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Changes in the live birth profile in Henan, China: A hospital registry-based study

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Abstract

Background: Preterm complications and neonatal asphyxia are the leading causes of death in those under 5 years of age. However, little information exists for the province of Henan, China. The purpose of this study was to explore changes in the live birth profile in a provincial hospital over the past 32 years in Henan, China.

Methods: A retrospective analysis was conducted to reveal the characteristics of live neonates from 1987 to 2018.

Results: There were 118 253 live births during the period, including 19 798 (16.74%) preterm births. The neonatal death rate was 6.45‰, and the top risk factor was preterm birth complications and birth asphyxia. Before 1998, neonatal death occurred primarily among term infants. Between 1999 and 2018, preterm infants, especially extreme and very preterm infants with very low birthweight, constituted more than half of all mortalities, and the preterm birth rate increased from 5.94% in 1999 to 16.69% in 2018. The risk factors associated with preterm birth were being male (aOR = 1.18, $P < 0.001$), advanced maternal age (>35 years old; aOR = 1.08, $P = 0.008$), gravidity ≥2 (aOR = 1.15, $P < 0.001$), parity ≥2 (aOR = 1.50, $P < 0.001$), placenta previa (aOR = 7.41, $P < 0.001$), twin or multiple births (aOR = 10.63, $P < 0.001$), hypertension (aOR = 2.08, $P < 0.001$), and rupture of membrane (aOR = 5.03, $P < 0.001$).

Conclusions: The preterm birth rate has increased over the past 32 years from 4.98% to 16.69% in a provincial hospital in China. Preterm birth was the leading

reason for neonatal death, and birth asphyxia was the major risk factor for death in term infants.

KEYWORDS
live birth, neonatal death, preterm birth, risk factors

1 | INTRODUCTION

Over the past two decades, substantial political, economic, and research efforts have been made to reduce child mortality, and a total of 195 countries and territories have seen declining rates of communicable, neonatal, and nutritional diseases between 1980 and 2016.[1] However, even as recently as 2016, the three leading causes of death in children under 5 years were lower respiratory infections, neonatal preterm birth complications, and neonatal encephalopathy because of birth asphyxia and trauma, and together, these result in about 1.8 million deaths each year.[1] China has made great progress in reducing child mortality, with a 37% decline from 2009 to 2015[2]; however, the neonatal death rate is still higher than in high-resource countries.[1] The leading causes of neonatal deaths in China are preterm birth complications, birth asphyxia, congenital abnormalities, and pneumonia.[2] Preterm birth is responsible for one third of neonatal deaths and nearly one half of all cases of congenital neurologic disability, including cerebral palsy.[3-5] Furthermore, the preterm birth rate has been increasing in most countries, and China has the second highest number of preterm infants born each year.[6]

The aim of this investigation was to analyze temporal changes in live births from 1987 to 2018, including preterm birth, birth asphyxia, and neonatal death, in one provincial hospital in Henan—the largest province in China with a population of more than 100 million. We aimed to identify the factors that influence neonatal death and to use findings to develop strategies to reduce the incidence of neonatal death and to improve neurological outcomes in high-risk infants.

2 | MATERIALS AND METHODS

This was a retrospective study using data from January 1987 to December 2018 to identify changes in live births. The study was based on data from the hospital registration system and the Medical Service Department of the hospital. We checked and extracted the maternal characteristics and obstetric information manually because both paper and electronic records were used during the study period. The recorded information was anonymized and de-identified before analysis, and the analysis was approved by the ethics committee of the hospital and was exempted from the need for informed consent. Data included only live infants and excluded stillbirths with no sign of life during labor or delivery, and we did not include newborns transferred from other hospitals after the delivery. For the purposes of this study, live birth was defined as a newborn showing any sign of life (breathing, beating of the heart, pulsation of the umbilical cord, or definite movement of voluntary muscles irrespective of the duration) at any gestational age after birth. Neonatal death was defined as the death of a newborn occurring during the first 28 days of life (0-27 days) after a live birth. The data collected from each fiscal year included sex, birthweight, gestational age, single or multiple births, maternal age, and delivery type.

