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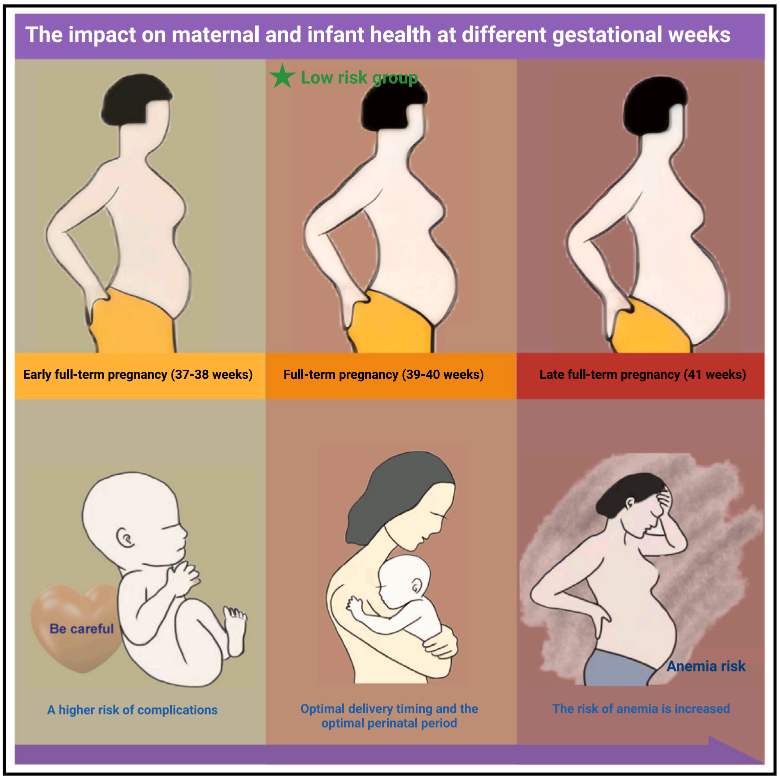
Neonatal and maternal morbidity rates in low-risk nulliparous women across different gestational ages

Graphical abstract



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In brief

Female reproductive endocrinology; Public health

Highlights

- Neonatal complications peak at 37–38 weeks in low-risk nulliparous women
- Delivery at 41 weeks raises maternal anemia risk compared to 39–40 weeks
- Deliveries at 39–40 weeks best minimize neonatal and maternal health risks
- Non-genetic factors likely influence anemia during pregnancy, per Mendelian analysis

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CellPress

Article

Neonatal and maternal morbidity rates in low-risk nulliparous women across different gestational ages

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SUMMARY

This study examines perinatal outcomes in low-risk nulliparous women and their neonates across different gestational ages. Using data from 18 hospitals, we analyzed maternal and neonatal complications for deliveries at 37–38 weeks, 39–40 weeks, and 41 weeks, focusing on the risks associated with early- and late-term deliveries. Neonatal complications were highest at 37–38 weeks, while maternal complications, primarily anemia, were more prevalent at 41 weeks. These findings suggest that deliveries closer to 39–40 weeks may offer optimal outcomes for maternal and neonatal health. By providing insights into the impact of gestational timing, this study aids clinical decision-making for safe delivery timing, potentially improving perinatal outcomes for low-risk pregnancies.

INTRODUCTION

Over the past decades, the relationship between gestational ages and perinatal outcomes has become central in perinatal medicine research.[1] Traditionally, full-term infants are neonates born after 37 weeks but before 42 weeks of gestation.[2,3] However, advancements in clinical practice have revealed that even among infants deemed full-term, specific gestational ages significantly influence their prognosis and health outcomes.[4,5] In response to these findings, the American College of Obstetricians and Gynecologists refined the classification of full-term infants into early full-term pregnancies (37–38 weeks), full-term pregnancies (39–40 weeks), and late-term pregnancies (41 weeks).[6] This classification underscores the importance of considering specific gestational ages when assessing the health outcomes of full-term infants.[7–9] Studies have shown that infants born during the early full-term period are more susceptible to perinatal risk factors and have higher morbidity rates compared to those born late-term.[10–13] These risks and morbidities may be related to the physiological immaturity and incomplete development of critical organ systems in infants born at earlier gestational ages.[14,15]

Infants born in the early full-term period may face challenges such as respiratory dysfunction, poor temperature regulation, feeding difficulties, and neurodevelopmental issues.[16–18] In contrast, infants born during the standard full-term period (39–40 weeks) typically exhibit better health outcomes compared to those born either early or, in some cases, late-term.[19–22] This finding highlights the reduced risk of adverse perinatal outcomes and the likelihood of optimal development and well-being for infants born around 40 weeks.[23] Recognizing the significance of gestational age in assessing the health outcomes of full-term infants is crucial, as deviations from the optimal gestational range can have profound effects on an infant's short-term and long-term well-being.[24–27]

In the United States, approximately 1.5 million nulliparous women give birth each year,[28] with over half of these pregnancies classified as low-risk.[29–33] For these low-risk nulliparous women, the morbidity rates for both neonates and mothers show a moderate increase from 39 to 41 weeks of gestation.[34,35] In China, there were about 14.55 million live births in 2019,[36] yet information on nulliparous women and full-term births is less frequently published, with research on related morbidity being scarce.[37,38] Although the incidence of adverse pregnancy outcomes in full-term infants is relatively low,[39,40] given the large birth population, these adverse outcomes remain a significant public health concern.[41] Particularly in China, and specifically in Hunan Province, the lack of research on gestational age-related perinatal morbidity underscores the urgent need for comprehensive studies in this area.[42–44]

Therefore, based on the hypothesis that an increase in gestational weeks may reduce the likelihood of experiencing various complications, this study aims to compare the rates of neonatal and maternal complications in low-risk primiparas delivering at different gestational weeks (37–38 weeks, 39–40 weeks, and 41 weeks). This will help to reveal the potential impact of delivery timing on maternal and neonatal health outcomes in low-risk pregnancies. This analysis aims to provide empirical evidence

