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Vitamin D-related risk factors for preterm and full-term infants at birth: a retrospective study

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Abstract

Background Preterm birth affects a child's development and health. Vitamin D may influence the health of neonates. Our objective was to evaluate vitamin D levels and contributing factors in preterm and full-term newborns in Wuxi, China.

Methods A retrospective study was performed on neonates at the Affiliated Women's Hospital of Jiangnan University from May 2020 to May 2022. The neonates were classified into three categories: very preterm ($<32^{+0}$ weeks, $n=167$), preterm (32^{+0}-36^{+6} weeks, $n=454$), and full-term ($\geq 37^{+0}$ weeks, $n=192$). Serum concentrations of 25-hydroxyvitamin D were assessed. We employed the Kruskal-Wallis test, Mann-Whitney U tests, or chi-squared tests to compare categorical variables. The binary logistic regression study aimed to identify potential risk variables.

Results The median blood 25-hydroxyvitamin D concentration was 35.9 nmol/L, with roughly 82.7% categorized as vitamin D deficiency. However, the frequency of vitamin D insufficiency did not vary significantly across the three groups. Serum 25-hydroxyvitamin D levels at birth in full-term, preterm, and very preterm children exhibit substantial differences when mother body mass index exceeds 30 kg/m^2 ($P<0.001$). Newborn vitamin D levels shown considerable variations among three groups categorized by maternal body mass index, maternal age, and season of birth. In terms of the preterm birth phenotypes, deficiency was significantly associated with fetal growth restriction, fetal distress, and neonatal infections. No significant differences in vitamin D levels were observed among the three groups for mode of conception, number of gestations, or maternal gestational age. Furthermore, the deficiency rates of vitamin D were not markedly different among full-term, preterm, and very preterm newborns.

Conclusion Vitamin D levels in newborns were correlated with maternal obesity, maternal age, season of birth, preeclampsia, fetal growth restriction, neonatal infection, and fetal distress. At delivery, full-term infants born to women with a BMI exceeding 30 kg/m^2 or those delivered in winter exhibit significantly elevated levels of 25-hydroxyvitamin D compared to preterm and very preterm newborns.

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Keywords Vitamin D, Newborn, Preterm birth, Neonatal phenotype, Pregnant woman

Background

The global prevalence of vitamin D deficiency is a public health issue, underscored by its critical importance in human health, particularly for newborns and pregnant women [1, 2]. Vitamin D deficiency, with a frequency of 84%, is common among pregnant Chinese women. Living in regions with diminished ambient Ultraviolet B radiation elevates the risk of vitamin D insufficiency, such as in the northwest area. Moreover, the peak incidence was noted throughout winter and spring [3, 4]. Maternal vitamin D is the sole source of vitamin D for newborns. 25-hydroxyvitamin D (25(OH)D) crosses the placenta from mother to fetus. If the mother is vitamin D deficient, the newborn will also suffer from it [5, 6].

Preterm birth is a leading cause of neonatal mortality, with China ranking second in the number of preterm births globally, following only India [7]. Preterm newborns are at risk for various morbidities, including cognitive disabilities, developmental delay, and immune system dysfunction. Extensive research has demonstrated that vitamin D is critical in early immune system development and innate immune defense against bacterial infections in infants [8, 9]. Individuals with poor vitamin D status are also more susceptible to cognitive disorders [10]. Therefore, ensuring adequate vitamin D levels enhances immune responses and promotes cognitive development in premature newborns.

The vitamin D status in fetuses and newborns primarily depends on the maternal vitamin D status during pregnancy [11]. Several studies have revealed a high prevalence of vitamin D deficiency among Chinese pregnant women [4, 12]. Maternal vitamin D deficiency is associated with multiple perinatal complications, including gestational diabetes mellitus (GDM) [13] and preeclampsia [14], which are the primary causes of elective preterm delivery. However, limited information is available regarding the nutritional vitamin D status among preterm and full-term infants at birth in China.

25(OH)D, a vitamin D metabolite, exhibits relative stability with an extended half-life of approximately 3 weeks in serum, rendering it widely employed as a serum biomarker for assessing vitamin D status. This study aimed to determine the vitamin D status and preterm phenotypes by evaluating serum 25(OH)D concentration in full-term and preterm newborns in Wuxi, thereby potentially contributing to the development of effective early-life vitamin D intervention strategies.

