated measures.[16,17]

For the observer sustainability, the outcome of interest was a change from having an observer to having no observer. Time to outcome (change to self administration) was estimated, and the hazard ratio (HR) was computed between the different types of practical observer in a Cox proportional hazard model.[18] Censoring occurred at the time of death, treatment interruption, transfer to another area, end of treatment, or end of follow-up (31 July 2000), whichever came first.

The main predictors were the types of practical observer: health professional, community member, or family member. A number of covariates were considered as potential confounders and divided into three groups: 1) demographic and socio-economic characteristics (sex, age, marital status, ethnic group, formal education, understanding of Thai language, income, ability to take time out of work/study, number of living places, and independent means of travel), 2) health services (type of TB clinic, use of fixed-dose combinations, and initial DOT assignment), and 3) disease condition (initial weight, initial AFB result, initial drug resistance, human immunodeficiency virus (HIV)/acquired immune-deficiency syndrome (AIDS) status, and other co-morbidity, including heart disease, hypertension, cerebrovascular accident, diabetes mellitus, psychosis, alcoholic consumption, liver cirrhosis, drug abuse and imprisonment).

We identified associations between two variables by cross-tabulation and by using Pearson's χ^2 test. Variables that were associated with the specific outcome ($P < 0.05$) were selected for testing in the models. Four specific models of increasing numbers of covariates were applied to determine the association between the exposure and the outcome, 1) without covariates, 2) with inclusion of the first group of covariates, 3) with inclusion of the first and second

Table 1 Type of DOT observer during treatment

Month*	A	0	1	2	3	4	5	6	7	8	9	End
Number of patients being treated	411	411	402	391	375	366	353	61	23	9	5	411
Observer type												
Health personnel	177	94	74	52	38	29	25	3	0	0	0	28
Community member	21	31	30	32	32	30	28	6	2	1	1	30
Family member	181	210	219	225	217	210	203	36	16	4	2	233
Self administration	32	76	79	82	88	97	97	16	5	4	2	120

* Month: A = initially assigned observer (data from the records); 0-End = practical observer (data from the interviews); 0 = at the start of treatment, 1–9 = at the end of that month, End = at the end of the final month which varied according to the different periods of received treatment (standard regimen: 6 months; extended or changed regimen: 7–18 months; incomplete treatment: death, interruption, transfer to another area, or failure.). Five patients who received long-course chemotherapy were still on treatment after 9 months.
DOT = directly observed treatment.

groups of covariates, and 4) with inclusion of all three groups of covariates. At each step at which additional covariates were incorporated, only those that fulfilled the following criteria were retained: 1) having a significant association with the outcome (Wald test, $P < 0.05$) or 2) being associated with the outcome ($P < 0.1$) and leading to a change of more than 15% of OR or HR for any observers in the larger model, if removed.

The confounders for the effect of the practical observer on each outcome were controlled by multivariate analysis. The results were presented as OR and HR with 95% confidence interval (95%CI) of no practice over practice of actual DOT and change to self administration, respectively. Hosmer-Lemeshow statistic was used to check the fit of the logistic regression models.[19] Likelihood ratio tests were used to determine the significance of the presence of covariates in the Cox regression models. A P value of less than 0.05 was considered statistically significant. All analyses were done using STATA.[20]

RESULTS

Of the 455 patients enrolled, 44 were excluded because the interviewer was unable to establish contact with them or their DOT observers. Compared with the remaining patients, the excluded patients were younger (median age 31 vs. 42 years), more likely to have HIV/AIDS (27% vs. 11%), and more often treated at a general or regional hospital (48% vs. 29%).

The remaining 411 patients were 6 to 86 years of age (mean 44, SD [standard deviation] 17), and 70% were male. Of the 323 patients with data available on income, 76% earned less than the official minimal daily wage in the study area (about 3.5 US$).

Initially assigned observer vs. practical observer

The distribution of patients by type of initially assigned and practical observer is shown in Table 1. The numbers decreased markedly by the end of the sixth month, as 71% of 411 patients reached cure or treatment completion. Of 379 patients assigned to an observer, 212 (56%) changed their initially assigned observers during the treatment period, and 130 did so on the day of assignment. Of 177 patients assigned to health personnel, 84 changed on the day of assignment. Most changes during treatment (84%) were toward a less preferred category according to the national guidelines.

No practice of actual DOT

During the first 5 months of treatment, the proportions of patients who practised no actual DOT were between 7%–15% among HP, 20%–26% among CM, and 32%–38% among FM observers (Table 2). The adjusted OR of no practice over practice of actual DOT was similar between CM and FM, but was only about 1/8 among HP over FM (Model 4 in Table 3). The OR in non-FM (CM+HP) compared with FM was 0.3 (95%CI 0.2–0.5).

The odds of no practice of actual DOT were higher among patients who had no formal education, who had a higher income, who were treated at a general or regional hospital, or who had no other co-morbidity.

Change to no observer

During the first 5 months of treatment, between 12%–16% of patients with HP observers changed to

Table 2 No practice of actual DOT during the first 9 months of treatment by type of observer

Type of practical observer	Month of treatment*								
	1	2	3	4	5	6	7	8	9
Family member	72/223	78/234	80/224	76/213	79/207	77/202	6/32	3/15	0/5
Community member	8/31	8/32	7/32	7/31	6/30	6/26	1/5	0/1	—
Health personnel	5/75	7/52	6/39	4/30	3/26	3/24	0/3	—	—

* No. of patients with no practice of actual DOT/No. of patients analysed in that month.
DOT = directly observed treatment.

Table 3 Odds ratios of not practising actual DOT: crude and adjusted analyses

Included variable	Actual DOT* No	Actual DOT* Yes	Odds ratios (95% confidence interval)† Crude Model 1	Adjusted analyses Model 2	Model 3	Model 4
Practical observer						
Health personnel	28	221	0.13 (0.07–0.24)*	0.12 (0.06–0.21)*	0.14 (0.07–0.26)*	0.13 (0.07–0.24)*
Community member	43	145	0.64 (0.39–1.05)	0.63 (0.38–1.04)	0.88 (0.50–1.53)	0.90 (0.51–1.58)
Family member	471	884	1	1	1	1
Formal education						
Educated	396	1018	—	0.54 (0.36–0.82)*	0.55 (0.36–0.84)*	0.57 (0.37–0.87)*
None	147	232	—	1	1	1
Minimal income						
>Minimal daily wage	122	209	—	2.31 (1.48–3.62)*	2.40 (1.51–3.81)*	2.38 (1.49–3.80)*
<Minimal daily wage	293	810	—	1	1	1
No information	128	231	—	1.88 (1.23–2.87)*	2.42 (1.53–3.81)*	2.73 (1.71–4.34)*
Independent travel						
Travel alone	368	780	—	1.48 (1.03–2.12)*	1.36 (0.94–1.98)	1.31 (0.90–1.91)
Travel with other	175	470	—	1	1	1
TB clinic						
Community hospital	329	736	—	—	0.62 (0.42–0.90)*	0.58 (0.39–0.86)*
General/regional hospital	183	291	—	—		1
Zonal TB centre	31	223	—	—	0.18 (0.09–0.39)*	0.23 (0.11–0.49)*
Co-morbidity						
Yes	73	329	—	—	—	0.41 (0.25–0.65)*
No	470	921	—	—	—	1

* Number of patient-months with actual DOT: No = no practice of actual DOT; DOT = practice of actual DOT for any dose.
† Model 1 = crude analysis; Model 2 = Model 1 + demographic and socio-economic covariates; Model 3 = Model 2 + covariates related to health services; Model 4 = Model 3 + covariates related to disease condition.
* $P < 0.05$.
DOT = directly observed treatment.

self administration, compared to 0%–3% with CM and 0.5%–4% with FM observers (Table 4). The risk of change to self administration was four-fold higher among HP over FM, but was only about a half among CM compared with FM (Model 2 in Table 5, Figure). The relative risk for change in the non-FM compared with the FM group was 2.6 (95%CI 1.5–4.5).

Change to self administration was about two-fold more likely among patients who had no living partner than those with a living partner, and about 2.6-fold more likely among patients who lived in more than one place than those who lived in only one place during treatment.

DISCUSSION

Compliance with the DOT principle was poor. HP observers practised actual DOT more often than CM or FM observers. However, changing from HP observer to self administration occurred more frequently than changing from other types of observer to self administration.

DOT has been recommended for all patients with TB because of the expected difficulties in predicting whether a patient will adhere to treatment.[7,8] However, in practice, the reality is different. The proportion of patients with no observer assignment was high (34%) in a previous study in north-eastern Thailand,[14] compared with 8% in our study. A higher proportion of patients with observer assignment may suggest greater agreement with DOT among service providers. The remaining non-assignment was claimed to be due to a lack of suitable observers in this study. This challenges the feasibility of trying to implement DOT for all.[21,22]

The national guidelines recommend HP as the first choice of observer, but HPs are not always available or accepted by the patients. A study from India

Table 4 Changing to no observer during the first 9 months of treatment by type of observer

Type of practical observer	Month of treatment* 1	2	3	4	5	6	7	8	9
Family member	4/219	10/225	7/217	3/210	1/203	0/36	1/16	0/4	—
Community member	0/30	1/32	1/32	0/30	0/28	0/6	0/2	0/1	—
Health personnel	8/74	5/52	6/38	3/29	3/25	0/3	—	—	—

* No. of patients with change to self administration/No. of patients analysed in that month.

Table 5 Hazard ratios of changing to no observer: crude and adjusted analyses

Included variable	Change to SA* Yes	Change to SA* No	Hazard ratio (95% confidence interval)† Crude Model 1	Adjusted analyses Model 2	Model 3	Model 4
Practical observer						
Health personnel	25	196	4.98 (2.85–8.68)‡	4.19 (2.38–7.36)‡	4.66 (2.51–8.64)‡	4.54 (2.43–8.49)‡
Community member	2	159	0.53 (0.13–2.22)	0.46 (0.11–1.93)	0.53 (0.12–2.27)	0.54 (0.13–2.34)
Family member	26	1104	1	1	1	1
Living partner						
Having no partner	28	415	—	2.16 (1.25–3.74)‡	2.18 (1.26–3.79)‡	2.16 (1.25–3.75)‡
Having partner	25	1044	—	1	1	1
Living place						
Only one	23	419	—	0.39 (0.23–0.67)‡	0.38 (0.22–0.66)‡	0.38 (0.22–0.67)‡
More than one	23	1040	—	1	1	1
TB clinic						
Community hospital	21	875	—	—	0.55 (0.29–1.02)	0.53 (0.28–1.00)‡
General/regional hospital	19	381	—	—	1	1
Zonal TB centre	13	203	—	—	0.53 (0.24–1.14)	0.51 (0.23–1.11)
HIV/AIDS						
Yes	10	136	—	—	—	1.27 (0.62–2.60)
No	43	1323	—	—	—	1
Log likelihood			−284.90	−274.55	−272.47	−272.27
Degrees of freedom			2	4	6	7

* Number of patient-months with change to no observer or self-administration.
† Model 1 = crude analysis; Model 2 = Model 1 + demographic and socio-economic covariates; Model 3 = Model 2 + covariates related to health services; Model 4 = Model 3 + covariates related to disease condition.
‡ $P < 0.05$.
SA = self administration; HIV = human immunodeficiency virus; AIDS = acquired immune-deficiency syndrome.

showed that HPs were assigned to all patients but without an alternative, and that 27% of 200 patients did not or could not attend the clinic as scheduled.[23] Outreach approaches have been used in New York City to solve the problem of low accessibility of HP-DOT, but this requires more staff and supervision.[24] In our setting, with its financial limitations, incentives or outreach approaches were rarely used, and patients had to bear all the costs of travel. For patients with limited income or with limited options for transport, it was clearly not feasible to assign HP-DOT without an alternative. As about half of the HP observer assignments were immediately rejected, acceptability may be an additional obstacle to accessibility.

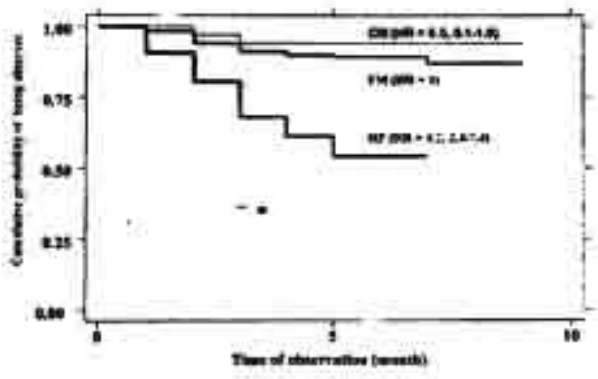

Figure Survival curve for each type of observer during 9 months of treatment. HR = hazard ratio of changing to having no observer adjusted for having/not having a living partner, number of living places, type of TB clinic, and HIV/AIDS status. CM = community member; FM = family member; HP = health personnel.

As in the study from India,[23] modification of HP-DOT occurred. Some patients met their health workers once or twice weekly or monthly because they were unable, or unwilling, to visit the hospital or health centre every day. In other cases, assigned health personnel transferred their observer role to community and/or family members. Applying an intermittent regimen apparently improved the sustainability of HP-DOT, but the benefit was not statistically significant (data not shown). Sustaining HP observers was not only a result of the patients' accessibility and willingness to accept a HP observer, but it was also associated with monitoring the DOT observer in practice and the providers' ability to counteract non-compliance.

Using community members is a promising alternative because good outcomes have been reported,[25–27] although there are no data available on actual DOT. In our setting, CM observation changed to self administration less often than non-CM, and CMs complied with the DOT principle better than FMs. However, CMs were less often assigned. The sustainability of increasing assignment to this group may need further exploration.

The Centers for Disease Control and Prevention in

the United States suggest that family members may not make good observers due to emotional ties.[7,15] Family bonds in our setting may, however, have more advantages than disadvantages with regard to general care and psychological support. The reason for not practising actual DOT was not family bonds but a lack of perceived need, and FM observation may be the only remaining option for the patients with poor performance status. Supervision of FM observers, with staff members of TB clinics or health centres making unannounced home visits, has been applied in Thailand, but the effectiveness of this activity has not yet been reported.

Our study may be subject to information bias. Misclassification of observers was often inevitable when there was more than one observer in a month. DOT practice could be overstated in the interviews because patients and observers considered the interviewers as health personnel. The 'practice of actual DOT' group included patients who practised actual DOT for any doses, and it may have included undisclosed 'no practice of actual DOT', which would bias our estimates. Furthermore, data were missing for 44 cases who were more often assigned to HP (60% vs. 43%) and more often assigned to CM (11% vs. 5%) than the patients included in the analyses. If the non-FM group maintained the observer status but did not practise actual DOT, we may have overestimated the compliance with the DOT principle among non-FM compared with FM groups.

CONCLUSIONS

Actual DOT practice was quite different from the initial assignment. Actual DOT was more often reported for health personnel than for other types of observer, but it was more difficult to maintain health personnel as observers. To improve the coverage of actual DOT, strategies to enhance the sustainability of health personnel observers and the practice of actual DOT among family member observers are needed.

Acknowledgements

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RÉSUMÉ

CONTEXTE : Le système de santé gouvernemental en Thaïlande du Sud avec la mise en œuvre d'une stratégie de traitement directement observé et de courte durée.
OBJECTIF : Comparer les pratiques réelles du traitement directement observé (TDO) et la possibilité de maintenir un observateur selon les différents types d'observateurs.
MÉTHODES : Ont été suivis en 1999 et 2000, 411 nouveaux patients atteints d'une tuberculose pulmonaire à bacilloscopie positive. Les patients et/ou leurs observateurs ont été interviewés au sujet de la présence d'une personne quelconque à côté du patient au cours de la prise du médicament et au sujet des pratiques de surveillance de la déglution du médicament par le patient (TDO réel). Les données ont été enregistrées mensuellement et analysées par les modèles de Cox et de régression logistique.
RÉSULTATS : Au cours des 9 premiers mois de traitement, les proportions de sujets ne pratiquant pas un TDO réel ont été respectivement de 11%, de 23% et de 35% pour le personnel de santé (HP), les membres de la collectivité (CM) et les membres de la famille (FM) ; la proportion de sujets qui sont passés à une administration sans observateur ou à une auto-administration a été respectivement de 11%, de 1% et de 2%. C'est le personnel de santé qui avait le risque le plus faible de ne pas recourir à un TDO réel (odds ratio HP/FM 0,1 ; IC95% 0,1–0,2 ; CM/FM 0,9 ; IC95% 0,5–1,6), mais le risque le plus élevé de passer à l'auto-administration.
CONCLUSION : Pour augmenter la couverture par un TDO réel, des stratégies s'imposent pour maintenir le personnel de santé comme observateur du TDO et pour pousser à un TDO réel les observateurs familiaux.

RESUMEN

MARCO DE REFERENCIA : El sistema de salud gubernamental de Tailandia del Sur, con la implementación de una estrategia de tratamiento directamente observado de corta duración (DOTS).
OBJETIVO : Comparar la práctica del tratamiento directamente observado (TDO) real y la permanencia del observador junto al paciente a lo largo del tratamiento, según los diferentes tipos de observadores.
MÉTODO : Se practicó el seguimiento de 411 pacientes nuevos con tuberculosis pulmonar con baciloscopia positiva, en 1999–2000. Se entrevistaron a los pacientes y/o a sus observadores acerca de la presencia de cualquier persona que hubiera permanecido con el paciente durante la toma de los medicamentos y acerca de la práctica de supervisión de la deglutición de los medicamentos (TDO real). Los datos fueron registrados mensualmente y analizados por los modelos de Cox y de regresión logística.
RESULTADOS : Durante los primeros 9 meses de tratamiento, se constató que la proporción de observadores que no realizaban el TDO real era de 11% para el personal de salud (HP), 23% para los miembros de la comunidad (CM) y de 35% para los miembros de la familia (FM) ; la proporción de sujetos que pasan a un tratamiento sin observador o a una autoadministración era de 11%, 1% y 2%, respectivamente. El personal de salud tenía el riesgo más bajo de no practicar el TDO real (odds ratio : HP/FM 0,1 ; IC95% 0,1–0,2 ; CM/FM 0,9 ; IC95% 0,5–1,6), pero el riesgo más alto para cambiar a la autoadministración.
CONCLUSIÓN : Se necesitan estrategias para mantener el personal de salud como observadores del TDO y promover el TDO real entre los observadores familiares, a fin de aumentar la cobertu... del TDO real.

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Associated factors of tooth wear in southern Thailand

P. CHUAJEDONG, U. KEDJARUNE-LEGGAT, D. KERTPON, V. CHONGSUVIVATWONG* & P. BENJAKUL *Faculty of Dentistry and *Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkla, Thailand*

SUMMARY The purpose of this study was to evaluate the possible risk factors connected with tooth wear. Using the Tooth Wear Index (TWI) and the charting of pre-disposing factors tooth surface loss was recorded in 506 patients, of the Dental Hospital, Prince of Songkla University. We found that age, sex, number of tooth loss, frequency of alcohol, sour fruit and carbonate intake were significant risk factors. Regarding the tooth position, the first molar showed the greatest degree of wear, while the canine and premolar showed the least, respectively. The occlusal surface showed the greatest wear and the cervical, lingual and buccal surfaces showed the least, respectively.