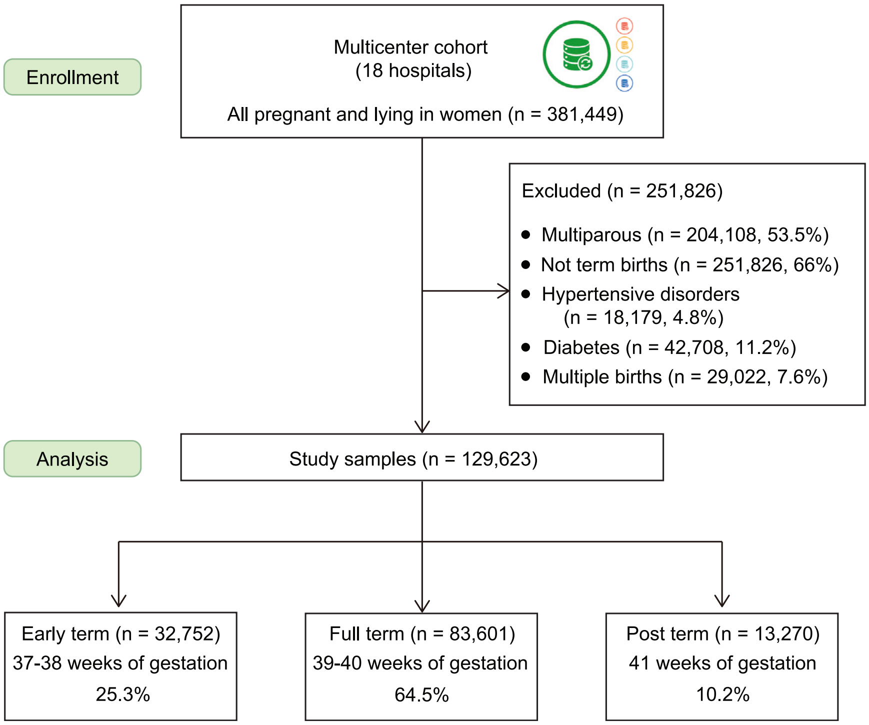

Figure 1. Study cohort selection flowchart (2015–2019)

to guide clinical decision-making on optimal timing for delivery, ultimately optimizing the health outcomes for low-risk nulliparous women and their neonates.

RESULTS

Association analysis between gestational ages and maternal characteristics

Between 2015 and 2019, data from 381,449 pregnancies were recorded across 18 hospitals in Hunan Province. After screening, 129,623 pregnant women met the study criteria (for detailed selection criteria, refer to the Methods section, Figure 1). Of these, 32,752 women (25.3%) delivered at gestational ages of 37–38 weeks, 83,601 women (64.5%) at 39–40 weeks, and 13,270 women (10.2%) at 41 weeks (Figure 1). The American College of Obstetricians and Gynecologists categorizes these stages as early full-term, full-term, and late-term, respectively.

Table 1 stratifies the characteristics of pregnant women by stages of gestational age. Compared to those in the early and full-term stages, women delivering at 41 weeks were younger (below 35 years), had a higher level of education, and received more prenatal care. Furthermore, the rates of cesarean delivery varied significantly across gestational ages: 30.4% ($n = 9{,}954$) for 37–38 weeks, 29.9% ($n = 25{,}022$) for 39–40 weeks, and 39.1% ($n = 5{,}190$) for 41 weeks, indicating that the rate of cesarean delivery was similar between 37–38 weeks and 39–40 weeks, with a notable increase at 41 weeks ($p < 0.001$).

Comprehensive assessment of neonatal morbidity

The overall rate of comprehensive neonatal morbidity was 25.04 cases per 1,000 live births. At gestational ages of 37–38 weeks, the rate was 47.11 cases per 1,000 live births (1,543/32,756), compared to 17.92 cases per 1,000 live births (1,498/83,601) at 39–40 weeks and 15.45 cases per 1,000 live births (205/13,268) at 41 weeks. Adjusted multivariate Poisson regression model results indicated that the risk of comprehensive neonatal morbidity was significantly higher at 37–38 weeks (ARR = 2.627, 95% CI = 2.450–2.818) and significantly lower at 41 weeks (ARR = 0.860, 95% CI = 0.744–0.994) compared to 39–40 weeks. Apart from the Apgar score below 5 at 1 min, all other indicators of comprehensive neonatal morbidity significantly decreased in risk when comparing 39–40 and 41 weeks to 37–38 weeks (Figure 2). Therefore, these results suggest that increased gestational age is associated with improved neonatal health outcomes. Further stratified by mode of delivery, showed that the risk of composite neonatal morbidity decreased more significantly with increasing gestational age among cesarean section deliveries. Compared to gestational age of 39–40 weeks, the risk of a 1-min Apgar score below 5 was lower in neonates delivered vaginally at 37–38 weeks, whereas there was no significant difference observed among neonates delivered by cesarean section (Figure S1).

Statistical analysis of maternal comprehensive morbidity rate

The overall maternal composite morbidity rate was 293.96 per 1,000 live births (38,104/129,623). For composite complications, the risk was slightly lower at 37–38 weeks compared to 39–40 weeks (aRR = 0.957, 95% CI = 0.938–0.976), but significantly increased at 41 weeks (aRR = 1.134, 95% CI = 1.105–1.164). Among the three gestational age groups, there were no significant differences in the risks of obstetric hemorrhage, obstetric infection, or maternal transfusion. However, the risk of anemia was significantly higher at 39–40 weeks and 41 weeks compared to 37–38 weeks (Figure 3). This finding may indicate that the risk of maternal anemia increases with longer gestation. Further stratification by mode of delivery revealed that the risk of maternal transfusion was significantly lower for vaginal deliveries at 37–38 weeks, while there was no significant difference for cesarean section deliveries (Figure S2).

