Hospitalized Infant Morbidity in the Prospective Cohort Study of Thai Children Project

Vorasith Sornsrivichai MD*, Virasakdi Chongsuvivatwong MD, PhD*,
Ladda Mo-suwan MD, MSc**, Utcharee Intusoma MD**

** Epidemiology Unit, Faculty of Medicine, Prince of Songkla University, Songkhla*
*** Department of Pediatrics, Faculty of Medicine, Prince of Songkla University, Songkhla*

Background: *Infant morbidity causes a substantial resource burden, however, its magnitude and pattern in developing countries is still unknown.*
Material and Method: *The authors prospectively followed a cohort of 2,739 children over a one-year period in three rural areas of Thailand to detect the hospitalized infant morbidity.*
Results: *The incidence of morbidity was 454.9/1,000 live births. The top five morbidities were perinatal conditions, respiratory diseases, pneumonia, infectious diarrhea, and disorders related to short gestation/ low birth weight, and had an incidence of 88.7, 35.4, 34.3, 30.3, and 23.0 diagnoses/1,000 live births, respectively. They accounted for 1,973 days (76.6%) of hospital stay. Of all morbidities, 34.8% occurred in the early neonatal period and 3.1% occurred in the late neonatal period.*
Conclusion: *The present study confirmed that perinatal conditions in the early neonatal period and pneumonia and diarrhea in the post neonatal period are still an important health problem. Further attempts for prevention and control will be needed.*

Keywords: *Cohort studies, Developing countries, Diarrhea, Hospitalisation, Infant, Morbidity, Pneumonia, Respiratory tract infections, Thailand*

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Most mortality and morbidity occur in the first year of life and cause a substantial portion of the national resource burden. The association between morbidity experienced during infancy and diseases and disabilities in adulthood have been confirmed[1-3]. From a large hospital registry, the majority of serious infant morbidities needing hospitalization in Thailand in 1998 were respiratory tract infections, gastrointestinal tract diseases, diarrhea, and injuries[4]. However, similar to most developing countries, studies of infant morbidity in Thailand have been based on a limited number of specific diseases in the hospital-based registry, surveillance system, or periodic cross-sectional surveys that have limitations in terms of coverage, validity, and representativeness[5-7]. The magnitude and burden of infant morbidity, as well as its pattern, is still unknown.

The Prospective Cohort Study of Thai Children Project (PCTC) is a multi-center cohort study that aimed to follow five birth cohorts of children from intrauterine to the age of twenty-four to collect information about holistic development of Thai children. The overall study comprises of four community-based cohorts in four districts from different parts of Thailand *i.e.* Panomtuan District in the West, Thepa District in the South, Kranuan District in the Northeast, Muang Nan District in the North, and a hospital-based cohort in Bangkok. All children who were born over a one-year period in the present study areas were included in the cohort. Information was collected extensively, prospectively and repeatedly, over time on 4,245 children, their families, and communities. In the present report, the authors investigated the pattern of infant morbidity for the rural part of the PCTC. The first PCTC child was

Correspondence to: Sornsrivichai V. Epidemiology Unit, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla 90110, Thailand. Thailand. Phone: 0-7445-1166, Fax: 0-7445-5150, E-mail: vorasith@msn.com

born in October 2000 and the last child completed the first year of life in January 2002. The information is to be used for priority setting, planning of current health strategies, and testing associations with other health outcomes in the future.

Objective

To enrich the PCTC data with medical record review to obtain the incidence of hospitalized morbidity by causes, patterns, and length of hospital stay during the first year of life.

Material and Method

The National Ethics Committee of the Ministry of Public Health gave their approval for the PCTC. All the families involved in the study were briefed on all the study procedures and possible risks before signing a consent form. The research protocol was approved by the Ethics Committee of Faculty of Medicine, Prince of Songkla University.

To maintain homogeneity of the data sources, the rural sites of the PCTC in Panomtuan, Thepa, and Kranuan Districts were used. Each study site has a community hospital that served as a base for the field and clinical research and health services. A special system was created to link the data from the fieldwork and medical record when the children came to the hospital. However, there was the possibility some children might utilize the health service from other nearby hospitals. To minimize the failure to detect the hospitalization, parents were interviewed during a scheduled home visit at ages 1, 3, 6, and 12 months to check for prior hospitalization then their medical records were subsequently checked in the admitting hospitals. This research project, therefore, attempts to detect the morbidity that needed hospitalization from all those sources *i.e.* the community hospital and the nearby hospitals.

