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Estimation of birth population-based perinatal-neonatal mortality and preterm rate in China from a regional survey in 2010

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Abstract

Objective: To estimate birth population-based perinatal-neonatal mortality and preterm rate in China from a regional survey in 2010.
Study design: Data of total births in 2010 obtained from 151 level I–III hospitals in Huai'an, Jiangsu, were prospectively collected and analyzed.
Results: From 61 227 birth registries (including 60 986 live births and 241 stillbirths), we derive a birth rate of 11.3‰ (of 5.4 million regional population), a male-to-female ratio of 116:100 and valid data from 60 615 newborns. Mean birth weight (BW) was 3441 ± 491 g with 13.6% macrosomia. Low BW was 2.8% (1691/60 372) with 8.83% mortality. Preterm rate was 3.72% (2239/60 264) with 7.61% mortality. Cesarean section rate was 52.9% (31 964/60 445), multiple pregnancy 1.8% (1088/60 567) and birth defects 6.7‰ (411/61 227). There were 97.4% healthy newborns and 2.2% (1298) requiring hospitalized after birth. The perinatal mortality was 7.7‰ (471/61 227, including 241 stillbirths, 230 early neonatal deaths). The neonatal mortality was 4.4‰ (269/60 986). The main causes of neonatal death were birth asphyxia (24.5%), respiratory diseases (21.5%), prematurity related organ dysfunction (18.5%) and congenital anomalies (7.7%), whereas incidence of congenital heart disease and respiratory distress syndrome was 8.6‰ and 6.1‰, respectively.
Conclusions: This regional birth population-based data file contains low perinatal-neonatal mortality rates, associated with low proportion of LBW and preterm births, and incidences of major neonatal disease, by which we estimate, in a nationwide perspective, in 16 million annual births, preterm births should be around 800 000, perinatal and neonatal mortality may be 128 000–144 000 and 80 000–96 000, respectively, along with 100 000 respiratory distress syndrome.

Keywords

Birth defects, morbidity, mortality, neonate, perinatology, prematurity, respiratory distress syndrome, stillbirth

History

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Introduction

Although China is one of the highest population countries in the world, perinatal-neonatal mortality and morbidity and the associated risk factors are only estimated by vital statistics derived from a surveillance system through nationwide sampling of birth and death data from certain numbers of city districts and rural counties over the past decade for the children under five years mortality rate (U5MR) [1–4]. It may answer questions in public health in general, regarding death rate and related causes, but lacks details in terms of assessment of perinatal and neonatal care efficiency, specified death rate such as fetal deaths or stillbirths [5] and major morbidities in relation to perinatal risks, clinical intervention and response from delivery to neonatal special care. There are quite a few studies [6–12] focusing on these issues derived from either urban birth population data or hospital delivery and hospitalization, but they were neither associated with well-defined regional population nor valid for estimation of nationwide incidence and outcome of birth-related major perinatal-neonatal disorders and deaths or major complications and related risks. It has been the great concern in recent years in detection and alteration of birth defects (BD; 13–15), gender imbalance [16–18], high cesarean section delivery [19,20], resuscitation for birth asphyxia and preterm rate, all

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of which are compelling but requiring appropriate approach to investigate. From our previous surveys of neonatal respiratory failure requiring extensive respiratory and intensive care, we estimated a 50% survival rate in those with 27–29 weeks of gestation [21–23], but overall preterm rate and their death rate related to regional incidence of specific disease were unknown yet. As most people in China are from low income and/or rural families and living in regions with low-to-intermediate health care facilities, insufficient care management-related outcome should have been missed or biased in the analyses of vital statistics from Chinese perinatal-neonatal surveys [1–4,6–12], and it may have profound impact on estimation of overall perinatal-neonatal status and burden for comparison with that reported internationally.

In this study, we hypothesized that by collecting and analyzing regional birth population-based data, we may derive perinatal and neonatal mortality and preterm rate according to internationally accepted definitions. We also aimed at understanding gender imbalance in the region, and associated incidences of major neonatal diseases, including BD-related congenital malformations, requiring hospitalization from all the newborns in Huai'an in 2010. We anticipate that by analyzing these data it may be feasible to estimate the nationwide status and establish an alternative investigational approach in the surveillance of perinatal and neonatal health care. To answer these questions, we conducted a complete birth population-based prospective survey in Huai'an, an emerging rural prefectural region of Jiangsu province. This city has 5.4 million populations as permanent resident in 2010, with 50% living in rural areas and approximately 5% being migrant residents. The average annual gross domestic production (GDP) per capita was 23 000 Chinese Yuan (CNY, 6.7 = 1 USD) in 2010, very close to the national GDP at an average of 24 000 Yuan. It represented approximately 50% of the population in Jiangsu province (totally 78.7 millions in 2010), and up to 50% of the total population of China (1.34 billion in 2010), corresponding to regional GDP ranges equivalent to 3000–4000 USD, in the mid-level of regional economics and maternal and infant health care standard. It should also fall into both type I and II rural areas with health care facilities as proposed by Feng et al. [1,2].

