Neonatal mortality rate and risk factors in northeast China: analysis of 5,277 neonates in 2005

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Summary

Background: Healthcare has dramatically improved for both mothers and neonates over the last three decades in China. However, the reported rates of morbidity and mortality vary among different regions of China, and the exact rates in Northeast China are unknown. This study aimed to determine neonatal morbidity and mortality rates and the associated risk factors in Northeast China. *Materials and Methods:* Neonates born in 2005 at seven hospitals in five major cities of Heilongjiang province in Northeast China were recruited. Standardized questionnaires on both the mother and neonate were conducted by trained investigators**.** The questions included demographic data on the mother, the mother's weight, gestational age (GA), complications during pregnancy, method of delivery, neonate's gender, weight, general health situation, and complications after delivery. *Results:* A total of 5,277 neonates were included, with a male to female ratio of 1.07. The incidence of preterm delivery was 8.7%, which was associated with an increased age of the mother, a history of preeclampsia-eclampsia, premature rupture of membranes, and intrauterine distress. Morbidity occurred in 7.0% of neonates, including hypoxic ischemic encephalopathy (2.4%), asphyxia (1.6%), pneumonia (1.6%), hyperbilirubinemia (0.5%), intracranial hemorrhage (0.5%), meconium aspiration syndrome (0.2%), and ingestion syndrome (0.2%). The overall mortality was 9.5‰. Preterm delivery, maternal history of preeclampsia-eclampsia, hypoxic ischemic encephalopathy, intracranial hemorrhage, pneumonia, asphyxia, and meconium aspiration syndrome were independent risk factors for mortality with odds ratios (95% confidence interval) of 17.42 (7.31-38.9), 12.52 (Table 3) (3.91-16.82), 10.13 (2.52-19.86), 9.77 (2.35-19.93), 4.15 (1.78-9.52), 2.18 (1.21-5.47), and 2.76 (2.11-6.32), respectively (all $P < 0.01$). *Conclusions:* In 2005, the overall morbidity and mortality was 7.0% and 9.5‰, respectively in northeast China, and preterm delivery was the highest risk factor for neonatal mortality. The prevention on preterm delivery should be a top priority for the improvement of neonatal healthcare.

Key words: Neonates; Morbidity; Mortality; Preterm delivery.

Introduction

With the accelerated development of the social economy and culture, as well as the improvement of public health care coverage and prophylactic and therapeutic techniques in China, the morbidity and mortality of both mothers and neonates have dramatically decreased over the last couple of decades [1]. However, some data from various regions of China have demonstrated significant variation in neonatal morbidity and mortality, presumably due to the imbalanced development and progression of economy and culture among the regions [2]. For example, studies conducted in southern and southeastern China have demonstrated significant decreases in morbidity and mortality [1-3]. In contrast, no reports on morbidity and mortality are available for Northeast China.

Heilongjiang province is located in Northeast China with middle level economic and cultural development. As a consequence of economic development and increases in education and hygienic levels in Heilongjiang province, the healthcare system, including maternal and child health care, has improved significantly over the past three decades. The major objective of maternal and child health care is to lower the mortality of both the mothers and neonates. Thus, data on the mortality and morbidity of mothers and neonates are not only major indicators of the effectiveness and success of the healthcare system, but are also the basis for policies that further improve the healthcare system. However, there has been a relative lack of large-scale clinical data in China, especially in northeast China.

Therefore, the aim of the present study was to determine the mortality of neonates and the related risk factors, based on data prospectively collected from seven hospitals in five cities in Heilongjiang province.

Materials and Methods

Participating hospitals

The seven hospitals involved in the study included three teaching hospitals (Hongqi Hospital affiliated to Mudanjiang Medical College, The First Hospital affiliated to Jiamusi University Medical College, and The Second Hospital affiliated to Harbin Medical University) and four municipal and specialty hospitals (Daqing People's Hospital, The First Municipal Hospital of Qiqihar City, Mudanjiang Maternity Hospital, and Jiamusi Maternal and Child Health Care Center). Each of the aforementioned hospitals had over 100 beds in the Department of Obstetrics and Gynecology.