Mendelian randomization analysis: Exploring the potential causal link between pregnancy and anemia

This Mendelian randomization analysis investigated the potential causal relationship between pregnancy (exposure) and anemia (outcome). Initially, data were extracted from the VCF

Table 1. Maternal characteristics

Characteristic	Total (N = 129623)	Gestational Age (wk) 37–38 (n = 32752)	39–40 (n = 83601)	41 (n = 13270)	P
Maternal age					
<20	1756 (1.4)	728 (2.2)	898 (1.1)	130 (1.0)	p < 0.001
20–34	120341 (92.8)	30234 (92.3)	77639 (92.9)	12468 (94.0)	
≥35	5517 (4.3)	1308 (4.0)	3715 (4.4)	494 (3.7)	
Unknown	2009 (1.5)	482 (1.5)	1349 (1.6)	178 (1.3)	
Maternal education					
Less than high school	20715 (16.0)	5206 (15.9)	13423 (16.1)	2086 (15.7)	p < 0.001
High school	52582 (40.5)	13338 (40.7)	33763 (40.4)	5481 (41.3)	
More than high school	55978 (43.2)	14111 (43.1)	36196 (43.2)	5671 (42.8)	
Unknown	348 (0.3)	97 (0.3)	219 (0.3)	32 (0.2)	
Marital status:married	128839 (99.4)	32187 (98.3)	83601 (100.0)	13051 (98.3)	p < 0.001
Prenatal care					
0	234 (0.2)	62 (0.2)	154 (0.2)	18 (0.1)	p < 0.001
1–5	8670 (6.7)	2511 (7.7)	5401 (6.5)	758 (5.7)	
≥5	118312 (91.3)	29533 (90.1)	76468 (91.4)	12311 (92.8)	
Unknown	2407 (0.8)	646 (2.0)	1578 (1.9)	183 (1.4)	
Cesarean delivery	40166 (31.0)	9954 (30.4)	25022 (29.9)	5190 (39.1)	p < 0.001
Neonatal sex:male	66127 (51.0)	18073 (55.2)	41855 (50.1)	6199 (46.7)	p < 0.001
Year					
2015	33521 (25.9)	8205 (25.1)	21570 (25.8)	3746 (28.2)	p < 0.001
2016	27096 (20.9)	7375 (25.5)	17308 (20.7)	2413 (18.2)	
2017	24347 (18.8)	6156 (18.7)	15768 (18.9)	2423 (18.3)	
2018	22908 (17.7)	5629 (17.2)	14889 (17.8)	2390 (18.0)	
2019	21751 (16.8)	5390 (16.5)	14065 (16.8)	2296 (17.3)	

file "ukb-b-17553.vcf.gz," selecting genetic variants with p values below 5e-06 for further analysis. Manhattan plots (Figures S3A and S3B), generated using the CMplot package, displayed the genetic variants and their associations with pregnancy.

Subsequently, the TwoSampleMR package was utilized for Mendelian randomization analysis. We analyzed the association between pregnancy and anemia by applying methods such as the IVW, MR Egger regression, and the weighted median approach. The results indicated no significant causal link between pregnancy and anemia (Figures S3C and S3D; Table S1). Furthermore, heterogeneity tests (Table S2) and pleiotropy tests (Table S3) did not reveal significant issues, enhancing the consistency and reliability of our analysis. Additional assessments of robustness were conducted through scatterplots, forest plots, funnel plots, and leave-one-out sensitivity analyses, demonstrating the consistency of the genetic instrumental variants used and the stability of the analysis results (Figures S3C–S3F).

In conclusion, although our Mendelian randomization analysis did not find a significant causal relationship between pregnancy and anemia, this outcome suggests that the association may be more influenced by non-genetic factors such as environment, nutrition, and other health conditions. This finding is significant for understanding and managing anemia during pregnancy.

Sensitivity analysis of the impact of gestational ages

In the sensitivity analysis (Table 2), no significant differences were observed in the overall maternal composite morbidity (excluding anemia) among women delivering at 37–38 weeks, 39–40 weeks, and 41 weeks. This result suggests that the maternal health risks may be similar across different gestational ages, though further research is needed to identify specific risk factors.

Impact of perinatal period on mode of delivery

To explore the impact of different perinatal periods and maternal characteristics on the mode of delivery, univariate, and multivariate logistic regression analyses were conducted (Table 3). Compared to deliveries at 37–38 weeks, the likelihood of cesarean section was lower for deliveries at 39–40 weeks (OR = 0.11, 95% CI = 0.86–0.95) and higher for deliveries at 41 weeks (OR = 1.10, 95% CI = 1.03–1.18). The risk of cesarean section increased with advancing maternal age (OR = 1.08, 95% CI = 1.08–1.09). Compared to other education levels, both high school (OR = 0.35, 95% CI = 0.33–0.37) and college education (OR = 0.11, 95% CI = 0.10–0.12) were significantly associated with a reduced risk of cesarean section. The number of medical interventions during pregnancy was significantly related to the mode of delivery, though this association does not necessarily imply causality. In summary, women who are full-term, younger,

Multivariate Poisson Regression Model

Characteristics		Number (rate/1000)	aRR (95%CI)
Copmosite neonatal morbidity	**Total**	**3246 (25.04)**	
	37–38W	1543 (47.11)	2.627(2.450,2.818)
	39–40W	1498 (17.92)	1
	41W	205 (15.45)	0.860(0.744,0.994)
Apgar score below 5 at 1min	**Total**	**1334 (10.3)**	
	37–38W	442 (13.54)	1.253(1.119,1.404)
	39–40W	796 (9.52)	1
	41W	96 (7.23)	1.158(0.982,1.365)
Apgar score below 5 at 5min	**Total**	**171 (1.32)**	
	37–38W	72 (2.21)	2.008(1.469,2.746)
	39–40W	89 (1.06)	1
	41W	10 (0.75)	0.693(0.361,1.330)
Low weight (< 2500g)	**Total**	**1749 (13.5)**	
	37–38W	1132 (34.6)	4.951(4.484,5.466)
	39–40W	587 (7.02)	1
	41W	30 (2.26)	0.323(0.224,0.466)
Death of the newborn	**Total**	**39 (0.3)**	
	37–38W	15 (0.46)	1.412(0.702,2.842)
	39–40W	21 (0.25)	1
	41W	3 (0.23)	0.543(0.160,1.835)