KEYWORDS: wear, tooth surface loss, erosion, attrition, abrasion, risk factors

Introduction

Although tooth wear can be a physiological process (Milosevic, 1998),clinical problems due to tooth wear have increased, because people are keeping their own teeth for many more years. Tooth wear is regarded as pathological if the teeth become so worn that they no longer function effectively or seriously effect appearance (Kidd & Smith, 1993).

Tooth wear is a common term used to describe the surface loss of dental hard tissue, which may be a result of erosion, attrition and abrasion (Smith & Knight, 1984a). Tooth wear is usually regarded as multifactorial, but the aetiology is still unclear (Smith, Bartlett & Robb, 1997). Although many studies have investigated the cause of tooth wear, it has been difficult to differentiate among erosion, abrasion and attrition because of the combination of possible causes (Hattab & Yassin, 2000).

Many kind of foods and beverages have been linked to the problem. These include sports drinks, carbonated drinks, fruit juice, lactovegetarian diet, alcohol, fresh fruits and pickled foods (Linkosalo & Markkanen, 1985; Smith & Shaw, 1987; Rytomaa *et al.*, 1988; Meurman *et al.*, 1990). When, tooth wear is positively associated with age it can be called a physiological process (Johansson *et al.*, 1993; Milosevic, 1998). Some studies have shown that men have more tooth wear than women (Molnar *et al.*, 1983; Smith & Robb, 1996), although occasionally this view has not been supported (Abdullah *et al.*, 1994). The number of teeth present have also shown a correlation with wear, fewer teeth leading to more wear of the remainder (Dahl, Carlsson & Ekfeldt, 1993; Johansson *et al.*, 1993), although a contrary view was recorded by Smith and Robb (1996).

In addition, there are other factors effecting the process of tooth surface wear. Patients with gastro-oesophageal reflux disease or other diseases that provoke reflux may be prone (Gregory-Head *et al.*, 2000). It has also been observed among battery workers associated with the acid environment and people living in conditions with fine particulate material in the air, such as deserts (Johansson, Fareed & Omar, 1991; Petersen & Gormsen, 1991). Salivary factors and bruxism have also been investigated to see if they contribute to tooth surface loss (Jorvinen, Rytomaa & Heinonen, 1991; Gudmundsson *et al.*, 1995; Milosevic & Dawson, 1996; Khan, Young & Daley, 1998). Known factors can explain only 41% of tooth wear, with the majority of tooth wear remaining unexplained (Dahl & Oilo, 1996).

Differences in cultural, dietary, occupational, environmental and geographical factors may influence the manifestation of tooth wear in different countries. Little

is known about the aetiology of the problem in our country. The aim of this present study was to analyse the relative contributions of various aetiological factors contributing to tooth wear in Southern Thailand.

Materials and methods

Sample population

The sample comprised of patients who were over 15 years of age and presented in the Dental Clinic at the Prince of Songkla University during April and May, 1999. There were 506 (151 males and 355 females) with a mean age of 32 years. All of the subjects were fully informed and agreed to take part in the study. Patients who had received orthodontic treatment or surgery of the temporomandibular joint were excluded.

Questionnaire

The questionnaire comprised of questions on medical status, sign and symptoms of any temporomandibular joint disorder (TMD), parafunctional habits, chief complaints, the general environment of patients, the frequency of intake of sour food and drinks were all recorded. The first author performed the questionnaire interview then completed the questionnaire for each of the sample.

Clinical examination

The severity of tooth wear was recorded utilizing Tooth Wear Index (TWI)described previously (Smith & Knight, 1984b) by the same examiner. It was an ordinal scale grading severity of tooth wear. The bruxism was defined as the presence of both historical and clinical criteria (Pavone, 1985). The intra-examiner reliability was tested by re-examining both the interview and the clinical examination of 10 cases after an interval of 1 week. Intra-examiner agreement was evaluated by Weighted Kappa statistic.

Statistical methods

Data management and statistical analyses were performed by using Stata Release 6. For univariate analysis, Spearman correlation was used to analyse the correlation between severity of tooth wear and the continuous independent variables. A Kruskal–Wallis test was performed the category independent variables. For dichotomous independent variables the Wilcoxon Rank Sum test was performed. Multiple regression analysis was performed using the generalized least squared (GLS) with the random effects model (taking repeated measures of the same subjects into account). Variables that were significant at 0·1 level in univariate analysis were put into multivariate modelling.

Results

The kappa statistic of this agreement was 0·82 which represented a high level of agreement between the first and second examination. Table 1 presents the demographic characteristics of the sample. Table 2 shows the distribution of chief complaints, medical status and the need for daily medication. Table 3 indicates the distribution of tooth wear risk factors.

From Table 3, the number of teeth available per patient range from 10 to 32 with an average of 28 (s.d. = 3·04). Of several symptoms that may be related to tooth wear, unilateral chewing habit was the most common while bruxism was present in only 17·8% of the sample.

In Table 4, univariate analysis shows several significantly associated factors for tooth wear of the occlusal and cervical surfaces. The level of association with risk factors was lower on the buccal and lingual surface.

Table 1. Distribution of demographic characteristics

	Frequency (%)
Sex	
Male	151 (29·8)
Female	355 (70·2)
Age (years)	
< 20	91 (18·1)
20–29	136 (27·0)
30–39	127 (25·0)
40–49	115 (22·8)
50–59	33 (6·5)
> 60	3 (0·6)
Occupation	
Government official	193 (38·1)
Student	155 (30·6)
Worker	60 (11·9)
Unemployed	35 (6·9)
Merchant	29 (5·7)
Business man	14 (2·8)
Farmer	11 (2·2)
Other	7 (1·4)

Table 2. Distribution of chief complaints, systemic diseases and need for daily medication

	Frequency (%)
Chief Complaint	
Check up	155 (30·6)
Teeth pain	91 (18)
Filling	58 (11·5)
Teeth sensitivity	47 (9·3)
Scaling	25 (4·9)
Other	130 (25·7)
Systemic diseases	
Other	53 (10·5)
Gastritis	47 (9·3)
Allergy	35 (6·9)
Asthma	10 (2·0)
Alcoholism	1 (0·2)
Hernia	1 (0·2)
No	359 (70·9)
Needed daily medication	67 (13·2)

Table 3. Distribution of tooth wear factors

	Frequency (%)
Number of tooth (teeth)*	
10–19	12 (2·4)
20–29	381 (75·3)
>30	113 (22·3)
Clicking sound during mouth opening	132 (26·1)
Experienced sour in the mouth	142 (28·1)
Facial pain and tenderness	92 (18·2)
Bruxism	90 (17·8)
Unilateral chewing habit	244 (48·2)
Long-term dust exposure	88 (17·4)
Brushing technique	
Upward and downward technique	246 (48·6)
Forward–backward technique	65 (12·8)
Brass technique	42 (8·3)
Roll technique	3 (0·6)
Others technique	150 (29·7)

*Average = 28, s.d. = 3·04.

When multiple repeated measurements with random effects was used, 5, 3, 1 and 1, factors were still associated with tooth wear of these respective surfaces. Increased age is associated with increased tooth wear of all surfaces excepted the lingual. Males had a higher risk of tooth wear only on the cervical surface and not on other surfaces. Reduced number of teeth lost is associated with increasing tooth wear on the occlusal surface. Carbonated drinks are associated with only lingual surface tooth wear whereas alcohol and sour fruits are association with occlusal tooth wear.

Regarding tooth position, there was a significant difference ($P < 0·05$) in the tooth wear score among tooth positions. The first molar showed the highest score. The scores were less in canine, premolar and anterior teeth, respectively. However, there was no difference among quadrants ($P < 0·05$). These are shown in Fig. 1. Furthermore, this study found that when regarding tooth surface variation, the significantly different tooth wear($P < 0·05$) demonstrated the greatest at the occlusal surface. Less wear was found at the cervical, lingual and buccal surface, respectively. The tested risk factor could explain almost 60% of occlusal tooth wear and about one-fourth of the cervical tooth wear but could not provide explanation of loss of the buccal and lingual surfaces (adjust $r^2 = 0·03$).

Discussion

Tooth surface, tooth position, sex, age, number of teeth lost and the frequency of sour fruits, alcohol and carbonate intake may play an important role in tooth wear. From Table 4 it was shown that the occlusal surface was a clearer predictor effecting the severity of tooth wear than other surfaces. These findings imply that wearing of the occlusal surface was dependent on many factors other than another surface. Buccal and lingual tooth wear have very few statistical predictors. As expected, this study found that the severity of tooth wear was the greatest at the occlusal surface and less at cervical, lingual and buccal, respectively. In relation to its prevalence relative to tooth position (Fig. 1) the first molar showed the greatest degree of wear while the canines and premolars showed the least. The findings of this study were somewhat different from a previous study (Smith & Robb, 1996) that showed that incisors had the most severe wear. However, another study has shown that tooth wear into the dentine was seen most frequently on the central incisor and lower first molar (Milosevic, Young & Lennon, 1994). These results may be explained by the fact that the first molar is the first permanent tooth that erupts into the oral cavity. Therefore, the first molar can be more exposed to various factors that can lead to tooth wear.

As expected, tooth wear increased with age, which is consistent with other studies (Johansson *et al.*, 1993; Smith & Robb, 1996). Moreover, this study found that age is a common risk factor for tooth wear of all surfaces except for the lingual surface for which the frequency

Table 4. Statistical significance of factors associated with tooth wear from univariate analyses and multiple regression

Predictor	Statistic method use in univariate analysis	*P*-value from univariate/*P*-value from multivariate*			
		Occlusal	Cervical	Buccal	Lingual
Personal data					
Age	Spearman†	<u>< 0·001/< 0·001</u>	<u>< 0·001/< 0·001</u>	<u>< 0·001/0·01</u>	0·002/0·08
Sex	Mann–Whitney	< 0·001/0·36	<u>< 0·001/< 0·001</u>	0·03/0·15	0·13/–
Occupation	Kruskal–Wallis	< 0·001/0·88	< 0·001/0·14	0·99/–	0·99/–
Sports	Kruskal–Wallis	< 0·001/0·85	0·28/–	1·00/–	1·00/–
General health					
Systemic diseases	Kruskal–Wallis	< 0·001/0·89	0·03/0·35	1·00/–	0·99/–
Taking medication daily	Mann–Whitney	< 0·001/0·89	< 0·001/0·75	0·33/–	0·33/–
Dental status					
Bruxism	Mann–Whitney	< 0·001/0·36	0·009/0·9	0·69/–	0·12/–
Unilateral chewing	Mann–Whitney	< 0·001/0·36	0·001/0·99	0·89/–	0·29/–
Sour taste in mouth	Mann–Whitney	0·37/0·19	0·001/0·18	0·86/–	0·23/–
Facial pain	Mann–Whitney	< 0·001/0·56	< 0·001/0·52	0·73/–	0·41/–
Brush technique	Kruskal–Wallis	< 0·001/0·16	0·21/–	0·99/–	0·99/–
Number of teeth lost	Spearman	<u>< 0·001/0·004</u>	0·001/0·16	0·95/–	< 0·001/0·19
Tooth position	Kruskal–Wallis	<u>< 0·001/< 0·001</u>	<u>< 0·001/< 0·001</u>	1·00/–	0·99/–
Dietary factor					
Fruit juice	Spearman	< 0·001/0·21	< 0·001/0·69	0·10/–	0·61/–
Carbonate	Spearman	< 0·001/0·25	< 0·001/0·07	0·003/0·31	<u>0·004/0·017</u>
Hard food	Spearman	< 0·001/0·46	< 0·001/0·63	0·24/–	< 0·001/0·28
Alcohol	Spearman	<u>< 0·001/0·001</u>	0·015/0·17	0·10/–	< 0·001/0·21
Sour food	Spearman	< 0·001/0·41	0·60/–	0·06/0·39	< 0·001/0·54
Sour fruit	Spearman	<u>0·001/< 0·001</u>	0·19/–	0·67/–	0·12/–
Adjust *r*-squared for multiple linear regression		0·59	0·21	0·03	0·03

*P-value from using univariate statistic method/P-value from multivariate analysis with parameter test.
†Spearman correlation.
Underlined value indicates that the factor is of statistical significance both in univariate and multivariate analysis.

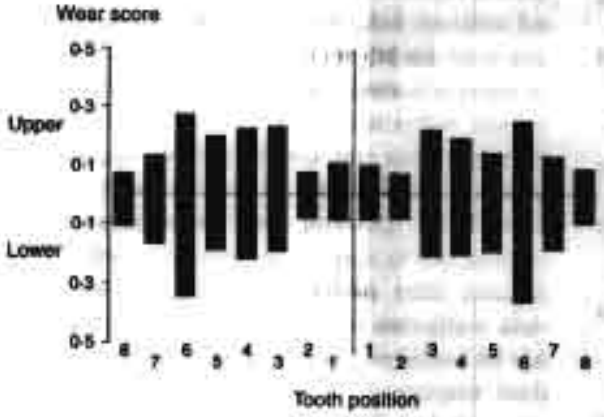

Fig. 1. Wearing score of teeth according to tooth position in the dental arch.

of carbonate intake was a more powerful erosive factor. Tooth wear also correlated positively with the number of teeth lost. As previously stated, several studies have demonstrated that tooth wear is more extensive in men than women. At least part of the explanation is that men have a more powerful masticatory musculature than women (Dahl & Qilo, 1996). However, this study showed only a significant increase in cervical surface loss in males may be because of greater abrasion from their tooth brushing technique.

Alcohol may induce tooth wear indirectly as it causes irritation of the gastric mucosa. This provokes reflux, especially in alcoholics (Bartlett, 1997). The erosion caused by reflux has been emphasized as more important than dietary factors by Smith and Knight (1984a). However, direct erosive effects were also documented. Rees, Burford and Loyn (1998) reported that alcoholic lemonade beverages can erode enamel and Sarrett, Coletti and Pelaso (2000) reported increasing of composite wear by ethanol content of wine.

Some fruit intake can also contribute erosive effects and the correlation between tooth wear and the

mapping using Ethnograph software, version 4.0 (Qualis Research Associates, Utah, USA).

Results

Quantitative study

Eligible medical records were available in 95%, 93% and 94% of study records in the university hospital, the regional hospital, and the general hospital, respectively. After exclusion by the above criteria, the final numbers were 879, 923, and 924, for the university, regional and general hospitals, respectively. Most women were less than 35 years old with similar proportions of nulliparous and multiparous women across three hospitals (see Table 1). The proportion of women in private cases was higher in the university and the general hospital than in the regional hospital. Elective CS were more common in the general hospital.

There were 73 physicians in total: 31, 29, and 13 in the university, regional, and general hospitals, respectively. The proportions of gender (male *vs* female) and professional status (intern or resident *vs* faculty member) were similar in the three hospitals (see Table 2).

Use and timing of antimicrobial prophylaxis

The prophylactic use of antimicrobial agents in the three hospitals is shown in Figure 1. Antimicrobial prophylaxis was used in 94% of all women undergoing CS with prescribing after cord clamping in 87%. Eighteen percent of women in the university hospital did not receive any prophylactic antimicrobial agents. The proportions of the prophylactic use and intraoperative prescription were significantly different across hospitals ($P<0.01$). Intraoperative prescription was consistently used by the physicians in the regional and

Table 1 General characteristics of cases undergoing cesarean section

Characteristics	Hospitals			Total
	University ($n=879$) N(%)	Regional ($n=923$) N(%)	General ($n=924$) N(%)	($n=2726$) N(%)
Age (years)				
<25	108 (12.3)	267 (28.9)	276 (29.9)	651 (23.8)
25–29	255 (29.0)	273 (29.6)	309 (33.4)	837 (30.7)
30–34	305 (34.7)	243 (26.3)	222 (24.0)	770 (28.3)
≥35	211 (24.0)	140 (15.2)	117 (12.7)	468 (17.2)
Parity				
Nulliparity	437 (49.7)	403 (43.7)	390 (42.2)	1230 (45.1)
Multiparity	442 (50.3)	520 (56.3)	534 (57.8)	1496 (54.9)
Type of service				
Ward	337 (38.3)	445 (48.2)	244 (26.4)	1026 (37.6)
Private	542 (61.7)	478 (51.8)	680 (73.6)	1700 (62.4)
Type of cesarean section				
Elective	344 (39.1)	344 (37.3)	457 (49.5)	1145 (42.0)
Non-elective	535 (60.9)	579 (62.7)	467 (50.4)	1581 (58.0)

Table 2 Characteristics of physicians

Characteristics	Hospitals			Total
	University ($n=31$) N(%)	Regional ($n=29$) N(%)	General ($n=13$) N(%)	($n=73$) N(%)
Age (years)				
<30	18 (58.1)	16 (55.2)	8 (61.5)	42 (57.5)
30–39	5 (16.1)	7 (24.1)	1 (7.7)	13 (17.8)
≥40	8 (25.8)	6 (20.7)	4 (30.8)	18 (24.7)
Gender				
Male	17 (54.8)	16 (55.2)	7 (53.8)	40 (54.8)
Female	14 (45.2)	13 (44.8)	6 (46.2)	33 (45.2)
Professional status				
Intern	-	13 (44.8)	8 (61.5)	21 (28.8)
Resident	15 (48.4)	3 (10.4)	-	18 (24.6)
Faculty member	16 (51.6)	13 (44.8)	5 (38.5)	34 (46.6)

general hospitals, but not by those in the university hospital.

Type and doses of antimicrobial agents

Types and doses of intraoperative antimicrobial agents are shown in Table 3. Two grams of intravenous ampicillin was the most common prescription in all hospitals. Other antimicrobial agents such as cefazolin, cefoxitin, or amoxicillin/clavulanate potassium were prescribed more often in the regional hospital.

Physicians in the university hospital usually prescribed multiple doses of prophylactic antimicrobial agents (91%). The proportion of single dose and multiple doses within the first operative day were similar in the general hospital. In contrast, physicians in the regional hospital mostly prescribed a single dose of antimicrobial agents (84%). The proportions of single-dose regimen differed significantly across hospitals ($P < 0.01$) and had a high variation among physicians within each hospital.

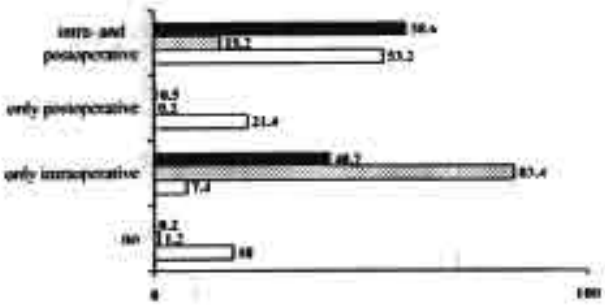

Figure 1 Percentages of prophylactic antimicrobial prescription in the university, regional and general hospitals. ■, general; ▨, regional; □, university.

