Original Article

Impact of maternal age on neonatal outcomes among very preterm infants admitted to Chinese neonatal intensive care units: a multi-center cohort study

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Background: The percentage of advanced maternal age (aged over 35 years) mothers has been rising across the world, the evidence of maternal age on neonatal outcomes from low- and middle-income countries is scarce. Our objective was to evaluate the effect of maternal age on mortality and major morbidity among very preterm infants admitted to Chinese neonatal intensive care units.

Methods: Data from a retrospective multi-center cohort of all complete care very preterm infants admitted to 57 neonatal intensive care units that participated in the Chinese Neonatal Network from January 1st to December 31st, 2019 were analyzed. Neonatal outcomes including mortality or any major morbidity, defined as necrotizing enterocolitis stage 2 or 3, moderate & severe bronchopulmonary dysplasia, severe intraventricular hemorrhage, cystic periventricular leukomalacia, severe retinopathy of prematurity, or sepsis. A multiple logistic regression model was constructed to analyze the independent association between maternal age and neonatal outcome.

Results: Among 7,698 eligible newborns, 80.5% of very preterm infants were born to mothers between the ages of 21 and 35 years, with 18.0% born to mothers >35 years and 1.5% born to mothers <21 years. Higher rates of maternal hypertension, maternal diabetes, cesarean deliveries, antenatal steroid usage were noted as maternal age increased. The proportion of prenatal care, cesarean section, antenatal steroid usage and inborn for very preterm infants born to mothers <21 years was lower than those of mothers of other ages. Compared to the ages of 21–35 years group, the odds of severe intraventricular hemorrhage (adjusted odd ratio: 2.00, 95% CI: 1.08–3.71) was significantly higher in the ages of 15–20 years group. Increasing maternal age was associated with higher rates of small for gestational age and lower birth weight of very preterm infants, but no correlation between advanced maternal age and very preterm infants mortality or major morbidity.

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Conclusions: Among very preterm infants, increasing maternal age was associated with higher rates of small for gestational age but not neonatal mortality or major morbidity. Young maternal age may increase the risk of severe intraventricular hemorrhage of very preterm infants.

Keywords: Maternal age; very preterm infants; neonatal morbidity; neonatal outcome

Submitted Jan 01, 2022. Accepted for publication Apr 27, 2022.
doi: 10.21037/tp-22-1
View this article at: https://dx.doi.org/10.21037/tp-22-1

Introduction

Very preterm infants (VPIs, gestational age <32 weeks) account for about 16% of premature births (1), but representing the majority of preterm deaths and major morbidities (2). With the rapid development of perinatal medicine in China, the number of very premature infants cared in neonatal intensive care units (NICUs) has been increasing rapidly, but the overall survival rate and survival without major morbidity are still lower than that in the developed countries (3).

Young or advanced maternal age is a significant problem in the field of clinical and public health in developing countries (4,5). The Chinese government enacted the universal two-child policy 5 years ago to address the country's aging issue (6), and the incidence of advanced maternal age (aged over 35 years) nearly tripled (7). Many population studies have demonstrated an association between young or advanced maternal age and adverse birth outcomes, including increased neonatal mortality (8,9), the higher proportion of preterm birth (10), low birth weight (11,12), genetic anomalies (13) or birth defects (14), and reduced the 5-min Apgar score (15,16). In contrast to the birth outcomes of newborns, a few studies linking maternal age with neonatal outcomes of preterm infants indicated that advanced maternal age has improved the prognosis of less than 33 weeks' gestation at birth or extremely low birth weight infants (17-19). However, these studies were completed in the developed countries, and the association between maternal age and neonatal outcome in VPIs in the medium- and low-income countries is scarce. In this study, we evaluate the effect of maternal age on mortality and major morbidity among very preterm infants admitted to Chinese NICUs. We present the following article in accordance with the STROBE reporting checklist (available at https://tp.amegroups.com/article/view/10.21037/tp-22-1/rc).