The researcher and a physician independently abstracted all the PCTC children's medical records from the hospitals using a prepared data abstraction form. The information abstracted included infant morbidity (illness or adverse events that lead to hospitalization) and clinical information (history of illness, physical examination, laboratory investigation, diagnosis, onset of illness, duration of illness, severity, treatment, place of treatment, treatment outcome, complication and length of stay in hospital.) The initial assessments made by each individual reviewer were blinded. However, they were subsequently validated against each other. The final diagnoses were separately given by the researcher and a pediatrician, and then they were coded independently by the researcher and a coder with the ICD-10 four-digit codes. The authors used the four ICD-10 categories. The first category is the principal diagnosis. It is the condition that is primarily responsible for the patient's need for the treatment or investigation. A second category is comorbidity, or the conditions that co-exist with the principle diagnosis during the episode of healthcare and affect the management of the patient. Complications are the third category; they are conditions that develop during the episode of healthcare and affect the management of the patient. The final category is other diagnosis, that is to say, the conditions that co-exist or develop during the episode of healthcare but do not affect the management of the patient[8]. Disagreement was solved to get a consensus of the researcher and the pediatrician. The final ICD-10 codes were automatically grouped to ICD-10 tabular list for morbidity using relational database. In the analysis, all morbidities were first tabulated and the top ten in each ICD-10 category were reported in the table.

Descriptive statistics were carried out using Stata software version 7[9]. Nelson-Aalen cumulative hazard plot was done by R software version 2.6.1[10].

Results

There were 791 children enrolled in Panomtuan District, 1,076 in Thepa District, and 872 in Kranuan District. Of all the 2,739 children, 496 children were admitted in their first year of life contributing altogether 671 admissions (average number of admissions per admitted child = 1.35, range = 1-9). Of these admissions, 1,246 morbidities were diagnosed (average number of diagnosis of each admission = 1.86, range = 1-8). Twenty two percent of these children were admitted more than once.

Morbidities in the ICD-10 categories are shown in Table 1-3. From Table 1, more than half of all infant admissions were accounted for by the top five morbidities in principal diagnosis/comorbidity category *i.e.* "other conditions originating in the perinatal period", "other diseases of the respiratory system", "pneumonia", "diarrhea and gastro-enteritis of presumed infectious origin" and "slow fetal growth, fetal malnutrition, and disorders related to short gestation and low birth weight", with incidence of 88.7, 35.4, 34.3, 30.3, and 23.0 diagnoses/1,000 live births, respectively. They were altogether responsible for 1,973 days (76.6%) of hospital stay. Documented complication and other diagnosis were relatively low. There were only 51

complications diagnosed (details in Table 2), of which the majority were "other conditions originating in the perinatal period" and "diarrhea and gastro-enteritis of presumed infectious origin". There were 117 other diagnoses (details in Table 3), of which the majority was "other anemias". Many children were ill repeatedly with the same morbidity, especially with pneumonia and other diseases of the respiratory system.

Concerning the morbidities, 34.8% occurred in the first seven days of life (early neonatal period) and 3.1% occurred in the 2nd-4th weeks (late neonatal period). The average length of hospital stay during

Table 1. Top ten ICD-10 tabular list for morbidity of all and principal diagnoses/comorbidities. Numbers are frequency (incidence per 1,000 live births) and length of stay [percentage of total]

ICD-10 Tabular List for Morbidity	All*	Dx**	Child***	Days of total LOS**** [%]
Rank	(n = 1,246)	(n = 1,078)	(n = 2,739)	(n = 2,574)
253 Other conditions originating in the perinatal period	256 (93.5)	243 (88.7)	193 (70.5)	984 [38.2]
179 Other diseases of the respiratory system	101 (36.9)	97 (35.4)	83 (30.3)	287 [11.1]
169 Pneumonia	94 (34.3)	94 (34.3)	76 (27.7)	418 [16.2]
005 Diarrhoea and gastro-enteritis of presumed infectious origin	93 (34.0)	83 (30.3)	74 (27.0)	264 [10.3]
246 Slow foetal growth, foetal malnutrition and disorders related to short gestation and low birth weight	63 (23.0)	63 (23.0)	59 (21.5)	426 [16.6]
006 Other intestinal infectious diseases	60 (21.9)	58 (21.2)	52 (19.0)	210 [8.2]
167 Other acute upper respiratory infections	58 (21.2)	58 (21.2)	56 (20.4)	157 [6.1]
270 Other symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	58 (21.2)	53 (19.4)	51 (18.6)	133 [5.2]
170 Acute bronchitis and acute bronchiolitis	49 (17.9)	49 (17.9)	39 (14.2)	20 [0.8]
110 Volume depletion	44 (16.1)	40 (14.6)	37 (13.5)	111 [4.3]