Postoperative oral antimicrobial agents were used in 52% of the women in the university hospital whereas the corresponding proportions in the general hospital and the regional hospital were 19% and 6%, respectively. The most commonly used oral prophylactic antimicrobial agent was amoxicillin: 98%, 76%, and 96% in the university, regional and general hospitals, respectively. Cloxacillin was the second most common oral antimicrobial agent in the regional hospital.

Qualitative interview

Use of prophylactic antimicrobial agents

Complete interview response was obtained from 50 study physicians. All physicians said that they did prescribe prophylactic antimicrobial agents for at least some women undergoing CS and had not changed their practices in the last 2–3 years. Frequency of prophylactic use of antimicrobial agents ranged from routine use to selective use for high-risk women undergoing CS, the details of which are depicted in Table 4. Among physicians using prophylaxis for only indicated cases, the five most common indications were ruptured membranes, vaginal examinations, labor, maternal obesity and unplanned CS, respectively. The reason statements given by the physicians who used antimicrobial agents routinely varied such as 'I use prophylactic antimicrobial agents because they have been shown to reduce the incidence of post-cesarean infection in all cases', 'Antimicrobial prophylaxis indeed prevents infection in high-risk CS but it is customary to prescribe in the cases of elective CS. In

Table 3 Type and number of doses of prophylactic antimicrobial agents

Prophylactic antimicrobial agents	Hospitals			Total
	University *N*(%)	Regional *N*(%)	General *N*(%)	*N*(%)
Intraoperative drug type				
Ampicillin	531 (99.6)	718 (78.9)	899 (98.1)	2148 (91.0)
Cefazolin	1 (0.2)	144 (15.8)	2 (0.2)	147 (6.2)
Cefoxitin	–	37 (4.1)	15 (1.6)	52 (2.2)
Amoxicillin/Clavulanate	–	11 (1.2)	–	11 (0.5)
Gentamicin	1 (0.2)	–	1 (0.1)	2 (0.1)
Number of doses[†]				
Single	65 (9.0)	770 (84.4)	376 (40.8)	1211 (47.4)
Multiple	656 (91.0)	142 (15.6)	546 (59.2)	1344 (52.6)
One day only[‡]	279 (38.7)	85 (9.3)	373 (40.4)	737 (28.8)
More than one day[§]	377 (52.3)	57 (6.3)	173 (18.8)	607 (23.8)

[†]After excluding postoperative infection cases
[‡]Intravenous antimicrobial agents
[§]Intravenous and subsequent oral antimicrobial agents

Table 4 Indications for prescribing antimicrobial prophylaxis for cesarean section according to 50 physicians' opinions

Main indications for prescription	Number of physicians (%)
Routine for all cases	26 (52)
Indicated cases	24 (48)
Ruptured membrane	24 (100)
Vaginal examination	17 (71)
Labor	16 (67)
Maternal obesity	14 (58)
Unplanned cesarean section	9 (38)
Vaginal bleeding	6 (25)
Contamination or postoperative complications	6 (25)
Diabetes mellitus	7 (29)
On immunosuppressive drugs	6 (25)
Anemia	4 (17)
HIV infection	4 (17)
Malnutrition	3 (12)

addition, rate of turnover of cases in the operating room in my hospital is high, easily leading to contamination', or 'I would like to avoid any adverse consequences of infection; moreover, the adverse reactions of used antimicrobial agents are low so I use prophylaxis routinely'.

The selective users perceived that the benefit of prophylaxis was only in the women at higher risk of infections, for example, 'I think that antimicrobial prophylaxis is beneficial but not in all cases. Drug administration in all cases may reduce infection; however, this application is not cost-effective'. A few physicians did not believe in the benefit of such prophylaxis but prescribed it because other colleagues were practicing it or to protect them from any criticism: 'I don't like to give antimicrobial agents but other assistants prepare antimicrobial agent to operating room and the nurse asks me for administration so I don't refuse' or 'Indeed, post-cesarean infection depends on surgical techniques and operative time rather than prophylactic antimicrobial prescription but I prescribed because I would be blamed if I didn't prescribe and infection occurred'.

Timing of antimicrobial agent administration

Almost all physicians preferred administering the antimicrobial agents after cord clamping because they would like to avoid antimicrobial agents passing to the baby. Some physicians in the university hospital started prophylactic antimicrobial agents only postoperatively either to combat the contamination or prevent infection due to complications that occurred during the operation.

Type of antimicrobial agents

Ampicillin was the most commonly used antimicrobial agent as the first choice by all physicians, except one who used cefazolin, because ampicillin was perceived to cover organisms in the genito-urinary tract and it is simple, cheap, readily available, and with very few side-effects. An economic crisis in the country since 1997 compelled some physicians at the general and the regional hospitals to choose ampicillin (e.g. 'Ampicillin was chosen because it was the hospital recommendation when the hospital and government were facing with an economic crisis' or 'In choosing a type of antimicrobial agent for prophylaxis in cesarean section, I consider the patient's economics and ability to afford'). In case of penicillin allergy, gentamicin, cefazolin or cefoxitin were used in high-risk or emergency CS but not in elective operations.

Number of doses

Physicians in the regional hospital mostly prescribed a single dose of ampicillin or cefazolin as they perceived that it was the recommended practice of the hospital. Almost all physicians in both the university and the general hospitals used multiple doses. Most physicians said that they received the knowledge of this practice from textbooks rather than journals, for example, 'I have learned the principle of antimicrobial prophylaxis from the textbooks', 'The knowledge from textbooks is important but it should be modified to suit our country', or 'My current practice for number of doses is not only from obstetric textbooks but also from my ideas or surgical textbooks'.

Only a few physicians were aware of the literature on the appropriateness of single-dose antimicrobial prophylaxis: 'I don't know the effectiveness of single dose because I have never practiced but I think it may be effective; however, continuous doses after surgery are more effective in my opinion' or 'Single dose is effective in cases where there is no problem such as difficulty of surgery, long operative time, or tissue trauma during cesarean section'.

Most of the physicians still believed that multiple doses had better outcomes in their situation based on personal experience. Some physicians' reasons for prescribing multiple doses from their experience were 'I believe that additional postoperative antimicrobial agents are better than single dose', 'I usually use additional two-dose postoperative antimicrobial agents and don't get any problems so I continue to prescribe them', or 'In my experience, women during postpartum period were so troubled that I didn't want to give them more problems from postoperative infection'.

The main reasons for prescribing prophylactic oral antimicrobial agents postoperatively were also based on their positive experiences or preventing any infection due to intraoperative complications or contamination: 'Antimicrobial prophylaxis depends on my feeling during operation. If I think that this operation is difficult or has some problems, I may change the methods of prescription'. However, some physicians prescribed them because of their lack of confidence in the infection prevention systems of the hospital. The examples of their reasons were: 'If sterile techniques of patient preparation, surgical team, and operating room are adequate, antimicrobial prophylaxis is required only in high-risk cases, not in elective cases, and a single dose of antimicrobial agent is appropriate' or 'Antimicrobial prophylaxis for cesarean section should be considered with many situations such as the standard of operating room or infection rate'.

Discussion

The practices of prophylactic antimicrobial agents for CS varied across three different hospitals. Practice of single-dose antimicrobial prophylaxis after cord clamping was most commonly found in the regional hospital, as the physicians perceived it to be the recommended practice of the hospital. In the other two hospitals, either no prophylaxis or prolonged prophylactic antimicrobial agents were common. Main physicians' reasons for these practices depended upon individual perception of knowledge and adopted experiences. Ampicillin was the most common antimicrobial agent in all three hospitals. The reasons were its properties and the financial appropriateness.

The finding of variation in practice is similar to the surveys by Huskins *et al.*[6] and Pedersen and Blaakaer.[7] Both surveys evaluated the overall practices without any assessments for the physicians' reasons for use or variation. Our results of practices from quantitative data consistently correlated with those from the qualitative interview, although the time interval from the actual practice to interview was 2 years. This is likely to be because none of the physicians had changed their practices in the last 2 or 3 years.

Most randomized controlled trials of antimicrobial prophylaxis for CS have been carried out in Western countries where more expensive drugs such as cefotetan, cefoxitin, ceftizoxime, cetriaxone, cefotaxime or piperacillin were used.[3,8-10] However, systematic review showed no statistically significant difference in reducing post-cesarean infection between ampicillin and more expensive drugs.[3] Ampicillin was the drug of choice not only in this study but also in most centers in developing countries[6] because it is cheap and accepted by physicians. Furthermore, it was shown to be effective in one randomized study in Thailand.[11]

Many randomized trials and systematic reviews have shown that a single dose was as effective as multiple doses[3] and additional prolonged use of oral antimicrobial agents is associated with an increased risk of penicillin-resistant *Streptococcus pneumoniae* carriage.[12] Despite these findings, multiple-dose prescription and/or additional oral antimicrobial agents were still a common practice found in this study. This is because most of the physicians had the knowledge of multiple-dose prophylaxis and it was perceived to be better for reducing the incidence of postoperative infection in their particular conditions. However, single-dose practice was more common in the hospital where the physicians perceived it to be recommended. Therefore, the practice variation might be explained by the differences in knowledge, past experience and hospital recommendation.[13-17]

This study showed that there was a knowledge–behavior gap between research findings in the literature and the actual clinical practice. Such gaps have been shown to be narrowed by continuing medical education or setting up hospital clinical practice guidelines.[16-19] This is supported by our finding that in the regional hospital, where common hospital practice was established, the practice was more appropriate. In

addition, confidence in the hospital infection control may play an important role in physicians' decisions. As seen in our results, some physicians working in well-equipped and well-functioning conditions, such as the university hospital, ignored antimicrobial prophylaxis in low-risk women undergoing CS. On the other hand, some physicians who believed that the aseptic techniques might not be up to standard used a multiple-dose prophylaxis frequently.

Our literature review indicated that this is perhaps the first study exploring the reasons for the prophylactic practice of antimicrobial agents for CS using a combination of quantitative medical record review and qualitative physician interview at various levels of hospitals in a developing country. It is very likely that this disparity is also common in many other countries. Proper understanding of the nature and the factors influencing clinical practice should lead to a development of effective interventions for appropriate prescription.

In conclusion, each physician prescribed antimicrobial prophylaxis for CS in a way that depended on his/her knowledge, personal experience and the established clinical practice recommendations. However, the study showed a high variation of practice even where there were established clinical practice recommendations. Perhaps the development of written clinical practice guidelines followed by in-service training and the monitoring of subsequent practice should be recommended. The observation that guidelines may have some role in a more appropriate practice may be anecdotal and should be confirmed by a more specific study design in the future.

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A Randomized Controlled Educational Intervention on Emergency Contraception Among Drugstore Personnel in Southern Thailand

CHAVEEWAN RATANAJAMIT, PHD
VIRASAKDI CHONGSUVIVATWONG, MD, PHD
ALAN F. GEATER, PHD

Objective: to document the effectiveness of an educational intervention in improving knowledge of and practice in dispensing emergency contraception (EC) among drugstore personnel in Thailand.
Methods: Sixty of 120 drugstores in Hat Yai, a city in Southern Thailand, were randomly selected, and half of them were randomly assigned to participate in an educational program. Well-trained "secret" shoppers went into each store before the intervention and at 1 and 3 months after the program to assess the knowledge of and practice in dispensing EC among the drugstore personnel.
Results: Dispensing practices at baseline were poor to fair and knowledge was fair in both groups. Sellers in the intervention group improved significantly in choice of drug, advice provided, and knowledge of the time limit for initiating EC, but those in the control group did not. However, proper history taking on the time of intercourse and menstrual cycle was poor in both groups at all study periods.
Conclusion: All drugstore personnel should be educated on the importance of history taking and on the time limit for initiating EC. (*JAMWA*. 2002;57: 196-199)

Dr. Ratanajamit is in the Department of Clinical Pharmacy in the Faculty of Pharmaceutical Sciences and Drs. Chongsuvivatwong and Geater are in the Epidemiology Unit of the Faculty of Medicine, all at Prince of Songkla University in Thailand.

Emergency contraception (EC) can be used to prevent pregnancy after unprotected sexual intercourse if taken within a certain time limit.[1,2] Three regimens of EC pills, including high-dose oral contraceptives (HCP, known as the Yuzpe regimen), high-dose levonorgestrel (LNG), and mifepristone, and postcoital insertion of a copper intrauterine device are the methods currently available.[1,3] LNG (0.75 mg tablet)[4] and HCP[1] are the 2 regimens available over the counter in many countries, including Thailand.[5-10]

Unintended pregnancies are a problem worldwide.[11,12] The number of women who initiate sex early, have more than one sex partner, and are unmarried but sexually active has been increasing in many countries.[13-15] Government contraceptive programs in Thailand are restricted to married women, leaving unmarried sexually active women and adolescents with potential unintended pregnancies and induced abortions. EC has been used widely and inappropriately among Thai adolescents (N. Matananpun et al, unpublished data, 1997). Our previous survey found that drugstore personnel had insufficient knowledge of and used improper practices in dispensing EC.[16] Product package inserts are inadequate or incorrect and also lead to improper dispensing practice.

Improving drugstore providers' knowledge of EC and dispensing practice could help reduce unintended pregnancies. Our hypothesis was that the EC knowledge and practice of drugstore personnel could be improved through educational intervention.

Methods

Thailand has approximately 10 000 drugstores, 45% of which are run by pharmacists,[17] although most dispensing (60%-75%) is done by nonpharmacist staff.[18,19] At the time of this study, LNG was available over the counter in a 2-tablet blister package containing instructions that 1 tablet be taken within an hour after unprotected sexual intercourse and cautioning that no more than 4 tablets per month should be taken.[4]

The study was conducted between late 2000 and early 2001 in Hat Yai, the largest city in southern Thailand with a population of 150 000 and 120 drugstores, 65 of which were pharmacist owned. The Ethics Committee of the Faculty of Medicine at Prince of Songkla University approved the study protocol.

Study Design. The study was a randomized controlled intervention conducted over 5 months and including pre- and postintervention measurement of knowledge of and practice in dispensing EC. Secret shopping, also known as the simulated client method, sends standardized clients to gather data and has proven to be a valid measure of actual practice.[20] A survey of EC knowledge and dispensing practice was carried out in the study sample in 1999 to assess basic knowledge and to plan intervention contents.[16] The second assessment, including revised questions to assess EC dispensing, was carried out in 60 drugstores in late 2000 immediately before the intervention. Three male and 3 female secret shoppers age 20 to 22 years were randomly (and alternately) assigned to different phases of data collection. All secret shoppers were blinded to the intervention status of the assigned drugstores.

Sample. The intervention would be considered effective if the postintervention mean score was at least 15% higher in the intervention group than in the control group. To detect such a difference as significant (at α=.05 with a power of 80%) required a sample of 23 drugstores for each group. However, to increase the power, we used 30 drugstores in each group. This sample size would also be adequate to detect postintervention differences in dispensing behaviors

Table 1. Weighting of Emergency Contraception (EC) Knowledge and Practice Variables Measured Among Drugstore Personnel in Thailand

Variable	Weighting	Score
History taking	13	
Coitus history		5
Cycle history		2.5
History of EC use		2.5
Pregnancy		3
Drug dispensed	10	
EC advice	19	
Dosing		10
Side effects		4
Evaluation of effectiveness		5
Knowledge of EC	30	
Time limit for starting EC		5
EC indication		5
Effectiveness of EC compared to regular oral contraceptives		5
EC mechanism of action		5
Adverse effect of consistent use of EC		5
Whether EC can be used as regular oral contraception		5

of 35% to 40%; for instance, 45% and 10% or 58% and 20% in intervention and control groups, respectively.

The list of drugstore owners was used as the sampling frame. EC practice at pharmacist-owned drugstores has been shown to be generally better than that at nonpharmacist-owned drugstores,[16] so we stratified the eligible drugstores before randomization. Thirty pharmacist-owned and 30 nonpharmacist-owned drugstores were randomly selected. Drugstores were then randomly allocated into the intervention or the control group.

Intervention. The intervention was designed to increase knowledge of EC and improve dispensing skills. The intervention consisted of a lecture about EC and good dispensing practice and a demonstration and role-play activity that engaged the provider, the shopper, and the observer in various case studies. All material used in the training course was approved by a clinical pharmacist and a gynecologist.

The owners and staff of each drugstore in the intervention group were invited to the intervention course, with the suggestion that at least 2 people from each drugstore attend. The intervention was conducted as a daylong course on a Sunday to increase attendance and was repeated on another Sunday to accommodate those who could not attend the first day. The average number of trained drugstore personnel per drugstore was 2.2.

Each intervention drugstore was visited between phases of postintervention data collection for a discussion of EC to reinforce performance. All control drugstores were given the written material after the final data collection.

Variables. The variables measured were based on the essential elements for proper dispensing of EC: coitus history, EC history, and contraindications. Data on the type and amount of EC dispensed and advice provided on dosing, common side effects, and how to evaluate effectiveness were collected. The providers' knowledge of EC (whether it can be used as a regular contraceptive method, indications for use, effectiveness, actions, time limit, and adverse effects associated with consistent use) was also measured. All items measured were recorded in the observation checklists, which we created, tested, modified, and used in all secret shoppings.

The scenario used in secret shopping was adapted from a situation commonly found among new EC seekers: A college

Table 2. Characteristics of Drugstore Personnel by Group and Time of Data Collection*

Characteristic	Preintervention		1 Month Postintervention		3 Months Postintervention	
	Intervention	Control	Intervention	Control	Intervention	Control
Sex, n						
Male	29	36	30	34	28	34
Female	31	24	30	26	32	26
Age, n						
<40	35	29	27	30	33	26
≥40	25	31	33	30	27	34
Education level, n						
Lower secondary or less	6	3	4	2	4	2
Upper secondary but no bachelor's degree	26	28	23	31	20	31
Bachelor's degree or higher	28	29	33	27	36	27
Pharmacist, n						
Yes	21	25	21	23	19	25
No	39	35	39	37	41	35
Trained personnel, n (%)	...	...	42 (70)	...	41 (68)	...

*Thirty drugstores were each shopped by 1 male and 1 female secret shopper for a total of 60 shopping incidents.