Gestational age was estimated from the last menstrual period and/or by ultrasound. Preterm birth was defined as a neonatal born alive before 37 completed weeks of pregnancy. The subcategories of preterm birth were defined based on gestational age and included extremely preterm (less than 28 weeks), very preterm (28-32 weeks), moderately preterm (32-34^{+6} weeks), and late preterm (35-36^{+6} weeks). Newborns were also classified according to their body weight at birth as very low birthweight (≤1500 g), low birthweight (1501-2500 g), normal birthweight (2501-4000 g), or macrosomic (>4000 g).[7] Delivery modes were divided into vaginal delivery and cesarean birth.

Hypertension included chronic hypertension (blood pressure >140/90 mm Hg) and pregnancy-induced hypertension (elevated blood pressure after 20 weeks of pregnancy), and preeclampsia was diagnosed by the presence of hypertension plus the new onset of any one of the following: thrombocytopenia, renal insufficiency, liver dysfunction, pulmonary edema, or cerebral or visual disturbances. Rupture of membranes referred to a rupture of the amniotic sac, and prolonged rupture of membranes referred to durations longer than 18 hours before delivery. Gestational diabetes mellitus (GDM) was defined as any degree of glucose intolerance (fasting plasma glucose ≥5.9 mmol/L or 1 h postprandial whole blood glucose ≥7.8 mmol/L) with onset or first recognition during pregnancy.[8-10]

SPSS software (version 19.0) was used for data analysis. Quantitative data are presented as means ± SD and were analyzed by one-way ANOVA. A confounding factor

is a variable that influences both the dependent variable and independent variable, causing spurious association. Intermediate variables occur in a causal pathway from a causal (independent) variable to an outcome (dependent) variable. Following the literature, univariate and multivariable logistic regression analysis was performed to identify possible risk factors of preterm birth, including gender, maternal age, gravidity, parity, hypertension, rupture of membrane, placenta previa, GDM, and multiple births. Risk factors were selected when $P < 0.1$ in the univariate logistic regression model, and the limit of statistical significance was $P < 0.05$.

3 | RESULTS

3.1 | The basic characteristics of live births

From January 1987 to December 2018, there were 118 253 live infants delivered at the hospital (Figure 1A), including 64 023 (54.14%) males and 54 230 (45.86%) females (mean annual male/female ratio of 1.18:1, with a range of 1.03:1 to 1.34:1). The average birthweight decreased from 3227 g ± 281 g for males and 3268 g ± 428 g for females in 1987 to 3190 g ± 697 g and 3076 g ± 687 g, respectively, in 2018 ($P < 0.001$). The mean gestational age decreased from 40.08 weeks ±1.22 weeks in 1987 to 38.47 weeks ±2.65 weeks in 2018 ($P < 0.001$). There were 19 798 preterm infants (16.81%) born during the study period, and 57.31% of these preterm births were males. The preterm birth rate (<37 weeks) increased from 4.42% in 1987 to 21.30% in 2007, remained at 21.00% between 2007 and 2013, and then decreased to 18.28% in 2018 (Figure 1B). Notably, there was an increase in preterm births for newborns less than 32 gestational weeks or with very low birthweight (<1500 g) starting in 2007 (Figure 1C,D). The percentage of twin or multiple births increased from 1.35% in 1987 to 8.48% in 2018 ($P < 0.001$; Figure 1E).

3.2 | Risk factors for preterm birth

There were 19 798 preterm infants born during the study period, which made up 16.74% of the total live births. Among the preterm infants, 39.00% of them were late preterm, 35.70% were moderate preterm, and 25.30% were very or extremely preterm. The total rate of transfer from delivery ward to neonatal ward was 62.90% for preterm infants, 70.06% for very preterm infants, 73.31% for moderate preterm infants, and 45.33% for late preterm infants. For term infants, the rate was only 4.71%.