* "All" denotes frequency and incidence of diagnosis present anywhere among principal diagnosis, comorbidity, complication and other diagnosis categories; ** "Dx" denotes frequency and incidence of diagnosis present either at principal diagnosis or comorbidity categories; *** "Child" denotes frequency and incidence of children diagnosed either in principal diagnosis or comorbidity categories; **** "Days of LOS" denotes length of stay of diagnosis presence either at principal diagnosis or comorbidity categories and percentage of total length of stay

Table 2. Top ten ICD-10 tabular list for morbidity of complications. Numbers are frequency (incidence per 1,000 live births)

ICD-10 Tabular List for Morbidity	Dx
Rank	(n = 51)
253 Other conditions originating in the perinatal period	9 (3.3)
005 Diarrhoea and gastro-enteritis of presumed infectious origin	9 (3.3)
110 Volume depletion	4 (1.5)
111 Other endocrine, nutritional and metabolic disorders	4 (1.5)
179 Other diseases of the respiratory system	4 (1.5)
249 Other respiratory disorders originating in the perinatal period	3 (1.1)
288 Certain early complications of trauma and complications of surgical and medical care, not elsewhere classified	3 (1.1)
006 Other intestinal infectious diseases	2 (0.7)
098 Other anaemias	2 (0.7)
099 Haemorrhagic conditions and other diseases of blood and blood-forming organs	2 (0.7)
139 Other diseases of the eye and adnexa	2 (0.7)

Table 3. Top ten ICD-10 Tabular List for morbidity of other diagnoses. Numbers are frequency (incidence per 1,000 livebirths)

ICD-10 Tabular List for Morbidity	Dx
Rank	(n = 117)
098 Other anaemias	75 (27.4)
253 Other conditions originating in the perinatal period	4 (1.5)
270 Other symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	4 (1.5)
257 Cleft lip and cleft palate	3 (1.1)
264 Other congenital malformations and deformations of the musculoskeletal system	3 (1.1)
266 Chromosomal abnormalities, not elsewhere classified	3 (1.1)
099 Haemorrhagic conditions and other diseases of blood and blood-forming organs	2 (0.7)
124 Epilepsy	2 (0.7)
173 Chronic disease of tonsils and adenoids	2 (0.7)
199 Other diseases of the skin and subcutaneous tissue	2 (0.7)
220 Hydrocele and spermatocele	2 (0.7)
245 Fetus and newborn affected by maternal factors and by complications of pregnancy, labour and deliver	2 (0.7)
260 Undescended testicle	2 (0.7)
295 Liveborn infants according to place of birth	2 (0.7)

infancy was 3.8 days, the early neonatal was 4.8 days, the neonatal period was also 4.8 days, and for those that took place after the 4th week (post neonatal period), it was 3.3 days. Total admission days during the early neonatal and neonatal period were 1,128 days and 1,216 days, which accounted for 43.8% and 47.2% of the total days of admission respectively. Regarding the treatment outcome, 88.8% of the overall PCTC's admissions had a recovery or improved results, 7.7% being referred to other referral hospitals and 1.0% died.