Table 3. Emergency Contraception (EC) Knowledge Scores by Group and Time of Data Collection

Knowledge Item, possible maximum score	Knowledge Scores, mean ± standard deviation					
	Preintervention		1 Month Postintervention		3 Months Postintervention	
	Intervention	Control	Intervention	Control	Intervention	Control
Time limit for starting EC, 5	1.3±1.9	1.6±2.1	4.2±1.7*	1.4±2.0	4.8±1.0	2.3±2.3
EC indication, 5	3.0±1.7	3.1±1.6	3.6±1.6	3.3±1.7	4.1±1.4	4.0±1.4
EC should not be used as regular contraception, 5	3.3±0.9	3.4±0.8	3.7±1.0	3.7±1.0	3.9±1.0	3.9±1.0
EC effectiveness, 5	3.8±2.1	4.4±1.6	5.0±0.0	4.8±0.9	5.0±0.0	4.8±0.9
Mechanism of action, 5	4.3±1.8	4.6±1.7	4.8±1.2	4.7±1.3	5.0±0.0	4.9±0.6
Adverse effects if EC is consistently used, 5	2.5±1.2	2.7±1.1	0.8±1.4	0.6±1.3	3.2±1.6	2.7±1.4
Total knowledge, 30	18.2±4.1	19.9±4.0	22.1±3.0*	18.5±4.5	26.0±3.0*	22.7±4.4

*Mann-Whitney U test was used to test the statistical significance of differences between the intervention and control groups, and these differences were significant ($p<.001$).

student experienced unprotected midcycle intercourse 24 hours earlier. What can drugstore personnel do to prevent an unwanted pregnancy?

The inter-rater reliability was assessed among 5 full-time pharmacist drugstores. All 6 raters rated all 5 selected drugstores. The inter-rater kappa in each domain ranged from 0.31 to 1.

The main independent variables—treatment group, demographic data of seller, and owner status—were collected. Outcome variables measured were history taking, dispensing EC, advising customers about EC, and specific knowledge of EC.

Data Analysis. Our analysis was based on the strategy suggested by Assmann[31] and Moher.[32] Tests for significance (Mann-Whitney U test and Pearson χ^2) were performed for comparisons between intervention and control groups at months 1 and 3.

Categorical variables were tabulated to reveal the frequencies between the 2 groups. Variables were recorded as 0 for incorrect knowledge or practice and 1 for correct knowledge or practice, and this value was then multiplied by the weighting (Table 1) to form the scores. Weighting was based on the relative importance of each variable in EC practice, which was determined by the research team. For example, time of

Table 4. Numbers of Drugstore Personnel Who Took Histories, Dispensed Emergency Contraception (EC), and Gave Correct Advice, by Group and Time of Data Collection*

Variable	Preintervention		1 Month Postintervention		3 Months Postintervention	
	Intervention	Control	Intervention	Control	Intervention	Control
History taken						
EC ever used	2	1	5	2	7	1
Cycle	6	9	9	4	4	1
Coitus history	9	8	13	6	10	3
Coitus frequency	0	0	2	0	1	0
Pregnancy	0	0	0	0	0	0
Drug dispensed						
Levonorgestrol	33	34	48†	27†	56†	39
High-dose combined pills	9	9	6	4	4	2
Mifepristone	1	0	0	0	0	0
Correct advice						
Dosing						
Levonorgestrel	9	12	45†	12	49†	25
High-dose oral contraceptives	4	7	6	4	4	2
Side effects‡	34	33	46‡	30	46	41
Client evaluation of effectiveness‡	48	54	60	58	60	60

*Thirty drugstores were each shopped by 1 male and 1 female secret shopper for a total of 60 shopping incidents.
†Difference between groups was statistically significant: $p<.001$ (χ^2).
‡Difference between groups was statistically significant: $p<.01$ (χ^2).
§Advice about side effects and evaluating EC effectiveness was collected whether EC was dispensed or not, and only correct advice was counted.

coitus had the highest weighting (5) among history-taking variables because it determined whether EC could be used or not, and cycle history was weighted less. Advice on dose was weighted higher than that on side effects or evaluation of EC effectiveness. The weighting scheme was developed and discussed among the research team and the expert panel in the university.

Results

Characteristics of drugstore personnel are shown in Table 2. There were 15 pharmacist-owned and 15 nonpharmacist-owned drugstores in each group. Approximately one-third of drugstore staff in each group were pharmacists in each phase of data collection. The staff in both groups were similar with respect to sex, age, and educational level. Other baseline data were also similar between groups. Approximately 70% of sellers in the intervention group had been trained at postintervention data collection.

Knowledge of most items was moderate to high, and there were few differences between the 2 groups at any time of data collection (Table 3). Knowledge of the time limit for EC use increased remarkably in the intervention group, but not in the control group. A temporary drop in knowledge of adverse effects in case of consistent use was found at 1 month after intervention in both groups.

Table 4 shows that history taking was incomplete in most cases in all groups at all times. LNG was increasingly dispensed throughout the course of observation in the intervention group, but not in the control group, as was advice on the dose of LNG. Advice about EC side effects was given approximately half the time at baseline in both groups, but increased significantly in the intervention group at month 1 postintervention and in the control group at month 3 postintervention. Advice about evaluating effectiveness was quite good (80% to 90%) at baseline in both groups and improved slightly in the intervention group, but not significantly.

Discussion

The intervention group improved significantly in dispensing and advising about EC after training. The knowledge that EC should be initiated within 72 hours after unprotected sexual intercourse was poor at baseline in both groups, but much improved by the intervention. History-taking practice, especially regarding contraindications of EC use, was not improved by the training.

Although LNG, the best current choice for EC,[23] has been available in the study area and in many other developing countries[5,24] for more than a decade, availability does not determine use. We found that only slightly more than half of both groups dispensed LNG before the intervention, but that it increased in the intervention group.

We found that knowledge of the time limit for starting EC and of EC dosing was insufficient at baseline, which might arise from lack of training.[25] In 1997, the Thai Food and Drug Administration instructed pharmacists that LNG must be started within 1 hour after unprotected sexual intercourse,[26] which contradicts the findings of a multicenter study supported by the World Health Organization.[27] Misunderstandings of negative health effects (infertility, cancer of uterus or cervix) among drug sellers might lead to underuse of EC.[28] Drugstore personnel's knowledge that LNG can be dispensed up to 24 hours after unprotected intercourse was much improved by the training, but some still failed to dispense it.

History taking was the only domain not improved by the training, which was consistent with previous studies conducted among drugstore personnel in Thailand.[16,25] EC is a very sensitive issue in Thailand, and drugstore personnel usually dispense it without asking any questions about sexual intercourse.[29]

Practice guidelines for dispensing EC should be developed.

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Are health personnel the best choice for directly observed treatment in southern Thailand? A comparison of treatment outcomes among different types of observers

Petchawan Pungrassami[1] and Virasakdi Chongsuvivatwong[2] *[1]Zonal Tuberculosis Centre 12, Amphur Muang, Yala, Thailand; [2]Epidemiology Unit, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand*

Abstract

A prospective study was conducted in 24 districts in southern Thailand in 1999 with directly observed treatment, short-course strategy (DOTS) implemented to determine treatment outcomes in relation to the practical observer among 455 enrolled patients with tuberculosis. Health personnel (HP), community members (CM), family members (FM) and self-administration (SA) were initially assigned to be DOT observers in 43%, 5%, 44% and 8% of 411 analysed patients, respectively. In practice, 56% of the 379 patients with assigned observers changed their observers. The practical observer was the assigned observer among 17% of patients assigned to HP, 57% to CM, 75% to FM, and 34% to SA, respectively. There were no significant differences in treatment success between different types of main observers. Adjusted odds ratios (95% confidence interval) of treatment non-success were 1·1 (0·3–4·7), 0·7 (0·2–3·3), and 0·5 (0·2–1·1) for HP, CM, and FM, over SA groups, respectively. HP may not be the best choice in our setting due to poor sustainability and the availability of another promising choice (CM).

Keywords: tuberculosis, control, directly observed treatment, Thailand

Introduction

Thailand is among the 22 countries with 80% of the estimated cases of tuberculosis (TB) in the world (WHO, 2000) and the 10 countries with the highest prevalence of primary multidrug resistance (WHO/IUATLD, 1997). The WHO reviewed Thailand's National TB Programme (NTP) in 1995 and found low cure rates (17–68%) (THAILAND MINISTRY OF PUBLIC HEALTH & WHO, 1995). The NTP adopted the strategy of directly observed treatment, short-course (DOTS), in 1996 with the aim of covering all 810 districts in the country by the year 2001 (PAYANANDANA *et al.*, 1999).

Directly observed treatment (DOT), one element of DOTS, has been recommended for the improvement of patient adherence to TB treatment (US DEPARTMENT OF HEALTH AND HUMAN SERVICES, 1994; WHO, 1999). Most of the success stories of DOT designate health personnel (HP) and/or community members (CM) as DOT observers and the US Centers for Disease Control suggests that family members (FM) may not be strict observers due to emotional ties (US DEPARTMENT OF HEALTH AND HUMAN SERVICES, 1994; WHO, 1998). All 3 types of observer are used in Thailand, national guidelines recommend that the preferred choice in descending order is HP (staff members of TB clinics, hospital wards and health centres), CM (village health volunteers, community leaders, and friends), and FM (close and distant relatives) (MINISTRY OF PUBLIC HEALTH, 1998), but the majority are FM (AKKSLIP *et al.*, 1999; KAMOLRATANAKUL *et al.*, 1999). We, noticed, however, that DOT observers in practice were not always the same as those noted in patient records, and often changed over time. Accordingly, reports based on the records may not accurately represent the contribution of observer type to treatment outcomes.

We conducted this study with 2 objectives: to describe the pattern of transition from assigned to practical observer; and to determine treatment outcomes in relation to practical observer.

Methods

Study population and design

The study population covered 1·2 million people in 24 districts in southern Thailand. Using TB Registers at 22 TB clinics (1 zonal TB centre, 1 regional hospital, 3 general hospitals, and 17 community hospitals), we identified and followed-up all 455 patients with new, smear-positive, pulmonary TB according to WHO criteria (WHO, 1998) who started treatment between 1 February and 30 September 1999.

Treatment

As recommended by WHO (1998) the standard daily drug regimen combined a 2-month initial phase of 4 drugs (isoniazid, rifampicin, pyrazinamide, and ethambutol) and a 4-month continuation phase of 2 drugs (isoniazid and rifampicin). A thrice-weekly treatment was used on 21 patients at the zonal TB centre. If a patient's sputum smear was still positive for acid-fast bacilli (AFB) at the end of the second month, the initial treatment phase was extended for one or 2 months. For patients who could not tolerate the standard treatment the drug regimen was changed to a 9-month regimen without pyrazinamide, or to an 18-month regimen without rifampicin and pyrazinamide.

Initial assignment of DOT observer vs. the observer in practice

Assigned DOT observers were chosen by TB clinic staff on the first day of treatment. In practice, the person who actually stayed with the patient during drug intake, defined as 'practical observer', may not be the same as the assigned observer, and the practical observer may change during the treatment period.

Data collection and management

The patient records and registers relevant to TB were reviewed. In addition, the patients and/or their observers were interviewed at least one month after starting the treatment by the first author and/or one of 24 health professionals working in the study clinics. Data on the type of practical DOT observers were recorded for each month until the end of treatment (shown in Tables for only 9 months). When more than one type of observer was involved within one month, the one with the highest number of treatment observations in that month was used in the analyses.

Exposure variable: main type of practical observer

Data on the initial assignment of observers were not used in the comparative analyses. We defined the 'main type of practical observer' as the observer who actually observed more than 60% of the patient's treatment period. A patient was defined as having a 'mixed type of observer' if no type of observer observed more than

Address for correspondence: Petchawan Pungrassami, Zonal Tuberculosis Centre 12, Amphur Muang, Yala 95000, Thailand; phone +66 73 212332, fax +66 73 211727, e-mail ppetch@cscoms.com

60% of a patient's treatment period. Accordingly, the comparative analyses were made among 5 main types of practical observer; HP, CM, FM, no practical observer (or self-administration, SA), and mixed observer.

Outcome variable: treatment outcomes

The WHO (1997) definitions of treatment outcomes were applied at the end of each month until the end of treatment. Accordingly, we classified treatment outcomes into 6 mutually exclusive categories: (i) 'cure' (AFB-negative sputum at the end of treatment), (ii) 'completed treatment' (no AFB result at the end of treatment), (iii) 'failure' (AFB-positive sputum at or after the fifth month), (iv) death (died of any cause during the treatment), (v) 'default' (treatment interruption for at least 2 consecutive months), and (vi) 'transferred out' (changed treatment place with unknown sputum result). Cure and completed treatment was combined as 'treatment success'.

Controlling confounders

We divided covariates that might be associated with treatment outcome into 3 groups: (i) demographic and socio-economic characteristics (gender, age, ethnic group, marital status, education, understanding Thai language, income, feasibility to be free from work/study, number of living places, and independence in travelling), (ii) health services (TB clinic, drug regimen, use of fixed-dose combination, and DOT assignment), and (iii) disease condition (severity of disease, drug resistance, adverse drug effects, HIV/AIDS and other co-morbidities/conditions including heart disease, hypertension, cerebrovascular accident, diabetes mellitus, psychosis, alcoholic consumption, liver cirrhosis, drug abuse, and imprisonment). Univariate analyses were performed using cross-tabulation and Pearson's χ^2 test. Only covariates with at least a marginal association with the outcome ($P < 0{\cdot}2$) were selected to be tested in the models, described in the following paragraph.

Four logistic regression models of increasing numbers of covariates were applied to determine the association between the exposure and the outcome: (i) without covariates, (ii) with inclusion of the first group of covariates, (iii) with inclusion of the first and second groups of covariates, and (iv) with inclusion of all 3 groups of covariates. At each step of incorporating an additional group of covariates, only covariates fulfilling the following criteria were retained: (i) having significant association with the outcome (Wald test, $P < 0{\cdot}05$) or (ii) having association with the outcome ($P < 0{\cdot}1$) plus leading to a change of more than 15% of odds ratio (OR) for any main observers in the larger model, if removed. The results were presented as OR of treatment non-success over treatment success, with 95% confidence interval (95% CI). The likelihood ratio test was used to determine the significance of the presence of covariates or covariate groups in the models (KLEINBAUM, 1994). The Hosmer–Lemeshow statistic was used to check the fit of the logistic regression models (HOSMER & LEMESHOW, 2000). A P value of less than 0·05 was considered statistically significant in interpreting the resulting models. The analyses used Stata statistical software, version 6 (StataCorp, College Station, TX, USA).

Results

Excluded vs. analysed subjects

Of the 455 enrolled patients, 44 were excluded because the interviewer was unable to establish contact with them or their DOT observers. Compared with the remaining patients, the excluded patients were younger, more often Buddhist, people living with HIV/AIDS, treated at general/regional hospitals, assigned to HP, and had poorer outcomes (data not shown).

The remaining 411 patients (Table 1) were 6–86 years of age (mean = 44·1, SD = 17·4). Of the 323 patients with available data on income, 76% earned less than the official 'minimal daily wage' in the study area (US$ 3–3·5). The prevalence of multidrug resistance (resistance to at least isoniazid and rifampicin) in the 104 who were examined at the zonal TB centre where drug resistance could be tested, was 2% (95% CI 1–3%).

Table 1. Characteristics of analysed TB patients

Patient characteristics	Number (%) ($n = 411$)
Gender	
Male	308 (74·9)
Age (years)	
≤ 30	105 (25·6)
31–59	216 (52·6)
≥ 60	90 (21·9)
Ethnic group	
Muslim	242 (58·9)
Buddhist	169 (41·1)
Initial acid-fast bacilli	
+	122 (29·7)
++	120 (29·2)
+++	169 (41·1)
Initial drug resistance	
No	85 (20·7)
Resistant, not MDR	17 (4·1)
MDR	2 (0·5)
Not tested	307 (74·7)
HIV/AIDS	
Yes	47 (11·4)
Treatment place	
Community hospital	236 (57·4)
General/regional hospital	119 (29·0)
Zonal TB centre	56 (13·6)
Assigned observer	
Health personnel	177 (43·1)
Community member	21 (5·1)
Family member	181 (44·0)
No assigned observer	32 (7·8)

MDR, multidrug resistant.

Assigned vs. practical observer

The HP, CM, and FM were initially assigned to be DOT observers in 177, 21, and 181 of the 411 analysed patients, respectively. Of the 379 patients assigned an observer, 212 (56%) changed the observer during the treatment period, 130 of them on the day of the assignment. Among the 177 patients assigned to HP, 153 changed observer, 84 on the day of the assignment. The number of changes of observer per patient ranged between 0 and 3 (median = 1). Of 258 changes during treatment, 84% were to a less preferred category according to the national guidelines.

By definition, 8%, 7%, and 56% of the 411 patients had HP, CM, and FM as their main observers, respectively; whereas 24% mostly took medicine alone and 5% had mixed types of observer. Of the 177 patients assigned to HP, only 17% actually had HP as their main observer. The corresponding proportions for those assigned to CM, FM, and SA were 57%, 75%, and 34%, respectively (Table 2).

Overall distribution by month

Table 3 shows the distribution of patients by practical observer and treatment outcome from the start of treatment and at the end of each month. The proportion of HP observers decreased from 23% at the start of treatment to 7% at the end of the fifth month; in contrast, the proportion of SA increased from 18% to 27%. The number of those receiving treatment markedly decreased by the end of the sixth month as 71% of

Table 2. Comparison between the type of initially assigned observer and the main type of practical observers

Assigned observer	Main type of practical observer*					
	HP	CM	FM	SA	Mixed	Total
Health personnel (HP)	30	14	75	39	19	177
Community member (CM)	0	12	2	7	0	21
Family member (FM)	1	1	136	41	2	181
Self-administration (SA)	0	2	19	11	0	32
Total	31	29	232	98	21	411

*Observer who actually observed > 60% of a patient's treatment period.

Table 3. Distribution by practical observer and treatment outcome during the course of treatment

Month*	0	1	2	3	4	5	6	7	8	9
Observer type										
Health personnel	94	74	52	38	29	25	3	0	0	0
Community member	31	30	32	32	30	28	6	2	1	1
Family member	210	219	225	217	210	203	36	16	4	2
Self-administration	76	79	82	88	97	97	16	5	4	2
Still on treatment	411	402	391	375	366	353	61	23	9	5
Treatment outcome										
Cure	0	0	0	0	0	0	258	291	303	306
Completed treatment	0	0	0	0	0	0	32	35	37	38
Failure	0	0	0	0	2	4	4	5	5	5
Death	0	4	12	21	25	31	33	34	34	34
Default	0	5	8	15	18	23	23	23	23	23
End of treatment	0	9	20	36	45	58	350	388	402	406

*Month 0, practical observer at the start of treatment. Months 1–9, practical observer and treatment outcome at the end of that month. Five patients who were receiving long-course chemotherapy were still on treatment after 9 months.

the 411 patients were cured or had completed treatment.

Treatment outcome by practical observer

The overall treatment success rate in the study area was 85%. Table 4 shows the outcomes at the end of treatment by main practical observer. Logistic regression models were constructed to examine the effects of main observers and variable groups on lack of treatment success, and it was found that male gender, dependence in travel, being treated at a general or regional hospital, HIV and other co-morbidity, but not observer type, were all significantly asociated with lack of treatment success (Table 5).