Methods

A collaborative study group for data collection of birth population-based perinatal-neonatal care was established and epidemiologic approaches adopted. We collected birth data from all the level I–III hospitals (129 township, 15 county and 7 municipal by location) and their pediatric wards for neonatal care (8 in level II and 3 in level III hospitals), with the aid of regionally already established maternal-neonatal-infant information network system which provided nearly total birth registries of the regional hospitals. Coordination center for this study was based at Huai'an Women and Children's Hospital, and directors from all level II and III acted as co-investigators for all surrogated low-level clinics. The study protocol was approved by the scientific committee of the Children's Hospital of Fudan University and adopted by the scientific committees of the Huai'an hospitals, according to Chinese regulations for woman and child health care investigation. As data were collected from observational parameters and no specific intervention as diagnosis or treatment was applied in the protocol, informed consent was waived. All the recorded information for the births, stillbirths and hospitalized neonates from January 1 to December 31, 2010, were collected and analyzed at the coordination center.

Definitions of birth and death recordings and perinatal complications

Live birth, fetal death or stillbirth, and death during delivery, are defined according to the 10th revision of the international classification of diseases [24]. In brief, for definition of gestational age (GA), full term is defined as 37–42 complete weeks of gestation using the first day of last menstrual period; preterm is defined as born before 37 weeks of GA; and post-term as born after 42 weeks of GA. For definition of birth weight (BW), it should be obtained as immediate measurement record (usually in the first hours) by the attending care givers, and low BW (LBW) is defined <2500 g, very LBW (VLBW) <1500 g, extremely LBW (ELBW) <1000 g and macrosomia ≥ 4000 g. The perinatal period commences at 22 complete weeks (154 days) of GA, ends at 7 postnatal days. The neonatal period is the first 28 complete days after birth. For definition of death rates, fetal death is synonymous of stillbirth and is defined as fetal deaths per 1000 total births (including live births, fetal deaths); early neonatal mortality rate refers to early neonatal death (first 7 days)/1000 live births, including those of immediate deaths during delivery who had life signs; perinatal mortality rate refers to fetal deaths and early neonatal deaths/1000 total births; and neonatal mortality rate refers to neonatal deaths/1000 live births in the first 28 complete days after birth. Preterm death rate was based on total numbers of preterm deaths versus total live births of preterm births. The fetal status, perinatal complications, BD and major neonatal diseases are defined according to Fanaroff and Martin [25] and presented as incidence rates using numbers of total births (or live births) as denominator. Incidence of specific neonatal disease is expressed by using either total live births as denominator or total hospitalized numbers as constitutive rate where appropriate.

Quality control

To minimize bias among hospitals and investigators, we provided systematic training for the staffs committed to the survey to ensure that all the records to be cross-checked by on-site physician/investigator and coordinators. The routine quality control was focused on completeness and accuracy of the contents in records by the on-site investigators or representative staffs, along with visiting, telephone or e-mail communication, for verification and correction of the data. We also did periodically general quality control inspections that involved with birth registration or medical records from all the municipal and county hospitals and 20% township hospitals. At the end of the survey, we checked the numbers of records with the live births or the hospitalized neonatal numbers. The patients referred to other tertiary centers (mainly in Nanjing) were also retrieved for the relevant information of hospitalization.

Statistical analysis

The EPIDATA database was used for datasheet recordings, and statistical analysis was performed using SPSS software (v. 16.0). Numerical data were presented by the mean (standard deviation, SD) or median (interquartile range, IQR) where appropriate, using one-way analysis of variance (ANOVA) for comparisons of continuous variables between subset data. Categorical variables were represented as frequencies or rates, using Chi-square test for comparison of differences. A p value <0.05 was considered statistically significant. Missing data for each variable in the analysis ranged in 0.2–0.8% and were considered acceptable.