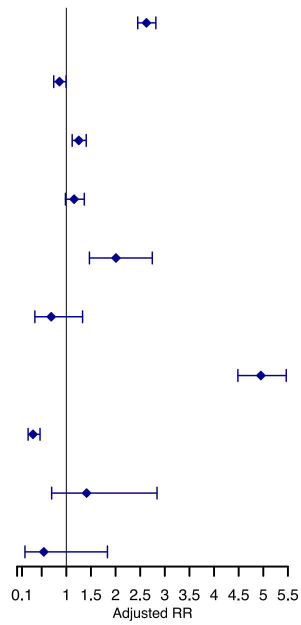

Figure 2. Risk comparison of various neonatal morbidities under multivariate Poisson regression model

This figure presents the adjusted relative risks (aRR) and their 95% confidence intervals (CIs) for neonatal complications across different gestational ages (37–38 weeks, 39–40 weeks, 41 weeks). The data are derived from a multivariable Poisson regression analysis, with 39–40 weeks as the reference group.

and have higher education levels are more likely to have a natural delivery.

Factors influencing gestational age at delivery

Logistic regression analysis (Table 4) revealed that nulliparous women's age, educational background, and marital status do not significantly impact their perinatal medical decisions. Additionally, the number of prenatal care visits is strongly correlated with perinatal choices, with women closer to their due date tending to have more prenatal care visits. However, this result does not definitively indicate a direct causal relationship between the number of prenatal care visits and perinatal choices, suggesting the need for further exploration of other potential influencing factors.

DISCUSSION

This population-based study aimed to investigate the relationship between gestational ages and morbidity rates in low-risk nulliparous women. Our findings highlight the significant impact of the delivery timing on outcomes for neonates and mothers. The data show that a majority (64.5%, n = 83,601) of low-risk nulliparous women delivered at 39 or 40 weeks, underscoring the prominence of this gestational age range in the overall population. However, our analysis indicates that the rates of comprehensive neonatal morbidity are significantly higher for early full-term (37–38 weeks) and late-term (41 weeks) pregnancies compared to full-term (39–40 weeks). In particular, early-term infants are more likely to experience respiratory issues due to the immaturity of their organs, while late-term infants face a higher risk of birth weight-related problems and intrauterine distress. Additionally, individual components of comprehensive neonatal morbidity exhibited a similar pattern, with risks being higher at the extremities of the full-term period.

Supported by sensitivity analysis, our findings confirm an association between overall composite neonatal complications and gestational age within the 37 to 41-week range among low-risk women. These results underscore the critical role of optimal timing of delivery in reducing adverse neonatal outcomes. Previous studies have also reported an increase in the frequency of adverse outcomes as gestational age progresses from 39 to 41 weeks, further supporting the importance of our findings. Compared to previous studies, our research further reveals the heightened sensitivity of early-term infants (37–38 weeks) to perinatal risk factors. The study by Ozgul Bulut et al. also found a significantly increased risk of respiratory diseases in early-term newborns, mainly due to immature lung development.[45] However, our study is based on a larger data sample and includes a comprehensive analysis of various perinatal complications, such as respiratory diseases, neonatal hypoglycemia, jaundice, and other common neonatal complications. It not only confirms the high sensitivity of early-term newborns to risks but also provides broader epidemiological evidence. The multidimensional data analysis allows us, for the first time, to systematically assess the incidence risk of early-term newborns across various complications, providing a new evidence base for understanding the impact of different gestational ages on neonatal health.

When comparing the composite neonatal complication rate observed in our study (25.04 per 1,000 live births) with other studies, we found significant differences. Our rate was higher than the composite neonatal complication rate reported in the U.S. Vital Statistics study (8.8/1,000 live births)[39] but lower than the rate reported in the ARRIVE trial (55.6/1,000 live births).[46] These differences may stem from variations in study design and inclusion criteria. The U.S. Vital Statistics study focuses on macro-level statistics with limited analysis of individual characteristics, while the ARRIVE trial emphasizes clinical interventions with a smaller sample size concentrated on a specific population. In contrast, our study adopts stricter inclusion criteria, focusing on perinatal outcomes in low-risk primiparas. Through a comprehensive analysis of complications, our research offers more precise clinical guidance for the timing of

Multivariate Poisson Regression Model

Characteristics		Number (rate/1000)	aRR (95%CI)
Copmosite maternal morbidity	**Total**	**38104 (293.96)**	
	37–38W	9173 (280.07)	0.957(0.938,0.976)
	39–40W	24494 (292.99)	1
	41W	4437 (334.36)	1.134(1.105,1.164)
Obstetric Hemorrhage	**Total**	**9458 (72.97)**	
	37–38W	2389 (72.94)	0.998(0.954,1.045)
	39–40W	6115 (73.15)	1
	41W	954 (71.89)	0.968(0.906,1.034)
Obstetric infection	**Total**	**2111 (16.29)**	
	37–38W	494 (15.08)	0.931(0.840,1.031)
	39–40W	1383 (16.54)	1
	41W	234 (17.63)	1.052(0.917,1.207)
Maternal transfusion	**Total**	**1081 (8.34)**	
	37–38W	267 (8.15)	1.028(0.892,1.184)
	39–40W	675 (8.07)	1
	41W	139 (10.47)	1.279(1.065,1.535)
Anemia	**Total**	**31457 (242.68)**	
	37–38W	7440 (227.16)	0.942(0.920,0.964)
	39–40W	20163 (241.18)	1
	41W	3854 (290.43)	1.200(1.165,1.235)