Discussion

Of 379 patients assigned to an observer, 56% changed their observer, and 84% of observer changes during the treatment were to a less preferred category. Of 17%, 57%, 75%, and 34% patients assigned to HP, CM, FM, and SA, respectively, the main type of practical observer was the assigned observer. We found no significant differences in the probability of treatment success among different types of main practical observer.

The DOT strategy has been recommended for all patients with TB because of the expected difficulties in predicting whether a patient will adhere to treatment (US DEPARTMENT OF HEALTH AND HUMAN SERVICES, 1994; WHO, 1999). The success of universal DOT programmes has been reported (WEIS, 1997; FUJIWARA *et al.*, 1997) but was followed by questions on their necessity and contribution to programme success (GALANOWSKY *et al.*, 1996; BAYER *et al.*, 1998). In our setting DOT was not universal as not all patients were assigned an observer, but it was not a selective strategy as in a policy of selective DOT for some patients (WEIS, 1997). The initial non-assignment of patients to DOT in our study was claimed to be due to lack of suitable observers. Though most of these pa-

Table 4. Main practical observers and treatment outcomes at the end of treatment

Main practical observer*	Treatment outcome at the end of treatment [*n* (%)]					
	No.	Cure	Completed treatment	Failure	Death	Default
Health personnel	31	24 (77·4)	3 (9·7)	1 (3·2)	1 (3·2)	2 (6·5)
Community member	29	25 (86·2)	1 (3·5)	0	2 (6·9)	1 (3·5)
Family member	232	175 (75·4)	23 (9·9)	3 (1·3)	21 (9·1)	10 (4·3)
Self-administration	98	70 (71·4)	10 (10·2)	1 (1·0)	8 (8·2)	9 (9·2)
Mixed	21	15 (71·4)	2 (9·5)	0	2 (9·5)	2 (9·5)
Total	411	309 (75·2)	39 (9·5)	5 (1·2)	34 (8·3)	24 (5·8)

*Observer who actually observed > 60% of a patient's treatment period.

Table 5. Odds ratios of treatment non-success over success by main type of practical observer: crude and adjusted analyses

Included variable[a]	Compared group	Crude OR of potential confounders	OR (95% CI) of treatment non-success[b]			
			Model 1	Model 2	Model 3	Model 4
Main type of practical observer	HP/SA	–	0·66 (0·20–2·12)	0·74 (0·22–2·48)	1·19 (0·32–4·40)	1·14 (0·27–4·73)
	CM/SA	–	0·51 (0·14–1·88)	0·29 (0·07–1·15)	0·58 (0·14–2·38)	0·71 (0·15–3·28)
	FM/SA	–	0·76 (0·41–1·43)	0·56 (0·28–1·11)	0·50 (0·25–1·00)	0·49 (0·23–1·08)
	Mix/SA	–	1·05 (0·31–3·48)	0·72 (0·20–2·59)	1·00 (0·27–3·70)	1·25 (0·31–5·07)
Gender	Male/Female	3·67 (1·53–8·79)*	+	5·35 (2·16–13·25)*	5·88 (2·34–14·75)*	4·54 (1·72–11·96)*
Independence in travel	Yes/No	0·34 (0·20–0·59)*	+	0·22 (0·12–0·41)*	0·19 (0·10–0·36)*	0·19 (0·10–0·38)*
TB clinic	CH/GH-RH	0·60 (0·34–1·06)	+	–	0·55 (0·30–1·01)	0·46 (0·24–0·90)*
	ZTC/GH-RH	0·20 (0·06–0·70)*	+	+	0·11 (0·03–0·46)*	0·06 (0·01–0·29)*
HIV/AIDS	Yes/No	7·76 (4·01–15·01)*	+	+	–	9·98 (4·13–19·51)*
Other co-morbidity	Yes/No	2·44 (1·38–4·33)*	+	–	–	2·53 (1·29–5·03)*
P[d]			–	< 0·0001	0·0015	< 0·0001

OR, odds ratio; 95% CI, 95% confidence interval; HP, health personnel; CM, community member; FM, family member; SA, self administration; CH, community hospital; GH, general hospital; RH, regional hospitals; ZTC, zonal TB centre.

[a]Criteria of variable inclusion: preliminary selection if having at least marginal univariate association with the outcome ($P < 0{\cdot}2$), keep in the models if having significant association with the outcome ($P < 0{\cdot}05$) or having probable association with the outcome ($P < 0{\cdot}1$) plus leading to a change of more than 15% of OR for observer type in the larger model, if removed.

[b]Model 1 = crude analysis; Model 2 = Model 1 + demographic and socio-economic covariates; Model 3 = Model 2 + covariates related to health services; Model 4 = Model 3 + covariates related to disease condition.

[c]Calculated by the likelihood ratio test comparing the current with the preceding model.

* $P < 0{\cdot}05$

tients had observers later on, more than one-third of them mostly took their medicine alone. These problems challenge the feasibility of trying to implement universal DOT.

As an intervention that requires not only patients willing to participate but also responsible observers, DOT should be evaluated for its practicality. Our findings confirm that DOT assignment or DOT by record will not always guarantee direct observation or even the presence of the 'observers' during drug intake. The transition of observer type should be monitored to detect and avoid patients being without a practical observer. The SA group in our study, though statistically not significant, had a higher default rate than the FM, CM, or HP groups and uncured defaulters may be the source of multidrug resistance in the community.

While HP had a non-significant higher success rate and the lowest death rate, it is clear that the sustainability of having HP as observers is poor and a considerable number of patients changed directly to SA. This may be explained by poor patient acceptability or provider–patient relationship (ZWARENSTEIN *et al.*, 1998; DAVIDSON *et al.*, 1999), and may also be due simply to poor accessibility. The patients and/or their supporters in our study bore all the transportation costs and constraints as the outreach approach (FUJIWARA *et al.*, 1997) and the enhanced DOT with multiple incentives and enablers (CHAULK & KAZANDJIAN, 1998) were rarely used.

As reported in previous studies (CHOWDHURY *et al.*, 1997; WILKINSON & DAVIES, 1997; ZWARENSTEIN *et al.*, 2000), CM appeared to be the other promising choice in terms of patients' convenience, sustainability, and desirable treatment outcome; however, they were less often assigned. The involvement of this group may need further exploration. The majority of observers in our study was FM as they were most often initially assigned and had the highest sustainability. However, treatment outcomes in this group were average. Comparable outcomes between patients observed by FM and non-FM have been reported, though without data on the practical observers (WAN, 1993; KAMOLRATANAKUL *et al.*, 1999). The apparently good outcome in FM-observed groups in the previous randomized controlled trials may also be due to restrictive inclusion criteria and the Hawthorne effect on the trials (LAST, 2001).

Our study may be subject to information bias. SA may be under-reported as patients and/or their 'observers' considered the interviewers to be health personnel. Choices and changes of observer type during treatment were not random processes, but were probably influenced by the patient's performance status, the severity of the disease/co-morbidity, the feasibility of meeting the observer as scheduled, the availability of family/social support, or the quality of health services. Without adjustment, the treatment outcomes among particular observer types may be confounded. For example, only 'healthier' patients would be able to travel to the TB clinics/health centres for HP-DOT, and this would be a contributory factor to lower death rates; whereas those who were incapable of travelling alone and had no supporters inevitably became SA and defaulted. We adjusted for all potential confounders and found some strong predictors of treatment success, e.g. gender, independence in travelling, health services, and HIV/AIDS and other co-morbidity. Further research, however, may be needed to identify any residual confounders or predictors.

The presence of a mixed observer group and the poor outcomes reflects the necessity for careful classification of observer type. However, we may still underestimate the death and default rates among the SA group as most patients in the mixed observer group finally changed from having observers to SA. Furthermore, data were missing in 44 cases, more of whom died or

defaulted than the analysed patients. If most of the missing cases had HP as their main observer, we may underestimate the death and default rates, and overestimate the failure rate among the HP group. With the current sample size, the power of our study to detect significant differences in treatment success among different types of observers was limited (2–11%); as the proportions of non-FM practical observers in the study population were low and the absolute differences in treatment success rates were between 1% and 9%.

In conclusion, for control programmes DOT observers should not just be assigned but should be ascertained from the start of treatment. HP may not be the best choice in many settings due to poor sustainability and the availability of promising alternatives such as CM. Changes of observer types during treatment may be unavoidable but changes to SA should be avoided.

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Prophylactic antibiotic prescription for cesarean section

TIPPAWAN LIABSUETRAKUL[1], PISAKE LUMBIGANON[2] AND VIRASAKDI CHONGSUVIVATWONG[3]

[1]Department of Obstetrics and Gynecology and [3]Epidemiology Unit, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla, [2]Department of Obstetrics and Gynecology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

Abstract

Objectives. To assess the use of prophylactic antibiotics for cesarean section, and to identify factors associated with a doctor's intraoperative prescription.

Design. A hospital-based, cross-sectional study.

Study participants. All 967 medical records of women undergoing cesarean section from January 1998 to February 1999 in a university hospital, Southern Thailand.

Main measures. Independent variables consisted of patient and doctor factors. The outcome variable was whether any antibiotics were given intraoperatively. Multivariate logistic regression with random effects was used to identify factors associated with the doctor's prescription.

Results. Prophylactic antibiotics were prescribed in 82% of all patients. One hundred and eighty-eight patients (21%) received antibiotics postoperatively. Of the patients receiving intraoperative antibiotics after cord clamping, 8% received only a single dose and 53% received an additional postoperative prescription. The most commonly used antibiotic was ampicillin. Intraoperative prescription was significantly associated with longer duration of ruptured membranes, higher number of vaginal examinations and doctors' age. Doctors aged 30–39 years had three and seven times the likelihood of prescribing intraoperative antibiotics compared with their younger and older colleagues, respectively.

Conclusions. Administration of single-dose prescriptions was still an uncommon practice. Prophylaxis was given more commonly to patients with well known risks for infection, and was given by doctors aged 30–39 years.

Keywords: antibiotic prescription, cesarean section, prophylactic antibiotics

A systematic review in the Cochrane Library concluded that antibiotic prophylaxis in all cases of cesarean section significantly reduced the incidence of puerperal infection [1]. Time of drug administration was different from other general surgeries because of the fetus. The intraoperative administration of a drug shortly after cord clamping is considered to be as effective as administering the drug preoperatively. The recommended duration of prescribed antibiotics in many trials has been reduced from ≥ 5 days to 3 days, then to 24 hours, then to three doses and finally to a single dose [2–4]. A second review of the Cochrane Library concluded that a single dose of ampicillin or first-generation cephalosporins has similar efficacy in reducing puerperal infection. In addition, the benefits are not different from broad-spectrum cephalosporins [4].

Despite such well established evidence, there have been very few studies on how doctors prescribe antibiotic prophylaxis to patients who have had cesarean section [5,6]. One survey study investigated the guidelines for patient selection and drug regimens in an obstetric department in Denmark [5]. Another study evaluated the change of antibiotic prophylaxis in cesarean section through an educational program [6]. Neither study focussed on the actual practice or predictor analysis for prophylactic antibiotic prescription. Documented guidelines regarding antibiotic prophylaxis for cesarean section have never been established in our department. Therefore, this study aimed to assess prophylactic antibiotic prescription with regard to usage, time of administration, type of antibiotics, and number of doses, and to identify factors associated with intraoperative antibiotic prescription.

Address reprint requests to Tippawan Liabsuetrakul, Epidemiology Unit, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla 90110, Thailand. E-mail address: ltippawa@ratree.psu.ac.th

Methods

This study was undertaken in a university hospital in Southern Thailand. Setting a confidence interval (CI) of 95%, the estimated prevalence of single-dose antibiotic prophylaxis in cesarean section from a pilot study of 10% and an acceptable error of 2%, at least 865 patients undergoing cesarean section were required to estimate the prevalence of single-dose antibiotic prescription. Therefore, all medical records of patients who underwent cesarean sections from January 1998 to February 1999 were reviewed retrospectively. Patients with a history of penicillin allergy or any evidence of infection before the cesarean sections were excluded. These were because the doctor's decision for giving antibiotic prophylaxis may be constrained by a history of penicillin allergy in some cases of elective cesarean sections, and women with evidence of infection before their cesarean sections were given antibiotic treatment for specific underlying infections.

The patterns of prophylactic antibiotic prescriptions were classified as no antibiotics, intraoperative antibiotics only, postoperative antibiotics only, and combined intra- and postoperative antibiotics. Prophylactic antibiotics are defined as antibiotics given to prevent infections [7]; therefore, women having puerperal morbidity classified as the evidence of febrile morbidity in this study were excluded to rule out the therapeutic treatment. Puerperal morbidity was defined as temperature $\geq 38°C$ occurring on any two of the first 10 postpartum days, exclusive of the first 24 hours, taken by mouth using a standard technique at least four times daily [8].

In the analysis for predictors of intraoperative antibiotic prescription, the dependent variable was modeled as prescribing (1)/not prescribing (0) intraoperative antibiotics. The potential predictor variables consisted of both patient and doctor variables. Patient variables included age, parity, gestational age at delivery, body mass index (BMI), type of service (non-private versus private), duration of labor, duration of ruptured membranes, number of vaginal examinations, and indication for cesarean section (elective versus non-elective). Elective cesarean section was defined as cesarean sections performed before the presence of labor and/or ruptured membranes. Doctor variables comprised gender, age, and years after residency training. The doctors who performed the cesarean sections were either residents or faculty members who decided on the use of prophylactic antibiotic prescription.

The association between the independent and dependent variables was evaluated by univariate analysis using chi-square test. Multivariate logistic regression with random effects was employed for identification of factors associated with the doctor's intraoperative prescription because the observed patients were nested in an individual doctor; therefore, models with random effects were taken into account. All patient and doctor variables were initially included in the full multiple logistic regression model. The exploratory significant variables were defined by the likelihood-ratio test with a probability value of 0.2. The significant variables for intraoperative prophylactic prescription were concluded in the final model with a P-value of 0.05. Missing data in this study were handled as one stratum of the variable for analysis. Any significant variables with missing data were tested for a significance of stratum of known data.

Table 1 Patient characteristics

Characteristics	# (%)
Age[1] (years)	
<25	108 (12.3)
25–29	255 (29.0)
30–34	305 (34.7)
≥35	211 (24.0)
Antenatal care[2]	
No	9 (1.0)
Yes	870 (99.0)
Gestational age[3] (years)	
<34	17 (1.9)
34–36	47 (5.4)
≥37	815 (92.7)
Most common indications for cesarean section	
Previous cesarean section	328 (37.3)
Cephalopelvic disproportion	249 (28.3)
Fetal distress	102 (11.6)
Breech presentation	67 (7.6)
Placenta previa	33 (3.7)
Premature ruptured membranes with failed induction	26 (3.0)
Pregnancy induced hypertension	12 (1.3)
Twins pregnancy	11 (1.2)
Failed induction	9 (1.0)
Transverse lie	6 (0.7)

[1]Mean ± standard deviation (SD), 30.7 ± 5.3 years.
[2]Mean of number of antenatal care ± SD, 9.2 ± 3.2.
[3]Mean ± SD, 38.4 ± 1.7 weeks.

Results

There were 967 cesarean deliveries in this period, and 923 patients were eligible according to the inclusion and exclusion criteria. Forty-four patients were excluded, 21 for a history of penicillin allergy, 13 for antibiotic use within the previous 7 days, four for fever (>37.8°C), one for chorioamnionitis (fever, uterine tenderness, maternal and fetal tachycardia), and five for combined fever and antibiotic use within the previous 7 days. Medical records were available for 879 (95%) patients. Table 1 shows patient characteristics. The obstetric complications were the five most common indications for cesarean section: previous cesarean section, cephalopelvic disproportion, fetal distress, breech presentation, and placenta previa.

Eleven of 12 patients with gestational diabetes (92%) received one to four doses of prophylactic antibiotics. One hundred and fifty-eight patients (18%) did not receive any

antibiotics. Among patients who received prophylactic antibiotics, 188 patients (21%) received only postoperative antibiotics while 533 patients (61%) received intraoperative antibiotics after cord clamping (8% for single dose only and 53% for additional postoperative prophylactic antibiotics). Ninety-four percent of patients who were prescribed intravenous postoperative antibiotics received them within the first postoperative day. After excluding the cases with puerperal morbidity, subsequent oral antibiotics were still prescribed in 55% of patients. The most common intraoperative prophylactic antibiotic was 2 grams of ampicillin (99.2%).

Thirty-one doctors who managed the eligible patients consisted of 15 residents and 16 faculty members. All doctors prescribed prophylactic antibiotics in at least some patients undergoing cesarean section. The predictor and outcome variables are shown in Tables 2 and 3. Prophylactic intraoperative antibiotic prescription was more common in nulliparous patients, in patients with a high body mass index (BMI), longer duration of labor or ruptured membranes, and higher number of vaginal examinations, and in those undergoing emergency cesarean section. Senior doctors prescribed prophylactic antibiotics less frequently than younger ones. Ten percent of the patients had missing data on BMI because of no record of height or weight on the day of surgery.

Table 4 demonstrates the procedures for developing the logistic model with random effects using probability values of the likelihood-ratio test. In the full model analysis, missing data on BMI (10%) in this study were handled as one stratum of the variable. The data showed that known values of BMI were not significant predictors, but missing values of BMI were independently associated with an increased probability of intraoperative antibiotic prescription [adjusted odds-ratio (OR) 1.8, 95% CI 1.1–3.0]. In-depth exploration of missing BMI data indicated that the patients in this group were not related to other independent factors for intraoperative prescription, but were more likely to be private patients and to be patients of one doctor who often prescribed intraoperative antibiotics. When that doctor was excluded from the model, the status of BMI as known or missing was no longer a significant predictor.

In the final model of multiple logistic regression analysis, the factors significantly associated with the prescription of intraoperative antibiotic prophylaxis were duration of ruptured membranes, number of vaginal examinations, and age of doctor (Table 5). The presence of ruptured membranes was a highly significant factor associated with intraoperative prophylactic antibiotic prescription. There was no significant random-effects variance among doctors for prescribing intraoperative prophylactic antibiotics ($P = 0.09$).

Among 671 patients who did not develop febrile morbidity or other postoperative infections, 429 patients (64%) received one to three doses of perioperative antibiotics, and 242 patients (36%) received more than three doses and/or oral prophylactic antibiotics. Only 'years after residency training' was a significant predictor for giving less or more than three doses of perioperative antibiotics. Doctors who completed their residency training >5 years ago gave more than three doses of perioperative antibiotics ($P = 0.03$; OR 1.8; 95% CI 1.0–3.1), but those who completed their residency training 1–5 years ago gave that regimen less (OR 0.6; 95% CI 0.2–1.2) when compared with residents.

