Perinatal Death Pattern in the Four Districts of Thailand: Findings from the Prospective Cohort Study of Thai Children (PCTC)

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Objective: *To determine the magnitude and investigate causes of perinatal deaths of a cohort of the Prospective Cohort Study of Thai Children.*

Material and Method: *A semi-structured verbal autopsy questionnaire and review of medical records were used to ascertain the causes of deaths during the perinatal period in four districts of Thailand.*

Results: *The total numbers of 3,522 babies (with 28 pairs of twins) were born from 3,494 pregnant women. The perinatal mortality rate was 10.69 per 1,000 total births, the stillbirth rate was 6.75 per 1,000 births, and the early neonatal mortality rate was 3.97 per 1,000 live-births. About 37.8% of the perinatal deaths were agreed to by two pediatricians and a neonatologist as preventable. About 90% of the preventable stillbirths occurred in the antepartum period.*

Conclusion: *Findings from the present study indicates that to further reduce the perinatal death rate, attention should be focused on reducing the stillbirths by a quality antenatal care.*

Keywords: *Cohort studies, Fetal death, Perinatal mortality, Prospective studies, Stillbirth*

Infant mortality rate is one of the important indices of a nation's health condition. In recent decades, with the advancement of medical care and public health service, post-neonatal deaths in most countries have declined dramatically. As in the United States, deaths in the first month of life consequently account for about two-thirds of all infant deaths[1]. From 1956 to 1990, the neonatal mortality rate fell from 24.2-3.8 per 1000 live-births, a decrease of about six-fold, whereas the postneonatal mortality rate dropped from 36.7-2.2 per 1000 live-births, a decrease of almost 17-fold[2].

In Thailand, the Ministry of Public Health has routinely calculated mortality rates by using data retrieved from birth certificates and death certificates. Like most other developing countries[3,4], registration of births and deaths is incomplete and the data is of poor quality, especially in rural and remote areas. Not surprisingly, the infant death rate (26.1 per 1,000 live-births) from the 4th national survey of population change[5] in 1994-5 was five times that of the vital statistics report of the same period (5.2 per 100 live-births)[6]. Discrepancies in these figures were due to under-registration of neonatal deaths during the first two weeks of life. Most deaths at this age take place at home. Causes of deaths given by non-medical persons can be inaccurate. Furthermore, the present system could not reveal the exact magnitude and causes of

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pregnancy termination due to under-reporting of abortion and stillbirths. This unreliable information may reduce the effectiveness of intervention programs to prevent perinatal deaths. Thus more reliable statistics are needed to identify potentially preventable causes as well as areas of health care service that are most in need of improvement.

The Prospective Cohort Study of Thai Children is the first longitudinal study of children in Thailand. It plans to follow children from about the 28th week of gestation to 24 years of age. This report describes the pattern and causes of perinatal deaths of the subjects from the data collected by an active surveillance system.

Material and Method
Study sites

The Prospective Cohort Study of Thai Children (PCTC) is an observational community-based study designed to follow different regional birth cohorts from about the 28th to 38th week gestation onwards. A sample of the Thai population was achieved in four cohorts from a chosen district in each of the four regions and a hospital-based sample in Bangkok, the capital. Eligible sites were accessible year-round, averaged between 800 and 900 births annually, and, had a hospital director (and associates) committed to long-term management. The four sites were: Panomtuan district of Kanchanaburi province in the west, Thepa district of Songkhla province in the south, Kranuan district of Khon Kaen province in the northeast, and Muang district of Nan province in the north. The present report is based on the data of the four districts only. Data from the Bangkok sub-sample which the research design was different from the other sites is not included in the present report.

Subjects

All pregnant women who resided or planned to raise their children in the 4 selected districts and who expected to give birth during the defined period of one calendar year were registered. They were identified in the beginning of the third trimester by a community survey or by retrieval from registries of the Antenatal Care Clinics (ANC) of hospitals, health centers and private clinics. Registration of subjects in the project was introduced sequentially. The first pregnant woman was enrolled in Panomtuan district in July 2000 and the first child was born on 15 October 2000. The last child of these four districts was born in Muang district of Nan province on 19 March 2002.

Case identification

Baseline data of pregnant women and their families were collected by an interview at 28-36 weeks gestation. Home visits to these women were carried out weekly from 36 weeks onwards. Delivery outcome was retrieved from the records of health centers or district hospitals. In the case of delivery at home or termination of pregnancy before term or infant death, their families or village leaders would report directly to the PCTC branch office at each site.

Fetal death of 28-40 weeks gestation was defined as a stillbirth, while death during the first seven days of life was defined as an early neonatal death. Perinatal death included stillbirths and early neonatal deaths.