Results

Over the 12-month study period, we collected information of 60 615 newborns in 60 986 live births from the 151 participating hospitals which accounted for 99.0% of the total births registered (61 227), corresponding to a crude birth rate of 11.3‰ (60 986/5 400 000) with a male-to-female ratio of 116:100 (32 406:27 874) (Table 1). The missing numbers of registered births (1%) were home deliveries or those not accessible by the staffs of participating hospitals and clinics. With increasing order of pregnancy and delivery, gender differences are more prominent (Table 2). Tables 3 and 4 show stratified and cumulated data of death rate and gender in either BW-associated GA or GA-associated BW categories, respectively. As shown in Table 1, mean BW was 3441 ± 491 g with 13.6% macrosomia, and LBW infants accounted for 2.8% (1691/60 372) with a mortality of 8.8%. The preterm rate was 3.72% (2239/60 264) with a mortality of 7.6%. Birth rate from multiple pregnant was 1.8% (1088/60 567). From the total births, 411 were found with BD at birth (0.68% of 60 280). The mean maternal age for pregnancy was 25.9 ± 5.1 years old, delayed child-bearing (mother's age $\geq$35 years old) being 8.41% (5065/60 209). Approximately 10% deliveries had significantly prenatal risk factors. Cesarean section rate was 52.9% (31 964/60 445), vaginal delivery 46.5% (28 084/60 445) and assisted vaginal delivery 0.7% (397/60 445). There were 241 stillbirths or fetal deaths (including 23 death during delivery without life signs), with similar numbers in both genders. Early (0–7 days) and later (8–28 days of postnatal life) neonatal deaths were 230 (including 106 deaths during delivery with life signs) and 39 cases, respectively. Thus the perinatal mortality rate was 7.7‰ ([241 + 230]/61 227), and neonatal mortality rate was 4.4‰ (269/60 986). The stillbirth rate was approximately 3.9‰ (241/61 227). The main causes of perinatal deaths ($n = 344$) were BD (18%), intrauterine distress (17.1%), during therapeutic induction (12%), umbilical cord (6.6%),

Table 1. Comparison of perinatal and demographic birth data between genders from total live births in 2010 from Huai'an, Jiangsu, China.

Variables	Male	Female	Total births	p Values
N (%)	32 406 (53.8)	27 874 (46.2)	60 280 (100%)	
GA, mean $\pm$ SD (week)	39.6 ± 1.5	39.7 ± 1.5	39.6 ± 1.5	<0.001
Preterm birth rate	1240 (3.85)	979 (3.53)	2219 (3.70)	0.020
<32 weeks	164 (0.51)	135 (0.49)	299 (0.50)	0.370
<28 weeks	15 (0.05)	17 (0.06)	32 (0.05)	0.273
BW, mean $\pm$ SD (g)	3494 ± 496	3378 ± 477	3440 ± 491	<0.001
LBW	835 (2.58)	843 (3.03)	1678 (2.79)	<0.001
VLBW	73 (0.23)	79 (0.28)	152 (0.25)	0.090
ELBW	13 (0.04)	15 (0.05)	28 (0.05)	0.277
Macrosomia	5343 (16.5)	2842 (10.2)	8185 (13.6)	<0.001
Multi-birth rate	541 (1.67)	541 (1.94)	1082 (1.80)	0.007
Cesarean section	17 640 (54.6)	14 174 (51.0)	31 814 (52.9)	<0.001
Pregnant complications	3205 (9.89)	2805 (10.1)	6010 (10.0)	0.255
Pregnant hypertension	523 (1.61)	489 (1.75)	1012 (1.68)	0.096
PROM	1742 (5.38)	1522 (5.46)	3264 (5.41)	0.330
Pregnant anemia	392 (1.21)	352 (1.26)	744 (1.23)	0.290
Maternal age, mean $\pm$ SD (y)	26.0 ± 5.2	25.8 ± 5.1	25.9 ± 5.1	<0.001
Amniotic fluid volume				0.240
Normal	29 390 (92.7)	25 209 (92.4)	54 599 (92.6)	
Polyhydramnios	253 (0.80)	217 (0.80)	470 (0.80)	
Oligohydramnios	2047 (6.46)	1857 (6.81)	3904 (6.62)	
Amniotic fluid contamination				0.220
Normal	27 613 (86.0)	23 667 (85.6)	51 280 (85.8)	
Grade I	1739 (5.42)	1476 (5.34)	3215 (5.38)	
Grade II	1424 (4.44)	1306 (4.72)	2730 (4.57)	
Grade III	1327 (4.13)	1195 (4.32)	2522 (4.22)	
1-min Apgar $\leq$7	1256 (3.90)	1023 (3.68)	2279 (3.80)	0.092
1-min Apgar $\leq$3	191 (0.59)	155 (0.56)	346 (0.58)	0.309
5-min Apgar $\leq$7	305 (0.94)	231 (0.83)	536 (0.90)	0.075
5-min Apgar $\leq$3	117 (0.36)	116 (0.42)	233 (0.39)	0.156
Congenital anomalies	236 (0.73)	175 (0.63)	411 (0.68)	0.074
Mortality rate#	124 (0.38)	123 (0.44)	247 (0.41)	0.145
Preterm death rate	79 (6.43)	87 (8.94)	166 (7.61)	<0.001
Hospitalized rate	4332 (13.4)	2540 (9.11)	6872 (11.3)	<0.001

Abbreviations: BW, birth weight; LBW, Low BW; VLBW: Very LBW; ELBW: Extremely LBW; PROM, premature rupture of membrane. Statistics: Values are n (%) or mean $\pm$ SD; p values are for comparison between corresponding male and female value sets. #Data obtained in the first 7 days after birth.

placenta (5.1%), neonatal asphyxia (3.6%) and respiratory distress syndrome (RDS, 3.3%).