Table 2 Patient variables and outcome variable

Patient variables	Intraoperative antibiotic prescription	
	No, *n* (%) ($n = 346$)	Yes, *n* (%) ($n = 533$)
Parity[1]		
Nulliparity	112 (25.6)	325 (74.4)
Multiparity	234 (52.9)	208 (47.1)
Gestational age (weeks)		
<37	30 (46.9)	34 (53.1)
≥37	316 (38.8)	499 (61.2)
Body mass index[1]		
<24	64 (45.7)	76 (54.3)
25–29	167 (37.4)	280 (62.6)
≥30	75 (39.5)	115 (60.5)
Unknown	40 (39.2)	62 (60.8)
Type of service		
Non-private	133 (39.5)	204 (60.5)
Private	213 (39.3)	329 (60.7)
Duration of labor (hours)[1]		
0	202 (56.1)	158 (43.9)
1–6	58 (30.7)	131 (69.3)
7–12	60 (29.4)	144 (70.6)
>12	26 (20.6)	100 (79.4)
Duration of ruptured membranes (hours)[1]		
0	273 (53.1)	241 (46.9)
1–6	43 (21.9)	153 (78.1)
7–12	17 (14.7)	99 (85.3)
>12	13 (24.5)	40 (75.5)
Number of vaginal examinations[1]		
0	210 (56.4)	162 (43.6)
1–5	126 (29.5)	301 (70.5)
≥6	10 (12.5)	70 (87.5)
Indication of cesarean section[1]		
Elective	194 (56.4)	150 (43.6)
Non-elective	152 (28.4)	383 (71.6)

[1]Significant association between independent and dependent variables (P value <0.05).

Discussion

Prophylactic antibiotics were prescribed in cases of cesarean section in our study hospital with a proclivity of 2 grams of intraoperative ampicillin prescription. The proportion of patients receiving a single dose of antibiotics after cord clamping as suggested by the systematic review was very

Table 3 Doctor variables and outcome variable

Doctor variables	Intraoperative antibiotic prescription	
	No, *n* (%) (*n* = 346)	Yes, *n* (%) (*n* = 533)
Age (years)[1]		
<30	156 (38.8)	246 (61.2)
30–39	47 (17.7)	218 (82.3)
≥40	143 (67.4)	69 (32.6)
Gender[1]		
Male	232 (37.0)	395 (63.0)
Female	114 (45.2)	138 (54.8)
Years after residency training[1]		
0	128 (39.0)	200 (61.0)
1–5	44 (31.4)	96 (68.6)
≥6	174 (42.3)	237 (57.7)

[1]Significant association between independent and dependent variables (*P* value <0.05).

Table 5 Final model of patient and doctor factors for the prescription of intraoperative antibiotic prophylaxis from multiple logistic regression with random effects

Factors	OR	95% CI
Duration of ruptured membranes (hours)		
0	1	–
1–6	2.9	1.8–4.8
7–12	4.1	2.0–8.2
>12	2.5	1.1–5.5
Number of vaginal examinations		
0	1	–
1–5	1.5	1.0–2.4
≥6	3.2	1.3–7.9
Age of doctor (years)		
<30	1	–
30–39	3.0	1.7–5.5
≥40	0.4	0.2–0.9
Random-effects variance[1]	*P* = 0.09	

OR, odds ratio; 95% CI, 95% confidence interval.
[1]*P*-value of random-effects variance.

low, whereas a combination of intraoperative and additional postoperative prescription was common. Almost all patients who were prescribed postoperatively received intravenous antibiotics within the first postoperative day, and about half subsequently received oral antibiotics. Prescription of antibiotic prophylaxis was influenced by a 'high risk' status of the patient, but not on a universal basis as directed by the evidence of its efficacy.

Prophylactic antibiotics were most commonly used for patients who had undergone cesarean section; however, there was a wide variation in the time of administration, type of antibiotic, number of doses, and indications for prescription. In this study, most patients were prescribed antibiotics for prophylaxis after cord clamping, but some patients were prescribed postoperatively. A questionnaire survey from an obstetric clinics in Denmark found that 44% of prophylactic antibiotics were administered after cord clamping and 27% were applied before skin incision [5]. Evidence showed that antibiotics given after cord clamping did not give less protection than those given before the procedure [9]. In addition, early administration resulted in masking neonatal

Table 4 Model of multiple logistic regression with random effects for all patient and doctor factors using the significance of likelihood-ratio test

Variables	*P* value of likelihood-ratio test		
	Initial model[1]	Intermediate model[2]	Final model[2]
Age of patient	0.44	–	–
Parity	0.18	0.08	–
Gestational age	0.26	–	–
BMI	0.02	0.02 (0.08)[3]	–
Type of service	0.46	–	–
Duration of labor	0.38	–	–
Duration of ruptured membranes	<0.01	<0.01	<0.01
Number of vaginal examinations	0.13	0.03	0.01
Indication of cesarean section	0.31	–	–
Gender of doctor	0.77	–	–
Age of doctor	0.02	<0.01	<0.01
Years after residency training	0.90	–	–

[1]Probability value for inclusion in the model is 0.2 by the likelihood-ratio test.
[2]Test of the significant variables for including in the model (*P* value <0.05).
[3]*P* value for the likelihood-ratio test of all stratum of BMI is 0.02, but that of the known stratum of BMI is 0.08.

infections or increasing the cost for neonatal septic work up, thus it should be avoided [10]. Since 1978, most published trials have administered antibiotics after cord clamping [4].

Prescribed antibiotics varied among ampicillin, cefazolin, cefuroxime or cefoxitin in the observational study on post-cesarean infection after antibiotic prophylaxis [11,12]. The summary of a Swedish–Norwegian Consensus Conference for antibiotic prophylaxis in surgery recommended that second-generation cephalosporins as an intravenous single dose be used for all emergency and some elective cesarean sections [7]. A systematic review also recently concluded that a single dose of ampicillin or first-generation cephalosporins has been established to be as efficacious as the other extended broad-spectrum antibiotics [4]. Serum levels of free individual drug above the minimal inhibitory concentration are needed in antibiotic applications [13,14]. In addition, the degree of colonization and drug resistance of organisms causing antibiotic failure need to be considered in each area. Fortunately, healthy pregnant women undergoing cesarean section are unlikely to be colonized with drug-resistant organisms from the community prior to surgery [15]. Thus, high-spectrum antibiotics should not be required and this cost can be reduced, especially in developing countries. The most commonly used antibiotic in this study was ampicillin, which is cheaper and of lower spectrum than cephalosporins.

A single dose of prophylactic antibiotics should be sufficient if given intraoperatively after cord clamping. Additional antibiotics given prior to cord clamping or after (e.g. for 24-hour postpartum or longer) did not increase the protection [4]. Yet in our study and other previous studies [5,6,11, 12,16], these additional dosages were often administered, although most antibiotics were not prescribed beyond 24 hours. The question of why nearly half of the patients who received postoperative prophylactic antibiotics were prescribed subsequent oral antibiotics regardless of any post-cesarean infections in this study was unanswered and needs further study. The cases of post-cesarean infection were excluded for calculation of prophylactic oral antibiotics in order to reduce the bias of oral antibiotics for infectious treatment.

Administration of prophylactic antibiotics in this study was mostly confined to patients with a high risk for postoperative infection, as in many previous studies [5,7,8,17]. In contrast, the Cochrane Review, which collected trials to re-analyze by meta-analysis, revealed that antibiotic prophylaxis is beneficial for both elective and non-elective patients [1]. However, as our study collected data before this Cochrane Review was published, it is not surprising that prophylaxis was omitted among elective patients. One recent study examined the use of antibiotic prophylaxis in 50 consecutive cesarean sections in eight centers in five countries. There were wide variations in the time of drug administration, type of drug, and the percentage of single-dose regimen [18]. The only significant predictor among the doctor variables in our study was age of doctor. Intraoperative prophylactic prescription was more common in young faculty members, but less so in the senior faculty members when compared with residents. This may result from the fact that antibiotic prophylaxis for cesarean section was not commonly used in the past. However, when the antibiotics were given, the senior faculty members tended to use more than three doses of antibiotics and/or oral antibiotics, as in past practice. Why the middle-age group of doctors had the highest likelihood of giving antibiotics is not known. In-depth studies on behavioral aspects of the doctors should be carried out.

In the analysis of predictors for intraoperative prescription, patient and doctor variables were considered because individual doctors decided to prescribe prophylactic antibiotics with respect to not only patient factors, but also based on personal judgement. In addition, multivariate logistic regression with random effects was employed to deal with the nesting of two levels of data. However, all patients of each doctor and all doctors were studied, thus there was wide variation in the numbers of patients among individual doctors. In particular, a few doctors who had a high number of patients might predominate in the representative results. The practice of antibiotic prophylaxis for cesarean section in this university hospital had a discrepancy with evidence, especially practising long-term prophylactic regimen. Further studies to identify the doctors' reasons for the practices of prophylactic antibiotic prescription for cesarean section should be conducted so that proper intervention can be planned and successfully implemented. In addition, reliable and up-to-date evidence should be disseminated as soon as possible to all doctors to encourage the best evidence-based practice.

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Adverse Pregnancy Outcome in Women Exposed to Acyclovir During Pregnancy: A Population-based Observational Study

CHAVEEWAN RATANAJAMIT[1,2], METTE VINTHER SKRIVER[1], PETER JEPSEN[1], VIRASAKDI CHONGSUVIVATWONG[3], JØRN OLSEN[4] and HENRIK TOFT SØRENSEN[1]

From the [1]Department of Clinical Epidemiology, and [4]Danish Epidemiology Science Centre, Institute of Epidemiology and Social Medicine, Aarhus University, Aarhus, Denmark, and [2]Department of Clinical Pharmacy, Faculty of Pharmaceutical Sciences, and [3]Epidemiology Unit, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand

This study aimed to examine the risk of adverse pregnancy outcomes in children born to mothers who redeemed a prescription for systemic or topical acyclovir during pregnancy. Data on prescriptions of acyclovir were obtained from the Danish North Jutland Prescription Database and data on pregnancy outcomes from the Danish Medical Birth Registry and the County Hospital Discharge Registry. The risk of malformations, low birth weight, preterm birth and stillbirth in users of acyclovir were compared with non-exposed women using a follow-up design, while the risk of spontaneous abortion was examined using a case–control design. 90 pregnant women had redeemed a prescription for systemic acyclovir, and 995 women for topical acyclovir, during 30 d before conception, or during their pregnancies from 1 January 1990 to 31 December 2001. The odds ratios (95% confidence intervals) of the exposed relative to the non-exposed for the systemic and topical acyclovir were: malformations, 0.69 (0.17–2.82) and 0.84 (0.51, 1.39); low birth weight, 2.03 (0.50–8.35) and 0.48 (0.21–1.07); preterm birth, 1.04 (0.38–2.85) and 0.95 (0.70–1.28); stillbirth (for topical acyclovir), 1.70 (0.80–3.60); and spontaneous abortion, 2.16 (0.60–7.80) and 1.29 (0.80–3.60). There is increasing evidence that the use of systemic acyclovir is not associated with an increased prevalence of malformations at birth and preterm delivery. The data for low birth weight and spontaneous abortion are still inconclusive, although the risk of spontaneous abortion is increased in women exposed to acyclovir during the first month of pregnancy. The use of topical acyclovir does not seem to be associated with any adverse pregnancy outcome, although data on stillbirth are inconclusive.

C. Ratanajamit, Department of Clinical Pharmacy, Faculty of Pharmaceutical Sciences, Prince of Songkla University, Songkhla, 90110 Thailand (Tel./fax. +66 7442 8222, e-mail: rchaveew@ratree.psu.ac.th)

INTRODUCTION

Acyclovir is a widely used drug in the treatment of herpes simplex virus and varicella zoster virus (1). Appropriate use of antiviral drugs in pregnant women, in particular those infected with herpes simplex virus, reduces the transmission rates to the newborn (2). Acyclovir crosses the placenta and gives a maternal-to-cord plasma ratio of 0.83:1.9 (3). Being a nucleoside analogue, acyclovir has teratogenic, embryotoxic, carcinogenic and antiproliferative potential (4). Studies of rats exposed to acyclovir (50–100 mg/kg) during pregnancy showed an increased risk of gross structural defects (small or missing tympanic bone, missing tail and protruding tongue) in their offspring (5), although other studies in rats found no teratogenic effects (6–8). Data from registries established by the manufacturer of acyclovir between 1984 and 1998 showed a prevalence of 3% (19/581) [95% confidence interval (95% CI) 2.0–5.2%] of malformations in offspring of women who received acyclovir during pregnancy, but the route of administration was not specified (9). The registries were based on spontaneous reporting, which could result in bias owing to loss to follow-up.

This study examined the risk of adverse birth effects in offspring born to mothers who redeemed a prescription of systemic and/or topical acyclovir during pregnancy, based on registry data in North Jutland County, Denmark.

MATERIALS AND METHODS

Study population

A follow-up study and a case–control study were conducted in North Jutland County, Denmark, which has a population of 490 000 people. The follow-up study included data on all women who had had a live birth or a stillbirth after the 28th week of gestation between 1991 and 2001. The data were obtained from the Pharmacoepidemiological Prescription Database, the Danish Medical Birth Registry and the County's Hospital Discharge Registry (10–12). The risk of adverse birth outcome (malformations, low birth weight, preterm birth and stillbirth) was examined in a follow-up study, and the risk of spontaneous abortion in a case–control study.

Use of acyclovir

The population-based North Jutland Pharmacoepidemiological Prescription Database was used to identify potentially exposed pregnant women. The database, which was initiated on 1 January 1991, includes 63 659 pregnant women from a population of about 490 000 inhabitants, which corresponds to 10% of the Danish population. North Jutland is served by pharmacies equipped with electronic accounting systems that are used primarily to secure reimbursement from the National Health Service. The health service provides tax-supported health care for all inhabitants of Denmark, i.e. 50% of the cost of prescribed medicines, including acyclovir. Information including the customer's civil registration number, the type and amount of drug prescribed according to the anatomical therapeutical chemical (ATC) classification system, and the date of dispensing of the drug is transferred from the pharmacies to the prescription database. All women receiving prescriptions for acyclo-

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vir, systemic or topical, were identified subsequently, while the exposed and non-exposed pregnant women were identified in the Danish Medical Birth Registry. Cases with spontaneous abortion were identified in the Hospital Discharge Registry.

Outcome data

The data were linked to the Danish Medical Birth Registry and the County Hospital Discharge Registry, by means of the civil registration number.

Danish Medical Birth Registry. The Danish Medical Birth Registry contains information on all births in Denmark since 1 January 1973 (13). Data are recorded by the midwives and doctors responsible for the deliveries. The main variables in the registry are maternal age, birth weight, gestational age, birth order, maternal smoking status and data on delivery. The registry also includes a code that links the parents to the newborn.

County Hospital Discharge Registry. The computerized data from the medical birth registry do not include data about specific malformations. Therefore, data on malformations were obtained from the County Hospital Discharge Registry, which was established in 1977. This registry transfers the data to the nation-wide registry, where 99.4% of all discharges from Danish medical hospitals are recorded. These registries record civil registration number, dates of admission and discharge, the surgical procedure(s) performed, and up to 20 discharge diagnoses, classified according to the Danish version of the International Classification of Diseases (ICD), 8th revision until the end of 1993 and thereafter the 10th revision. The children were identified at birth and followed in the registry for the first year of life. The codes for congenital malformations were 740.00–759.99 in the ICD8 and Q0.00–Q99.9 in the ICD10, but congenital dislocation of the hip and undescended testes were excluded owing to poor validity of these diagnoses (14). Congenital malformations were recorded at birth or during the first year of life for malformations undiagnosed at birth. The codes for spontaneous abortion were 634.61, 643.8–9 and 645.1 in the ICD8, and O02 and O03 in the ICD10.

Record linkage between acyclovir and outcome data

The 10-digit civil registration number, assigned to all citizens shortly after birth by the Central Office of Civil Registration since 1968, was used to link the exposure and outcome data of each pregnant woman.

Study design

Follow-up analysis. Exposure to acyclovir was defined as redeeming a prescription for acyclovir, either systemic or topical, at any time during pregnancy. The exposure period for malformations included 30 d before pregnancy (since the drug may cause chromosome damage to developing follicles) up to the first 90 d of pregnancy. The pre-embryonic and embryonic periods are critical periods, in which certain drugs can produce congenital malformations (15). Non-exposed individuals comprised all pregnant women who did not redeem a prescription for acyclovir during their pregnancies.

Case–control analysis. A case–control design was used to study the association between redeeming a prescription for acyclovir and spontaneous abortion. Cases were identified as all women whose first pregnancy between 1 January 1991 and 31 December 2001 resulted in hospitalization with spontaneous abortion. None of them had given birth or had an abortion before 1991. Acyclovir exposure was determined as having redeemed a prescription for systemic or topical acyclovir less than 3 months before the date of admission with the diagnosis of spontaneous abortion. The control group was obtained from the Danish Medical Birth Registry and consisted of women whose pregnancy resulted in a live birth or stillbirth after the 28th gestational week between 1 January 1991 and 31 December 2001, and who had not given birth or had an abortion before 1991. The risk estimates were calculated for exposure time intervals of 0–4, 0–8 and 0–12 weeks before the date of admission with spontaneous abortion. 4 217 cases and 32 540 controls were identified.

Statistical analysis

Follow-up analysis. Logistic regression analysis was performed to quantify the risk of malformations, low birth weight, preterm birth and stillbirth in pregnant women who redeemed a prescription for acyclovir compared with non-exposed women. Systemic acyclovir and topical acyclovir were analysed separately. The analyses were adjusted for parital status (parous or non-parous women), maternal smoking status (smoker or non-smoker) and maternal age (< 25, 25–30 and > 30 y), using design variables. Only full-term births were included in the study of low birth weight. Multiple linear regression was used to estimate the effect of exposure on birth weight, adjusted for gestational age, squared gestational age, maternal smoking status, parity and maternal age (16).

Case–control analysis. Logistic regression analysis was performed to quantify the risk of spontaneous abortions related to redeeming acyclovir, adjusted for maternal age divided into 3 categories (< 25, 25–30 and > 30 y), using design variables. As the selected exposure time window might affect the exposure of controls, the odds ratios (ORS) were calculated for different exposure windows (0–4, 0–8 and 0–12 gestational weeks).

RESULTS

Systemic acyclovir

90 pregnant women redeemed a prescription for systemic acyclovir during pregnancy or 30 d before conception. These pregnant women were classified into different exposure periods as shown in Table I. There were no major differences in maternal age, parity and proportion of smoking mothers between the cohorts. The prevalence of birth outcomes is presented in Table I. One case with a defect of the atrial septum and unspecified congenital malformation of the heart was found among the exposed women. No stillbirths were observed. The OR for each pregnancy outcome among the exposed, compared with the non-exposed women, is shown in Table II. No difference in mean birth weight was found. The adjusted OR (95% CI) for low birth weight was 2.03 (0.50–8.35). The ORs (95% CI) for spontaneous abortion for different exposure time from redeeming a prescription to the date of hospitalization with spontaneous abortion were: 0–4 gestational weeks 2.16 (0.60–7.80), 0–8 gestational weeks 1.88 (0.62–5.66) and 0–12 gestational weeks 1.78 (0.60–5.53).