Investigation into the cause of death

Verbal autopsy is commonly used to investigate the cause of death in population based studies where most deaths occur at home or in the peripheral hospital and necropsy or physical autopsy cannot be performed. Symptoms and signs prior to death were collected by an interview of the parents or caregivers[7]. In the present study, a semi-structured questionnaire was designed to cover common causes of early neonatal death described in the recent national report[8].

The attending pediatrician of each site interviewed parents and caregivers at about two weeks after the event to allow time for the families to recover from their grief, but not later than one month. For the hospitalized cases, information was also retrieved from the hospital records. Causes of stillbirth and early neonatal death were then extracted from the verbal autopsy questionnaire by two pediatricians (L.M. and S.I.) and one neonatologist (P.C.). In the case of a non-agreement, a consensus was reached at a meeting of the group. Causes of death were defined based on Wigglesworth's classification into "stillborn", "congenital malformation", "neonatal asphyxia", "immaturity" and "specific causes"[9]. The classification was modified by further categorization of stillbirth into "obstetric problems", "medical problems of mother", "macerated fetus" and "congenital anomalies"; the "specific causes" category in the early neonatal death was replaced with "individual specific diseases".

At the end of the extract form, the raters were asked to conclude whether death of that case was preventable.

Ethical clearance

The present study was approved by the

National Ethical Committee, Ministry of Public Health. Families were fully informed of all study procedures and any possible risks before signing an informed consent form.

Data analysis

The stillbirth rate (SBR) and perinatal mortality rate (PNMR) were calculated per 1,000 total births while early neonatal mortality rates (ENMR) were calculated per 1,000 live births. Statistical analysis was performed using STATA version 7.0[10].

Results

A total of 3,494 pregnant women were registered in the present study. The total births were 3,522 with 28 pairs of twins. Twenty-four babies were dead at birth. The SBR was therefore 6.8 per 1,000 total births. Fourteen infants did not survive the first week of life. The ENMR was 4.0 per 1,000 live-births and the PNMR was thus 10.7 per 1,000 total births.

From the total of 38 deaths, 35 cases (92%) were completely investigated; the other 3 cases included only the diagnosis. Seventy-two per cent died in the hospital and the male to female ratio was 1.4:1 and 3.3:1 for stillbirth and early neonatal death, respectively. Weight was recorded in 25 cases of deaths (65.8%). A breakdown of the perinatal mortality by birth weight was: 307.6 per 1,000 total births for the under 1,500 g, 22.5 for the 1,500-2,499 g, 4.6 for the 2,500-3,499 g, and 4.3 for the 3,500 g and over.

Causes of stillbirth

The most common cause of stillbirth, as shown in Table 1, was obstetric problems of which intrauterine asphyxia contributed to about one-half. Macerated fetuses and congenital anomalies accounted for 20.8% and 12.5% of stillbirths, respectively. A case of diaphragmatic hernia was diagnosed intrauterine by ultrasound but the parents refused referral for delivery and corrective operation at the University hospital.

Causes of early neonatal death

The most common cause of death in the first seven days of life was congenital anomalies of which two-thirds were anencephaly. As shown in Table 2, perinatal asphyxia, meconium aspiration, and neonatal sepsis were next in importance. Hypothermia and neonatal sepsis were both considered the consequence of child neglect.

Maternal characteristics

Table 3 describes maternal characteristics and perinatal mortality rate. The pregnancies of 1.1% of women aged 20 years and older ended with perinatal deaths while for younger mothers the figure was 0.4%. The PNMR of the mothers who did laboring work or who were farmers (11.61 and 12.36 per 1,000 total births, respectively) were around 2 times that of those who did non-laboring work (5.78 per 1,000 total births). All babies of mothers in professions or who had university education were born alive and survived the first week. The PNMR of the primiparous mothers (7.39 per 1,000 total births) was two-thirds that of the multiparous mothers (10.89 per 1,000 total births). With regard to antenatal care, 3.8% of women did not register for the service or did, but visited only once. Of those who paid frequent or regular visits, the PNMR was 9.5 per 1,000 births whereas the non-registered group had a PNMR of 17.1. The cesarean section rate of the perinatal death group was 20% while that of the non-death group was 16.5%.