Fig. 1 shows the results of the cumulative hazard plot (Nelson-Aalen curve) of the major infant morbidities in the principal diagnosis category. The hazard for "pneumonia" was the highest and steadiest although there was a relative increase during the 8th and 9th months. The hazard for "other diseases of the respiratory system" was lower in the first 4 months but increased during the 5th and 6th months and eventually caught up with the "pneumonia" from the 6th month onwards. The hazard of the other three diseases were generally lower, approximately two thirds of "pneumonia". In contrast, "diarrhea and gastro-enteritis of presumed infectious origin" and "other intestinal infectious diseases" posed a greater hazard in the second half of the infancy. The hazards for "Diarrhea and gastro-enteritis of presumed infectious origin" increased during the 7th and 8th months and in the 12th month while that of "other intestinal infectious diseases" increased during the 6th and 8th months and again in the 12th month. The hazard for "acute bronchitis and acute bronchiolitis" was the lowest in the first 6 months with an increase during the 8th and 10th months, and eventually caught up with the other two diseases in the 10th month.

Discussion

During the first year of life, almost one-fifth of the PCTC children were hospitalized; more than one-fifth of which were admitted repeatedly with up to nine admissions. The top five main infant morbidities were diseases related to perinatal condition, other respiratory

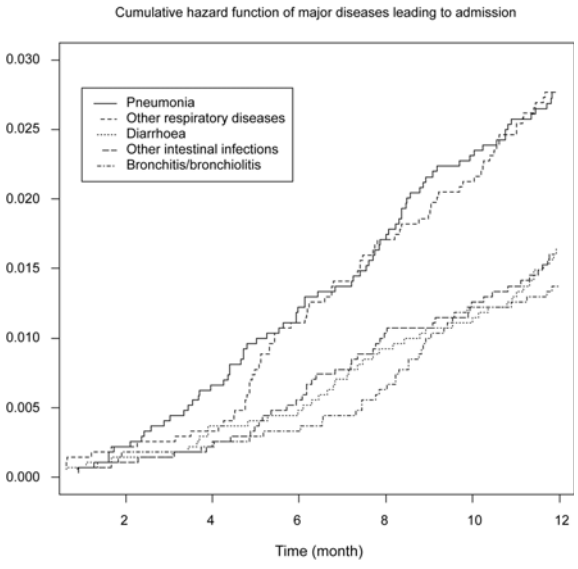

Fig. 1 Nelson-Aalen cumulative hazard plot of major hospitalized infant morbidities

diseases, pneumonia, diarrhea, and short gestation/ low birth weight. These five morbidities were altogether responsible for half of all the infant morbidities. One third of the total infant morbidities occurred in the early neonatal period. Pneumonia and other respiratory diseases, the major common cause of infantile admission comes early in the infant period whereas infectious diarrhea and other intestinal infection come later.

The incidence of infant hospitalized morbidity in the rural sites of the PCTC in the present report is higher than the country's previous studies[4]. This may be the results of the greater data coverage of the present study and a higher morbidity and admission rate in the rural areas. However, regarding the outcome of treatment and the relatively low documented complication rate found in the present study, there may be an implication that the admission was made in the early stage of the disease and/or the quality of care in these settings was good.

Half of all infant morbidities were accounted by the top five morbidities in principal diagnosis/ comorbidity category. They were "other conditions originating in the perinatal period", "other diseases of the respiratory system", "pneumonia", "diarrhea and gastro-enteritis of presumed infectious origin", and "slow fetal growth, fetal malnutrition and disorders related to short gestation and low birth weight". The incidence of these diseases in the present report is higher than those reported from a previous study of hospitalized infants in Thailand[4]. Early neonatal morbidities accounted for one third of infant morbidities and more than 90% of neonatal morbidities. Priority and resource allocation *e.g.* facility, equipment and personnel should be allocated for these morbidities. The early neonatal period is the most vulnerable period for infants, which is indicated by more than two fifths of the total infant admission days taking place in this period. The late neonatal period is less important, contributing only 3% of the total days of admission. Most of the main causes of early neonatal morbidities were perinatal conditions, which may be prevented by good maternal antenatal care (ANC) and intrapartum care. High perinatal morbidities, despite the fact that ANC utilization and proportion of birth occurred in hospital was high in this cohort[11], may indicate the need to improve the quality of ANC and intrapartum care.

