The correlation between vitamin D and maternal/infant outcomes, inflammatory response in pregnant women

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Abstract

Purposes

To analyze the effects of vitamin D deficiency in pregnant women on common adverse pregnancy outcomes and small for gestational age (SGA) and to detect the expression of inflammatory factors in pregnant women to provide a theoretical basis for the treatment of vitamin D deficiency in pregnant women.

Methods

Serum samples from pregnant women from January 2015 to December 2015 were collected to measure the 25-(OH)D level. The effects of maternal age, pregnancy, season, parity and temperature on vitamin D levels in pregnant women were recorded. Then, the relationship between vitamin D levels and gestational diabetes mellitus, gestational hypertension, premature rupture of membranes, cesarean section, premature delivery and spontaneous abortion, and neonatal gestational age were analyzed. The expression of IL-6 and TNF-α in serum was detected by RT-PCR and western blot.

Results

The incidence of vitamin D deficiency, insufficiency and sufficiency in pregnant women in this region was 83.28%, 15.36% and 1.36%, respectively. Age, pregnancy, sampling season and parity were the influencing factors on vitamin D level, and multivariate logistic regression analysis showed that summer, autumn and temperature were protective factors for adequate vitamin D in pregnant women ($P < 0.05$). Vitamin D levels in pregnant women were associated with preterm birth, spontaneous abortion and SGA. The incidences of preterm birth, spontaneous abortion and SGA were higher in the vitamin D deficiency group ($P<0.05$).

Conclusion

The serum vitamin D level of pregnant women in this area is low and is affected by multiple factors such as age, pregnancy, season, parity and temperature. Low vitamin D levels can increase the risk of premature birth, spontaneous abortion and SGA in pregnant women, and its low expression is common. As it also leads to inflammation, increasing the level of vitamin D in the serum of pregnant women can effectively reduce the occurrence of related diseases.

Backgroup

Vitamin D (VD) is a fat-soluble vitamin and is composed of a group of sterol derivatives with anti-caries effects and similar structures[1]. The main function of vitamin D is to promote the absorption of calcium and phosphorus by small intestinal mucosal cells, promote calcium renewal and new bone formation, and promote the absorption of phosphorus and reabsorb calcium and phosphorus from renal tubular cells, thereby improving calcium in the blood[2]. In addition, vitamin D also promotes skin cell growth, differentiation and regulation of immune function. The vitamin D required by the human body is mainly formed by the conversion of cholesterol in the body through ultraviolet light in sunlight and can also be supplemented by the diet. Vitamin D has multiple forms of metabolism in the body through multiple metabolic pathways. Since 25-(OH)D is relatively stable in the human body, the international level of 25-(OH)D is usually used to reflect the body's vitamin D level[3, 4].

Pregnant women are a special group whose metabolism and endocrine function will change subtly with the pregnancy cycle. At the same time, the nutrition of pregnant women needs to meet the needs of their own nutrition and fetal development[5]. With the rapid changes in modern lifestyles, vitamin D deficiency during pregnancy is becoming increasingly common and has gradually become a global problem. Clinical investigations show that vitamin D is essential for pregnancy and infant health[6]. Vitamin D deficiency during pregnancy has a significant impact on the health status of pregnant women and pregnancy outcomes, such as gestational diabetes, gestational hypertension, premature rupture of membranes, and premature birth; at the same time, vitamin D deficiency during pregnancy has an important impact on fetal growth and development, especially fetal bone development, which may adversely affect fetal weight, body length, and head circumference. Vitamin D is an important indicator of pregnancy[7]. However, due to the huge differences in the living environment of pregnant women in different regions, the factors affecting the serum vitamin D levels of pregnant women are also different[8]. Therefore, this study analyzed the effects of serum vitamin D levels and age, pregnancy, season, parity and temperature factors on serum vitamin D levels in pregnant women and explored serum vitamin D levels in pregnant women for common adverse pregnancy outcomes and small for gestational age newborns. The influence of the expression of inflammatory factors in the serum of pregnant women further elaborated the influence of different vitamin D expression levels on pregnant women and provided a sufficient theoretical basis for the prevention of vitamin D deficiency in maternal and child.