Materials and methods

Cohort selection

This study enrolled 813 infants born at Wuxi Maternity and Child Health Care Hospital from May 2020 to May 2022. Doctors advise women preparing for pregnancy to take Elevit (Bayer) supplements daily, as they contain essential minerals and vitamins the body needs. During prenatal examinations, physicians recommend that pregnant women adhere to a balanced diet comprising fresh vegetables and fruits while managing their weight. Either the pregnant woman or her spouse was suggested to be away from smoking, alcohol, or drugs before and during the pregnancy. Perinatal care guidelines recommend routine evaluation of vitamin D levels in pregnant women at 12–13 weeks of gestation, and when pregnant women exhibit vitamin D deficiency, clinicians typically recommend a daily intake of 400–800 IU of vitamin D_3. Additionally, healthcare professionals advise that pregnant women have regular sun exposure and partake in weekend outdoor activities, if possible. However, numerous pregnant women, regardless of being full-time homemakers or career professionals, typically remain indoors, resulting in limited solar exposure. The primary reasons for this are the nature of people's work and the preference of Chinese women for fair skin. Sunlight exposure is prone to darkening the skin and causing the formation of spots.

We analyzed the neonates in three groups according to the gestation age: very preterm ($<32^{+0}$ weeks, $n=167$), preterm (32^{+0}-36^{+6} weeks, $n=454$), and full-term ($\geq 37^{+0}$ weeks, $n=192$). The tertiary health care center has approximately 10,000 deliveries and 800 preterm newborn admissions annually. The exclusion criteria include: (1) infants with major congenital malformations and life-threatening illnesses; (2) mothers with conditions likely to affect vitamin D and calcium metabolism, such as parathyroid disorders and chronic renal or liver diseases; (3) either the pregnant woman or her spouse had been addicted to smoking, alcohol usage or drug before or during the pregnancy.

Standard protocol approvals, registrations, and patient consent

The Medical Research Ethics Committee of Wuxi Maternity and Child Health Care Hospital, Affiliated Women's Hospital of Jiangnan University, approved this study (2023-06-1213-64). It was a retrospective study utilizing the hospital's electronic medical records system. Due to the retrospective nature of our study, the Medical Research Ethics Committee waived informed consent from participants. The clinical trial number is not applicable.

Data collection

We collected demographic information on gestation number, mode of conception, season of birth, birth weight, and gestational age at delivery. The electronic medical record system indicated that blood collection occurred 24–48 h post-delivery. Researchers determined gestational age based on the mothers' reported date of the last menstrual period and confirmed it with ultrasound reports during the first trimester. Data regarding potential confounding factors, including maternal age, maternal pre-pregnancy body mass index (BMI), mode of conception, pregnancy complications, and preterm birth phenotype, were extracted from electronic medical record system. Pregnancy complications and phenotype of preterm birth encompassed fetal growth restriction (FGR), fetal distress, small for gestational age (SGA), premature rupture of membranes, pregnancy bleeding, GDM, preeclampsia (PE), and neonatal infections.

Definition and classification of research variables

Maternal BMI was classified according to WHO guidlines [15], with cutoff values of 25 kg/m^2 and 30 kg/m^2. Maternal age was categorized as <30, 30–40, and >40 years, according to recognized correlations between advanced age and negative obstetric outcomes. Gestational age was classified as <32 weeks (very preterm), 32–36 weeks (preterm), and ≥37 weeks (full-term), based on previous research assessing infant outcomes within these ranges [16].

Fetal distress, currently termed non-reassuring fetal state,is a condition in which the fetus exhibits indications of insufficient oxygen or nutrition supply, usually occurring during late pregnancy or childbirth. The diagnostic criteria include aberrant fetal heart rate, meconium-stained amniotic fluid, fetal acidosis, and atypical fetal movement. FGR refers to the inability of a fetus to achieve its growth potential, typically attributable to maternal, fetal, or placental causes. The diagnostic criteria include ultrasound findings (fetal weight below the 10th percentile for gestational age or abdominal circumference below the 10th percentile for gestational age), deviation from the growth curve (the fetal growth trajectory diverges from the norm, with a significant reduction in weight gain), and abnormal umbilical artery blood flow. Neonatal infection denotes infections that arise in newborns, either contracted in utero, during parturition, or postnatally. SGA is characterized by a birth weight that falls below the 10th percentile of the average weight for gestational age.

25(OH) D is the most abundant circulating form of vitamin D in the human body and serum 25(OH) D concentration has been a reliable indicator to assess the status of vitamin D. Vitamin D levels were recorded from patient files. The medical records indicate that the serum samples for measuring 25(OH) D in newborns were obtained during the neonatal screening within 24 h after birth. According to the concentration of serum 25(OH) D, the vitamin D status was categorized as deficient (25(OH)D level <50 nmol/L), insufficient (25(OH)D level: 50–75 nmol/L), or sufficient (25(OH)D level >75 nmol/L) according to previously described medical research guidelines [17].