Table 1. Causes of stillbirths (n = 24 babies)

Causes	Number of cases (%)	Details
Obstetric problems	9 (37.5)	Intrauterine asphyxia (5)[a], antepartum hemorrhage (3), velamentous cord (1)
Macerated fetus	5 (20.8)	
Congenital anomalies	3 (12.5)	Anencephaly (1), diaphragmatic hernia (1), Thanatophoric dysplasia (1)
Medical problems of mothers	2 (8.3)	Diabetes mellitus (1), maternal sepsis (1)
Difficult labor	1 (4.2)	
Others	1 (4.2)	Hydrops fetalis
Inconclusive	3 (12.5)	

[a] Figure in the parenthesis is the number of cases

Table 2. Causes of early neonatal deaths (n = 14)

Causes	Number (%)	Details
Principal causes		
Congenital anomalies	6 (42.9)	Anencephaly (4)[a], congenital heart disease (1), multiple anomalies (1)
Perinatal asphyxia	2 (14.3)	
Meconium aspiration	2 (14.3)	
Neonatal sepsis	2 (14.3)	
Preterm	1 (7.1)	
Hypothermia	1 (7.1)	
Precipitating causes		
Obstetric problems	5 (35.7)	Premature rupture of membrane (2), cord accident (1), pre-eclampsia (1), pregnancy induced hypertension (1)
Others	2 (14.3)	Child neglect (2)
Perinatal asphyxia	1 (7.1)	
Inconclusive	6 (42.9)	

[a] Figure in the parenthesis is number of cases

Table 3. Perinatal mortality rate by maternal characteristics

Maternal characteristics	Number (%)	Perinatal mortality rate (per 1,000 births)	Relative risk (95% confidence interval)
Age (y)			
< 20	620 (18.1)	4.30	0.39 (0.09,1.61)
≥ 20	2813 (81.9)	11.11	1
Occupation			
Laborer	1125 (32.7)	11.61	2.00 (0.83,4.80)
Farmer	970 (28.2)	12.36	2.12 (0.87,5.17)
Non-labor work	1346 (39.1)	5.78	1
Education			
Primary or lower	2083 (60.6)	12.00	2.06 (0.93,4.56)
Higher	1357 (39.4)	5.78	1
Parity			
0	1092 (35.0)	7.39	0.68 (0.30,1.52)
≥ 1	2027 (64.9)	10.89	1
Antenatal care visits			
No or once	40 (1.3)	17.09	1.78 (0.43,7.40)
Often or regular	3114 (98.7)	9.50	1
Mode of delivery			
Abnormal	741 (22.8)	13.94	1.66 (0.81,3.41)
Normal	2503 (77.2)	8.34	1

Preventable death

In the opinion of the three pediatricians, about one-third (37.8%) of perinatal deaths, 39.1% of stillbirths and 35.7% of early neonatal deaths, could have been prevented by appropriate antenatal or intrapartum care. About 90% of the preventable stillbirths occurred in the antepartum period.

Discussion

The present report describes the results of a study of an active surveillance of perinatal death in a community-based setting. Stillbirths accounted for 70% of death in the perinatal period. Causes of death could be concluded in 87.5% of stillbirths studied and in all of the early neonatal deaths. About

one-third of the deaths were judged to could have been preventable.

The PNMR of the PCTC sample of 10.69/1,000 total births was much lower than those of reports from other developing countries[11-14]. The PNMR was 34.9 per 1,000 births in a prospective study from Turkey[11]. A recent report from a prospective monitoring of pregnant women and newborns from September 2001 to August 2002 in the West Bank and Gaza Strip, the PNMR was 21.2 per 1000 births[12]. The rate was much higher in the rural areas than in the war zone. From a community based, cross sectional questionnaire study of 30 randomly selected areas in rural Tamil Nadu, South India, the stillbirth rate was 13.5/1000 births, the neonatal mortality rate was 35.3/1000 live-births, and the perinatal mortality rate was 42.0/1000 births[13]. In another retrospective cohort study from rural China, the PNMR was as high as 69 per 1,000 births[14]. The PCTC PNMR was closer to that of the Faroes, one of the Nordic communities. The perinatal mortality in the Faroes has been declining from 13.7 per 1,000 total births during 1976-1985 to 10.3 in the following decade[15]. Though the PNMR of the PCTC was low, it showed no improvement over the country's figure of five years ago (10.01 per 1,000 births)[8]. Given that the national figure was derived from provincial hospitals which have higher than usual complicated referral cases, the present figure from this community-based study should have been lower.

The surveillance system of the present study revealed stillbirths as a major contributor (63%) to perinatal mortality. Stanton et al[16] used the vital registration data, demographic and health surveys, and study reports to estimate stillbirth rates. The resultant stillbirth rates ranged from 5 per 1000 births in developed countries to 32 per 1000 in south Asia and sub-Saharan Africa. The estimated number of global stillbirths is 3.2 million (uncertainty range 2.5-4.1 million)[16] which is almost as high as the estimated number of global neonatal death of 4 million[17]. These global estimates support the importance of stillbirths. As the early neonatal deaths of the PCTC sample has declined to the level about two-thirds of the previous country survey (11.15 per 1,000 live-births)[8], to further reduce the PNMR attention should be focused on decreasing the stillbirths.