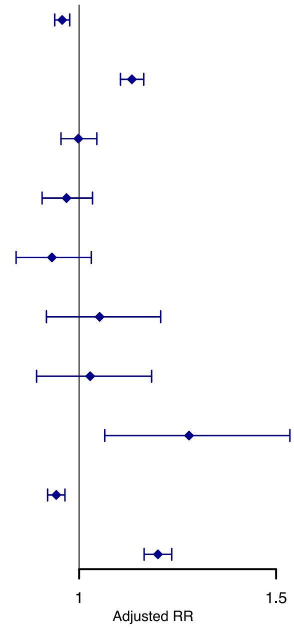

Figure 3. Comparison of maternal morbidity risks under multivariate Poisson regression model

This figure displays the ARRs and their 95% CIs for maternal morbidities across different gestational ages (37–38 weeks, 39–40 weeks, 41 weeks), derived from multivariate Poisson regression analysis, with 39–40 weeks as the reference group.

delivery in low-risk primiparas, particularly applicable to regions with relatively limited data, such as Hunan Province.[47–50]

Regarding maternal complications, our study found an association between gestational age and an increased risk. Specifically, we observed that women delivering at 39–40 weeks and 41 weeks had a higher overall composite maternal complication rate compared to those delivering at 37–38 weeks. Although no significant differences were observed between gestational age groups in the risks of obstetric hemorrhage, obstetric infection, or maternal transfusion, the incidence of anemia increased with gestational age. This may be related to the risk of perinatal blood loss associated with mechanical or surgical interventions during delivery as gestation progresses and the baby becomes larger.[51] Anemia during pregnancy is associated with adverse perinatal outcomes, including preterm birth, premature rupture of membranes, and increased maternal and neonatal mortality. However, since the samples in this study were all full-term infants (37–41 weeks), we were unable to assess the potential association between hemoglobin levels and the risk of preterm birth. This characteristic may limit our ability to analyze risks related to low birth weight or preterm birth. Therefore, future studies should consider including preterm samples to more comprehensively explore the impact of hemoglobin levels on adverse pregnancy outcomes.

Despite the generally low prevalence of adverse outcomes in pregnancies without morbidity, their clinical significance should not be overlooked. In China, with over 10 million live births annually, data on low-risk pregnancies without morbidity are limited.[52–56] Although infrequent, the cumulative impact of adverse outcomes can affect many individuals. These findings highlight the importance of increasing awareness of the potential risks associated with early full-term deliveries and preventing avoidable morbidity.[57]

The strength of our study lies in its population-based design. It encompasses data from 18 medical institutions over five years, providing a comprehensive overview of the morbidity rates for neonates and mothers among low-risk women. This data-driven approach lays a solid foundation for ensuring maternal and neonatal safety and improving the quality of neonatal care.

Our study holds significant value for clinical practice, especially in optimizing delivery timing to enhance maternal and neonatal health outcomes. By systematically analyzing the morbidity rates among low-risk nulliparous women delivering at different gestational ages, our findings offer empirical evidence to clinicians regarding the optimal timing for childbirth. Notably, our results underscore the importance of avoiding early full-term deliveries (37–38 weeks) unless medically indicated, as delivering during this period may increase the risk of neonatal morbidity. Additionally, our research supports delaying delivery to 39–40 weeks without morbidity to reduce adverse outcomes. This information aids in guiding pregnant women and healthcare providers to make more informed delivery plans, optimize perinatal care, minimize unnecessary medical interventions, and enhance the quality of maternal and neonatal health outcomes.

Despite the valuable insights provided, our study has limitations. Firstly, the retrospective, population-based design precludes establishing a causal relationship between gestational age and morbidity. Secondly, data collection relied on medical institutions' maternal and neonatal information systems, possibly subject to entry biases or incompleteness. Although we adjusted for maternal age, maternal education level, marital status, and year of delivery, residual confounding factors such as socioeconomic status cannot be entirely ruled out. Additionally, our study was limited to low-risk primiparas, so the findings may not be generalizable to women with high-risk pregnancies or multiple gestations. Finally, the study sample was concentrated in 18 hospitals in Hunan Province, which may limit the generalizability of our findings to broader geographic regions. Moreover, our study was limited to low-risk nulliparous women. Thus, the results may not apply to women with high-risk or multiple pregnancies. Finally, focusing on 18 Hunan Province hospitals may limit our findings' generalizability to a broader geographical area.

Table 2. Sensitivity analysis: composite maternal morbidity without anemia

	Gestational Age (wk)	Total Live Births	N	Rate/1000 Live Births	Unadjusted RR(95% CI)	Adjusted RR(95% CI)
Copmosite maternal morbidity	Total	129623	11335	87.45		
	37–38 W	32752	2855	87.17	0.994 (0.953,1.036)	1.002 (0.961,1.044)
	39–40 W	83601	7308	87.42	1	1
	41 W	13270	1172	88.32	1.005 (0.948,1.066)	0.996 (0.939,1.057)

RR, relative risk. Composite maternal morbidity includes admission to Composite maternal morbidity includes admission to obstetric hemorrhage, obstetric infection, and maternal transfusion.

Multivariate Poisson regression model were adjusted for maternal age, education, marital status, year.

Future research should address these limitations and further deepen our understanding of the relationship between gestational ages and maternal and neonatal health outcomes. Prospective cohort studies or randomized controlled trials could help establish a causal relationship between gestational age and morbidity. Expanding the study's geographical coverage and sample diversity, including women with high-risk and multiple pregnancies, would enhance the general applicability of our findings. Additionally, exploring the underlying mechanisms affecting the relationship between gestational ages and morbidity, such as genetic, environmental, and lifestyle factors, would provide a more precise basis for targeted prevention and intervention measures. Moreover, the sample selection in this study was limited to low-risk primiparas who delivered at term, which prevented a comprehensive evaluation of the potential impact of hemoglobin levels on adverse outcomes such as preterm birth or low birth weight. This sample choice may have limited our ability to observe certain potential associations. Future research should address this limitation by including samples from different gestational ages. Future studies should also consider evaluating the impact of delivery timing decisions on maternal mental health and how to maximally meet pregnant women's preferences and expectations while ensuring safety.