The preterm birth rate was slightly higher in male than in female infants from 1987 to 2018 (Figure 2A, OR = 1.18 [95% CI: 1.13-1.22], $P < 0.001$). Women over 35 years of age had greater chances of having preterm infants compared with mothers under 35 years old (25.93% vs 4.14% in 1987 and 20.45% vs 17.54% in 2018, Figure 2B, 1.31 [1.25-1.28], $P < 0.001$). The preterm birth rates were 3.20% and 14.90% in 1987 and 2018 in mothers with a first pregnancy,

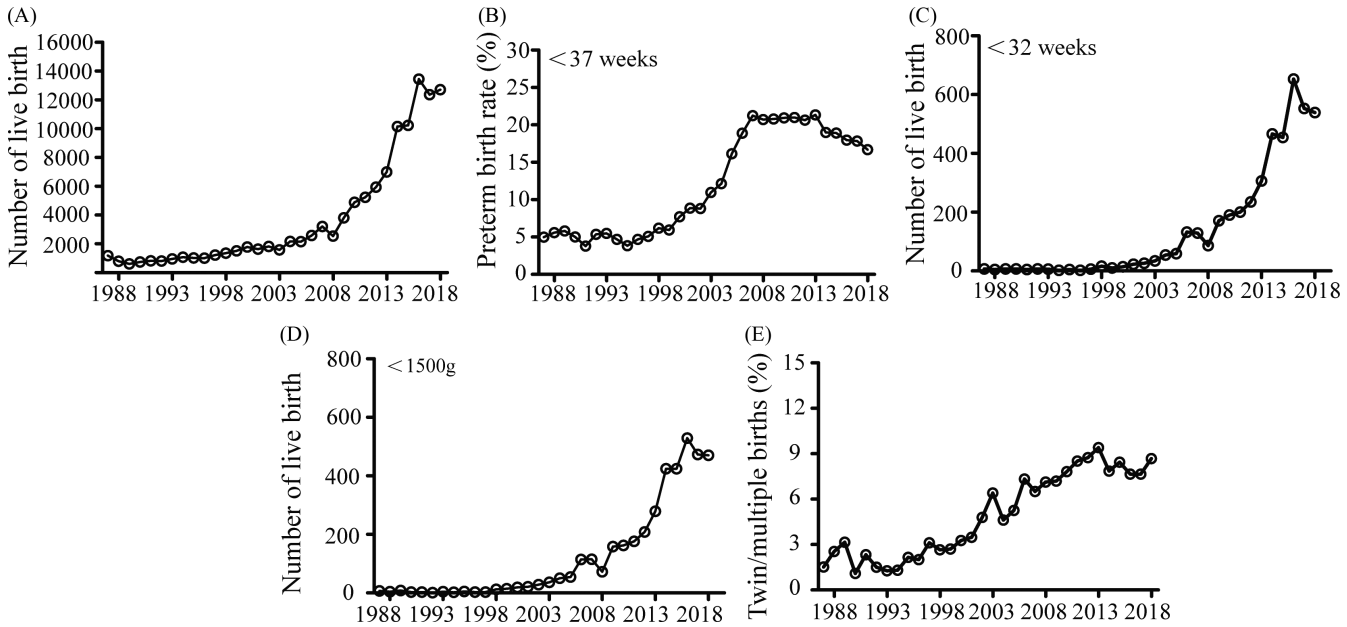

FIGURE 1 The live birth profile changes from 1987 to 2018. A, The absolute number of live births in the hospital each year. B, The preterm birth rate (<37 weeks). C and D, The numbers of very preterm infants (<32 weeks) and infants with very low birthweight (<1500 g) in each year. E, The percentage of twin or multiple births