Methods

Study design and settings

This was a retrospective cohort study based on the Chinese Neonatal Network (CHNN), which aims to carry out high-quality cooperative research to enhance the perinatal health (20). CHNN has established and maintained a standardized clinical database to monitor the outcome and clinical practice of all VPIs or infants with birth weight <1,500 g hospitalized in 57 participating NICUs starting from January 1, 2019. These 57 hospitals caring for approximately 5% of all VPIs in China, included: four national children's medical centers, four regional children's medical centers, 30 provincial perinatal or children's medical centers and 19 major referral centers in large cities across 25 provinces (21). Regular audit was performed to ensure the data quality. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by ethics board of Children's Hospital of Fudan University (No. 2018-296) and individual consent for this retrospective analysis was waived because this study did not directly intervene in the diagnosis and treatment of individual patients.

Study population

The inclusion criteria were VPIs admitted to 57 NICUs participating in the CHNN from January 1st, 2019 to December 31st, 2019. Newborns with major congenital anomalies (22), been transferred to other hospitals or discharged against medical advice, missing maternal age and information on newborn outcomes, and extreme values for maternal age currently over 55 or under 15 were excluded.

Data collection

Detailed clinical data were collected prospectively by

trained abstracters using the CHNN standardized database, according to the abstractor's manual (20).

Definitions

Gestational age was the best obstetric estimate based on early prenatal ultrasound results and obstetric history. If the obstetric estimate was not available or was different from the postnatal estimate of gestation by more than two weeks, the gestational age was estimated using the Ballard Score (23). Antenatal steroid usage refers to have received the antenatal steroids if at least one dose was administered to the mother before delivery. Maternal diabetes and hypertension included any type of these diseases that occur before or during pregnancy. Inborn was defined as a preterm infant born in a perinatal center (24). Small for gestational age (SGA) was defined as birth weight <10th percentile for gestational age and sex (25). Pregnancy care refers to at least one obstetric visit during pregnancy. The Score of Transport Risk Index of Physiological Stability (TRIPS) was calculated to assess infant illness severity at admission and for up to 24 hours after (26).

Outcomes

The primary outcome was mortality or any major morbidity, including necrotizing enterocolitis (NEC, ≥ stage 2), moderate & severe bronchopulmonary dysplasia (BPD), brain damage, severe retinopathy of prematurity (ROP, ≥ stage 3) and sepsis. Brain damage was defined as the presence of either severe (grades III and IV) intraventricular hemorrhage (IVH) or cystic periventricular leukomalacia (cPVL). The secondary outcome was the individual components of brain damage (severe IVH and cPVL). The definition of NEC refers to Bell's criteria (27), and Moderate & Severe BPD refers to Jobe's criteria (28). IVH was defined according to Papile's criteria (29) and PVL was reported based on the presence of periventricular cysts on cranial ultrasound or MRI. ROP was classified according to the International Classification (30). Sepsis was defined as positive blood or cerebrospinal fluid culture and patient treated with antibiotics for 5 or more days (31).

Statistical analysis

The VPIs were divided into three discrete groups according to maternal age (15–20, 21–35, and 36–55 years). χ^2 test was applied to compare the categorical baseline characteristic and neonatal outcomes between three categories of maternal age with report of frequency and percent. Analysis of Variance (ANOVA) was employed for normally-distributed variables while Kruskal-Wallis test for highly-skewed baseline variables. Cochran-Armitage trend test or linear regression test, as appropriate, were used to determine the trend of baseline information and neonatal outcomes across three groups of maternal age.

Multi-variable logistic regression models were constructed, using generalized estimating equation approach (GEE) with a compound symmetric covariance structure to deal with cluster effect of infants within 57 CHNN sites. The independent variables including basic VPIs information (gestational age, birth weight, male, multiple birth), maternal health status (hypertension, diabetes and parity) and treatments before delivery (prenatal care, cesarean section, antenatal steroid and inborn). Regression analyses were performed using different combinations of the independent variables, which included basic VPIs information in Model 1, basic VPIs information and maternal health status in Model 2, basic VPIs information, maternal health status and treatment before delivery in Model 3. In order to further observe the overall trend of maternal age on neonatal outcomes, maternal age was treated as a continuous variable for logistic regression using GEE adjusted for the same independent variables as Model 3, which was stratified into three groups of maternal age. SAS Version 9.4 (SAS Institute, Cary, North Carolina) was used for all data management and analysis. The significance level was set as $P<0.05$ with two-tail test.