Here is a suggested "Limitations of Study" paragraph for the manuscript.

Limitations of the study

This study has several limitations that should be considered when interpreting the findings. First, as a retrospective analysis using data from the Maternal and Child Health Surveillance database, there is potential for selection and reporting biases, which may affect the generalizability of results. The study sample was limited to low-risk nulliparous women with singleton pregnancies, potentially limiting the applicability of these findings to women with high-risk or multiple gestations. Additionally, while we adjusted for key factors, such as maternal age, education level, and year of delivery, residual confounding from unmeasured variables, such as socioeconomic status and lifestyle factors, cannot be fully ruled out. The study's reliance on administrative data also precluded detailed clinical assessments that

Table 3. Logistic regression outcomes of potential effects on delivery mode

Delivery mode	Eutocia (N = 87489)	Cesarean (N = 39302)	OR (univariable)	OR (multivariable)
Gestational Age (wk)				
37–38	22175 (25.3%)	9728 (24.8%)		
39–40	57369 (65.6%)	24465 (62.2%)	0.97(0.95–1.00)	0.90(0.86–0.95)
41	7945 (9.1%)	5109 (13%)	1.47(1.40–1.53)	1.10(1.03–1.18)
Age (Mean ± SD)	26.2 ± 3.6	27.3 ± 4.0	1.08(1.08–1.09)	1.08(1.08–1.09)
Education				
Other	13179 (15.1%)	6605 (16.8%)		
High school	34004 (38.9%)	17580 (44.7%)	1.03(1.00–1.07)	0.35(0.33–0.37)
University	40306 (46.1%)	15117 (38.5%)	0.75(0.72–0.77)	0.11(0.10–0.12)
Marriage				
Married	85925 (98.2%)	38723 (98.5%)		
Unmarried	1561 (1.8%)	579 (1.5%)	0.82(0.75–0.91)	1.24(1.05–1.47)
Number of medical solution				
0–1	77269 (88.3%)	2785 (7.1%)		
More	10220 (11.7%)	36517 (92.9%)	99.13(94.90–103.56)	153.97(146.12–162.24)

OR, odds ratio, from univariate and multivariate logistic regression analyses are reported to assess the influence of gestational age, maternal age, education, marital status, and the number of medical interventions on the mode of delivery. ORs are accompanied by 95% confidence intervals (CIs), with significance indicated by p values. Higher ORs suggest a greater likelihood of cesarean delivery associated with the respective variable, adjusted for in the multivariate model.

Table 4. Logistic regression outcomes of potential effects on gestational age

Gestational Age(wk)		37–38 (*N* = 31311)	39–40 (*N* = 80401)	41 (*N* = 12892)	OR (univariable)	OR (multivariable)
Age	Mean ± SD	26.8 ± 3.9	26.6 ± 3.7	26.6 ± 3.6	0.99 (0.98–0.99, *p* <0 .001)	0.98 (0.98–0.98, *p* <0 .001)
Education	Other	4737 (15.1%)	12311 (15.3%)	1942 (15.1%)		
	High school	12853 (41%)	32717 (40.7%)	5374 (41.7%)	0.98 (0.95–1.02, *p* = 0.440)	
	University	13721 (43.8%)	35373 (44%)	5576 (43.3%)	0.99 (0.95–1.03, *p* = 0.675)	
Marriage	Married	30797 (98.4%)	79058 (98.3%)	12691 (98.4%)		
	unmarried	514 (1.6%)	1342 (1.7%)	201 (1.6%)	1.01 (0.91–1.11, *p* = 0.882)	
Number of prenatal care	0–4	2463 (7.9%)	5321 (6.6%)	748 (5.8%)		
	5–9	18581 (59.3%)	45126 (56.1%)	6977 (54.1%)	1.14 (1.08–1.20, *p* <0 .001)	1.17 (1.11–1.23, *p* <0 .001)
	10–14	10144 (32.4%)	29226 (36.4%)	5011 (38.9%)	1.37 (1.30–1.44, *p* <0 .001)	1.44 (1.37–1.52, *p* <0 .001)
	15-	123 (0.4%)	728 (0.9%)	156 (1.2%)	2.92 (2.40–3.54, *p* <0 .001)	3.02 (2.49–3.67, *p* <0 .001)

OR, odds ratio, are presented for both univariate and multivariate logistic regression analyses, with the univariate analysis examining each variable individually and the multivariate analysis adjusting for all variables simultaneously. ORs with 95% confidence intervals (CIs) are shown in brackets, with statistical significance indicated by a *p* value less than 0.05.

could offer deeper insights into specific complications. Lastly, as the data were collected from hospitals within a single province, the findings may not be generalizable to other regions with differing healthcare practices or population characteristics. Future prospective studies with broader geographic and demographic scope are needed to confirm these findings and explore additional contributing factors.

Conclusion

In summary, our population-based study analyzed the association between gestational ages and morbidity rates in neonates and mothers among low-risk nulliparous women (Figure 4). The findings highlight the increased risks to neonatal health during early full-term gestational ages and to maternal health during late-term gestational ages. These insights contribute to a better understanding of the optimal timing for delivery, emphasizing the need to prioritize maternal and neonatal safety. The experimental design of our study and the comprehensive data it utilized lay a foundation for enhancing care quality and promoting neonatal health in the population.

RESOURCE AVAILABILITY

Lead contact

Further information and requests for resources should be directed to and fulfilled by the lead contact, Fanjuan Kong (kfj8541684@sina.com).

Materials availability

This study did not generate new unique reagents or materials.

Data and code availability

- Data: the data generated during this study are available from the corresponding author on reasonable request.
- Code: custom statistical scripts used for analyses can also be requested from the corresponding author.
- Restrictions: due to privacy concerns, access to detailed clinical data requires institutional ethical approval.

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AUTHOR CONTRIBUTIONS

F.K. and Z.S. conceptualized and designed the study. B.L. contributed to data collection and management. J.L. and Y.C. performed the statistical analysis and interpretation of the data. F.K. drafted the manuscript, and Z.S. critically reviewed and revised the manuscript for important intellectual content. All authors have read and approved the final manuscript.