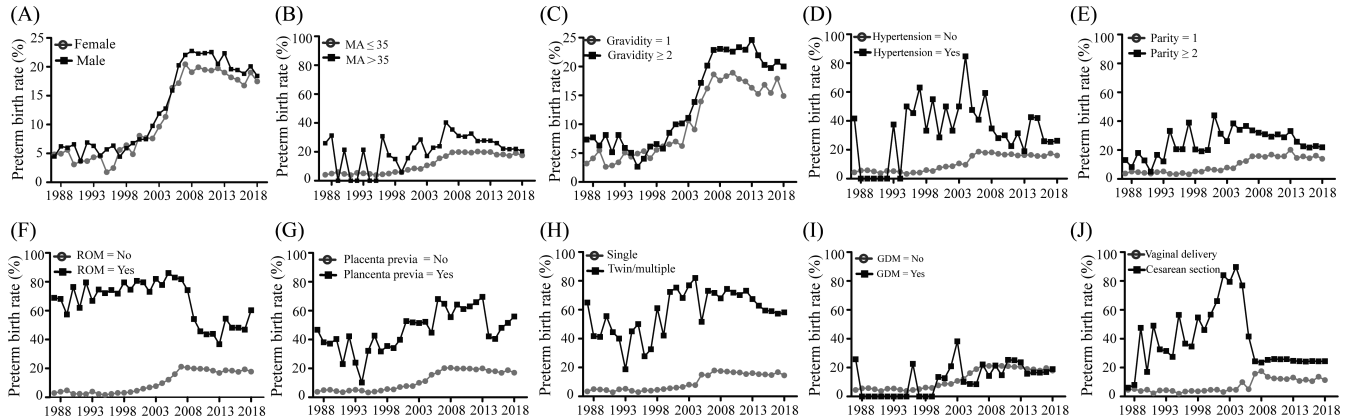

FIGURE 2 The preterm birth rate by different risk factors from 1987 to 2018. A, The preterm birth rate in male and female infants (OR = 1.18, 95% CI: 1.13-1.22, $P < 0.001$). B, The preterm birth rate in mothers ≤35 years and mothers >35 years (1.31 [1.25-1.28], $P < 0.001$). C, The preterm birth rate by gravidity (1.36 [1.31-1.41], $P < 0.001$). D, The preterm birth rate in mothers with or without hypertension (1.83 [1.76-1.89], $P < 0.001$). E, The preterm birth rate by different parity (2.21 [1.97-2.48], $P < 0.001$). F, The preterm birth rate in mothers with or without rupture of membrane (4.14 [3.87-4.44], $P < 0.001$). G, The preterm birth rate in mothers with or without placenta previa (5.38 [5.37-6.33], $P < 0.001$). H, The preterm birth rate in single or twin/multiple infants (10.40 [9.86-10.97], $P < 0.001$). I, The preterm birth rate did not show a significant difference between mothers with or without GDM (0.99 [0.90-1.09], $P = 0.836$). J, The dynamic changes in preterm birth rate each year showed an overall higher rate for cesarean section than for vaginal delivery (0.33 [0.32-0.34], $P < 0.001$)

whereas the rates were 7.34% and 20.00% in 1987 and 2018 in mothers with two or more pregnancies (Figure 2C, 1.36 [1.31-1.41], $P < 0.001$). Hypertension was associated with preterm birth, as seen in Figure 2D (2.21 [1.97-2.48], $P < 0.001$) from 1987 to 2018.

From 1987 to 2018, the preterm birth rate was higher for second or later born children as compared with first-born neonates (13.11% vs 3.76% in 1987 and 21.99% vs 13.98% in 2018, Figure 2E, 1.83 [1.76-1.89], $P < 0.001$). Similar results were seen in mothers with rupture of membrane (68.87% vs 2.95% in 1987 and 60.32% vs 17.81% in 2018, Figure 2F, 4.14 [3.87-4.44], $P < 0.001$), placenta previa (46.77% vs 3.80% in 1987 and 55.92% vs 17.08% in 2018, Figure 2G, 5.38 [5.37-6.33], $P < 0.001$), and twin/multiple births (65.00% vs 3.43% in 1987 and 58.20% vs 14.50% in 2018, Figure 2H, 10.40 [9.86-10.97], $P < 0.001$). GDM had no obvious impact on the rate of preterm births compared with the absence GDM (2.47% vs 5.15% in 1987 and 17.97% vs 18.98% in 2018, Figure 2I, 0.99 [0.90-1.09], $P = 0.836$).

With respect to the mode of birth, the mean preterm birth rate for cesarean birth was 38.75% compared with 7.56% for vaginal delivery over the entire study period. The preterm birth rate was much higher in the cesarean group during the first 20 years of the study period, although the rate declined sharply and then remained stable and high compared with the vaginal delivery group in the final 10 years of the study period (24.49% vs 11.36% in 2018) (Figure 2J, 0.33 [0.32-0.34], $P < 0.001$).