About 40% of stillbirths in the PCTC sample were rated as preventable by the three pediatricians. As almost all of the preventable stillbirths occurred in the antepartum period, they could have been prevented by higher-quality antenatal obstetric and medical care

and the appropriate mode of delivery. Timely cesarean section could have rescued some of these cases. Although the cesarean section rate in the present study was above the optimum rate of 15% as recommended by the WHO for the high-risk area[18], the needed cases might not have had the chance to receive appropriate care. Communication and the information provided for expectant mothers during the antenatal care visits are thus very important. It had been noted that the educational levels of mothers in the rural areas was often very limited; in the present study half of the mothers received only primary education and 6.3% were illiterate.

The findings of the present study showed that deaths of the preterm and low birth weight babies were 4 to 60 times more prevalent than that of the normal weight group. Prevention of preterm delivery as well as upgrading the quality of care of the very low birth weight (VLBW) infants would substantially reduce the PNMR. Since the advanced technology of VLBW care is not yet available country-wide, emphasis should be on prevention. As shown in a randomized controlled study in rural Gambia, maternal dietary supplementation and eradication of anemia can reduce stillbirth and early neonatal death rates by about half as well as decrease the low birth weight prevalence by 40%[19]. In the PCTC sample, anemia was not a significant risk factor but weight gain during pregnancy of less than 10 kg and maternal height below 145 cm increased the risk almost three times (Isranurug S, personal communication). Thus, intervention to prevent low birth weight in a setting like that of the PCTC study should include nutrition education and/or supplementation for pregnant women plus improvement of nutrition of pre-pubertal girls.

Like the mortality pattern of Western countries two decades ago[20], congenital anomalies were important causes of early neonatal deaths in this study. The most common anomaly in the present study was anencephaly, one form of neural tube defect. To prevent this condition, the United Kingdom MRC Vitamin study Research Group has recommended folic acid supplementation for pregnant women as well as women in the reproductive age[21]. Despite this, the importance of folic acid supplementation has not yet been recognized as a public health issue in Thailand.

Despite the fact that the verbal autopsy may not be as reliable as the postmortem autopsy, it is the only tool for assigning causes of deaths in the community setting. The authors have improved its reliability by using a semi-structured questionnaire

and having pediatricians as interviewers. Although the interview took place around 2 to 4 weeks after the incident, the issue of recall bias should be minimal as the event was so serious that the parents and caregivers would be less likely to forget.

Although the PNMR in this sample was not high, about one-third of them could have been prevented by appropriate antepartum and intrapartum care. Intervention should be strategically planned to serve the at risk groups especially the low education mothers. Improvement of the antenatal care should highlight the importance of nutrition and vitamin supplements as well as self care.

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รูปแบบการตายปริกำเนิดใน 4 อำเภอของประเทศไทย: รายงานข้อค้นพบจากโครงการวิจัยระยะยาวในเด็กไทย

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วัตถุประสงค์: เพื่อศึกษาขนาดและสาเหตุการตายปริกำเนิดในโครงการวิจัยระยะยาวในเด็กไทย

วัสดุและวิธีการ: ใช้แบบสอบถาม *verbal autopsy* และเวชระเบียนเพื่อสรุปสาเหตุการตายปริกำเนิดใน 4 อำเภอ
ของประเทศไทย

ผลการศึกษา: เด็กเกิด 3,522 รายจากหญิงตั้งครรภ์ 3,494 คน (มีแฝด 28 คู่) อัตราตายปริกำเนิดเท่ากับ 10.69/
การเกิด 1,000 ราย อัตราตายคลอดเท่ากับ 6.75/การเกิด 1,000 ราย และอัตราตายของทารกใน 28 วันแรกเท่ากับ
3.97/เกิดมีชีพ 1,000 ราย กุมารแพทย์ 2 คนและกุมารแพทย์ด้านทารกแรกเกิด 1 คนเห็นพ้องกันว่า ร้อยละ 37.8
ของการตายปริกำเนิดในการศึกษานี้ป้องกันได้และประมาณร้อยละ 90 ของการตายคลอดที่ป้องกันได้นี้เกิดขึ้น
ในช่วงก่อนคลอด

สรุป: หากลดการตายคลอดโดยการดูแลหญิงตั้งครรภ์อย่างมีคุณภาพจะช่วยลดการตายปริกำเนิดได้