DECLARATION OF INTERESTS

The authors declare no competing interests.

STAR★METHODS

Detailed methods are provided in the online version of this paper and include the following:

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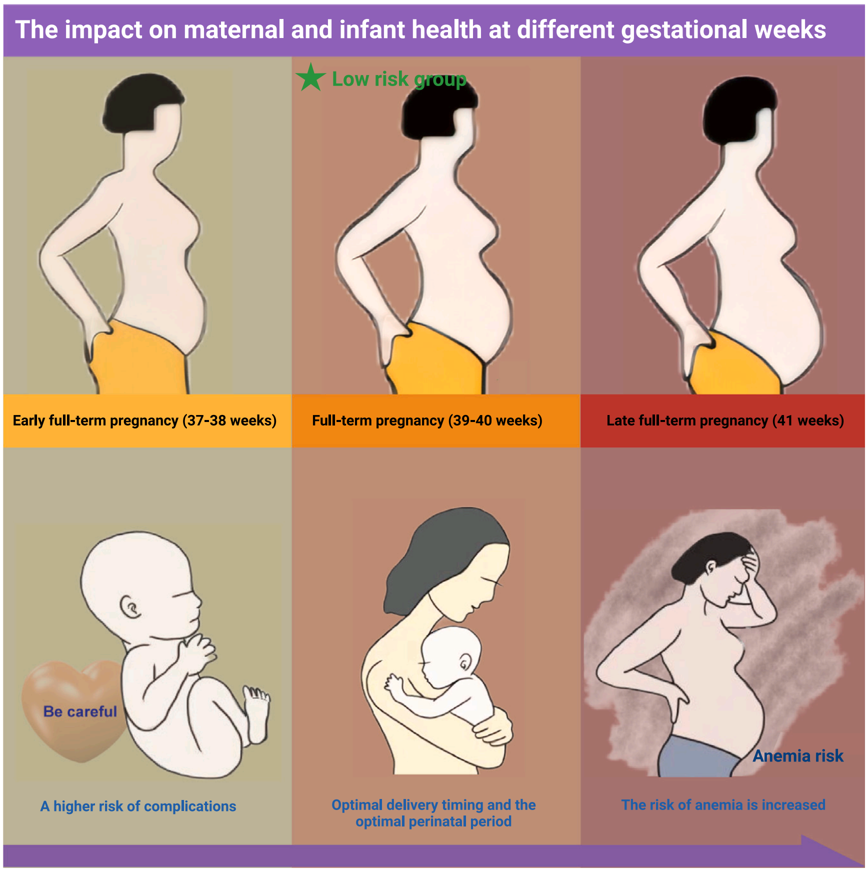

Figure 4. The impact of different gestational ages on maternal and neonatal health among low-risk nulliparous women

SUPPLEMENTAL INFORMATION

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STAR★METHODS

KEY RESOURCES TABLE

REAGENT or RESOURCE	SOURCE	IDENTIFIER
Biological samples		
	Hunan Maternal and Child Health Surveillance Database	Hunan Provincial Maternal and Child Health Hospital; Approval No.: 2020S072
Deposited data		
	Statistical code and metadata	This paper; Available upon request from corresponding author
Software and algorithms		
	IBM SPSS Statistics 23.0	IBM; https://www.ibm.com/products/spss-statistics
	R 3.6.1	The R Project for Statistical Computing; https://www.r-project.org/
	VariantAnnotation	CRAN: https://cran.r-project.org
	gwasglue	CRAN: https://cran.r-project.org
	dplyr	CRAN: https://cran.r-project.org
	tidyr	CRAN: https://cran.r-project.org
	CMplot	CRAN: https://cran.r-project.org
Other		
	Hunan Maternal and Child Health Surveillance Database	Hunan Provincial Maternal and Child Health Hospital; No publicly available data; subject to institutional data-sharing policy

EXPERIMENTAL MODEL AND STUDY PARTICIPANT DETAILS

The data for this study were sourced from the Hunan Province Maternal and Child Health Surveillance Database, covering the period from January 2015 to December 2019. This database, established by the national government, compiles comprehensive information on the childbirth process and clinical data of neonates from 18 designated medical institutions. Data collection was conducted by trained professionals, who systematically recorded information and followed standardized protocols to ensure data accuracy and completeness. Quality control measures included double-checking data entries and verification by higher authorities to maintain data integrity.

The database includes detailed personal information, maternal hospital admission records, comorbidities, and maternal and neonatal health outcomes. Participants in the study were classified into two groups: nulliparous (first-time mothers) and multiparous (mothers with previous births). The study included only those participants with complete clinical information.

Additionally, this study includes no personally identifiable information to ensure privacy. Eligible participants were required to meet the following criteria: (1) gestational ages of 37–41 weeks; (2) singleton pregnancies; (3) absence of gestational hypertension; (4) absence of gestational diabetes; (5) nulliparous; (6) absence of cardiovascular disease (CVD); (7) absence of chronic kidney disease (CKD); (8) absence of other comorbidities. The age of the included participants ranged from 18 to 45 years, with a median age of 28 years. The study included both maternal and neonatal data, and the majority of the newborns were full-term (39–40 weeks), with a balanced distribution of male and female neonates.

This study strictly adhered to ethical guidelines to protect participant privacy, ensuring that no personally identifiable information was included in the analysis. The study protocol received approval from the Hunan Provincial Maternal and Child Health Hospital's Medical Ethics Committee (Approval No.: 2020S072). Informed consent was obtained from all participants before data collection, ensuring that they understood the study's purpose and procedures.