Topical acyclovir

995 pregnant women redeemed a prescription for topical acyclovir during periconception or pregnancy. The numbers of pregnant women who redeemed a prescription for topical acyclovir at different exposure periods are shown in Table I. The total number of prescriptions redeemed for topical acyclovir was 1 148. As with the systemic acyclovir group,

Table I. *Descriptive characteristics of the study cohorts*

Variable	Exposed to acyclovir in the first trimester or 30 d before pregnancy		Exposed to acyclovir during pregnancy		
	Systemic	Topical	Systemic	Topical	Non-exposed
Pregnancies, *n*	72	474	73	906	62 685
Prescriptions, *n*	85	503	99	1 035	0
Mother's age (y)					
< 25	14 (19.5)	74 (15.6)	12 (16.4)	151 (16.6)	12 089 (19.3)
25–30	26 (36.1)	185 (39.0)	28 (38.4)	363 (40.1)	25 621 (40.9)
> 30	32 (44.4)	215 (45.4)	33 (45.2)	392 (43.3)	24 975 (39.8)
Proportion of smokers	(27.8)	(26.4)	(35.6)	(29.8)	(28.5)
Proportion of parous women	(80.6)	(73.4)	(83.6)	(74.1)	(78.1)
Birth weight	3 565 ± 592	3 535 ± 566	3 567 ± 632	3 571 ± 553	3 520 ± 587
Low birth weight	1 (1.5)	2 (0.4)	2 (2.9)	6 (0.7)	834 (1.4)
Preterm deliveries	4 (5.6)	27 (5.7)	4 (5.5)	46 (5.1)	3 297 (5.3)
Stillbirths	0	4 (0.8)	0 (0)	7 (0.8)	282 (0.4)
Malformations	2 (2.8)	16 (3.4)	2 (2.7)	37 (4.1)	2 496 (4.1)
Full-term births	68	447	69	860	59 337

Data are shown as *n* (%) or mean ± SD.

Table II. *Adverse pregnancy outcomes for systemic acyclovir*

Variable	Crude OR (95% CI)	Adjusted OR[a] (95% CI)
Redeemed a prescription for systemic acyclovir		
Malformations	0.69 (0.17, 2.81)	0.69 (0.17, 2.82)
Low birth weight	2.10 (0.51, 8.56)	2.03 (0.50, 8.35)
Preterm birth	1.05 (0.38, 2.86)	1.04 (0.38, 2.85)
Stillbirth	–	–
Spontaneous abortion[b]		
Exposure time (gestational weeks)		
0–4	2.11 (0.59, 7.55)	2.16 (0.60, 7.80)
0–8	1.93 (0.65, 5.78)	1.88 (0.62, 5.66)
0–12	1.82 (1.82, 5.40)	1.78 (0.60, 5.53)

[a]Odds ratio adjusted for parity, maternal smoking status and maternal age.
[b]Odds ratio adjusted for maternal age.
95% CI: 95% confidence interval.

Table III. *Adverse pregnancy outcomes for topical acyclovir*

Variable	Crude OR (95% CI)	Adjusted OR[a] (95% CI)
Redeemed a prescription for topical acyclovir		
Malformations	0.84 (0.51, 1.39)	0.84 (0.51, 1.39)
Low birth weight	0.49 (0.22, 1.10)	0.48 (0.21, 1.07)
Preterm birth	0.96 (0.72, 1.30)	0.95 (0.70, 1.28)
Stillbirth	1.72 (0.81, 3.66)	1.70 (0.80, 3.60)
Spontaneous abortion[b]		
Exposure time (gestational weeks)		
0–4	1.04 (0.55, 1.95)	1.06 (0.56, 1.99)
0–8	1.29 (0.82, 2.03)	1.29 (0.82, 2.03)
0–12	1.14 (0.76, 1.71)	1.14 (0.76, 1.72)

[a]Odds ratio adjusted for parity, maternal smoking status and maternal age.
[b]Odds ratio adjusted for maternal age.
95% CI: 95% confidence interval.

there were no differences in maternal age, parity and proportion of smoking mothers between exposed and control groups. The OR for each birth outcome in acyclovir exposed compared with controls is shown in Table III. The adjusted ORs (95% CI) for low birth weight and stillbirth were 0.48 (0.21–1.07) and 1.70 (0.80–3.60), respectively. The ORs and 95% CI for spontaneous abortion, adjusted for maternal age, at different times from redeeming a prescription for topical acyclovir to the date of hospitalization with spontaneous abortion were not increased. Children born to mothers who redeemed a prescription for topical acyclovir had a 30 g higher birth weight than those whose mothers did not redeem a prescription for acyclovir.

DISCUSSION

These results did not indicate that redeeming acyclovir during pregnancy poses a reproductive hazard. The amount of information for most outcomes, however, was limited and there were no data on early (preclinical) spontaneous abortions. The findings add to the increasing evidence that use of systemic acyclovir is not associated with an increased prevalence rate of malformations at birth or preterm delivery, but the data on low birth weight and spontaneous abortion are still too sparse. The use of topical acyclovir does not seem to be associated with any adverse pregnancy outcome, although data on stillbirths and spontaneous abortions are inconclusive.

As the registration of prescriptions and that of pregnancy outcomes are independent, differential misclassification should be prevented. Non-differential misclassification of exposure is, however, a problem since redeeming a prescription is only an indicator for use of medicine at that time. Patients are, however, required to pay part of the cost of acyclovir, which may reduce non-compliance with respect to a prescribed medicine. It was also anticipated that some women had obtained the drug from other sources, which may bias the risk estimates towards a null effect. However, this source of bias was not expected to be important owing to the large number of non-exposed women. If the disease for which acyclovir is prescribed had an effect on the outcomes under study, the study would be confounded by indication, but confounding by indication was apparently not a problem. Most results show no effect unless the disease prevents the outcome, which is unlikely.

The finding of no increased risk of malformations at birth in women who redeemed a prescription for acyclovir is consistent with the findings of the few other studies (9, 17). In the study by Rieff-Eldridge et al. (9), the observed risk (3.3%) of malformations was calculated as the number of malformations in reported live births and induced abortions divided by the total number of live births, which would not provide a valid prevalence rate. The data on acyclovir in the manufacturer pregnancy registry showed that 69 of 652 (10.5%) spontaneous abortions occurred after initial exposure to acyclovir during the first trimester. In addition, there were 78 induced abortions, all after initial exposure during the first trimester (no congenital malformations were reported). If these spontaneous abortions were the result of malformations, it could bias the risk estimate for malformations towards unity. In the present study, the risk of spontaneous abortions was increased in the systemic acyclovir group, while the risk of malformation at birth was decreased. It is possible that drug exposure may increase foetal death in the presence of malformations. In that case, the prevalence of malformations at birth would be low, or could be low even if the drug acts teratogenically. The underlying infection itself may also cause foetal death, resulting in spontaneous abortion. Most studies have to rely on data about malformations at birth, without information on spontaneous abortions. These studies have limited ability to detect a teratogenic effect if the exposure causes abortion.

In this study, data were available on spontaneous abortions leading to hospitalizations, but not on abortions in the preclinical phase. In addition, there were no data on the timing of the abortion. For these reasons, the requirement for density sampling of controls within the cohort had to violated when studying spontaneous abortions. Controls should have been matched on gestational time of the cases to provide comparable periods for drug use and proper effect measure. Therefore, a median gestational time for the abortions had to be assumed; this was set at 12 weeks, which is probably too long. The results are probably biased towards no association. Because of this uncertainty, an attempt was made to restrict exposure time to 8 weeks and 4 weeks. Each of these steps increased the OR (95% CI) to 2.2 (0.6–7.8) for systemic acyclovir, which is expected if the exposure cause abortion. Topical acyclovir exposure had no impact on risk estimates.

Redeeming prescriptions for systemic or topical acyclovir during pregnancy did not increase the risk of preterm birth. No stillbirths were found in the systemic acyclovir group, but the topical acyclovir group had a statistically insignificant increased risk for stillbirth of 80%, which may indicate that the underlying infection could cause stillbirth.

In conclusion, this study has provided some evidence to suggest that systemic acyclovir use during pregnancy does not increase the risk of malformations at birth or preterm birth. The use of topical acyclovir does not seem to be associated with any adverse pregnancy outcome, although the data on the risk of stillbirth are inconclusive.

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PREGNANCY LOSS IN THE PHILIPPINES

Metta Kuning[1], Don McNeil[2] and Virasakdi Chongsuvivatwong[3]

[1]Faculty of Science and Technology, Prince of Songkla University, Pattani, Thailand; [2]Department of Statistics, School of Economics, Macquarie University, Sydney, Australia; [3]Epidemiology Unit, Faculty of Medicine Prince of Songkla University, HatYai, Songkhla, Thailand

Abstract. In this cross-sectional study, 8,481 women aged 15-49 who had at least one pregnancy outcome were considered. This study aimed to examine the characteristics of Filipino women having had a pregnancy loss, and to test the association between domestic violence and pregnancy loss. To control for the confounding effect of the number of pregnancies, the sample was divided into seven groups classified by the number of pregnancies. The risk factors considered were demographic characters (age and partner's age, marital status, and place of residence), socioeconomic status (education and partner's education, having a paid helper at home, having a say in how income was spent), domestic violence (physical abuse and forced sex), sexual behavior of partner, whether the pregnancy was wanted, and disease history (tuberculosis, diabetes, hypertension, malaria, hepatitis, kidney disease, heart disease, anemia, goiter and other medical problems). The major risk factors were found to be physical abuse, region, faithfulness of partners, hypertension, hepatitis, kidney disease, anemia, and the other medical problems, respectively. The risk of pregnancy loss for the women suffering domestic violence was 1.59 (95%CI 1.28-1.97) times higher than for the women who did not. Women aged 15-19 years had a much higher risk of pregnancy loss than the other age groups (OR=1.49, 95%CI 1.22-1.82). There were similar risk for women aged 20-24 years (OR=1.08, 95%CI 0.94-1.25) and 35-39 years (OR=1.05, 95%CI 0.92-1.19). No association emerged with marital status, socioeconomic status, forced sex, the number of partners, unwanted pregnancy, tuberculosis, diabetes, malaria, heart disease, and goiter. Although women's age, partner's age, residence, women's education, partner's education, and paid helper at home were significantly associated with pregnancy loss, they were likely to be confounders rather than risk factors.

INTRODUCTION

Reproductive health has always occupied an important part of any discussion about women's health (Santow, 1995). Reproductive failure is represented by fetal loss (National Statistical Office, 2000). The risk of pregnancy loss has been justified as a useful health index in epidemiological studies of possible environmental hazards to man (Czeizel *et al*, 1984). Pregnancy loss occurs in 12 to 24% of pregnancies (Smith, 1988; Stirrat, 1990). Pregnancy loss adversely affects the mother's present health (Regan, 1991), grief response, subsequent pregnancy, psychological problems (Bowles *et al*, 2000), and social or economic condition (Ney *et al*, 1994).

Correspondence: Metta Kuning, Faculty of Science and Technology, Prince of Songkla University, Pattani, 94000, Thailand.
E-mail: kmetta@bunga.pn.psu.ac.th

Previous pregnancy losses have downstream impacts on the mother's health. Pregnancy loss has an adverse affect on subsequent live births. Thom *et al* (1992) suggested that women with three or more prior pregnancy losses were at higher risk of preterm delivery, placenta previa, having membranes ruptured for more than 24 hours, breech presentation, and having an infant with a congenital malformation.

Domestic violence against women is a public health problem. At least one woman in three has been beaten, coerced into sex, or otherwise abused in her lifetime, and up to 2 million women worldwide are assaulted by their partners each year [United Nations Population Fund (UNFPA), 2000]. Approximately 40-60% of battered women are abused during pregnancy (Parker and McFarlane, 1991) and these women are four times more likely to have a pregnancy loss than non-battered women (Bullock, 1989). The proportion

of women having had more than one pregnancy loss increases with increased severity of abuse (Webster *et al*, 1996).

The aims of the study were to examine this characteristics of Filipino women from the Safe Motherhood Survey (SMS) [(National Statistic Office (NSO), Philippines, and Macro International Inv (MI), 1994] having had a pregnancy loss, and to test the association between domestic violence and pregnancy loss.

MATERIALS AND METHODS

A total sample of 8,481 Filipino women aged 15-49 who had ever had a pregnancy outcome from the Safe Motherhood Survey (SMS) was used in this study. The Safe Motherhood Survey was the first national survey of the Philippines carried out as part of the global Demographic and Health Surveys program. This survey was conducted between October and December 1993, to investigate a variety of women's reproductive health issues, including pregnancy history, maternal morbidity, pregnancy outcomes, use of services for health problems, socio-demographic characteristics, domestic violence and sexual behavior. Pregnancy outcomes included live births and pregnancy. A pregnancy loss is defined as any non-live birth after pregnancy, either by spontaneous abortion (miscarriage or fetal loss before full term), induced abortion or stillbirth (children born dead after a gestation of seven or more complete months). The outcome, pregnancy loss, was measured by the questions 'Have you had any pregnancies that did not result in live births?' and 'How many pregnancies did not result in a live birth?'

In our analysis, we took the unit of analysis as the woman, rather than the pregnancy, and we measured the fetal loss rate as the number of women having at least one pregnancy loss divided by their total number of pregnancies.

Demographic factors, socioeconomic factors, maternal morbidity history, domestic violence, sexual behavior and unwanted pregnancy were the determinants of interest. The ages of the woman and her partner were their ages at interview. The Philippines is grouped geographically into three major islands: Luzon, Visayas, and Mindanao. Socioeconomic status was measured by the questions 'Do you have a paid helper at home?' and 'Do you have a say in how your household's overall income is spent?' Paid helpers were defined broadly as any nonrelatives who received cash for services in the home, regardless of whether or not they resided in the household. The maternal morbidity questions comprised 'Have you ever, at any time in your life, been told by a doctor or a nurse that you had (a) tuberculosis, (b) diabetes, (c) high blood pressure, (d) malaria, (e) hepatitis, (f) kidney disease, (g) heart disease, (h) anemia, (i) goiter, or (j) other medical problems?' The domestic violence items were 'Has anyone close to you, that is, family or friend, ever hit, slapped, kicked, or tried to hurt you physically?' and 'Have you ever been physically forced to have sex with someone?' The direct questions, 'Has your husband had sex with other women or with men?' and 'Does your husband ever pay other women to have sex with him?' explored the sexual behavior of their partner. Altogether, 'How many sexual partners have you had in your whole life?' is the question for evaluating the sexual behavior of the woman [National Statistic Office (NSO), Philippines, and Macro International Inv (MI), 1994].

The number of fetal losses per woman is expected to increase with the number of pregnancies. To remove this confounding effect, we separated the 8,481 women into the following seven groups: one pregnancy (n=945), two (n=1,333), three (n=1,441), four (n=1,258), five (n=1,007), six or seven (n=1,278), and eight or more pregnancies (n=1,219). The association can then be measured separately within each group, and an accurate estimate of the overall association is then obtained by comparing the resulting estimates.

All the determinants of interest were categorical. Pearson's chi-squared test and 95% confidence intervals for odds ratios were used to assess the associations between the outcome and the various determinants. For determinants with more than two categories, odds ratios were computed by comparing each category of the determinant with all other categories of that determinant combined (McNeil, 1996). Mantel-Haenszel adjusted odds ratios were used to examine the

associations between the outcome and the determinants after adjusting for the number of pregnancies, using a homogeneity test based on the chi-squared goodness of fit statistic (Breslow and Day, 1980).

RESULTS

In this section, results are given for three outcome measures, as follows: (a) the proportion of women who had a fetal loss, (b) the fetal loss rate per pregnancy, obtained by dividing the proportion (a) by the number of pregnancies, and (c) the odds ratios for the risk of ever having a fetal loss comparing two risk factors.

The mean age of the women was 34.5 years, with a standard deviation of 8.0 years. The average number of pregnancies was 4.4 and the maximum was 20. One in three women had at least one pregnancy loss in their lifetime.

Fig 1 shows the proportion of women who had a fetal loss classified by mother's age group for each number of pregnancies. As expected, this proportion increased with the number of pregnancies, but the rate of increase diminished with age.

The fetal loss rate per woman varied from 4.2% for women who had had one pregnancy, to 8.0% for women who had had six or seven pregnancies.

Demographic factors

Table 1 shows the fetal loss rate per pregnancy classified by pregnancy number for the demographic factors. As seen from the Table, the disparity of rates is most obvious when evaluated by the ages of the woman and her partner. In one pregnancy group, the fetal loss rates were highest among women aged 40 or more (12.9%) whose partners were aged 45 or more (8.6%). The fetal loss rates in the two-pregnancy group (overall 5.8%) were highest for women aged 35-39 years (8.2%) and for women with partners aged 17-29 years (6.8%). Among women who had had more than two pregnancies, the overall rates varied from 7.2% to 8.0%, and were highest among the younger women.

The women having had 1-4 pregnancies and living in de facto relationships had higher fetal loss rates than those who were married or widowed.

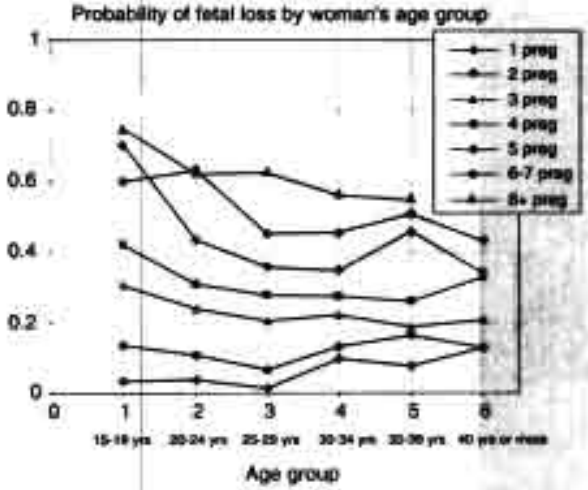

Fig 1–Proportion of women having a fetal loss by mother's age group.

There were relatively small differences between those living in urban and rural areas, and between the three island groups.

Socioeconomic status, domestic violence, sexual behavior and unwanted pregnancy

Table 2 shows the fetal loss rate classified by pregnancy number, with respect to socioeconomic status, domestic violence, sexual behavior and unwanted pregnancy status.

The fetal loss rate for women with more than two pregnancies increased with educational level for the woman and for her partner. For women who had 2-7 pregnancies, the fetal loss rate of those who had a paid helper at home was higher than for others. Among women who had had 1 and 5 pregnancies, the fetal loss rate had a higher difference between those who had a say in income spent and those who had not.

For women who had up to three pregnancies, those suffering physical abuse had higher fetal loss rates (7.8% to 10.6%) than others. Also, the fetal loss rate of women having been forced to have sex was high among women with 1, 2 and 4 pregnancies.