Results

A total of 9,510 VPIs were admitted to units participating in the CHNN in 2019. Of these, we excluded a total of 1,812 infants because of being transferred to other hospitals (n=344) or discharged against medical advice (n=1,349), born with a major congenital anomaly (n=48), missing maternal age (n=70), or having mothers of extreme maternal age (n=1). The remaining 7,698 VPIs composed the study population (*Figure 1*).

Comparison of the baseline characteristics of VPIs born to mother with different age groups (*Table 1*) revealed that the majority of VPIs were born to mothers between the ages of 21 and 35 years (n=6,199, 80.5%), with 1,382 (18.0%) born to mothers >35 years and 117 (1.5%) born to mothers <21 years. Increasing maternal age was associated with higher rates of maternal hypertension, maternal diabetes, cesarean

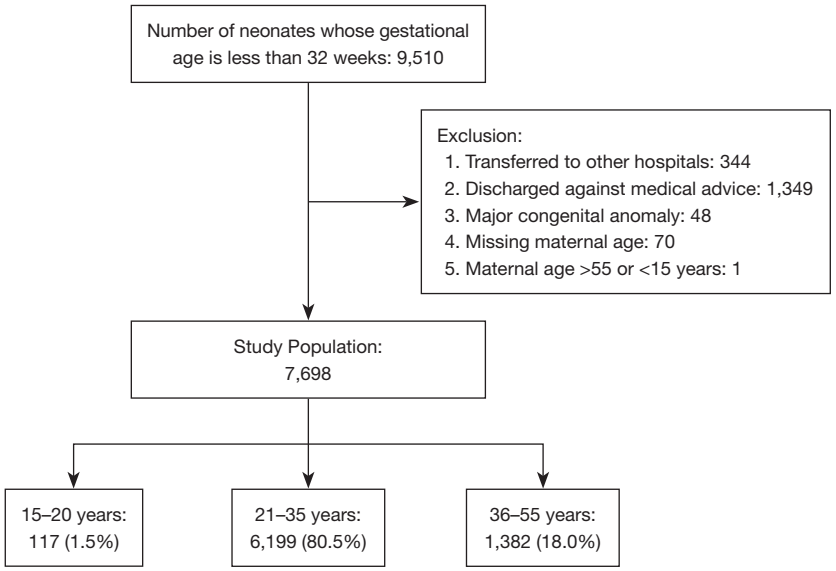

Figure 1 Study flow chart.

Table 1 Baseline characteristics in each group of maternal age

Outcomes	Maternal age (years)			Overall	P-value	P-value for Trend
	15–20	21–35	36–55			
N	117	6,199	1,382	7,698		
Maternal information, N (%)						
Primigravida	91/117 (77.8)	3,408/6,158 (55.3)	397/1,375 (28.9)	3,896/7,650 (50.9)	<0.01	<0.01
Hypertension	10/111 (9.0)	1,051/6,098 (17.2)	374/1,366 (27.4)	1,435/7,575 (18.9)	<0.01	<0.01
Diabetes	10/111 (9.0)	969/6,092 (15.9)	347/1,358 (25.6)	1,326/7,561 (17.5)	<0.01	<0.01
Perinatal care, N (%)						
Prenatal care	98/105 (93.3)	5,951/6,000 (99.2)	1,321/1,339 (98.7)	7,370/7,444 (99.0)	<0.01	0.71
Cesarean section	33/116 (28.4)	3,407/6,177 (55.2)	895/1,375 (65.1)	4,335/7,668 (56.5)	<0.01	<0.01
Antenatal steroid Usage	54/94 (57.4)	4,404/5,637 (78.1)	1,002/1,266 (79.1)	5,460/6,997 (78.0)	<0.01	0.02
Inborn	54/117 (46.2)	4,026/6,199 (64.9)	895/1,382 (64.8)	4,975/7,698 (64.6)	<0.01	0.17
Infants characteristics						
Gestational age, median [P25, P75]	30.00 [28.71, 31.14]	30.00 [28.71, 31.00]	30.00 [28.43, 31.00]	30 [28.57, 31.00]	0.10	0.04
Birth weight, mean (Std)	1,395.32 (301.16)	1,348.99 (308.63)	1,322.76 (324.67)	1,344.98 (311.64)	<0.01	<0.01
SGA, N (%)	5/117 (4.3)	375/6,196 (6.1)	108/1,380 (7.8)	488/7,693 (6.3)	0.03	<0.01
Multiple birth, N (%)	26/117 (22.2)	1,969/6,199 (31.8)	310/1,382 (22.4)	2,305/7,698 (29.9)	<0.01	<0.01
Male, N (%)	78/117 (66.7)	3,536/6,196 (57.1)	770/1,380 (55.8)	4,384/7,693 (57.0)	0.07	0.11
Apgar score <7 at 5 min, N (%)	5/105 (4.8)	362/5,845 (6.2)	90/1,295 (6.9)	457/7,245 (6.3)	0.48	0.24
TRIPS score on admission, median [P25, P75]	13 [7, 19]	12 [6, 19]	13 [6, 19]	12 [6, 19]	0.14	0.55