To further explore the effect of risk factors on the preterm birth rate, logistic regression was conducted, and the results showed that placenta previa (aOR = 7.41 [95% CI: 6.80-8.08], $P < 0.001$), twin or multiple pregnancies (10.63 [10.05-11.24], $P < 0.001$), and rupture of membrane (5.03 [4.67-5.42], $P < 0.001$) were the top risk factors for preterm birth (Table 1). Other contributing factors included being male (1.18 [1.14-1.23], $P < 0.001$), advanced maternal age (1.08 [1.02-1.14], $P = 0.008$), being the second or third pregnancies for the mother (1.15 [1.09-1.21], $P < 0.001$), parity ≥2 (1.50 [1.42-1.57], $P < 0.001$), and hypertension (2.08 [1.83-2.37], $P < 0.001$). However, GDM did not contribute to preterm birth (0.99 [0.90-1.09]) (Table 1).

3.3 | Neonatal deaths

The neonatal death rate was 10.96‰ in 1987 and 3.22‰ in 2018, with a peak of 29.85‰ in 1989 (Figure 3A). The average annual neonatal death rate during the period from 1987 to 2018 was 6.45‰. There were a total of 763 deaths (6.45‰) from 1987 to 2018, and 423 (55.46% of the total deaths) were preterm infants. Among the total deaths, 19.90% had birth asphyxia, 11.72% had neonatal infection, 4.95% had respiratory distress syndrome (RDS), and 7.98% had other diseases (Figure 3B). About 28.5% were $28\text{-}31^{+6}$ weeks of gestational age, and 52.90% had very low birthweight (Figure 3C,D). Before 1998, neonatal death occurred almost exclusively among term infants. However, preterm infants, especially extreme and very preterm with very low birthweight, consisted of more than half of the neonatal deaths after 1998 (Figure 3E,F).

TABLE 1 Risk factors in preterm infants

		Unadjusted			Adjusted[b]		
	Incidence (%)[a]	OR	95% CI	*P*	OR	95% CI	*P*
Gender							
Female	15.65	1.00			1.00		
Male	17.90	1.18	[1.13, 1.22]	<0.001	1.18	[1.14, 1.23]	<0.001
Maternal age							
≤35 years	19.05	1.00			1.00		
>35 years	25.06	1.31	[1.25, 1.28]	<0.001	1.08	[1.02, 1.14]	0.008
Gravidity							
1	14.33	1.00			1.00		
≥2	18.48	1.36	[1.31, 1.41]	<0.001	1.15	[1.09, 1.21]	<0.001
Parity							
1	13.38	1.00			1.00		
≥2	22.02	1.83	[1.76, 1.89]	<0.001	1.50	[1.42, 1.57]	<0.001
Hypertension							
No	16.68	1.00			1.00		
Yes	30.66	2.21	[1.97, 2.48]	<0.001	2.08	[1.83, 2.37]	<0.001
ROM							
No	15.80	1.00			1.00		
Yes	43.70	4.14	[3.87, 4.44]	<0.001	5.03	[4.67, 5.42]	<0.001
Placenta previa							
No	15.92	1.00			1.00		
Yes	52.45	5.38	[5.37, 6.33]	<0.001	7.41	[6.80, 8.08]	<0.001
GDM							
No	16.90	1.00			—	—	—
Yes	16.76	0.99	[0.90, 1.09]	0.836	—	—	—
Multiple births							
Single	13.22	1.00			1.00		
Twin/multiple	61.30	10.40	[9.86, 10.97]	<0.001	10.63	[10.05, 11.24]	<0.001
Constant					0.06		<0.001

Abbreviations: GDM, Gestational diabetes mellitus; ROM, Rupture of membrane.

[a]Incidence (%) = preterm infants / (preterm + term infants) × 100 in each subgroup.

[b]Adjusted ORs were adjusted for maternal age, gravidity, parity, hypertension, ROM, placenta previa, GDM, and multiple births.