There were 97.4% newborns discharged without any diseases whereas 2.2% required care in neonatal wards. Totally 6872 neonates were hospitalized for treatment and various care, with 1298 (2.2%) immediately after birth, 43% of them admitted in the first 24 h after birth, and 75% from rural families. The mean BW for all the hospitalized neonates was 3092 ± 706 g, or a median BW of 3200 g. Preterm infants accounted for 24.5% and LBW infants 19.4%. Table 5 shows incidence rate of major diseases of the hospitalized patients during neonatal period. There were four major types of disorders: pulmonary infection and sepsis, intracranial injury and neurological impairment, hyperbilirubinemia and acute bilirubin encephalopathy, and congenital malformation. Preterm birth-related organ system development insufficiency is present but dispersed mainly in RDS, which accounts for 46.3% (56/121) in the hospitalized or 36.4% (56/154) of all, VLBW infants. The incidence of RDS was 6.1‰, together with other major diseases that may develop respiratory failure, requiring extensive respiratory and intensive care. More BD-related congenital anomalies were found in later neonatal period. The incidence of congenital heart diseases (CHDs) requiring hospitalized (8.6‰) and other congenital anomalies (1.9‰) was also based on the diagnosis in the whole neonatal period, therefore exceeds the total numbers of BD (0.68%) identified at birth. The mortality rate for neonates whose parental residency was with urban or rural background was 1.2% or 2.8%, respectively, whereas total deaths were 2.37% (163/6872) for all the hospitalized. Death rate was 8.0% in those with congenital anomalies versus 1.8% in those without ($p < 0.01$). The main causes of neonatal death ($n = 233$) related to organ system dysfunction in hospitalization were birth asphyxia (24.5%), respiratory diseases (21.5%), prematurity and VLBW (18.5%) and congenital anomalies (7.7%). In hospitalized patients, 18.8% had

Table 2. Order of pregnancy and delivery related birth rate and gender difference from 60 144 births.

Gravidity	1st	2nd	3rd	4th	5th and higher
N	33 960	17 277	5418	2139	1296
Constitution rate, %	56.5	28.7	9.0	3.6	2.2
Parity	1st	2nd	3rd and higher		
N	39 118	18 850	2163		
Constitution rate, %	65.0	31.3	3.6		
Male-to-female ratio	1.08	1.29	1.57		

Table 3. Birth weight (BW) associated gestational age (GA), death rate and gender of all births.