SGA, small for gestational age; TRIPS, Transport Risk Index of Physiological Stability.

Table 2 Neonatal outcome in each group of maternal age

Outcomes	Maternal age (years)			Overall	P-value	P-value for Trend
	15–20	21–35	36–55			
N	117	6,199	1,382	7,698		
Composite outcome[a], N (%)	49/117 (41.9)	2,507/6,199 (40.4)	581/1,382 (42.0)	3,137/7,698 (40.8)	0.53	0.35
Mortality	7/117 (6.0)	297/6,199 (4.8)	67/1,382 (4.8)	371/7,698 (4.8)	0.84	0.90
NEC ≥ stage II	4/117 (3.4)	282/6,199 (4.5)	61/1,382 (4.4)	347/7,698 (4.5)	0.83	0.99
Moderate & severe BPD	39/117 (33.3)	1,650/6,183 (26.7)	393/1,378 (28.5)	2,082/7,678 (27.1)	0.12	0.45
Brain damage[b]	11/98 (11.2)	561/5,459 (10.3)	121/1,229 (9.8)	693/6,786 (10.2)	0.85	0.59
Severe IVH[b]	8/98 (8.2)	350/5,428 (6.4)	84/1,221 (6.9)	442/6,747 (6.6)	0.70	0.77
cPVL[b]	4/102 (3.9)	305/5,681 (5.4)	59/1,277 (4.6)	368/7,060 (5.2)	0.47	0.40
Severe ROP[b]	5/105 (4.8)	362/5,845 (6.2)	90/1,295 (6.9)	457/7,245 (6.3)	0.67	0.39
Sepsis	6/117 (5.1)	572/6,199 (9.2)	126/1,382 (9.1)	704/7,698 (9.1)	0.31	0.68

[a], composite Outcome included death or at least one of any morbidity including NEC ≥ Stage II, Moderate & Severe BPD, Brain damage, Severe ROP, and sepsis. [b], morbidity among newborns who have been screened. NEC, necrotizing enterocolitis; BPD, bronchopulmonary dysplasia; IVH, intraventricular hemorrhage; cPVL, cystic periventricular leukomalacia; ROP, retinopathy of prematurity.

deliveries and antenatal steroid usage. The incidence of prenatal care (93.3%), cesarean section (28.4%), antenatal steroid usage (57.4%) and inborn (46.2%) in the mothers aged 15–20 years were significantly lower than that of other age groups. Among the infant factors, the mean birth weight was (1,322.76±324.67) g and the incidence of SGA was 7.8% in the VPIs born to mothers aged 36–55 years. Increasing maternal age was associated with higher rates of SGA and lower birth weight of VPIs. No differences in sex were observed across the maternal age groups.

The assessment of VPIs outcomes (*Table 2*) revealed no differences in mortality and major morbidity of VPIs born to mothers in different maternal age groups. The regression models in model 3 (*Table 3*) revealed that compared to the ages of 21–35 years group, the odds of severe IVH (adjusted OR: 2.00, 95% CI: 1.08–3.71) was significantly higher in the ages of 15–20 years group. Infants born to mothers with advanced maternal age (36–55 years) were not found to have increased risk of developing adverse primary or secondary outcomes. The regression model with the mother's age as a continuous variable indicated maternal age was not found to be associated with mortality or major morbidity (*Table 4*).