Infectious diseases occurred more in the post neonatal period. Pneumonia began early and spread throughout this period (Fig. 1.) Compared to community longitudinal studies from developing countries in the past, the incidence in the present report is lower[12,13]. The difference may be the result of the implementation of a case management protocol for early acute respiratory tract infection and also be partly explained by a difference in case definition, frequency of surveillance and a small proportion of mild cases that did not need hospitalization. Pneumonia associated with measles or pertussis in the present study was low due to high vaccine coverage for these diseases. New vaccines against common causative organisms *e.g. S. Pneumoniae* or *H. influenzae* have not been included in routine immunization but under such a high incidence in Thai infants and the high percentage attributable to these two organisms[14-16], cost-effectiveness of implementation of these vaccinations should seriously be considered. Other known risk factors *e.g.* low birth weight, breast feeding, malnutrition, crowding and air pollution including environmental tobacco smoke[17-19], are not included in the present report but will be explored in a later article.

Infectious diarrhea and other intestinal infections had a higher incidence after the sixth month because the maternal immunity either tranplacental IgG or secretory IgA from breast milk had declined and the exposure to enteropathogens had increased. In the present report, the incidence is higher than 11.2 episodes per 1,000 children per year reported from a previous study in hospitalized infants in Thailand[4], possibly because of more data coverage of admissions. However, compared to previous community follow up studies from Thailand and other developing countries, the incidence in the present report is lower[19,20-22]. This may be explained partly through the result of a decreasing trend of the disease and partly by different case definition, frequency of surveillance and a high proportion of mild cases that did not need hospitalization. From other parts of this cohort study, rotavirus is a major causative organism in the infancy period with 16% prevalence. Cost-effectiveness of vaccination for rotavirus should be considered against other general hygienic measures, which have been shown to prevent infancy diarrhea in general[23-25].

Many children had been admitted repeatedly, some of whom had repeated morbidities especially pneumonia and other diseases of the respiratory system. Factors influencing the repetitiveness of morbidities need exploring further to ascertain whether there are biological factors *e.g.* malnutrition, epithelial cell damage from prior diseases or socioeconomic factors *e.g.* community or parents socioeconomic status, sanitation or disease prevention knowledge that contributed to the repetitiveness of infant morbidity[26,27].

The strength of the study was that it is a population-based cohort study with a greater coverage of detailed hospitalized morbidity data from the medical records with a relatively low percentage of ill-defined diagnosis. With certain limitations on the information of etiologic organisms, the present study did confirm that perinatal conditions, pneumonia, and diarrhea are still an important infant health problem. Further attempts will be needed to prevent and control the problem.

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การป่วยที่ต้องเข้ารับการรักษาในโรงพยาบาลในช่วงขวบปีแรกของเด็กในโครงการวิจัยระยะยาวในเด็กไทย

วรสิทธิ์ ศรศรีวิชัย, วีระศักดิ์ จงสู่วิวัฒน์วงศ์, ลัดดา เหมาะสุวรรณ, อัจฉรีย์ อินทุโสมา

***ภูมิหลัง**: การป่วยในวัยทารกมีภาวะโรคสูง แต่ในประเทศกำลังพัฒนายังขาดข้อมูลขนาดและลักษณะของปัญหานี้*
***วัสดุและวิธีการ**: ติดตามเด็ก 2,739 คน ที่เกิดใน 3 อำเภอเขตชนบท ตั้งแต่แรกเกิดจนอายุ 1 ปี เพื่อเก็บข้อมูลการป่วยในวัยทารกที่เข้ารักษาในโรงพยาบาล*
***ผลการศึกษา**: อุบัติการณ์การป่วยในวัยทารกเท่ากับ 454.9/1,000 การเกิดมีชีพ การป่วย 5 อันดับแรก คือ โรคปริกำเนิด โรคระบบทางเดินหายใจ ปอดอักเสบ อุจจาระร่วงติดเชื้อ และการเกิดก่อนกำหนด/น้ำหนักแรกเกิดน้อย มีอุบัติการณ์เท่ากับ 88.7, 35.4, 34.3, 30.3 และ 23.0/1,000 การเกิดมีชีพตามลำดับ คิดเป็นวันนอน โรงพยาบาล 1,973 วัน (ร้อยละ 76.6) ร้อยละ 34.9 ของการป่วยเกิดในช่วง 7 วันแรก ร้อยละ 2.8 ในช่วง 8-28 วันแรก*
***สรุป**: โรคปริกำเนิดในช่วง 7 วันแรก และโรคปอดอักเสบและอุจจาระร่วงในช่วงหลัง 28 วันยังเป็นปัญหาสาธารณสุขที่สำคัญ และจำเป็นต้องหามาตรการควบคุมป้องกันต่อไป*