Subjects and data collection procedures

Between January 1, 2005 and December 31, 2005, neonates who were born in the Department of Obstetrics and Gynecology, and those who were admitted to the Department of Neonates due

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Table 1. — *Gestational age (GA), birth weight, and mortality of the preterm, term and postterm neonates*

Category	Proportion (%)	Median GA (weeks)	Weight (mean±SD, g)	Mortality (n (‰))
Preterm				
< 28 weeks (n=18)	0.3	27	1000.2 ± 38.7 (range: 960-1150)*	6 (333.4)*
28-<37 weeks (n=439)	8.3	35	2769.2 ± 876.4*	27 (62.1) *
Term				
37-<42 weeks (n=4,452)	84.2	39	3789.3 ± 572.2	10 (2.2)
Post-term				
≥42 weeks (n=46)	0.9	42	3897.4 ± 361.1	0
Missing data (n=333)	6.3	NA	NA	7 (21.0)
Total (n=5,277)	100	NA	NA	50 (9.5)

* = P< 0.001, compared with term and postterm neonates.
NA = not available.

to certain diseases or adverse conditions in the seven participating hospitals**,** were enrolled in the present study. After birth, a standardized questionnaire was completed by a trained investigator for each neonate. The questionnaire covered information on both the mother and the neonate, which included demographic data on the mother, gestational age (GA), complications during pregnancy, the mother's weight, method of delivery, gender, weight, general health situation, and complications after delivery. Pregnant women were included if they stayed in the city for monitoring during their pregnancy. Neonates and mothers transferred from other hospitals were excluded. The Institutional Review Boards from each of hospital separately reviewed and approved the study protocol. All parents or guardians provided informed written consent.

Quality control and data input

At each hospital, one designated expert in data management was responsible for the quality assurance of the completeness and accuracy of the questionnaires. All investigators received training prior to the study. Unreliable or incomplete questionnaires (n = 500) were regarded as invalid, and were thus excluded. Upon the confirmation of data collection, data were entered into the database established with EPI data software (The EpiData Association, Odense, Denmark). Data verification was carried out by comparing input data to data on randomly selected questionnaires (1% of all questionnaires). If the errors exceeded 10%, all data had to be input again by another investigator.

Classification of GA and definitions of morbidity and mortality

GA was classified into three terms: preterm (<37 weeks), term (37-<42 weeks), and post-term (>=42 weeks). Preterm was also divided into two stages (<28 weeks and 28-<37 weeks). Neonatal morbidity was defined as the occurrence of preterm delivery, hypoxic ischemic encephalopathy (HIE), intracranial hemorrhage, hyperbilirubinemia, pneumonia, asphyxia, meconium aspiration syndrome (MAS), and/or ingestion syndrome (or swallowing syndrome of newborn) that occurred in all three terms. Fetal distress was judged entirely from the recorded evidence of instantaneous fetal heart rate and related parameters. Neonatal mortality was defined as deaths among live-born infants that occurred between the day of delivery and 28 days after delivery.

Statistical analysis

Continuous variables were presented as mean ± standard deviation (SD) when normally distributed, or as median (range) when abnormally distributed. Categorical variables were presented as counts or rates, with the odds ratios (ORs) and 95% confidence intervals (CIs) calculated. Comparisons between continuous variables were made using the student *t*-test, analysis of variance, or Mann-Whitney test, where appropriate. Univariate analyses on categorical data were performed by 2-tailed Pearson c^2 test or Fisher**'**s exact test. Multivariate logistic regression analysis on risk factors for neonatal morbidity and mortality were used. The maternal and neonatal variables such as GA, birth weight, age of mother, preeclampsia-eclampsia (PE-E), premature rupture of membrane (PROM) (which occurs in pregnancy when there is rupture of the membranes (rupture of the amniotic sac and chorion) more than an hour before the onset of labor), history of preterm delivery, and intrauterine distress were included in the logistic regression model for identification of the risk factors for morbidity. The maternal and neonatal variables and different morbidity variables were fitted into multivariate regression model to identify the risk factors for mortality. All statistical analyses were performed using SPSS 13.0 software (SPSS inc., Chicago, IL, USA).

Results

General information

A total of 5,277 neonates were born from 5,265 mothers during the period of the study, and were included in the data analysis. There were 12 pairs of twins. The neonatal male-female ratio was 1.07. GA was available for 4,944 (93.7%) of the neonates, with the shortest and longest GA being 25 and 44 weeks, respectively. Among the 5,277 neonates, 4,452 (84.2%) were classified as being term**,** with a median GA of 39 weeks and mean (±SD) birth weight 3789.3 ± 572.2 g (Table 1).

Neonatal morbidity and mortality

Morbidity occurred in 370 (7.0%) neonates, including hypoxic ischemic encephalopathy in 127 (2.4%), asphyxia

in 85 (1.6%), pneumonia 85 (1.6%), hyperbilirubinemia in 27 (0.5%), intracranial hemorrhage in 27 (0.5%), meconium aspiration syndrome in 11 (0.2%), and ingestion syndrome in 8 (0.2%) (Table 2).

Overall, 50 neonates died in the Department of Obstetrics and Gynecology during or after birth (n=43), or within four weeks after being transferred to the Department of Neonates (n=7), resulting in an overall mortality of 9.5‰. The mortality rate was 72.0‰ in preterm neonates with a GA of <37 weeks (333.4 ‰ in neonates with a GA of <28 weeks, and 62.1‰ in those with a GA between 28 and <37 weeks), which was significantly higher than that (2.2‰) of term neonates with a GA between 37 and 42 weeks (OR=9.87, 95% CI: 2.72-37.91, $P < 0.001$).