Statistical analysis

We categorized the season of birth as follows: spring (from March to May), summer (from June to August), autumn (from September to November), and winter (from December to February). We performed all the statistical analyses using IBM SPSS version 27.0 and considered differences statistically significant when $P<0.05$. For the study, we performed the Kolmogorov-Smirnov test to determine whether variables were normally distributed. Continuous variables were expressed as mean values and standard deviation ($\bar{x} \pm s$), and the difference was assessed using the Mann–Whitney U test. Non-parametric variables were assessed using the median and interquartile range (1st and 3rd quartiles, IQR) and compared via the Kruskal-Wallis test. Upon the Kruskal-Wallis test indicating significant differences among groups, pairwise comparisons were conducted using Dunn's test. The Chi-Square (χ^2) test assessed differences between categorical variables. The correlation between serum 25(OH)D level and gestational age was determined by linear regression analysis. Binary logistic regression analysis was used to investigate potential risk factors for vitamin D deficiency in newborns. The correlation between the phenotype of preterm birth and 25(OH)D level was analyzed using the χ^2 test.

Results

Figure 1 illustrates that most newborns (82.7%) had 25(OH)D levels below 50 nmol/L. There was a negative correlation between infants' serum levels of 25(OH)D and gestational age (Fig. 2).

Table 1 demonstrates that an examination of vitamin D status among very preterm, preterm, and full-term groups, considering variables such as gestational age, conception method, and maternal age, showed no statistically significant differences. Furthermore, the prevalence of vitamin D deficiency did not demonstrate notable variations across these three categories. Serum 25-hydroxyvitamin D levels at birth in full-term, preterm, and very preterm infants exhibit substantial differences when maternal BMI exceeds 30 kg/m^2 ($P<0.001$).

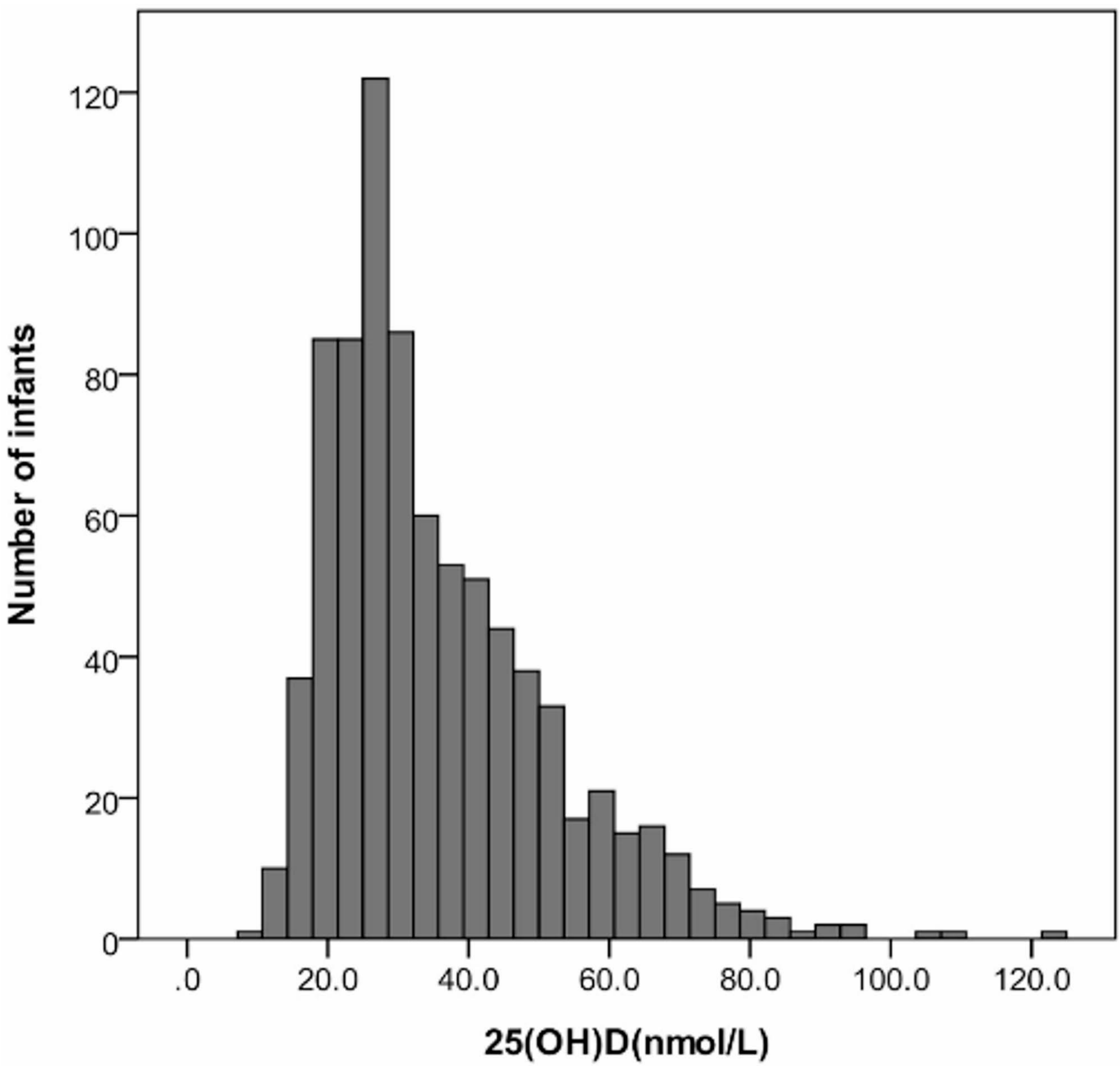

Fig. 1 Distribution of serum 25(OH)D levels among 813 infants at birth. 25(OH)D, 25-hydroxyvitamin D; Median value: 35.9 nmol/L; Range: 10.4-122.3 nmol/L