BW g	*n* (%)	Cumulated *n* (%)	GA weeks	Cumulated GA, weeks	Death *n* (%)	Cumulated deaths, *n* (%)	Male *n* (%)
500-	2	2	24.6 ± 3.2	24.6 ± 3.2	2	2	2
600-	5	7	27.2 ± 2.5	26.4 ± 2.8	5	7	0
700-	5	12	27.3 ± 2.1	26.7 ± 2.5	5	12 (100)	4 (80)
800-	10	22	30.3 ± 4.0	28.4 ± 3.7	3 (30)	15 (68.2)	5 (50)
900-	6	28	29.8 ± 4.2	28.8 ± 3.8	3 (50)	18 (64.3)	2 (33)
1000-	27	55 (0.1)	29.2 ± 2.9	29.0 ± 3.4	14 (51.9)	32 (58.2)	12 (44)
1100-	11	66 (0.11)	29.6 ± 4.1	29.1 ± 3.5	5 (45.5)	37 (56.1)	5 (46)
1200-	25	91 (0.15)	30.3 ± 2.6	29.4 ± 3.3	11 (44.0)	48 (52.7)	10 (42)
1300-	23	114 (0.19)	30.2 ± 1.9	29.6 ± 3.1	4 (17.4)	52 (45.6)	9 (41)
1400-	40	154 (0.25)	31.5 ± 1.9	30.1 ± 2.9	3 (7.5)	55 (35.7)	24 (60)
1500-	69 (0.11)	223 (0.36)	32.2 ± 3.0	30.7 ± 3.1	19 (27.9)	74 (33.2)	33 (48)
1600-	53 (0.1)	276 (0.45)	32.6 ± 2.0	31.1 ± 3.0	8 (15.4)	82 (28.7)	24 (45)
1700-	64 (0.1)	340 (0.57)	33.9 ± 3.0	31.6 ± 3.2	5 (7.8)	87 (25.6)	39 (62)
1800-	85 (0.14)	425 (0.7)	33.9 ± 3.1	32.1 ± 3.3	5 (5.9)	92 (21.6)	43 (52)
1900-	75 (0.12)	500 (0.8)	34.6 ± 2.4	32.5 ± 3.3	5 (6.7)	97 (19.4)	37 (49)
2000-	190 (0.3)	690 (1.1)	35.6 ± 2.9	33.3 ± 3.5	22 (11.6)	119 (17.2)	99 (52)
2100-	152 (0.3)	842 (1.4)	35.8 ± 2.3	33.8 ± 3.4	2 (1.3)	121 (14.4)	82 (55)
2200-	203 (0.3)	1045 (1.7)	36.3 ± 2.5	34.3 ± 3.4	9 (4.6)	130 (12.4)	98 (49)
2300-	245 (0.4)	1290 (2.1)	36.8 ± 2.4	34.8 ± 3.4	11 (4.5)	141 (10.9)	112 (46)
2400-	401 (0.7)	1691 (2.8)	37.3 ± 2.3	35.4 ± 3.3	7 (1.8)	148 (8.7)	195 (49)
2500-	737 (1.2)	2428 (4.0)	38.2 ± 2.0	36.2 ± 3.3	17 (2.3)	165 (6.8)	354 (48)
2600-	754 (1.2)	3182 (5.3)	38.6 ± 1.8	36.8 ± 3.2	7 (0.9)	172 (5.4)	339 (45)
2700-	1006 (1.7)	4188 (6.9)	38.8 ± 1.8	37.3 ± 3.0	5 (0.5)	177 (4.2)	467 (47)
2800-	1404 (2.3)	5592 (9.3)	39.0 ± 1.6	37.7 ± 2.8	7 (0.5)	184 (3.3)	593 (42)
2900-	1706 (2.8)	7298 (12.1)	39.2 ± 1.4	38.1 ± 2.6	1 (0.1)	185 (2.5)	772 (46)
3000-	4751 (7.8)	12 049 (20.0)	39.5 ± 1.3	38.6 ± 2.3	14 (0.3)	199 (1.6)	2132 (45)
3100-	3455 (5.7)	15 504 (25.7)	39.6 ± 1.2	38.8 ± 2.2	3 (0.1)	202 (1.3)	1634 (48)
3200-	4721 (7.8)	20 225 (33.5)	39.7 ± 1.2	39.0 ± 2.0	4 (0.1)	206 (1.0)	2276 (48)
3300-	4404 (7.3)	24 629 (40.8)	39.7 ± 1.1	39.2 ± 1.9	2 (0)′	208 (0.8)	2181 (50)
3400-	4807 (7.9)	29 436 (48.8)	39.8 ± 1.1	39.3 ± 1.8	4 (0.1)	212 (0.7)	2458 (51)
3500-	7805 (12.9)	37 241 (61.7)	39.9 ± 1.1	39.4 ± 1.7	12 (0.2)	224 (0.6)	4233 (54)
3600-	4603 (7.6)	41 844 (69.3)	39.9 ± 1.1	39.5 ± 1.7	7 (0.2)	231 (0.5)	2660 (58)
3700-	3825 (6.3)	45 669 (75.6)	40.0 ± 1.1	39.5 ± 1.6	3 (0.1)	234 (0.5)	2211 (58)
3800-	3615 (6.0)	49 284 (81.6)	40.0 ± 1.1	39.5 ± 1.6	0 (0)	234 (0.5)	2110 (59)
3900-	2857 (4.7)	52 141 (86.4)	40.1 ± 1.0	39.6 ± 1.6	2 (0.1)	236 (0.4)	1713 (60)
≥4000	8231 (13.6)	60 372 (100)	40.2 ± 1.0	39.6 ± 1.5	10 (0.1)	246 (0.4)	5243 (65)

All values are given in numbers and percentage (%) or means ± SD.

Table 4. Gestational age (GA) associated birth weight (BW), death rate and gender of all births.