Risk factors for mortality and preterm delivery

The incidence of preterm delivery was 8.7% (n=458). Maternal gestational hypertension-preeclampsia occurred in 199 (3.8%) mothers; the proportion of mild, moderate, and severe preeclampsia, and eclampsia was 24.1%, 21.1%, 21.8%, and 32.2%, respectively.

In univariate and multivariate analyses, preterm delivery, the maternal history of PE-E, HIE, intracranial hemorrhage, pneumonia and asphyxia, and MAS, were significantly related to the incidence of preterm neonatal death (Table 3). The multivariate adjusted ORS (95% CI) for preterm neonatal mortality were 17.42 (7.31-38.9), 12.52 (Table 3) (3.91-16.82), 10.13 (2.52-19.86), 9.77 (2.35-19.93), 4.15 (1.78-9.52), 2.18 (1.21-5.47), and 2.76 (2.11-6.32) for preterm delivery, maternal history of PE-E, HIE, intracranial hemorrhage, pneumonia, asphyxia, and MAS, respectively (Table 3, all $P < 0.01$).

Table 2. — *The incidence of major morbidities in 5,277 neonates*

Morbidity	Number [a] (%)
Hypoxic ischemic encephalopathy	127 (2.4)
Asphyxia	85 (1.6)
Pneumonia	85 (1.6)
Hyperbilirubinemia	27 (0.5)
Intracranial hemorrhage	27 (0.5)
Meconium aspiration syndrome	11 (0.2)
Ingestion syndrome	8 (0.2)
Overall	370 (7.0)

[a] = Some neonates had two or more morbidities

Since preterm delivery was a major factor that was associated with a neonatal mortality rate that was 33-fold higher than normal delivery, the risk factors for preterm delivery were also determined. In both univariate and multivariate analyses, the age of the mother, PE-E, PROM, a history of premature delivery, and intrauterine distress were significantly associated with the incidence of preterm delivery (Table 4).

Discussion

Neonatal morbidity and mortality are closely related to the developmental levels of the domestic economy, medical science, and the maternal-infant health care system. With the development of the economy and medicine, and the increase in the standard of living in China, the morbidity and mortality rates of neonates have significantly decreased [4, 5]. The five cities (Harbin, Jiamusi, Daqing,

Table 3. — *Related risk factors of neonatal mortality*

Factor	Incidence (%) of death	Univariate analysis		Multivariate analysis	
		OR (95%CI)	*P* value	OR (95%CI)	*P* value
Preterm delivery (yes *vs.* no)	68.0:0.3	9.87 (2.72-37.91)	< 0.001	17.42 (7.31-38.9)	<0.001
Maternal PE-E (yes *vs.*no)	57.5:3.2	4.73 (1.72-7.31)	<0.001	12.52 (3.91-16.82)	<0.001
HIE (yes *vs.* no)	32.7:1.8	3.12 (1.42-6.43)	0.005	10.13 (2.52-19.86)	<0.001
Intracranial hemorrhage (yes *vs.* no)	19.4:0.7	1.23 (1.02-2.76)	0.009	9.77 (2.35-19.93)	0.005
Pneumonia (yes *vs.* no)	9.3:2.7	1.93 (1.21-3.63)	0.008	4.15 (1.78-9.52)	0.007
Asphyxia (yes *vs.* no)	8.6:3.3	1.49 (1.13-2.86)	0.005	2.18 (1.21-5.47)	0.002
MAS (yes *vs.* no)	9.2:3.1	1.97 (1.17-3.46)	0.003	2.76 (2.11-6.32)	0.005

PE-E = preeclampsia-eclampsia; HIE = hypoxic ischemic encephalopathy; MAS = Meconium aspiration syndrome; OR = Odds ratio; CI = confidence interval.

Table 4. — *Risk factors for preterm delivery*

Factor	Incidence (%) of preterm delivery	Univariate analysis		Multivariate analysis	
		OR (95% CI)	*P* value	OR (95% CI)	*P* value
Mother age (> 30 *vs.*<30 years)	34.7:19.3	1.17 (1.01-1.43)	<0.001	1.78 (1.07-3.75)	0.008
PE-E (yes *vs.* no)	17.9:3.6	3.53 (2.91-3.97)	0.005	3.89 (1.96-5.98)	0.006
PROM (yes *vs.* no)	10.7:3.1	3.67 (1.98-4.23)	0.008	4.32 (1.69-7.31)	0.005
History of preterm delivery (yes *vs.* no)	21.2:9.3	1.41 (1.23-1.65)	<0.001	1.74 (1.56-2.37)	0.009
Intrauterine distress (yes *vs.* no)	34.6:21.3	1.56 (1.31-1.76)	0.004	1.87 (1.01-2.76)	0.008

PE-E = preeclampsia-eclampsia; PROM = premature rupture of membranes.