3.4 | Mother's age and delivery mode

Average maternal age increased from 25.9 years ± 3.7 years in 1987 to 30.7 years ± 4.6 years in 2018 ($P < 0.001$). The age of primiparous mothers increased from 25.5 years ± 2.5 years in 1987 to 28.9 years ± 3.7 years in 2018 ($P < 0.001$; Figure 4A). The percentage of cesarean deliveries among all mothers increased dramatically from 23.7% in 1987 to 65.5% in 2006 ($P < 0.001$), remained stable at around 65.0% between 2006 and 2013, and then showed a downward trend from 59.8% in 2014 to 50.5% in 2018. Similarly, there was a moderate decline in the proportion of cesarean births among primiparous mothers from 62.8% to 40.5% between 2013 and 2018 (Figure 4B).

4 | DISCUSSION

Based on our analysis, the preterm birth rate and the occurrence of twin or multiple births have increased in recent decades, whereas the number of neonatal deaths has been decreasing. Preterm complications and birth asphyxia were the leading causes of neonatal death over the study period. Being male, advanced maternal age, twin or multiple births, gravidity, parity, and maternal diseases also contributed to preterm birth.

The ratio of males to females has been shown to be affected by multiple factors, and there is globally a narrow male bias at birth with a male/female ratio of 1.05:1.[11] In Japan and the United States, the male/female ratio at birth

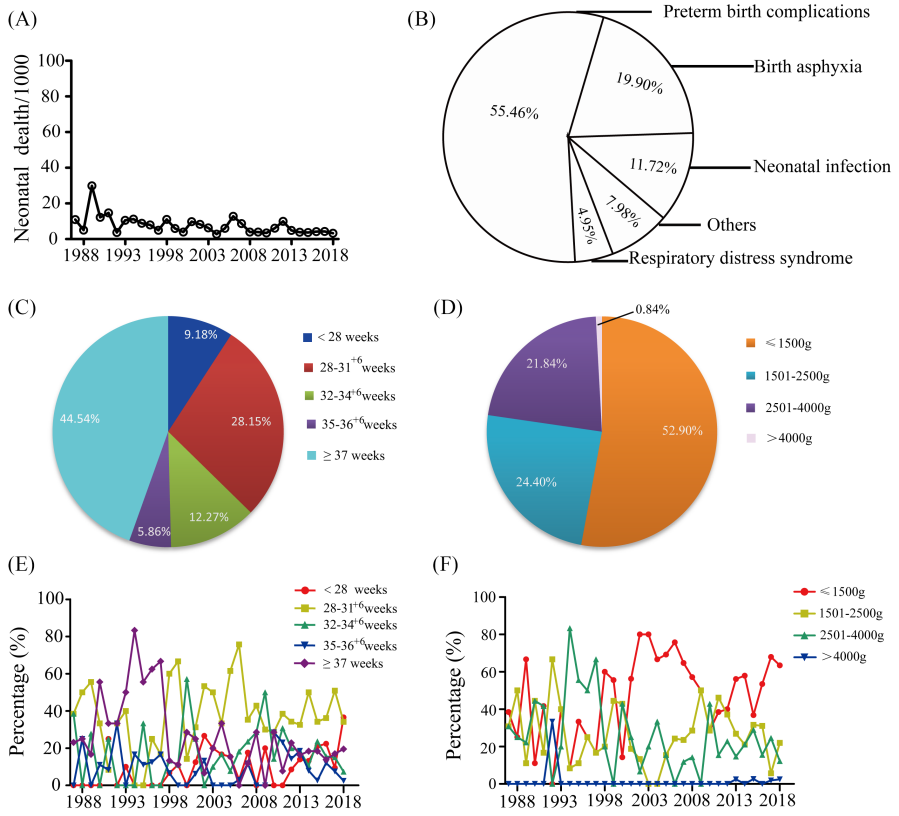

FIGURE 3 Incidence and causal factors of neonatal death. A, The incidence of neonatal death in the hospital each year (deaths within 28 days after birth). B, The causal factors for neonatal deaths. C, Neonatal death rate by gestational age. D, Neonatal death rate by birthweight. E, Neonatal death rate by gestational age over time. F, Neonatal death rate by birthweight over time [Colorfigure can be viewed at wileyonlinelibrary.com]