Discussion

In low- and middle-income countries, young or advanced maternal is associated with higher risks of preterm birth and neonatal mortality (32). However, most of these studies focus on the influence of mother's age on the birth outcomes (33), and less attention has been paid to neonatal outcomes of VPIs born to young or advanced maternal age. We analyzed relationships between maternal age and outcomes of VPIs in the Chinese population. To our knowledge, this study is the first to report the association between maternal age and neonatal outcome in VPIs in developing countries. Our findings suggest that increasing maternal age was associated with higher rates of SGA and lower birth weight of VPIs. Compared with the ages of 21–35 years, the incidence of severe IVH in VPIs with young maternal age (ages of 15–20 years) increased. We did not identify any significant association between advanced maternal age and VPIs mortality or major morbidity, after adjustment for relevant confounding factors.

Some studies about advanced maternal age and the prognosis of preterm infants have reported that the incidence of BPD in preterm infants <29 weeks gestational age decreased with increasing maternal age (18), and extremely low birth weight infants of mothers >40 years were more likely to survive and had a lower risk of neurodevelopmental impairment or death compared with mothers <20 (19). In the present study, we did not find improved VPIs neonatal outcomes with advanced maternal age. Although women with advanced maternal

Table 3 Adjusted odds ratio of neonatal outcome in each group of maternal age [OR (95% CI)]

Outcomes	Model 3		Model 2		Model 1	
Maternal age	15–20 (years)	36–55 (years)	15–20 (years)	36–55 (years)	15–20 (years)	36–55 (years)
Composite outcome	1.05 (0.69, 1.61)	1.03 (0.91, 1.17)	1.07 (0.68, 1.68)	1.03 (0.91, 1.17)	1.07 (0.68, 1.67)	1.04 (0.92, 1.16)
Mortality	1.03 (0.42, 2.54)	0.84 (0.63, 1.12)	1.21 (0.51, 2.87)	0.86 (0.65, 1.13)	1.27 (0.55, 2.91)	0.82 (0.63, 1.07)
NEC ≥ stage II	0.76 (0.24, 2.37)	0.91 (0.64, 1.30)	0.73 (0.24, 2.20)	0.92 (0.66, 1.29)	0.76 (0.25, 2.29)	0.87 (0.63, 1.21)
Moderate & severe BPD	1.14 (0.66, 1.96)	1.00 (0.88, 1.14)	1.13 (0.62, 2.04)	1.01 (0.88, 1.15)	1.13 (0.63, 2.02)	1.01 (0.89, 1.15)
Brain damage	1.69 (0.99, 2.88)	1.06 (0.91, 1.24)	1.78 (1.02, 3.09)*	1.06 (0.91, 1.23)	1.79 (1.02, 3.14)*	1.04 (0.90, 1.21)
Severe IVH	2.00 (1.08, 3.71)*	1.22 (0.97, 1.53)	2.04 (1.07, 3.89)*	1.20 (0.97, 1.48)	2.09 (1.10, 3.98)*	1.18 (0.95, 1.45)
cPVL	1.00 (0.42, 2.39)	0.92 (0.71, 1.18)	1.11 (0.47, 2.62)	0.92 (0.71, 1.17)	1.10 (0.46, 2.58)	0.91 (0.72, 1.16)
Severe ROP	0.77 (0.17, 3.57)	1.05 (0.71, 1.54)	0.86 (0.19, 3.85)	1.01 (0.69, 1.49)	0.87 (0.20, 3.88)	0.97 (0.66, 1.41)
Sepsis	1.11 (0.56, 2.21)	0.96 (0.79, 1.16)	1.07 (0.54, 2.11)	0.95 (0.79, 1.15)	1.02 (0.51, 2.01)	1.01 (0.84, 1.22)

VPIs born to mothers aged 21–35 years were used as the reference. Model 3 adjusted for gestational age, birth weight, male, multiple birth, maternal hypertension, maternal diabetics, primigravida, prenatal care, cesarean section, antenatal steroid usage and inborn. Model 2 adjusted for gestational age, birth weight, male, multiple birth, maternal hypertension, maternal diabetics and primigravida. Model 1 adjusted for gestational age, birth weight, male and multiple birth. *, P<0.05. OR, odd ratio; CI, confidence interval; NEC, necrotizing enterocolitis; BPD, bronchopulmonary dysplasia; IVH, intraventricular hemorrhage; cPVL, cystic periventricular leukomalacia; ROP, retinopathy of prematurity.