Mudanjiang, and Qiqihar) in Heilongjiang province of northeast China are representative of mid-level industrialized urban regions with an average level of domestic income.

This set of data exhibited that a male to female ratio of 1.07, which is lower than that of other regions nationwide [6]. The overall mortality rate was 9.5‰, which is lower than the nationwide average mortality rate (13.2‰) in 2005 [5]. The rate of preterm delivery was 8.7% in the present study, which is similar to that reported from developed countries, ranging from 9-12% in the last two decades [7]. Preterm delivery was closely related to neonatal death [8]. In the present study, the mortality was 333.4‰ for neonates with a GA of <28 weeks, and 62.0‰ for neonates with a GA of 28-<37 weeks. In contrast, the mortality was 2.2‰ and 0‰ for term and post-term neonates, respectively. However, the overall mortality rate (9.5‰) observed in the present study was much lower than the rate reported in southern China in the 1980's (24.5‰) [3] and nationwide data in 2005 (13.2‰) [5]. Moreover, the mortality rate in term neonates (2.2‰) was also much lower than the average rate of 33‰ (range 2 to 70 per 1000 live birth) in the developing world [9]. These findings imply that an improvement in maternal and neonatal healthcare has been achieved in northeast China.

The present study demonstrated that the age of the mother, history of PE-E, PROM, history of preterm delivery, and intrauterine distress were related to an increased risk of preterm delivery. Hsieh *et al.* reported that women aged 40 years and older in Taiwan were at an increased risk for preterm delivery (before 37 weeks of gestation) (adjusted OR 1.7, 95% CI 1.3-2.2) [10]. In women who had a completely uncomplicated pregnancy and a normal vaginal delivery, advanced maternal age was still significantly associated with early preterm delivery (before 34 weeks of gestation), a birth weight <1500 g, low Apgar scores, fetal demise, and neonatal death [10].

PE is one of the most common complications of pregnancy, with incidence rates of 2%-7% among healthy, primiparous women in the United States [11]. The only cure for PE is delivery, and it remains one of the most common complications resulting in a medically indicated preterm delivery [12]. In the present study, the incidence of maternal gestational hypertension-preeclampsia was 3.8%, which is lower than that previously reported in northeast Chinese women (4.5%) [13], but higher than American Chinese (1.8%) [14]. However, the characteristics of the patients in these three studies differed; thus these studies should be compared cautiously.

Maternal cervical anomaly and intrauterine infection and inflammation may be the major causes of some cases of PROM. The resulting premature neonates are more likely to have sepsis, respiratory distress syndrome, necrotizing enterocolitis, and intraventricular hemorrhage. Complications of infection include chorioamnonitis, maternal wound infection, and neonatal sepsis [15]. Prolonged oligohydramnios can result in pulmonary hypoplasia, pneumothorax, and skeletal deformities. In the present study, PROM increased the risk of preterm delivery (OR: 4.32, 95% CI: 1.69-7.31).

As reported, preterm neonates are at a higher risk of disease. Among these, respiratory diseases, such as pneumonia, asphyxia, HIE, and lung hemorrhage, are the most common complications due to immature lung development. Common nervous system diseases include intracranial hemorrhage. With the deep interaction of preterm cause and consequence, the mortality of preterm neonates further worsened. The present study demonstrated that the mortality of preterm neonates was correlated with GA; the shorter the GA, the worse the neonatal outcome. Thus, regular antenatal examination for pregnant females with advanced age and the aggressive prophylactic measures (such as use of antenatal steroid) of pregnancy complications are of the most importance for ultimately reducing the incidence of preterm delivery and the mortality of preterm delivered neonates.

Although late preterm delivery (before 37 completed weeks of gestation) has been reported to be related to a slightly increased risk of neonatal mortality with a small sample size [16], preterm delivery has been confirmed as the major determinant of infant mortality with the series reported here. Other factors, including PE-E, HIE, intracranial hemorrhage, pneumonia, asphyxia, and MAS were demonstrated to be related to an increased risk of neonatal death.

In summary, the overall mortality is approximately 10‰ in northeast China, with a mortality rate of approximately 2‰ in term neonates. Preterm delivery, maternal history of preeclampsia-eclampsia, hypoxic ischemic encephalopathy, intracranial hemorrhage, pneumonia, asphyxia, and MAS were identified as risk factors for mortality. Thus, the prevention of preterm delivery, strength of pregnancy monitoring, and improvement of preterm newborn support should be concentrated in the neonatal heath care management in this region. However, the success of improving the preterm infant outcome is closely related to regional economic development.

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