Significant differences in vitamin D levels are evident among newborns delivered in winter ($P = 0.002$).

There is a significant difference in vitamin D levels among infants born to mothers of varying ages ($p = 0.027$). Infants born to mothers under 30 years of age exhibit a higher likelihood of vitamin D deficiency compared to those born to mothers aged 30–40 years ($p = 0.011$); however, no significant difference is shown between infants of mothers under 30 years and those over 40 years ($p = 0.347$), nor between mothers aged 30–40 years and those over 40 years ($p = 0.764$). Newborns exhibited significantly reduced serum 25(OH)D levels when their mothers were obese prior to pregnancy, irrespective of the birth being full-term or not (<25 kg/m^2 vs. 25–30 kg/m^2, $p = 0.944$; <25 kg/m^2 vs. > 30 kg/m^2, $P < 0.001$; 25–30 kg/m^2 vs. > 30 kg/m^2, $P < 0.001$). Serum 25-hydroxyvitamin D levels in children born in various seasons exhibit significant differences, with the exception of the comparison between summer and autumn ($p = 0.680$). The disparity in vitamin D levels across newborns with varying birth weights is not statistically significant ($P = 0.864$). The levels of vitamin D exhibited substantial variations among three groups depending on

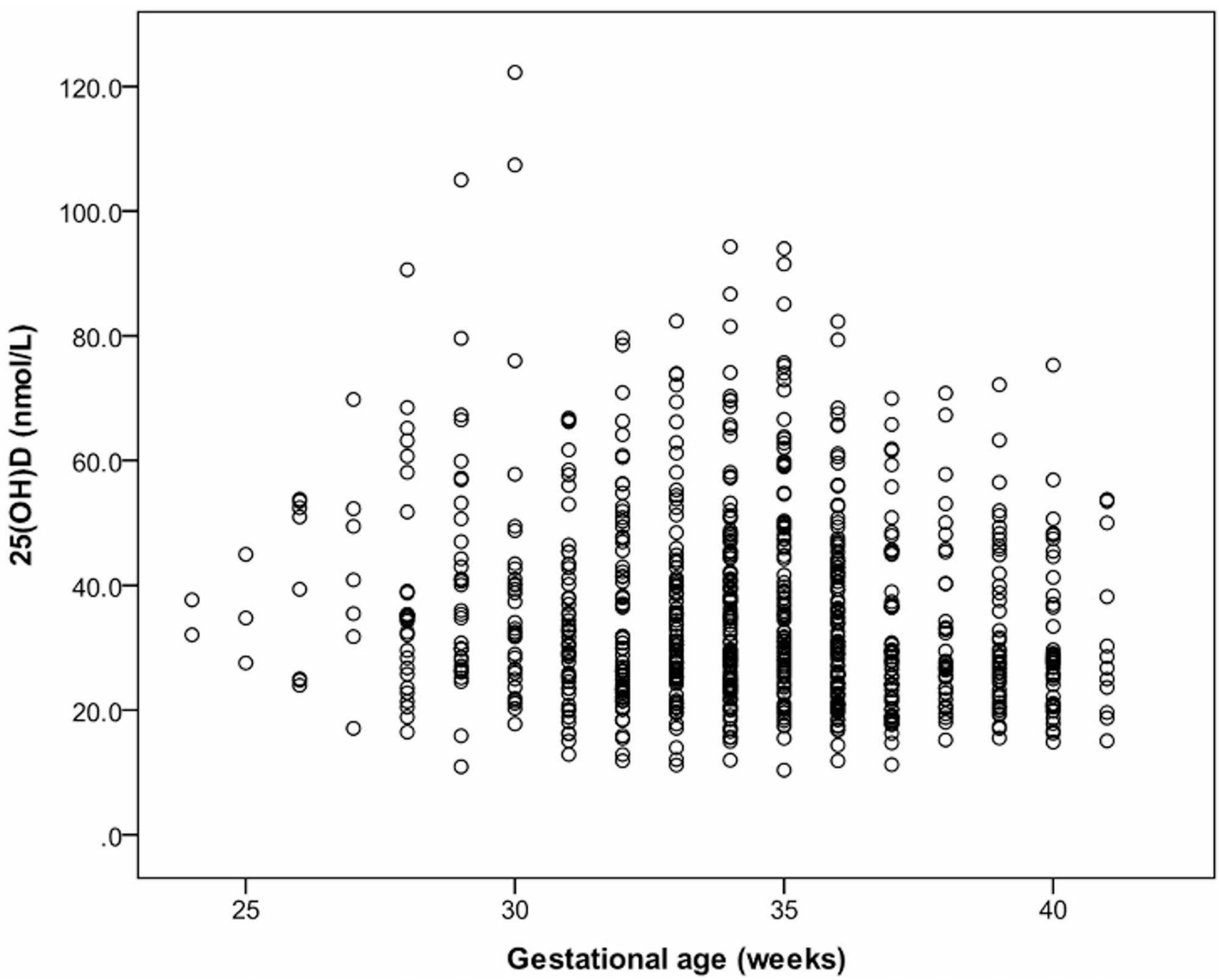

Fig. 2 Serum 25(OH)D levels from infants aged 24–41 weeks. 25(OH)D, 25-hydroxyvitamin D, $n=813$, $y=35.177+(-0.119)x$, $P<0.001$

maternal BMI, maternal age, and season of delivery in all babies.

*The serum 25(OH)D levels among different groups of newborns were compared using Kruskal-Wallis test; †data for maternal pre-pregnancy BMI was only available from 756 newborns.IQR, Interquartile Range; ab, < 25 kg/m^2 vs. 25–30 kg/m^2, $P=0.944$; < 25 kg/m^2 vs. > 30 kg/m^2, $P<0.001$; 25–30 kg/m^2 vs. > 30 