GA Weeks	*n* (%)	Cumulated *n* (%)	BW g	Cumulated BW, g	Deaths *n* (%)	Cumulated deaths, *n* (%)	Male *n* (%)
<25	9	9	928 ± 309	928 ± 309	9	9	3 (33)
25	7	16	979 ± 402	950 ± 341	7	16 (100)	4 (57)
26	4	20	875 ± 272	935 ± 323	4	20 (100)	3 (75)
27	12	32	1321 ± 481	1080 ± 427	5 (41.7)	25 (78.1)	5 (42)
28	33	65	1826 ± 926	1458 ± 811	11 (33.3)	36 (55.4)	16 (49)
29	58	123 (0.2)	1563 ± 693	1508 ± 756	23 (39.7)	59 (48.0)	31 (53)
30	82	205 (0.3)	1887 ± 730	1660 ± 767	14 (17.1)	73 (35.6)	43 (54)
31	97	302 (0.5)	1869 ± 543	1727 ± 709	20 (20.8)	93 (30.8)	59 (62)
32	152 (0.2)	454 (0.7)	2050 ± 586	1835 ± 687	17 (11.2)	110 (24.2)	93 (61)
33	159 (0.2)	613 (1.0)	2214 ± 504	1933 ± 665	14 (8.9)	124 (20.2)	96 (61)
34	298 (0.5)	911 (1.5)	2328 ± 467	2062 ± 635	12 (4.0)	136 (14.9)	171 (58)
35	467 (0.8)	1378 (2.3)	2575 ± 526	2236 ± 648	15 (3.2)	151 (11.0)	264 (57)
36	861 (1.4)	2239 (3.7)	2814 ± 477	2458 ± 652	18 (2.1)	169 (7.5)	452 (53)
37	2616 (4.3)	4855 (8.1)	3133 ± 467	2821 ± 653	11 (0.4)	180 (3.7)	1532 (59)
38	8241 (13.6)	13 096 (21.7)	3343 ± 433	3150 ± 583	15 (0.2)	195 (1.5)	4850 (59)
39	16 739 (27.6)	29 835 (49.5)	3468 ± 423	3328 ± 524	19 (0.1)	214 (0.7)	9256 (56)
40	21 614 (35.7)	51 449 (85.4)	3533 ± 426	3414 ± 495	24 (0.1)	238 (0.5)	11 104 (52)
41	7121 (11.7)	58 570 (97.2)	3597 ± 434	3436 ± 492	4	242 (0.4)	3392 (48)
42	1487 (2.4)	60 057 (99.7)	3600 ± 440	3440 ± 492	4 (0.3)	246 (0.41)	724 (49)
>42	207 (0.3)	60 264 (100)	3567 ± 461	3441 ± 491	0 (0)	246 (0.41)	114 (55)

Table 5. Incidences and constitutive proportions of major diseases of hospitalized neonates.

Diseases	*n*	Proportion in all hospitalized (%)	Incidence in all live birth (‰)
Total	6872	100	
Pulmonary infection	3874	56.4	63.5
Hyperbilirubinemia	1782	25.9	29.2
Sepsis	1559	22.7	25.6
Hypoxic ischemic encephalopathy	1268	18.5	20.8
Intracranial hemorrhage	1263	18.4	20.7
Asphyxia	810	11.8	13.3
Congenital heart disease	523	7.61	8.6
Respiratory distress syndrome	371	5.40	6.1
Impetigo	279	4.06	4.6
Omphalitis	272	3.9	4.5
Cephalhematoma	257	3.70	4.2
ABO hemolytic disease	219	3.19	3.6
Diarrhea	214	3.11	3.5
Aspiration syndrome	193	2.81	3.2
Hypoglycemia	177	2.58	2.9
Upper respiratory tract infection	136	1.98	2.2
Myocardial injury	126	1.83	2.1
Other congenital anomalies	115	1.67	1.9
Hypocalcemia	103	1.50	1.7
Anemia	85	1.24	1.4
Cold injury syndrome	82	1.19	1.3
Thrush	69	1.00	1.1
Gastric tract hemorrhage	62	0.90	1.0
Meningitis	56	0.81	0.9
Pneumothorax	53	0.77	0.9
Syphilis	43	0.63	0.7
Acute bilirubin encephalopathy	32	0.47	0.5
Necrotizing enterocolitis	22	0.33	0.4
Meconium aspiration syndrome	17	0.25	0.3

Disease incidences are derived from 60 986 live births. Some patients may have more than one diagnosis. Both congenital heart diseases and other anomalies exceed the numbers of birth defects as the data were collected through the whole neonatal period.

pregnant complications, in which 8.0% were premature rupture of membrane, 3.6% maternal infection and fever, 2.3% pregnant hypertension, 1.5% eclampsia, 1.1% placenta previa, 0.6% pregnant anemia, 0.6% placenta abruption and 0.4% gestational diabetes. Death rate was 4% in those with pregnant complications compared to 2% in those without ($p < 0.001$). VLBW and those of BW 1500-2499 g accounted for 43.8% and 40.2%, respectively, of the pregnant complication-related neonatal diseases. There were 32 (1:1906) cases of congenital hypothyroidism and 11 (1/5544) phenylketonuria by screening at birth.