Table 4 Trends in outcomes with respect to maternal age groups [OR (95% CI)]

Outcomes	Maternal age (years)					
	15–20		21–35		36–55	
	Unadjusted OR	Adjusted OR	Unadjusted OR	Adjusted OR	Unadjusted OR	Adjusted OR
Composite outcome	1.06 (0.75, 1.52)	1.73 (0.99, 3.03)	1.01 (0.99, 1.02)	1.01 (0.89, 1.15)	0.99 (0.94, 1.04)	1.02 (0.97, 1.08)
Mortality	0.86 (0.37, 2.02)	2.67 (0.37, 19.09)	1.00 (0.97, 1.04)	0.90 (0.67, 1.22)	1.04 (0.93, 1.16)	1.00 (0.88, 1.13)
NEC ≥ stage II	4.63 (1.51, 14.17)	N/A*	1.01 (0.98, 1.05)	1.04 (0.77, 1.41)	1.10 (0.98, 1.23)	1.06 (0.93, 1.22)
Moderate & severe BPD	1.27 (0.84, 1.92)	2.02 (0.95, 4.32)	1.01 (0.99, 1.03)	0.95 (0.82, 1.10)	0.98 (0.92, 1.04)	0.99 (0.92, 1.06)
Brain damage	0.78 (0.49, 1.24)	1.06 (0.37, 3.10)	1.00 (0.98, 1.02)	1.12 (0.91, 1.39)	0.98 (0.92, 1.05)	1.02 (0.91, 1.13)
Severe IVH	0.89 (0.49, 1.60)	1.27 (0.45, 3.60)	0.99 (0.97, 1.02)	1.22 (0.92, 1.63)	1.00 (0.93, 1.08)	0.98 (0.87, 1.12)
cPVL	0.63 (0.34, 1.16)	N/A*	1.01 (0.97, 1.04)	1.12 (0.85, 1.46)	0.98 (0.87, 1.11)	1.07 (0.92, 1.25)
Severe ROP	1.05 (0.22, 4.98)	N/A*	1.02 (0.98, 1.05)	1.07 (0.72, 1.59)	1.00 (0.90, 1.12)	1.10 (0.93, 1.31)
Sepsis	0.81 (0.52, 1.25)	0.45 (0.08, 2.46)	1.00 (0.98, 1.03)	0.99 (0.81, 1.22)	0.95 (0.88, 1.04)	1.02 (0.92, 1.13)

Models adjusted for gestational age, birth weight, male, multiple birth, maternal hypertension, maternal diabetics, primigravida, prenatal care, cesarean section, antenatal steroid usage, inborn. *, N/A is due to small number of cases. OR, odd ratio; CI, confidence interval; NEC, necrotizing enterocolitis; BPD, bronchopulmonary dysplasia; IVH, intraventricular hemorrhage; cPVL, cystic periventricular leukomalacia; ROP, retinopathy of prematurity.

age had higher proportion of pregnancy complications and SGA with a lower mean birth weight of infants, they are more willing to take routine prenatal care, have planned births (34), and have higher AN steroids use (35). These factors may have mitigated the adverse influence of pregnancy complications (36). And also, most of women with advanced maternal age are multi-gravid women, and the cesarean section rate was high, which may be

related to the favorable prognosis of VPIs (37). Women with advanced maternal age have more education, higher income, stable marital status (38), and a higher perception of pregnancy risk (39,40) but pregnancy-related anxiety was not significantly increased (39) which are the factors related to improving the outcome of VPIs (41-43). Research by Kanungo *et al.* showed that increasing maternal age was associated with increased survival without major morbidity and reductions in mortality, NEC and sepsis of preterm newborns younger than 33 weeks (17), which was inconsistent with the results of our study. Our findings are consistent with the Israeli study (44), but the reasons for the difference in our findings from those of prior studies are unclear, lower overall survival rate and survival without major morbidity of VPIs in China (3) could explain this difference.