kg/m^2, $P<0.001$; cd, < 30 years vs. 30–40 years, $P=0.011$; < 30 years vs. > 40 years, $P=0.347$; 30–40 years vs. > 40 years, $P=0.764$; efg, Spring vs. Summer, $P=0.011$; Spring vs. Autumn, $P<0.001$; Spring vs. Winter, $P=0.001$; Summer vs. Autumn, $P=0.680$; Summer vs. Winter, $P<0.001$; Autumn vs. Winter, $P<0.001$; hi, > 30 kg/m^2, very preterm vs. preterm, $P=0.475$; very preterm vs. full-term, $P=0.001$; preterm vs. full-term, $P=0.009$; jk, winter, very preterm vs. preterm, $P=0.249$; very preterm vs. full-term, $P=0.045$; preterm vs. full-term, $P<0.001$; l, < 25 kg/m^2 vs. 25–30 kg/m^2 vs.> 30 kg/m^2, $P<0.001$; m, < 30 years vs. 30–40 years vs. > 40 years, $P=0.027$; n, IVF vs. natural conception, $P=0.462$; o, singleton vs. multiple, $P=0.660$; p, spring vs. summer vs. autumn vs. winter, $P<0.001$; q, very preterm vs. preterm vs. full-term, $P=0.287$; r, <2500 g vs. 2500–4000 g vs. >4000 g, $P=0.864$.

When examining pregnancy complications, we observed a significant difference in serum 25(OH)D levels between newborns and those from mothers with preeclampsia. There were no significant differences in vitamin D levels in the groups with FGR or GDM. For detailed information, refer to Table 2.

*The comparison was conducted with the Mann–Whitney U test. GDM, gestational diabetes mellitus; PE, preeclampsia; FGR, fetal growth restriction.

*The comparison was conducted with the Chi-Square (χ^2) test. GDM, gestational diabetes mellitus; PE, preeclampsia; FGR, fetal growth restriction.

Table 3 lists the eight preterm-birth phenotypes that were found in 621 preterm births: neonatal infections (20.8%), fetal distress (11.8%), small for gestational age (9.8%), early rupture of membranes (45.0%), pregnancy

Table 1 The serum 25(OH)D levels among very preterm, preterm and full-term groups