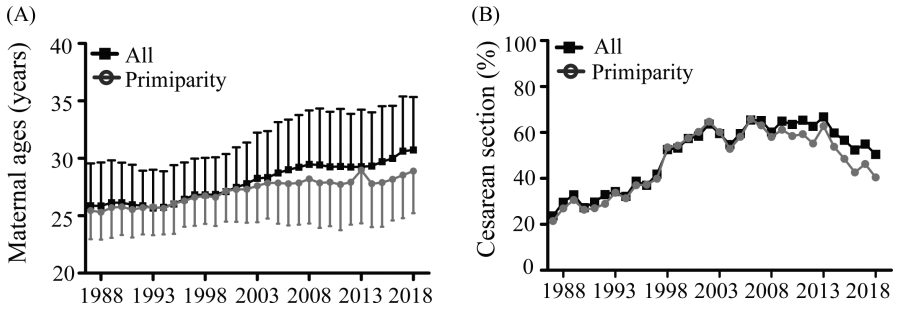

FIGURE 4 Changes in maternal age and cesarean section. A, The changes of maternal ages in pregnancy. B, The percentage of cesarean section delivery

has been decreasing in recent years and is now slightly lower than 1.05:1.[12] In this study, we found that the ratio of males to females at birth was 1.18:1, and although this decreased slightly starting in 2013, the ratio of males is still higher than reports from other countries.[13]

Infertility is estimated to affect between 8% and 12% of reproductive-aged couples worldwide, whereas in central Asia almost 30% of women of reproductive age suffer from infertility.[14] Thus, fertility treatments, including ovarian stimulation and assisted reproductive technology (ART), are increasingly being used. ART was approved for clinical use in China in 1999 starting with provincial and university-affiliated hospitals, and since then, its use has developed rapidly throughout the whole country. Although the use of single embryos for ART treatment has increased, two to three embryo transfers at the same time remains common in China,[15] which might explain our observation of increased twins and multiple births during the study period, which is similar to the increase reported in the United States.[16]

The cesarean birth rate increased dramatically from 23.7% in 1987 to 59.8% in 2014, and although it declined to 50.5% in 2018, this trend aligns with other reports that the cesarean rate has been rising since 1990 worldwide.[17,18] Apart from cesareans because of medical indications, the high rate of elective cesarean observed in the current study (10.40% of all cesarean cesarean) may partly be because of a high ratio of mothers who desired cesareans to avoid the pain of unmedicated vaginal delivery.[19] This may also be related to the one-child policy (since 1979) in that families may perceive cesareans as safer than vaginal births when complications arise. However, cesarean rates higher than 10% are not associated with reductions in maternal and newborn mortality rates,[20] and elective procedures can increase the risk of maternal morbidity, neonatal death, and neonatal admission to an intensive care unit.[21] The

cesarean rate in hospitals in China has decreased because pregnant women intending to have more than one child have been less likely to prefer cesarean section after the modification of the family planning policy in 2015.[21-23]

The preterm birth rate has risen in most countries and now represents the leading cause of neonatal death worldwide,[1] but the rate varies with geography and ethnicity ranging from 5%–6% in Europe to around 7.1% in China and 12% in the United States.[24] In the current study, the preterm birth rate has increased dramatically over the past 32 years, up to 18.28% in 2018 in this hospital, which is much higher than the previously reported 6.06%–10.52% preterm birth rate according to data from China.[24-26] The etiology underlying this disparity is poorly understood. The hospital where the study was conducted is a provincial hospital with a higher level of medical care. Thus, this facility may treat a higher percentage of women with high-risk pregnancy transferred in from other hospitals, which would likely contribute to the higher rate of preterm births. Other risk factors contributing to preterm birth include maternal characteristics (age, stress, infection, or other diseases), reproductive history (prior preterm birth), current pregnancy (such as short cervical length), social and economic inequalities,[27] and fetal diseases such as fetal distress and intrauterine growth restriction.[28] Nonetheless, this increase raises concern.