For women with one pregnancy, no fetal losses at all were reported by those whose partners had sex with other women. However, the fetal loss rates were higher among women with three or more pregnancies if their partners were not

Table 1
Rate of fetal loss classified by number of pregnancies for the demographic factors.

Demographic factors	Number of pregnancies						
	1	2	3	4	5	6-7	8+
Total number of women	945	1,333	1,441	1,258	1,007	1,278	1,219
Fetal loss rate (%)	4.3	5.8	7.6	7.4	7.9	8.0	7.2
Age (years)							
15-19	3.4	6.7	10.3	10.6	14.1	10.0	-
20-24	3.8	5.4	8.0	7.8	8.7	10.5	9.4
25-29	1.3	3.4	6.8	6.9	7.2	7.6	7.8
30-34	9.6	6.6	7.4	6.9	7.0	7.6	7.8
35-39	7.8	8.2	6.3	6.5	9.2	8.5	7.0
≥40	12.9	6.5	7.0	8.3	6.8	7.2	6.9
Partner's age (years)							
17-29	3.9	6.8	9.7	10.2	9.5	9.1	6.3
30-34	3.8	4.9	7.0	7.7	8.8	8.8	8.6
35-39	7.1	5.7	7.1	6.2	7.0	7.5	7.2
40-44	8.3	5.8	5.4	6.6	8.4	8.4	7.3
≥45	8.6	6.1	7.8	7.5	7.4	7.5	7.1
Missing	1.3	2.0	8.0	6.0	6.7	7.8	7.3
Marital status							
Married	4.3	6.0	7.4	7.3	8.0	8.0	7.2
Living together	6.7	6.3	9.7	9.9	7.5	7.5	7.3
Widowed	1.7	1.5	8.7	6.3	6.7	7.9	7.3
Residence							
Urban	4.9	5.8	7.2	7.7	8.0	8.9	7.6
Rural	3.6	5.7	8.0	7.1	7.8	7.2	7.1
Region							
Luzon	4.8	6.3	7.8	8.2	8.2	8.0	7.8
Visayas	6.0	6.4	6.9	7.1	7.9	8.6	7.0
Mindanao	2.0	4.2	8.0	6.1	7.4	7.5	6.7

faithful. Women who had more than one partner, and those who had unwanted pregnancies, had similar fetal loss rates to other women.

Mother's health status

Table 3 shows the fetal loss rate classified by number of pregnancies for mother's health status. The major health problems of the women who had fetal loss were hepatitis, diabetes, tuberculosis and malaria. Among women who had suffered hepatitis, the fetal loss rate was high for those with one pregnancy (14.3%), four pregnancies (12.5%), 6-7 pregnancies (12.8%), and more than seven pregnancies (11.5%). For women with diabetes, the fetal loss rate varied from 10.0% to 13.3% for women with 2-5 pregnancies. Among women who had suffered tuberculosis, fetal losses were high for those with three pregnancies (11.1%). For women who had experienced malaria, the fetal loss rate was 10.0% among those who had 6-7 pregnancies.

Associations between determinants and fetal loss

The Mantel-Haenszel odds ratios, used to measure the association between fetal loss and the risk factors after adjusting for the number of pregnancies, are shown in Table 4. Except for marital status, all the demographic factors were related to pregnancy loss. Age and partner's age were related to fetal loss ($p < 0.001$ in each case), with higher relative risk for women aged 15-19

Table 2
Rate of fetal loss classified by number of pregnancies for socioeconomic status, domestic violence, and sexual behavior.

Determinant variables	Number of pregnancies						
	1	2	3	4	5	6-7	8+
Total number of women	945	1,333	1,441	1,258	1,007	1,278	1,219
Fetal loss rate (%)	4.3	5.8	7.6	7.4	7.9	8.0	7.2
By socioeconomic status							
Woman's education							
No educ/primary	4.5	6.7	6.1	6.1	7.2	7.2	7.1
High school/voc-tech	4.7	5.3	7.9	7.8	7.9	8.4	7.8
College	3.7	5.6	9.3	9.2	9.9	11.1	8.7
Partner's education							
No educ/primary	4.3	5.6	7.2	5.9	6.9	7.1	7.0
High school/voc-tech	4.3	6.1	7.4	7.3	7.9	8.4	8.0
College	4.4	5.6	8.3	9.9	10.4	10.7	7.8
Paid helper at home							
Yes	2.2	6.9	9.2	8.7	9.2	10.8	6.4
No	4.6	5.6	7.5	7.2	7.8	7.8	7.3
Say in income spent							
Yes	4.6	5.8	7.6	7.5	8.0	8.0	7.2
No	1.4	3.8	8.9	6.1	4.9	7.2	8.1
By domestic violence							
Physical abuse							
Yes	7.8	8.4	10.6	7.5	8.1	9.2	7.9
No	4.0	5.5	7.3	7.4	7.9	7.8	7.2
Forced to have sex							
Yes	10.3	10.0	7.4	10.2	5.2	7.9	6.4
No	4.1	5.6	7.6	7.3	8.0	8.0	7.3
By sexual behavior							
Partner had sex other							
Yes	0.0	4.1	9.1	9.5	8.4	10.7	8.5
No	4.5	5.8	7.5	7.2	7.9	7.6	7.1
Partner pay women for sex							
Yes	8.3	5.6	12.9	10.7	7.6	10.6	8.6
No	4.2	5.8	7.4	7.2	7.9	7.8	7.2
Other partners							
Yes	7.5	6.7	8.9	8.5	9.1	7.9	6.5
No	4.2	5.7	7.6	7.3	7.8	8.0	7.3
By unwanted pregnancy							
Yes	4.9	4.6	7.1	7.0	8.0	7.6	7.6
No	4.3	6.0	7.8	7.5	7.9	8.2	7.0

years (OR=1.49, 95%CI 1.22-1.82) and for women whose partners were aged 17-29 years (OR=1.45, 95%CI, 1.25-1.70). Fig 2 shows a plot of the 95% confidence intervals for the individual odds ratios in each woman's age group before and after adjusting for the number of pregnancies. However the homogeneity test failed for woman's age group ($p = 0.003$), indicating an effect modification for this variable. Women living in urban areas had a higher risk of fetal loss (OR=1.14, 95%CI 1.03-1.26) than those living in rural areas. Luzon region had a higher risk of fetal loss than the other regions (OR=1.19, 95%CI 1.08-1.32).

Table 3
Rate of fetal loss classified by number of pregnancies for mother's health status.

Health status		Number of pregnancies						
		1	2	3	4	5	6-7	8+
Total number of women		945	1,333	1,441	1,258	1,007	1,278	1,219
Fetal loss rate (%)		4.3	5.8	7.6	7.4	7.9	8.0	7.2
Tuberculosis:	yes	-	9.5	11.1	9.4	7.3	8.6	7.8
	no	4.4	5.7	7.6	7.4	7.9	8.0	7.5
Diabetes:	yes	-	12.5	13.3	9.6	10.0	7.9	8.3
	no	4.4	5.7	7.6	7.4	7.8	8.0	7.5
Hypertension:	yes	5.4	7.1	9.3	8.8	8.1	8.0	8.0
	no	4.2	5.6	7.4	7.2	7.9	8.0	7.5
Malaria:	yes	8.7	6.5	7.1	8.2	6.8	10.0	7.7
	no	4.2	5.7	7.6	7.4	8.0	7.9	7.5
Hepatitis:	yes	14.3	3.6	2.2	12.5	9.1	12.8	11.5
	no	4.3	5.8	7.7	7.3	7.9	7.9	7.5
Kidney disease:	yes	7.8	8.0	5.3	9.1	9.1	9.7	8.0
	no	4.0	5.6	7.8	7.2	7.8	7.8	7.5
Heart disease:	yes	2.6	2.9	6.7	7.4	9.2	9.0	7.0
	no	4.4	5.8	7.7	7.4	7.9	7.9	7.6
Anemia:	yes	5.9	6.1	7.5	8.6	9.9	9.1	7.7
	no	4.2	5.6	7.7	7.2	7.4	7.7	7.5
Goiter:	yes	2.9	6.8	7.8	9.6	7.6	9.4	8.0
	no	4.4	5.7	7.6	7.3	7.9	7.9	7.5
Other medical	yes	6.6	6.4	8.6	9.1	8.8	9.5	6.9
problems:	no	4.1	5.7	7.6	7.2	7.8	7.8	7.6

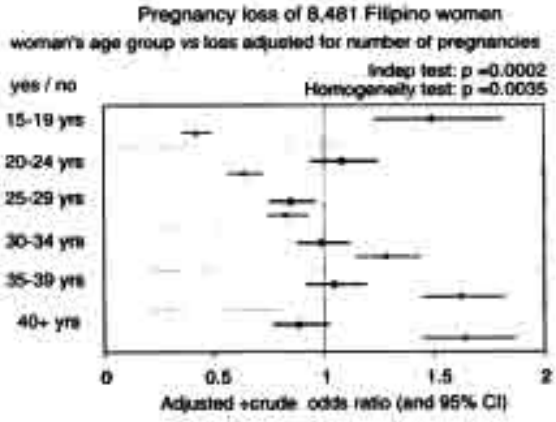

Fig 2–Odds ratios for age group *vs* fetal loss: association crude and adjusted association for number of pregnancies.

Turning to the social factors (Tables 5 and 6), no associations were found between fetal loss and the woman's say in how income was spent forced sex or the number of partners. The woman's education, her partner's education, having a paid helper at home and physical abuse were all risk factors. The risk of fetal loss increased with the level of education of the women and their partners. The odds ratio was 1.32 (95%CI 1.10-1.59) for women who had a paid helper at home. Women suffering physical abuse, or whose partner had sex with other women, or whose partner paid women for sex, had higher risks than others. Fig 3 shows the 95% confidence intervals for the odds ratios between physical abuse and fetal loss within each pregnancy number group. However, no increased risk was found for women who had an unwanted pregnancy. For this risk factor, the association was confounded by the number of pregnancies but there was no effect modification, as shown in Fig 4. Among the medical factors (Table 7) hypertension, hepatitis, kidney disease, anemia and other medical problems were all associated with fetal loss. However no associations were found between fetal loss and tuberculosis, diabetes, malaria, heart disease or goiter.

Table 4
Association between pregnancy loss and demographic factors after adjusting for number of pregnancies.

Predictors	Adjusted odds ratio and 95%CI		Crude odds ratio	Indep test	Homog test
Demographic factors					
Age (years)				<0.001	0.003
15-19	1.49	(1.22,1.82)	0.42		
20-24	1.08	(0.94,1.25)	0.64		
25-29	0.85	(0.75,0.97)	0.83		
30-34	0.99	(0.88,1.12)	1.29		
35-39	1.05	(0.92,1.19)	1.62		
≥40	0.89	(0.77,1.02)	1.64		
Partner's age (years)				<0.001	0.222
17-29	1.45	(1.25,1.70)	0.52		
30-34	1.07	(0.93,1.22)	0.80		
35-39	0.86	(0.76,0.98)	0.99		
40-44	0.99	(0.87,1.13)	1.46		
≥45	0.94	(0.83,1.05)	1.74		
Missing	0.79	(0.62,1.01)	0.62		
Marital status				0.102	0.330
Married	0.98	(0.83,1.14)	1.26		
Living together	1.17	(0.96,1.42)	0.89		
Widowed	0.82	(0.64,1.06)	0.69		
Residence				0.013	0.065
Urban	1.14	(1.03,1.26)	0.93		
Rural	0.88	(0.80,0.97)	1.07		
Region				<0.001	0.210
Luzon	1.19	(1.08,1.32)	1.04		
Visayas	1.00	(0.88,1.13)	1.04		
Mindanao	0.81	(0.72,0.91)	0.92		

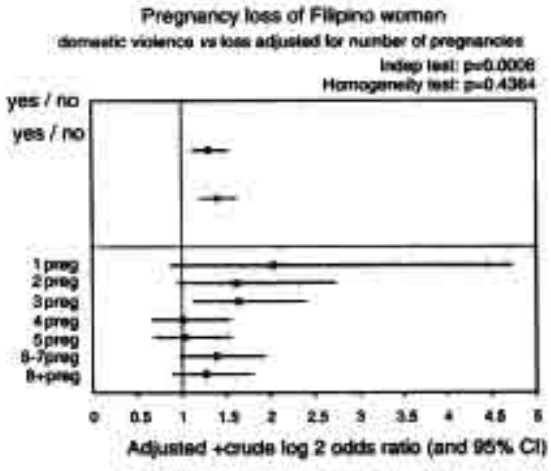

Fig 3–Domestic violence *vs* fetal loss, by number of pregnancies.

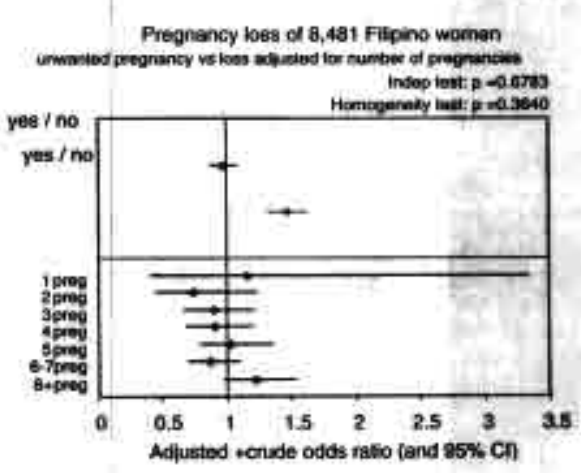

Fig 4–Unwanted pregnancy *vs* fetal loss, by number of pregnancies.

Table 5
Association between pregnancy loss and socioeconomic status, and domestic violence after adjusting for number of pregnancies.

Predictors	Adjusted odds ratio and 95%CI		Crude odds ratio	Indep test	Homog test
By socioeconomic status					
Women's education				<0.001	0.022
No. educ/primary	0.72	(0.65,0.81)	1.36		
High school/voc-tech	1.08	(0.97,1.21)	0.82		
College	1.49	(1.30,1.70)	0.82		
Partner's education				<0.001	0.016
No. educ/primary	0.71	(0.64,0.79)	1.24		
High school/voc-tech	1.07	(0.96,1.20)	0.90		
College	1.48	(1.31,1.68)	0.84		
Paid helper at home					
Yes	1.32	(1.10,1.59)	0.93	0.003	0.219
No	0.76	(0.63,0.91)	1.08		
How income spent					
Yes	1.15	(0.89,1.50)	1.24	0.294	0.233
No	0.87	(0.67,1.13)	0.81		
By domestic violence					
Physical abuse					
Yes	1.31	(1.15,1.47)	1.40	0.001	0.436
No	0.76	(0.65,0.89)	0.71		
Forced to have sex					
Yes	1.02	(0.75,1.37)	1.08	0.918	0.158
No	0.98	(0.73,1.33)	0.92		

Table 6
Association between pregnancy loss and sexual behavior after adjusting for pregnancy number.

Predictors	Adjusted odds ratio and 95%CI		Crude odds ratio	Indep test	Homog test
By sexual behavior					
Partner has sex other					
Yes	1.45	(1.22,1.72)	1.71	<0.001	0.074
No	0.69	(0.58,0.82)	0.58		
Partner pay women for sex					
Yes	1.59	(1.28,1.97)	1.72	<0.001	0.206
No	0.63	(0.51,0.78)	0.58		
Other partners					
Yes	1.05	(0.87,1.27)	1.29	0.581	0.438
No	0.94	(0.79,1.14)	0.77		
By unwanted pregnancy					
Yes	0.98	(0.87,1.09)	1.47	0.678	0.364
No	1.02	(0.92,1.15)	0.68		

Table 7
Association between pregnancy loss and mother's health status after adjusting for pregnancy number.

Predictors		Adjusted odds ratio and 95%CI	Crude odds ratio	Indep test	Homog test
Health status					
Tuberculosis:	Yes	1.28 (0.92,1.78)	1.72	0.918	0.158
	No	0.63 (0.51,0.78)	0.58		
Diabetes:	Yes	1.48 (0.95,2.29)	1.98	0.076	0.940
	No	0.68 (0.44,1.05)	0.52		
Hypertension:	Yes	1.20 (1.03,1.41)	1.34	0.023	0.859
	No	0.83 (0.71,0.98)	0.74		
Malaria:	Yes	1.17 (0.91,1.51)	1.51	0.234	0.698
	No	0.86 (0.66,1.10)	0.66		
Hepatitis:	Yes	1.83 (1.12,2.99)	1.67	0.019	0.069
	No	0.54 (0.33,0.89)	0.60		
Kidney disease:	Yes	1.30 (1.10,1.54)	1.39	0.002	0.123
	No	0.77 (0.65,0.91)	0.72		
Heart disease:	Yes	1.01 (0.81,1.25)	1.29	0.946	0.572
	No	0.99 (0.80,1.23)	0.77		
Anemia:	Yes	1.27 (1.15,1.40)	1.44	<0.001	0.357
	No	0.79 (0.69,0.89)	0.70		
Goiter:	Yes	1.23 (0.98,1.53)	1.39	0.073	0.821
	No	0.82 (0.65,1.02)	0.72		
Other medical problems:					
	Yes	1.21 (1.01,1.44)	1.26	0.033	0.587
	No	0.83 (0.69,0.99)	0.79		

DISCUSSION

Our primary objective was to investigate the associations between fetal loss and demographic, social and medical risk factors. We were particularly interested in the association between domestic violence and fetal loss. The outcome was whether or not a subject in the target population had had a fetal loss. We could have carried out a pregnancy-based analysis to model the risk of a fetal loss as a function of parity (and/or age) and the risk factors of interest. However, pregnancy outcomes are probably correlated within subjects, violating the statistical independence assumption, and thus necessitating a more complex method of analysis. To ensure independence of outcomes we chose to treat the woman rather than the pregnancy as the experimental unit. As a consequence, the risk of the outcome increases with the number of pregnancies, and thus the number of pregnancies is likely to be a confounder in the associations of interest. To eliminate this confounding effect we divided the sample into seven groups according to the number of pregnancies, and then recombined the estimates to obtain odds ratios, using the Mantel-Haenszel method. As Fig 1 shows, classifying by number of pregnancies largely eliminates the effect of age on fetal loss, as would be expected. Fig 2 shows very clearly the confounding effect of the number of pregnancies. The crude association between fetal loss and age group indicates increasing risk with age, as expected, but this association is reversed when one adjusts for the number of pregnancies. Fig 3, which is essentially a meta-analysis plot, graphically illustrates the association between domestic violence and fetal loss. For this risk factor, there is little if any confounding with the number of pregnancies, and it is interesting to note that the associations within each pregnancy-number group are mostly inconclusive; when these results are combined a substantial association emerges.

The association between fetal loss and whether or not the pregnancy was wanted is also shown graphically in Fig 4. Here the number of pregnancies is a very strong confounder. The crude odds ratio indicates a strong association between fetal loss and the pregnancy being unwanted, but after adjusting for the number of pregnancies this association completely disappears.

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