METHOD DETAILS

Study variables and outcomes

In this study, the primary exposure variable was gestational age at the time of delivery, with the primary outcome of interest being the comprehensive morbidity rate in neonates. This rate includes several indicators, such as Apgar scores below 5 at 1 and 5 min, low birth weight (below 2500 g), and neonatal death before maternal discharge. Moreover, maternal comprehensive morbidity rates were also examined, including postpartum hemorrhage (500 mL blood loss within 24 h of vaginal delivery, or more than 1000 mL for cesarean deliveries), obstetric infections, transfusions, and anemia (hemoglobin below 100 g/L). In calculating the incidence of comprehensive outcomes, if multiple outcomes occurred in a neonate or woman, it was counted only once to avoid data duplication.

Mendelian randomization analysis

We employed Mendelian randomization analysis to investigate the potential causal relationship between pregnancy and anemia. This analysis utilized the R package TwoSampleMR, with pregnancy (ID: "ukb-b-17553") as the exposure and anemia (ID: "ebi-a-GCST90038678") as the outcome. Initially, genetic instrumental variants associated with pregnancy were extracted from the GWAS database (https://gwas.mrcieu.ac.uk/) using the extract_instruments function, with significance thresholds set (p1 = 5e-06, p2 = 5e-08) and linkage disequilibrium filtering applied, ensuring only independent variants were included. Data manipulation and extraction of outcome data related to anemia were performed using the extract_outcome_data function. The data were then harmonized using the harmonise_data function to ensure alignment between the effect alleles of the exposure and outcome datasets, minimizing bias due to strand inconsistencies.

Data visualization was conducted using R packages such as CMplot for generating Manhattan and QQ plots, providing a visual overview of genetic variant distribution and p-value distributions. Additional data manipulation was performed using VariantAnnotation, gwasglue, dplyr, and tidyr to prepare the data for analysis.

The MR analysis applied multiple statistical methods to assess the robustness of the causal estimates, including inverse variance weighting (IVW), which provides a weighted average of the causal estimates assuming no horizontal pleiotropy. Egger regression was used to detect potential pleiotropy by allowing for a non-zero intercept, which indicates systematic pleiotropic effects. Weighted median estimation provided a robust estimate even when up to 50% of the instrumental variables were invalid. Simple mode and weighted mode methods offered additional sensitivity analyses to confirm the findings under different assumptions.

Heterogeneity analysis and pleiotropy testing were performed to evaluate the consistency of results across genetic variants, using scatterplots to visualize the relationship between SNP-exposure and SNP-outcome associations. Forest plots were used to show individual SNP effects and their confidence intervals, while funnel plots assessed potential asymmetry indicative of bias. A leave-one-out sensitivity analysis was conducted to assess the influence of each SNP on the overall causal estimate by iteratively removing one variant at a time. These analyses provided a comprehensive assessment of the potential causal relationship between pregnancy and anemia, contributing to a deeper understanding of the role of specific genetic variants in this association.

Perinatal period and delivery method association analysis

Delivery methods in the existing database were categorized into vaginal delivery and cesarean delivery. Due to the low number of births by other methods, they were excluded from this analysis. Additionally, the analysis incorporated variables such as gestational age, age, educational background, marital status, and medical interventions. Univariate and multivariate logistic regression analyses were conducted to assess the impact of these factors on the choice of delivery method, calculating the odds ratios (ORs) and their 95% confidence intervals (CIs).

Analysis of factors influencing perinatal choices

To explore the potential influencing factors on perinatal choices among pregnant women, data including gestational ages, age, educational background, marital status, and number of prenatal care visits were extracted from electronic health records. Logistic regression analysis, both univariate and multivariate, was utilized to evaluate the impact of these factors on perinatal decision-making. The ORs and their 95% CIs were calculated, with statistical significance assessed through *p*-values.

Analysis of factors influencing mode of delivery and gestational age at birth

Perinatal decisions include factors such as the timing of delivery, the mode of delivery (vaginal delivery vs. cesarean section), and other medical interventions during childbirth. This study extracted data from electronic health records, including variables such as mode of delivery, gestational age at birth, age, educational background, marital status, and the number of prenatal care visits. The modes of delivery in the existing database were classified into two groups: natural delivery and cesarean section. Due to the small number of deliveries by other methods, these were excluded from the analysis in this study. Univariate and multivariate logistic regression analyses were used to assess the potential impact of various factors on the choice of delivery mode and gestational age at birth, with the calculation of odds ratios (ORs) and their 95% confidence intervals (95% CIs).

QUANTIFICATION AND STATISTICAL ANALYSIS

The chi-square (χ^2) test was used to analyze the descriptive categorical variables of maternal characteristics across different gestational weeks. The overall neonatal and maternal morbidity rates, as well as the morbidity rates for each factor, were reported per 1,000 live births. Deliveries were categorized into three groups based on gestational age: early-term (37–38 weeks), full-term (39–40 weeks), and late-term (41 weeks). To explore the association between gestational age at delivery (with 39–40 weeks as the reference) and the risk of composite maternal and neonatal morbidity as well as individual morbidity factors, a multivariable Poisson regression model was employed. The regression model was adjusted for maternal age (categorized as <20 years, 20–34 years, and $\geq$35 years), maternal education level (categorized as below high school, high school, above high school, unknown), marital status (categorized as married, unmarried), and year of delivery (categorized as 2015, 2016, 2017, 2018, 2019). The results are presented as adjusted relative risks (aRRs) with 95% confidence intervals (CIs). Subgroup analyses were conducted based on the mode of delivery to investigate the impact of delivery mode (vaginal delivery vs. cesarean section) on the associations. For cases with missing data on maternal age, maternal education level, or prenatal care, a separate "unknown" category was created for analysis. Additionally, a sensitivity analysis was performed to explore the relationship between adverse outcomes in non-vertex deliveries and gestational age, excluding deliveries with breech, other, or unknown fetal positions. All statistical analyses and forest plots in this study were conducted using IBM SPSS Statistics 23.0 and R 3.6.1, ensuring precise data handling and efficient analysis, in line with international scientific research standards.

ADDITIONAL RESOURCES

Clinical Trial Registry: Not applicable as this study is a retrospective analysis.

Data Access: The data generated during this study are available from the corresponding author upon reasonable request.

Code Access: Statistical scripts can be provided upon request.