	Very preterm		Preterm		Full-term		H	P*
	n	Median (IQR)	*n*	Median (IQR)	*n*	Median (IQR)		
Maternal pre-pregnancy BMI†							36.973	<0.001[l]
< 25 kg/m[2a]	49	33.6 (28.7–57.4)	110	35.3 (25.2–52.2)	40	31.4 (26.0–45.0)	1.729	0.421
25–30 kg/m[2a]	48	39.1 (31.2–45.1)	212	35.7 (26.2–45.9)	106	37.2 (26.7–47.5)	1.045	0.593
> 30 kg/m[2b]	41	26.1 (21.5–30.5)[h]	110	27.1 (22.2–37.6)[h]	40	34.7 (26.9–43.7)[i]	13.992	<0.001
Maternal age							7.261	0.027[m]
< 30 years[c]	110	32.6 (25.9–40.9)	271	30.3 (23.6, 44.4)	128	36.5 (26.8–45.8)	4.273	0.118
30–40 years[d]	52	39.8 (26.9–53.2)	179	36.1 (25.6–47.6)	59	34.3 (26.4–48.1)	1.136	0.567
> 40 years[cd]	5	43 (26.3–58.8)	4	25.7 (16.1–43.6)	5	28.4 (26-45.8)	2.280	0.32
Mode of conception							0.542	0.462[n]
IVF	22	39 (31.3–53.6)	59	35.5 (24.2–47.6)	4	35.8 (24.0–46.0)	3.155	0.206
Natural conception	145	33.1 (25.9–43.5)	395	31.9 (24.2–45.4)	188	35.1 (26.8–46.3)	2.034	0.362
Gestation number							0.194	0.660[o]
Singleton	112	33.9 (26.1–43)	325	31.6 (24.3–46)	182	35.1 (26.6–46.3)	1.489	0.475
Multiple	55	35.6 (26.6–46.5)	129	34.5 (24.2–45.5)	10	36.4 (27.8–48.7)	1.617	0.446
Season of birth							44.606	<0.001[p]
Spring[e]	46	35.5 (28.8–46.6)	139	29.6 (24-47.2)	106	29.2 (26.7–44.5)	4.628	0.099
Summer[f]	30	36.6 (23.8–58.3)	86	35.8 (28.1–48)	16	46.3 (41.5–49.2)	2.892	0.235
Autumn[f]	46	35.4 (27.6–51)	125	39.3 (28.8–49.6)	23	37.6 (27.9–47.8)	0.404	0.817
Winter[g]	45	29.9 (23.5–38.3)[j]	104	26.5 (20.9–35.6)[j]	47	38.2 (25.2–45.5)[k]	12.625	0.002
Gestational age	167	34.3 (26.2–45)	454	32.1 (24.2–45.5)	192	35.1 (26.7–46.3)	2.50	0.287[q]
Birth weight							0.291	0.864[r]
< 2500 g	167	34.3 (26.2–45)	342	33.3 (24.8–47)	34	30.3 (26.7–48)	0.617	0.735
2500–4000 g	/	/	112	30.6 (23.9–42.9)	146	36.2 (26.7–46.3)	3.689	0.055
> 4000 g	/	/	/	/	12	34.7 (26.1–45.5)		
serum 25(OH)D (n, %)								
< 50 nmol/L	133	79.6%	370	81.5%	169	88.0%		0.069
50–75 nmol/L	28	16.8%	71	15.6%	22	11.5%		0.288
> 75 nmol/L	6	3.6%	13	2.9%	1	0.5%		0.088

bleeding (6.3%), GDM (15.9%), PE (12.6%), and FGR diagnosed (8.1%). There was no significant difference in the percentage of preterm membrane rupture, small for gestational age, GDM, PE, and pregnancy bleeding between the vitamin D deficient, insufficient, and sufficient groups ($p > 0.05$). Fetal distress rates were 13.3%, 5.1%, and 5.3%, respectively, in the deficient, insufficient, and sufficient 25(OH)D groups ($p > 0.05$). There was a significant difference ($p < 0.05$) in the vitamin D status according to FGR and neonatal infections (Table 3).

*The comparison was conducted using multifactorial binary logistic regression analysis. OR, odds ratio; CI, confidence interval; BMI, body mass index.

Due to missing data on maternal pre-pregnancy BMI for 57 out of 813 cases, we analyzed 756 newborns to identify risk factors for vitamin D deficiency using multifactorial binary logistic regression analysis. After

Table 2 Pregnancy complications and serum 25(OH)D levels among 813 infants

Subgroup	*n*	Serum 25(OH)D (nmol/L)		*P**
		Median	Interquartile Range	
GDM				0.684
yes	103	31.0	24.2–44.4	
no	710	32.5	24.2–46.4	
PE				< 0.001
yes	86	26.3	26.3–35.2	
no	727	32.1	24.7–45.3	
FGR				0.779
yes	51	31.1	24.3–44.9	
no	762	29.9	23.0-43.5	

Table 3 The correlation between phenotype and vitamin D in 621 preterm and very preterm births

Phenotype (%)	Serum 25(OH)D			*P**
	< 50 nmol/L *n* (%)-503	50–75 nmol/L *n* (%)-99	≥ 75 nmol/L *n* (%)-19	
Premature rupture of membranes (45.0%)	247 (49.1%)	45 (45.5%)	6 (31.6%)	0.279
FGR (8.1%)	47 (9.3%)	3 (3%)	0	0.046
Fetal distress (11.8%)	67 (13.3%)	5 (5.1%)	1 (5.3%)	0.044
Small for gestational age (9.8%)	50 (9.9%)	9 (9.1%)	2 (10.5%)	0.962
Neonatal infections (20.8%)	114 (22.7%)	14 (14.1%)	1 (5.3%)	0.038
PE (12.6%)	69 (13.7%)	7 (7.1%)	2 (10.5%)	0.183
GDM (15.9%)	80 (15.9%)	16 (16.2%)	3 (15.8%)	0.998
Pregnancy bleeding (6.3%)	32 (6.4%)	6 (6.1%)	1 (5.3%)	0.977

adjusting for gestational age, birth weight, and maternal age, we discovered a robust association between neonatal vitamin D deficiency and both the season of birth and maternal pre-pregnancy BMI, as detailed in Table 4. Notably, infants born in winter and those with mothers who were obese before pregnancy were at a significantly higher risk of vitamin D deficiency.