Discussion

This report is our first attempt to prospectively survey a complete birth population-based vital statistics, according to the international definitions, from a prefectural region with intermediate conditions of economics and maternal and infant health care in the nation. The major findings as characterized by relatively low rate of preterm birth, VLBW and ELBW, and details of major pregnant- and delivery-related mortality and morbidity of the fetuses and neonates, should represent the status in domestic regions approximate to 50% of the total population of similar economics and health care conditions in China. We found an annual regional birth rate of 11.3‰ in 2010, which is lower than, but very close to, an average of 11.8‰ birth rate in 1.34 billion as total population in 2010 (26). We estimate that annually total births should be close to 16 million with 5% (or lower) as preterm births (800 000), 128 000–144 000 perinatal deaths (8–9‰, including half as fetal deaths or stillbirths) and 80 000–960 000 neonatal deaths (5–6‰), in average; whereas in the neonatal deaths, 3/4 or 60 000 should be preterm (approximate to 7–8% of the total preterm births). There are disparities in the neonatal and infant mortality rates among the coastal, inland and remote (western) regions, or between rural and urban areas, in China [4,27], hence there are variations in either coastal or remote regions, which are not suitable for estimation of the national averages of perinatal and neonatal mortality and morbidity. As Chinese population accounts for 20% of the total population in the world, the current approach should be an alternative means by which more accurate and approximate

estimation of the birth rate, preterm rate, and perinatal and neonatal mortality and morbidity and related risks should be feasible. The high proportion of macrosomia, as shown in Table 3, should be related to the maternal rest and nutrition status in later pregnancy as social and cultural factors nowadays commonly reported from many domestic urban deliveries.

However, such approach for data access has both advantages and limitations. As reflected by a high efficiency in collecting perinatal data based on the investigational protocol, it should have a high reliability to answer the questions listed in the introduction, not yet available by current national sampling survey-based vital statistics [1–4]. The limitation exists as to variation and inadequacy of service standard and staffs competence in the lower level clinics participated for the accomplishment of the study, and to the numbers of home delivery that were not provided. Moreover, as the region had more than 99% deliveries in hospital, the data may not differentiate covariates affecting perinatal outcome due to access to the care facilities or socioeconomic confounders as seen in underdeveloped regions. The ''new rural cooperative medical scheme'' as health insurance policy was implemented in Huai'an since 2010, which covers more than 90% of the rural families including newborns. As there was a well-established perinatal-neonatal health care and information system in Huai'an hospital system, such limitation should be acceptable for conducting current survey in order to estimate the nationwide status of regions with similar conditions.

The high perinatal-neonatal mortality is mainly from developing and underdeveloped countries and regions [28]. The perinatal and neonatal mortality were 6.64‰ and 4.19‰, respectively, in the United States in 2005–2009 [29,30], and even lower in other high-income countries and regions of the world as demonstrated by Rajaratnam et al. [31]. It was not until recent years over decade effort that U5MR in China reached an average level around 15 per 1000 births, along with proportional reduction of neonatal and postneonatal death rate, similar to Singapore, South Korea and Taiwan in transition from 1980s to 1990s. Constitution of the preterm birth rate, LBW and VLBW in our data are much lower, hence are the perinatal and neonatal mortalities, which should be considered in interpreting the regional status and progression of the perinatal-neonatal care standard. Likewise, there was a very low level of stillbirth rate (3.9‰, 241/61 227), which should be much lower than the level estimated by Stanton et al. for 2000 or earlier era [5]. This may be attributed to underreport for stillbirths as officially later abortion (mostly therapeutic) before 28 weeks of GA was not included in the statistics of fetal death. Thus Huai'an data-based estimation of the nationwide situation still requires further work to verify.