Methods

Subjects

In this study, single-pregnant pregnant women who were born and delivered in Wuxi Maternal and Child Health Hospital of Jiangsu Province from January 2017 to December 2018 and their normal delivery were selected. Inclusion criteria: gestational age is not less than 8 weeks; regular single birth pregnant women in our hospital and normal delivery; sampling time is early pregnancy (pregnancy week <13 weeks), second trimester (13 weeks ≤ gestational weeks <28 weeks) and late pregnancy (gestational weeks > 28 weeks); and no calcium supplements were added during the study period. Exclusion criteria: multiple pregnancies, pregnancy complications, chronic metabolic diseases, neurological diseases, incomplete data or withdrawal. Ethical review: The treatment and grouping of the subjects in this study were informed by pregnant women and were reviewed by the Ethics Committee of Wuxi Maternal and Child Health Hospital.

Sample collection and vitamin D level detection

Blood samples were collected from pregnant women at 8-10 am on the sampling day. The samples were centrifuged, and the serum was stored at -80°C. All samples were tested for 25-(OH)D content using the Vitamin D test kit (IDS Ltd, UK) and operated in strict accordance with the test procedure. The detection method was enzyme-linked immunosorbent assay (ELISA)[9].

Grouping

In this study, maternal age, pregnancy, sampling season, parity and local temperature were considered factors influencing maternal serum vitamin D levels. Pregnant women were grouped as follows: pregnant women were grouped by age, including the low age group (15 years old ≤ age <25 years old), middle age group (25 years old ≤ age <35 years old) and high age group (35 years old ≤ age ≤ 46 years old); pregnant women were grouped according to gestational age, including early pregnancy (10 weeks ≤ gestational weeks <13 weeks), mid-gestation (13 weeks ≤ gestational weeks < 28 weeks) and late pregnancy (28 weeks ≤ gestational weeks ≤ 32 weeks); according to the climate distribution characteristics of Wuxi, the groups included were the spring group (March, April, May), summer group (June, July, August), autumn group (September, October, November) and winter group (December, January, February); and based on the number of births, women were divided into the primiparous group (first child) and multiparous group (second child or above).

Vitamin D deficiency standards

Vitamin D status was classified as follows: vitamin D deficient (25-(OH)D<50 nmol/L), vitamin D insufficient (50 nmol/L≤25-(OH)D<75 nmol/L) and vitamin D sufficient (25-(OH)D≥75 nmol/L) (quote). According to the vitamin D level of pregnant women, the study was divided into the vitamin D deficient group, vitamin D insufficient group and vitamin D sufficient group[10].

SGA Standard

Birth weight is less than the 10th percentile of the same-age fetal weight or less than 2 standard deviations of the same gestational age[11].

RT-PCR analysis

Total RNA was extracted with TRIzol reagent (Life Technologies) following the manufacturer's instructions, and extracted RNA was quantified. IL-6 and TNF-α expression was examined via standard RT-PCR and normalized to β-actin expression as an endogenous control[12]. The primer sequences were as follows: IL-6: F: GTCCAGTTGCCTTCTCCC; R: GCCTCTTTGCTGCTTTCA; TNF-α F: GATTCAGGGATGTGTGGCCT R: GCCACATTCCAGATGTCCCA; :β-actin: F: CCCGAGCCGTGTTTCCT; R: GTCCCAGTTGGTGACGATGC

Western blot analysis

Cells were lysed in radioimmunoprecipitation assay buffer with Protease Inhibitor Cocktail (Sigma), separated in sodium dodecyl sulfate polyacrylamide gels, and transferred to a polyvinylidene fluoride membrane. The membrane was incubated with anti-IL6, anti-TNF-α and anti-β-actin (Abcam, Cambridge, MA, USA) at 4°C overnight, followed by incubation with horseradish peroxidase-conjugated secondary antibody for 1 h. Bands were visualized with ECL[12].

Statistical analysis

SPSS 25.0 was used for statistical analysis. Serum vitamin D levels in pregnant women are expressed as the median and interquartile range; the incidence of serum vitamin D deficiency and SGA incidence in pregnant women are shown as incidences; the comparison between serum vitamin D levels in two or more groups of pregnant women is based on the Kruskal-Wallis Rank sum test; the comparison between the serum vitamin D deficiency rate and the adequacy rate in different groups of pregnant women was performed by chi-square test; age, pregnancy, sampling season and parity were used to analyze the serum vitamin D levels of pregnant women by multivariate logistic regression analysis. The effect of serum vitamin D levels in pregnant women was analyzed by single factor linear regression analysis. The comparison of common adverse pregnancy outcomes in serum vitamin D levels of different pregnant women was performed by the chi-square test. The serum vitamin D levels of different pregnant women were lower in those with small for gestational age (SGA) newborns[13]. The chi-square test was used for comparison, and the difference was statistically significant at $P < 0.05$.