Discussion

Vitamin D is believed to play a crucial role in the early immune development of infants. However, there is limited national data on the vitamin D status of newborns in China. Therefore, this study aimed to assess the vitamin D status by evaluating the serum 25(OH)D concentration in full-term and preterm newborns in Wuxi, providing valuable insights for future strategies regarding early-life vitamin D interventions. This study observed a remarkably high prevalence (82.7%) of vitamin D deficiency among neonates at birth in Wuxi, situated in southeast China. Among our cohort, 88% of full-term newborns exhibited serum 25(OH)D levels below 50 nmol/L. There's no significant difference regarding the prevalence

Table 4 Multivariable regression analysis of factors affecting serum 25(OH)D levels below 50 Nmol/L at birth

Variable	OR (95% CI)	*P**
Gestational age		
$< 32^{+0}$ week	0.946 (0.434–2.061)	0.946
32^{+0}-36^{+6} week	0.895 (0.484–1.657)	0.725
$\geq 37^{+0}$ week	reference	
Season of birth		
Spring	0.263 (0.128–0.541)	< 0.001
Summer	0.223 (0.101–0.491)	< 0.001
Autumn	0.222 (0.106–0.465)	< 0.001
Winter	reference	
Maternal pre-pregnancy BMI		
< 25 kg/m^2	0.278 (0.150–0.514)	< 0.001
25–30 kg/m^2	0.504 (0.277–0.916)	0.025
> 30 kg/m^2	reference	
Birth weight		
< 2500 g	0.486 (0.056–4.25)	0.515
2500–4000 g	0.737 (0.078–6.251)	0.780
> 4000 g	reference	
Maternal age		
< 30 years	3.025 (0.657–13.92)	0.155
30–40 years	1.908 (0.409–8.894)	0.411
> 40 years	reference	

of vitamin D deficiency among very preterm, preterm and full-term groups. Furthermore, we identified significant associations between neonatal vitamin D deficiency and season of birth, marenal age and maternal pre-pregnancy BMI.

Existing evidence suggests a high prevalence of vitamin D deficiency among pregnant women in many countries, which may have potentially adverse consequences for both fetuses and growing infants/children [2, 18, 19]. A meta-analysis of randomized controlled trials has indicated that appropriate prenatal vitamin D intervention improves maternal vitamin D status and enhances birth weight and length [20]. Moreover, several studies have highlighted the common occurrence of maternal vitamin D deficiency during pregnancy in China [21, 22], implying an increased risk for neonatal deficiencies when Chinese pregnant women with inadequate intake receive insufficient amounts of this essential nutrient. A few other studies have evaluated neonatal vitamin D status among preterm infants across different regions worldwide [11, 23]. Socioeconomic status, geographic characteristics, and ethnicity are crucial factors in determining vitamin D status [24].

Consistent with the findings of earlier studies [25, 26], our study found that When infants born to mothers with a BMI over than 30 kg/m^2 or in those born in winter, the risk of vitamin D deficiency is increased in preterm and very preterm infants. Furthermore, similar to findings from other studies [27, 28], neonates born during winter showed significantly lower serum 25(OH)D levels than those born in summer and autumn. Reduced cutaneous production of vitamin D_3 during winter due to decreased sunlight exposure leads to a higher prevalence of vitamin D deficiency among pregnant women during this season. Considering that the dataset covers the period from May 2020 to May 2022, coinciding with the COVID-19 epidemic, it is probable that pregnant women had diminished opportunities for outdoor activities during this time. Consequently, infants born in winter face a heightened risk for vitamin D deficiency at birth. In addition, this study found that serum 25(OH)D levels in very preterm and preterm infants were significantly lower than those in full-term infants in winter.

The study highlighted a significant correlation between vitamin D deficiency and PE, fetal distress, FGR, and neonatal infections. The incidence rates of these phenotypes were consistent with those reported in previous studies [29, 30]. Vitamin D deficiency contributes to preterm birth phenotypes through the biological mechanisms: (1) Vitamin D affects placental efficiency by modulating placental angiogenesis and nutrition transport, influencing the preterm phenotype [31, 32]. (2) Vitamin D facilitates trophoblast invasion by initiating epithelial-mesenchymal transition, a crucial phase in the differentiation of the trophoblast layer [33]. (3) Vitamin D mitigates proinflammatory indicators, particularly TNF-α in the mother and IL-6 in cord blood, and enhances newborn outcomes [34].