The lower LBW rate (2.8%) appears to coincide with the lower preterm birth rate (3.72%) in Huai'an, compared with 8.2% and 12.2%, respectively, in the United States in 2009 [30]. In our previous survey, a 4.5% preterm birth rate from 5822 hospital deliveries, along with 3.8% LBW and 0.5% VLBW, was found in Julu county, Hebei province in 2007–2008 [32]. As mentioned above, these findings suggest that Chinese birth population might have lower proportion of LBW and preterm birth rate, presumably both under 5%. Shin reported 7.2% LBW rate in Korea birth population [33]. Although we found only 2.8% LBW, 0.26% VLBW and 28 (0.05%) with BW <1000 g, we cannot rule out the underreport, by level I and II hospitals, of those as extremely preterm (<28 weeks of gestation) that may be missed in our final data analysis. The preterm birth rate in current survey was 3.72%, quite similar to that (3.5%) found in a nationwide survey in 1998 by means of sampling [11,12], but lower than that of 7.8% reported by nationwide retrospective surveys in 2003 [6], which included only tertiary centers with high-risk pregnancies and deliveries. Considering higher preterm birth rate is associated with a trend of urbanization, living style changes and social cultural diversities, as well as ethnicity differences [29,30,34], the targeted birth population in Huai'an has characteristics approximate to that of the nationwide averages in 2010 [27], and with homogenous social tradition and cultural identities. Therefore, we consider an average of 4–5% of preterm birth rate for nationwide total births to be more realistic. It suggests that with improved living style, preterm birth rate in Chinese pregnant women may differ, but social cultural tradition may play an important role in maintaining its rate still low compared to other western countries and already industrialized Asian regions.

Chinese community has been worrying with high male prevalence in gender imbalance since the implementation of ''one child per family'' policy in 1980s for family planning and population control. The data in Table 1 listed such difference at delivery, but it does not demonstrate any increased risks for females at delivery in general, although the female preterm death rate was significantly higher than the males. The gender ratio 116:100 at birth in the present survey is the same as we found in Julu county in 2007 [32], and also associated with even higher male dominance with birth delivery order increment (Table 2). Similar trend happens in other Asian countries and regions not subjected to ''one child family'' policy. Pham et al. [35] reported it at 114:100 at birth in Vietnam in 2000–2006; while the first baby being a girl, the sex ratio of the second birth increased significantly. A recent report indicates a male-to-female ratio at 111:100 in Taiwan resident in 2005 [36], where the Chinese cultural tradition remains despite the region is already industrialized for decades and birth rate has fallen to below 10‰ for many years. The high gender ratio at birth could be explained for by strong socio-cultural preference for boys in a family, often from rural residents.

The cesarean section rate was over 50% in China [19,20] compared to 32.9% in United States [30], which also rose by 50% in the past 10 years. We found the cesarean section rate at 52.9%, which should be close to its average level in Chinese hospitals with maternal care and delivery, although we found only 30.2% in Julu county [32]. Such a high level of cesarean section rate is mainly a compromise of both maternal (parental) and care giver sides as most of the costs of fetal and neonatal disorders were born mainly on the family up to 2010, especially for those from rural areas. We also report 10% pregnant complications, similar to the 11% found in our previous survey in Julu county [32], but lower than reported in the international literature. It might be underreported as the low-level hospitals or clinics offering delivery might lack adequate routine to identify the pregnant complications. The cesarean section rate was 54.2% in the hospitalized neonatal

infants, whereas neonatal diseases related to the pregnant complications were associated with higher death risks. A recent survey from Asian countries revealed an average of 27.3% of cesarean section delivery [37]. Our results suggest a need to confine the cesarean section according to medical indication, and alter delivery mode-associated neonatal morbidities.

BD is one of the main reasons for perinatal deaths. Chen reported a rate of BD at 0.73% in Taiwan [38]. The relatively lower BD rate in this study could be explained for by improved perinatal care of the region; however, it may also suggest inefficient diagnostic facilities and experience in recognizing, for example, CHD, inherited metabolic diseases, chromosomal disorders. From Table 5, we demonstrated that more CHD were identified in later neonatal period, together with other congenital anomalies accounting for totally 1.05% live births. We report incidence of congenital hypothyroidism (1:1906) and phenylketonuria (1:5544) first time from a well-defined regional birth population (94.1% neonates screened). Compared to a report of 1:2034 and 1:11 681, respectively, from >13 million neonatal samples in the past 22 years in China [39], the rate of congenital hypothyroidism was slightly higher, but that of phenylketonuria was doubled. The incidence of RDS was 6.1‰ from all live births (Table 5) who were diagnosed and cared for similar to that in our previous multicenter studies [21–23]. These patients were mostly born premature as VLBW. Taken above estimated annually nationwide total birth rate of 16 million, an incidence of RDS approximate to 100 000 should be expected.

In conclusion, these regional data profiles reflect status of birth population-based perinatal and neonatal mortality and morbidity in Huai'an in 2010, and its protocol and methodology should be applicable for regions with intermediate levels of women and children's health care, to represent up to 50% of the total national population. The current data should be served as a reference for future comparison of the transition, especially for high-risk pregnancy and neonate requiring modern infrastructure and technology to offer decent perinatal and neonatal care. We anticipate a trend to come in the next 5–10 years for steady improvement of perinatal-neonatal care in the whole China, some of the estimations may be verified, and robust approaches developed for more comprehensive evidence.

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Declaration of interest

The authors report no conflicts of interest.

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