Results

Basic information for 3,080 pregnant women<

In this study, 3,080 pregnant women were included as subjects. Their age range was 15–46 years old, the average age was 26.94 ± 3.95 years old, and most pregnant women were younger than 35 years old (94.19%). The sampling gestational age range was 10–32 weeks, and the average age was 17.89 ± 6.60 weeks. Most pregnant women were sampled during early or mid-gestation (90.75%), and the season was distributed in spring, summer, autumn and winter, but mostly in summer and autumn, which accounted for 29.87% and 31.23%, respectively; in this study, the parity includes the first and second or more, and most of the pregnant women were pregnant with their first child (86.30%). The age, pregnancy, sampling season and parity of 3,080 pregnant women are shown in Table 1.

Table 1
Demographic characteristics of pregnant women(N = 3080)

projects		**Number(n)**	**percentage(%)**
Age	$15 \leq Age < 25$	870	28.25
	$25 \leq Age < 35$	2031	65.94
	$35 \leq Age \leq 46$	179	5.81
Pregnancy staging	Early pregnancy(10 week ≤ GW < 13 week)	1025	33.28
	Second trimester(13 week ≤ GW < 28 week)	1770	57.47
	Late pregnancy(28 week ≤ GW ≤ 32 week)	285	9.25
Season	Spring	578	18.77
	Summer	920	29.87
	autumn	962	31.23
	Winter	620	20.13
Number of fetuses	First child($p = 1$)	2658	86.30
	Second child or above($p > 1$)	422	13.70

Vitamin D Expression In Maternal Serum

The serum vitamin D test results showed that the serum 25-(OH)D level of the pregnant women included in the study ranged from 10.0-93.9 nmol/L, and the median and quartile levels were 33.7 (24.7, 44.7) nmol/L. Among them, the number of pregnant women with severe deficiency, deficiency and sufficient vitamin D levels were 2,565 cases, 473 cases and 42 cases, accounting for 83.28%, 15.36% and 1.36%, respectively. The above results showed that the majority of pregnant women in the region had 25-(OH)D levels of less than 50 nmol/L and were in a state of vitamin D deficiency (Fig. 1A, 1B).

The influence of age and other factors on the expression of serum vitamin D in pregnant women

1. Single factor analysis of the influence of age and other factors on serum vitamin D levels in pregnant women

In this experiment, we performed a single factor analysis of age, pregnancy, sampling season, parity and serum 25-(OH)D levels in pregnant women. The results showed that there was a statistically significant difference in the effect of age on serum vitamin D levels in pregnant women ($H=15.677$, $P<0.001$). The expression level of vitamin D was the lowest in the lowest age group and the highest in the highest age group. The difference in pregnancy also had a significant effect on the serum vitamin D level of pregnant women ($H=12.334$, $P=0.002$). The level of vitamin D was the lowest in the early pregnancy group but the highest in the third trimester group.

In order to investigate the effect of the season on serum vitamin D levels in pregnant women, serum was collected in different seasons, and the results showed that the season was statistically significant ($H=74.736$, $P<0.001$). We also confirmed that parity affects the expression of serum vitamin D in pregnant women ($H=26.192$, $P<0.001$). The severe deficiency rate, deficiency rate and sufficiency rate of serum vitamin D in pregnant women with different influencing factors showed that factors such as high age, third trimester, summer and autumn, and second or higher pregnancy could significantly increase the expression of vitamin D (Table 2).