Obesity is associated with alterations in the vitamin D endocrine system [35]. Increased adipose mass can influence the transportation and metabolism of vitamin D, a group of fat-soluble prohormones. Previous reports have shown an inverse correlation between the percentage of body fat content and serum 25-OHD levels in healthy women [35]. Moreover, our research has pointed to the pre-pregnancy BMI of mothers as a contributing factor to vitamin D deficiency in their unborn children. Extensive data consistently show that infants born to obese mothers are more likely to have reduced levels of serum 25(OH)D [36, 37]. This research underscores the importance of advising women planning to become pregnant about the critical role of weight management in ensuring the health of their future offspring. Moreover, our findings indicate that babies born to mothers who experienced preeclampsia also tend to have significantly lower serum 25(OH)D levels. This finding is in line with a previously published study [14].

In conclusion, inadequate sun exposure and insufficient vitamin D supplementation contribute to the high prevalence of vitamin D deficiency in many societies. As demonstrated in previous studies, empirical evidence has shown that frequent vitamin D supplementation during pregnancy is a potent strategy for reducing the risk of vitamin D deficiency [38].

Maternal vitamin D serves as the primary source for the newborn, and effective supplementation can gradually correct deficiencies and lessen their adverse effects [39]. So, we advocate for personalized and sufficient vitamin D supplementation. The previous study [40] indicates that vitamin D supplementation of up to 4000 IU daily during pregnancy is safe. This would reduce the risk of preterm birth and enhance mother and baby health outcomes. Furthermore, emphasis must be placed on vitamin D supplementation and monitoring during prenatal care. Modifying the dosage of vitamin D supplementation, enhancing food and lifestyle, and focusing on high-risk populations can significantly mitigate the risk of preterm birth and improve mother and infant health outcomes.

Limitations

This retrospective study possesses many limitations. This study did not analyze confounding variables like as nutrition, sun exposure, vitamin D levels, gestational weight growth, and skin features. Secondly, it was not practicable to account for the time of the commencement of vitamin D treatment in this retrospective study. The restricted sample size and the constrained data distribution represent further restrictions. Comprehensive, rigorously designed randomized controlled trials evaluating clinically significant outcomes will be crucial for conclusive determinations. The environment, culture, and many characteristics of distinct countries and locations will influence the dissemination of local data. This will enhance our comprehension of vitamin D's involvement in pregnancy and neonatal health, establishing a scientific basis for the formulation of targeted preventative initiatives to promote mother and child health.

Conclusion

In summary, neonatal vitamin D levels were correlated with maternal obesity, maternal age, season of delivery, preeclampsia, fetal growth restriction, neonatal infection, and fetal distress. Newborns born to mothers with a BMI exceeding 30 kg/m^2 have an elevated risk of vitamin D insufficiency, particularly in preterm and very preterm newborns. Moreover, blood 25(OH)D concentrations in very preterm and preterm infants were markedly lower than those in full-term infants during winter.

Future research should aim for better-designed randomized controlled trials to determine the appropriate dosage of vitamin D supplementation across various groups and investigate alternate supplementation methods beyond conventional oral forms. This will enhance our comprehension of vitamin D's significance in pregnancy and neonatal health. Moreover, vitamin D supplementation should be integrated with lifestyle modifications (including increased outdoor exercise and dietary adjustments) to enhance health results. We advocate for regularly monitoring public health policies to assess the prevalence and trends of vitamin D deficiency across various groups, facilitating informed and rational policy modifications. These interventions are essential for improving health outcomes for both mothers and infants, therefore tackling the significant problem of vitamin D deficiency during the neonatal phase.

Abbreviations

25(OH)D	25-hydroxyvitamin D
GDM	Gestational diabetes mellitus
FGR	Fetal growth restriction
SGA	Small for gestational age
IQR	Interquartile range
PE	Preeclampsia
BMI	Body mass index
OR	Odds ratio
CI	Confidence interval

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Author contributions
Man Wu conceived and designed the research study. Man Wu and Min Zhao drafted the paper. Xin Jin and Yun Zhang collected the clinical data and performed the analysis. Xiaomin Zheng and Xiao Xiao contributed to the revision of the paper. All authors read and approved the final manuscript.

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Data availability
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This study followed the Declaration of Helsinki and was approved by the Medical Research Ethics Committee of Wuxi Maternity and Child Health Care Hospital (2023-06-1213-64). It was a retrospective study utilizing the hospital's electronic medical records system. Due to the retrospective nature of our study, the Medical Research Ethics Committee waived informed consent from participants.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Clinical trial number
Not applicable.

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