At present, the results on the relationship between maternal age and the incidence of severe IVH in preterm infants are not consistent. Research from the Canadian Newborn Network showed that there was no relationship between maternal age and severe IVH in preterm infants <29 weeks gestational age (18). The study conducted in the United States reported that extremely low birth weight infants with young maternal age had a higher incidence of severe IVH (19), which is consistent with our study. Many studies have demonstrated that obstetrical interventions were associated with the risk of IVH in preterm infants (45). A multicenter cohort study of VPIs in Germany showed that elective cesarean section was associated with lower IVH rates (46). Korea's case-control study suggested that antenatal steroid usage decreased the risk of IVH in preterm infants (47). Shipley *et al.*'s research (48) showed that the additional burden of postnatal transport could be a vital reason for severe IVH in VPIs. Similar to previous study in the United States (19), here, mothers aged 15–20 years had lower rates of antenatal steroid usage, cesarean section and inborn, which may increase the risk of severe IVH in VPIs.

In our study, women with young maternal age had lower rates of prenatal care, which may associate with their low education, low income and unstable marital status (49). At the same time, due to the lack of social support, the accessibility of prenatal care for women with young maternal age was lower (50). This may lead to poor prognosis and increase the risk of severe complications of VPIs (51). In addition to the perinatal factors, environmental tobacco smoke exposure and infection during pregnancy also contribute to an increased risk of IVH in preterm infants (52). Previous studies have shown that cigarette smoking was more prevalent in young women (53), and infection more common because of reduced blood supply to the uterus and cervix in adolescent mothers (8), which may increase the incidence of IVH in VPIs whit young maternal age. Young mothers may involve mother-fetus competition for nutrients and reduce placental transportation, which leading to more immature of germinal matrix (8) and caused an increase in risk of severe IVH in VPIs.

Our study has several strengths. We reported the association between maternal age and neonatal outcome in VPIs in China for the first time. We conducted a large population study representative of major tertiary hospitals across the country. The definitions of outcomes were standardized and multiple measures were applied to ensure the quality of data collection. Our study also has several limitations. Our study is a retrospective investigation. We have excluded 17.8% of infants due to incomplete of NICU care, which may likely represent infants of worse neonatal outcomes. Among the included VPIs, some data on maternal information and infant characteristics were missing. In the regression model, other variables related to the outcome of VPIs were not included, such as the sociodemographic status of the mothers, the quality of prenatal care and the mental status during pregnancy, which were described in similar population studies. Because our study was limited to VPIs, we cannot extrapolate findings to newborns born at a later gestational age.

In summary, our study demonstrated that young maternal age may be associated with increased risk of severe IVH among VPIs. Advanced maternal age was not associated with neonatal mortality or major morbidities despite higher prevalence of pregnancy complications. Further work is needed to explore the best way to provide better support to mothers at the age of 20 or below.

Acknowledgments

We thank the support of all site investigators from the Chinese Neonatal Network. The authors would like to thank all the staff at the Chinese Neonatal Network coordinating center for providing organizational support (Jianhua Sun, MD; Lin Yuan, MD, PhD; Yulan Lu, PhD; Tongling Yang, RN; Hao Yuan, RN; Li Wang, RN). We also thank two professors from Children's Hospital of Fudan University (Bo Sun, PhD and Weili Yan, PhD) and a professor from Department of Pediatrics, University of Alberta (Joseph Y. Ting, MD) for editorial assistance in the preparation of this manuscript.

Funding: This work was supported by the Canadian Institutes of Health Research (Grant number CTP87518 to SKL), and Shanghai Science and Technology Commission's Scientific and Technological Innovation Action Plan (Grant number 21Y21900800 to LQ).

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://tp.amegroups.com/article/view/10.21037/tp-22-1/rc

Data Sharing Statement: Available at https://tp.amegroups.com/article/view/10.21037/tp-22-1/dss

Peer Review File: Available at https://tp.amegroups.com/article/view/10.21037/tp-22-1/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tp.amegroups.com/article/view/10.21037/tp-22-1/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by ethics board of Children's Hospital of Fudan University (No. 2018-296) and individual consent for this retrospective analysis was waived because this study did not directly intervene in the diagnosis and treatment of individual patients.

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Cite this article as: Qi Z, Wang Y, Lin G, Ma H, Li Y, Zhang W, Jiang S, Gu X, Cao Y, Zhou W, Lee SK, Liang K, Qian L; on behalf of Chinese Neonatal Network. Impact of maternal age on neonatal outcomes among very preterm infants admitted to Chinese neonatal intensive care units: a multi-center cohort study. Transl Pediatr 2022;11(7):1130-1139. doi: 10.21037/tp-22-1

Supplementary

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https://dx.doi.org/10.21037/tp-22-1