Table 2
Single factor analysis of the influence of age and other factors on serum vitamin D levels in pregnant women

Groups		samples(n)	V D level(nmol/L)	Z/P	deficiency(%)	X^2/P	insufficiency (%)	X^2/P	sufficiency(%)	X
Age	Low(15 ≤ Age<25)	870	32.1(24.1,43.1)	10.588/ 0.005	85.06	3.389/0.184	13.91	3.368/0.186	1.03	1
	Medium(25 ≤ Age<35)	2031	33.9(24.7,45.1)		82.77		15.66		1.58	
	High(35 ≤ Age ≤ 46)	179	37.3(28.7,48.0)		80.50		18.99		0.56	
Period	Early pregnancy(10 week ≤ GW<13 week)	1025	32.4(24.2,42.6)	4.771/ 0.092	82.63	0.461/0.794	15.71	0.147/0.929	1.66	1
	Second trimester(13 week ≤ GW<28 week)	1770	50.7(25.0,44.8)		83.62		15.20		1.19	
	Late pregnancy(28 week ≤ GW ≤ 32 week)	285	35.1(26.7,47.4)		83.51		15.09		1.40	
Season	Spring	578	32.3(22.5,40.5)	44.736/ <0.001	86.16	4.851/0.183	13.15	3.262/0.353	0.69	9
	Summer	920	40.3(28.3,58.5)		81.85		16.30		1.85	
	autumn	962	39.0(27.7,56.8)		83.06		15.18		1.77	
	Winter	620	28.9(20.8,39.6)		83.06		16.29		0.65	
Number of fetuses	First child(p = 1)	2658	35.5(24.9,46.8)	1.064/ 0.287	83.52	0.614/0.433	15.35	0.279/0.598	1.13	0
	Second child or above(p > 1)	422	38.3(25.3,47.2)		81.99		16.35		1.66	
	Total	3080			83.28		15.36		1.36	

2. Multivariate logistic regression analysis of the influence of age and other factors on serum vitamin D levels in pregnant women

Univariate analysis showed that age, pregnancy and other factors had significant effects on serum vitamin D levels in pregnant women. Therefore, multivariate logistic regression was used to comprehensively analyze the influence of various factors. During the analysis, the vitamin D level was used as a dependent variable, where serum vitamin D levels < 75 nmol/L (deficiency or insufficiency) were assigned a value of 0 and serum vitamin D levels ≥ 75 nmol/L were assigned a value of 1. The independent variable X1 (age) used as the reference level 15 years ≤ age < 35 years old, the independent variable X2 (pregnancy week) used as the reference level 10 weeks ≤ gestational age < 28 weeks, and the independent variable X3 (season) used as the reference winter and spring. The independent variable X4 (parity) used the first child as the reference level, and the respective variable assignment is shown in Table 3.

Table 3
Logistic regression independent variable assignment

Factor	variable	X = 0	X = 1
Age	X1	15 ≤ Age<35	35 ≤ Age ≤ 46
Period	X2	10 weeks ≤ GW<28 weeks	28 ≤ GW ≤ 32
Season	X3	Winter/spring	Autumn/summer
Number of fetuses	X4	First child	Second child or above(p > 1)

The results of stepwise regression analysis showed that there was no collinearity between the independent variables. Multivariate logistic regression analysis showed that the summer and autumn were protective factors for vitamin D in pregnant women (Table 4).

Table 4

Multivariate logistic regression analysis

Factor	B-value	S.E-value	Wald X^2-value	Sig-value	OR-value	OR-value 95%CI
X1	1.251	0.216	9.132	0.121	2.872	1.523~4.615
X2	1.204	0.198	13.085	0.086	2.675	1.231~4.162
X3	2.326	0.187	15.732	< 0.001	4.383	2.532~5.967
X4	2.051	0.232	3.824	0.158	2.796	1.015~5.168

3. Linear regression analysis of the effect of temperature on serum vitamin D levels in pregnant women

In order to prove whether the effect of the season on vitamin D is due to temperature changes, we conducted a linear regression analysis of the local monthly mean temperature and the serum vitamin D level of pregnant women during the study period. The analysis showed that the serum vitamin D level of pregnant women was highly positively correlated with temperature. The higher the temperature, the higher was the serum 25-(OH)D level ($R^2 = 0.823$, $t = 6.818$, $P < 0.001$) (Fig. 2A, 2B).

Correlation between serum vitamin D levels and common adverse pregnancy outcomes in pregnant women

In this experiment, we grouped pregnant women according to vitamin D levels, including the deficiency group, insufficient group and sufficient group. Univariate analysis showed that the incidence of preterm birth and spontaneous abortion was the highest in the deficiency group, and the difference was statistically significant ($P < 0.05$, Table 5).