In our analysis, preterm birth complications made up 55.46% of the total deaths, and over half of these preterm babies were early preterm births. This aligns with other reports showing that preterm birth is the leading cause of death in children under 5 years,[29-31] especially infants with low gestational age and very low birthweight. Currently, there is no efficient therapeutic strategy that can reduce death related to very preterm complications,[32-34] and it is not always possible to prevent or reduce preterm birth even when risk factors are identified.[35] Several high-risk factors contributed to the preterm birth rates observed here, including being male, gravidity, parity, advanced maternal age, rupture of membrane, multiple pregnancy, hypertension, and placenta previa, and most of these are not modifiable.

In this study, 44.10% of preterm infants were born with rupture of membrane, which was still a risk factor for preterm birth after adjusting for other factors. The underlying causes of rupture of membrane include intrauterine infection and a history of preterm birth.[36,37] Advanced maternal age also contributes to preterm birth and is associated with many complications because of chronic and pregnancy-induced hypertension, GDM, and macrosomia. Hypertension was found to be another independent risk factor for preterm birth in this study because such disorders might lead to preeclampsia and result in medical induction of the birth before term.[38] Placenta previa usually results in medically induced preterm birth. Our results also showed that preterm babies were more likely to be born to mothers with parity ≥2, which is consistent with previous reports,[39,40] but a systematic review in 2010 reported that grand multiparity and great grand multiparity were not associated with preterm birth.[41] GDM was removed from our logistic model even though it has been reported that GDM plays a role in preterm delivery and mortality.[42]

With respect to neonatal death in our study, the incidence of neonatal death has decreased and remained at low levels in recent years. One reason for this could be the wide use of pulmonary surfactants and ventilation after birth, which has improved survival in preterm infants. Some studies have reported beneficial effects of antenatal magnesium sulfate, but the decreased deaths seen here cannot be attributed to antenatal magnesium sulfate because it has not been used routinely in this hospital.[43-45]

Apart from preterm birth complications and birth asphyxia, the causes of neonatal death included neonatal infection and respiratory distress syndrome, similar to other reports from China in 2019.[46] Although infection rates have modestly decreased in the neonatal intensive care unit as a result of ongoing quality improvement measures, 4 out of every 10 infants with sepsis die or experience major disability.[47] Pneumonia may be transmitted vertically from the mother or acquired from the postnatal environment, and the resultant inflammatory response leads to cellular injury that impairs gas exchange, alters pulmonary circulation, interferes with normal respiratory mechanics, denudates alveolar surfaces, and interferes with surfactant function, which results in respiratory failure leading to morbidity and mortality in newborn infants regardless of gestational age.[48] Respiratory distress syndrome primarily affects preterm infants, but RDS was also one of the leading causes in death of term infants in our study. It has been reported that the incidence of RDS increases in term infants with elective cesarean births,[49] and the reason for increased RDS in these infants is delayed removal of lung fluid and a lack of cortisol response associated with spontaneous labor.[50] In our study, there was an excessively high rate of cesarean birth.

A limitation of this study is that the data were only collected from a high-level provincial hospital. This creates a bias and overestimates the preterm birth rate and twin or multiple birth rate because this hospital often receives high-risk pregnant mothers transferred from local hospitals.[51] Thus, caution must be used in interpreting these data. Second, the current analysis is based on the discharge database, which is insufficient for analyzing critical risk factors such as socioeconomic status, occupation, stress, environment, lifestyle, nutrition, and heredity,[52-55] which are also related to preterm birth. Third, Henan Province has a population of around 105 million

inhabitants with imbalanced economic development and pronounced differences in health care resources between urban and rural areas, and thus the results of this study cannot be extrapolated to the whole province.

4.1 | Conclusions

In summary, the preterm birth rate increased over the past 32 years from 4.42% to 18.28% in one large provincial hospital in China, with placenta previa, twin or multiple pregnancies, and hypertension as the top risk factors for preterm birth. Preterm birth was the leading cause of neonatal death, and birth asphyxia was the major risk factor for death in term infants in this hospital. More efforts to improve perinatal care are required to reduce the rate of preterm births in China.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are openly available in article. if anyone need information in detail, please contact the corresponding author.

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