Table 5

Univariate analysis of vitamin D levels in maternal serum and common adverse pregnancy outcomes

Serum V D level	Number	Gestational diabetes			Hypertension during pregnancy			Premature rupture of membra		
		Samples	X2/P	RR/95%CI	Samples	X2/P	RR	Samples	X2/P	R
Deficiency group	2565	209	1.717/0.424	0.86(0.334~2.193)	192	0.582/0.748	0.79(0.306~2.016)	498	1.064/0.587	1
Insufficiency group	473	47		1.04(0.395~2.755)	32		0.71(0.264~1.912)	83		1
sufficiency group	42	4		1.00	4		1.00	7		1

To investigate the effects of different serum vitamin D levels on pregnancy outcomes, we performed a univariate analysis and found no significant effect of vitamin D expression on pregnancy outcomes, including gestational diabetes mellitus and hypertensive disorder complicating pregnancy ($P > 0.05$, Table 6).

Table 6

Univariate analysis of maternal serum with vitamin D levels and common adverse pregnancy outcomes

Serum V D level	Number	Cesarean section			Premature birth			Natural abortion	
		Samples	X2/P	RR/95%CI	Samples	X2/P	RR	Samples	X2/P
Deficiency group	2565	1202	2.560/0.278	0.90(0.669~1.197)	195	8.373/0.015	3.19(0.458~22.246)	204	11.727/0.003
Insufficiency group	473	239		0.97(0.713~1.305)	20		1.78(0.244~12.906)	18	
sufficiency group	42	22		1.00	1		1.00	1	

Correlation analysis of vitamin D levels in maternal serum and small for gestational age (SGA) neonates

In this study, 3,080 pairs of mothers and children met the criteria included in the study, of which 423 were born with SGA, for an incidence rate of 13.71%. A single factor analysis of the serum vitamin D levels and incidence of SGA in pregnant women revealed that the incidence of SGA in the deficiency group, the insufficient group and the sufficient group were 15.52%, 5.07%, and 2.38%, respectively. After statistical analysis, we found that the serum vitamin D level had a statistically significant effect on the incidence of SGA ($X2 = 41.390$, $P < 0.001$), and the incidence of SGA was highest in the deficient group. The risk of SGA in the deficient group and the insufficient group was 6.52 times and 2.13 times the sufficient group, respectively (Table 7).

Table 7

Univariate analysis of the incidence of 25-(OH)D levels in maternal serum and small for gestational age (SGA)

VD Level	Total	SGA	Incidence rate(%)	X^2/P	Relative risk(RR)	95%CI
Deficiency group	2565	230	8.97	10.827/0.004	3.77	0.541~26.218
Insufficiency group	473	23	4.86		2.04	0.283~14.749
sufficiency group	42	1	2.38		1.00	—

Vitamin D levels inhibit the expression of inflammatory factors

In order to demonstrate the effect of vitamin D expression on inflammatory factors, RT-PCR was used to detect the gene expression of IL-6 and TNF-α. In this experiment, subjects with higher serum vitamin D levels and lower vitamin D levels were used for experimental studies, of which 46 subjects had high serum vitamin D and 42 subjects had low vitamin D, named the high VD group and low VD group, respectively. The results showed that compared with the low VD group, the expression of IL-6 and TNF-α mRNA in the high VD group was significantly decreased, indicating that the expression of inflammatory factors may be negatively correlated with the content of vitamin D (Fig. 2A, 2B).

High vitamin D expression can inhibit the production of inflammation-related proteins

To investigate the effect of vitamin D on IL-6 and TNF-α protein expression (Fig. 3A, B), we detected IL-6 and TNF-α protein by western blot. The results showed that IL-6 and TNF-α protein expression was low in the high VD group compared with the low VD group ($P < 0.01$). These results indicate that IL-6 and TNF-α proteins are expressed at low levels when vitamin D levels are higher, while low levels of vitamin D can activate the expression of IL-6 and TNF-α protein, indicating that vitamin D and IL-6 and TNF-α protein may be negatively correlated. However, the specific mechanism requires further research.

Discussion

Studies have shown that people who are exposed to sun or ultraviolet light-irradiated olive oil and linseed oil can resist rickets, and further research has found that the active anti-chondrosis component in humans is vitamin D[14]. Vitamin D (referred to as VD) is a fat-soluble vitamin consisting of a group of sterol derivatives with anti-caries effects and a similar structure[15]. Adequate vitamin D can promote calcium absorption and promote bone calcification. The cholesterol derivative 7-dehydrocholesterol in the human body is stored under the skin and can be converted into cholecalciferol under the irradiation of sunlight or ultraviolet rays. It is an endogenous vitamin D that can promote the absorption of calcium and phosphorus. A large number of studies have shown that multivitamins have a significant regulatory effect on the occurrence and development of diseases, and vitamin D is closely related to various diseases such as hypertension, diabetes and inflammation.

In recent years, domestic and foreign research has found that vitamin D deficiency during pregnancy is a very common phenomenon[16, 17]. Therefore, this paper aims to investigate the expression of vitamin D in the serum of pregnant women in Wuxi. It was found that 83.28% of the pregnant women have serum vitamin D levels < 50 nmol/L, which is a state of vitamin D deficiency. However, only 1.36% of pregnant women have serum vitamin D levels ≥ 75 nmol/L, reaching a sufficient state. This study found that the vitamin D deficiency rate in Wuxi was even higher than the vitamin D deficiency rate in pregnant women in Shanghai. This indicates that the vitamin D deficiency in pregnant women in Wuxi is already quite serious.

At present, there are many factors that affect the serum vitamin D level of pregnant women, including age, pregnancy, season, outdoor exercise time and vitamin D supplementation preparation. Studies have shown that pregnant women of lower ages are more prone to vitamin D deficiency. Pregnant women in the early stage have more obvious vitamin D deficiency than pregnant women in the middle and late stages. At the same time, the expression of vitamin D in pregnant women's serum also has an obvious regulatory effect[18]. The expression of serum vitamin D in spring is significantly higher than that in winter. The serum vitamin D level of pregnant women with their second or more pregnancy is higher than that of pregnant women with first pregnancies. Increasing outdoor exercise time and vitamin D supplementation are protective factors for serum vitamin D in pregnant women. In this study, univariate analysis showed that there were statistically significant differences in serum vitamin D levels and sufficiency rates among pregnant women of different ages, pregnancy stage, sampling season and parity. Linear regression analysis showed that serum vitamin D levels in pregnant women were highly positively correlated with temperature. The higher the temperature, the higher was the serum 25-(OH)D level. Regarding pregnancy factors, deficiency is prevalent during early pregnancy, during which the loss of nutritional elements in pregnant women is common, which affects the absorption of vitamin D in pregnant women, resulting in relatively low levels of serum vitamin D in these pregnant women. Wuxi City is located at 31°7' to 32°2' north latitude and 119°33' to 120°38' east longitude. The subtropical monsoon climate has four distinct seasons; the sunshine duration and temperature are different in different seasons, and the summer and autumn seasons are sunny and the temperature is high. Pregnant women in the summer and autumn are more likely to participate in outdoor activities and be exposed to sunlight for a longer period than those in winter and spring, thus affecting serum vitamin D levels in pregnant women. In addition, the age of women pregnant with their second or more child is generally higher than that of women pregnant with their first child, and their awareness of the importance of outdoor activities and vitamin D supplementation is more profound, resulting in higher serum vitamin D levels in multiparous pregnant women than that in the primiparous group.

SGA, also known as a small size or intrauterine growth retardation, indicates a newborn born below the 10th percentile of the same-age fetal weight or a newborn born 2 standard deviations below the average fetal weight of the same gestational age[18, 19]. The perinatal mortality and risk of SGA are significantly higher than those of normal weight newborns. There are also cognitive impairments in adulthood, low learning ability, and low adult quality of life.

Infection and inflammation are important causes of premature birth and spontaneous abortion in pregnant women. Vitamin D has important functions, such as immune regulation and infection prevention[20]. It can increase anti-inflammatory factors in serum and reduce the level of proinflammatory factors. Vitamin D deficiency during pregnancy may occur through pregnancy. Because the inflammatory pathway increases the risk of premature birth and spontaneous abortion, this experiment tested the expression of inflammatory factors in the serum of pregnant women and found that adequate vitamin D can reduce the incidence of inflammation and reduce the possibility of miscarriage.

However, this study also has some shortcomings. Data on the duration of outdoor activities and vitamin D supplementation preparations for pregnant women were not included in the data analysis, which may produce some bias in the data analysis of this study. In addition, the mechanism of preterm birth, spontaneous abortion and SGA in pregnant women with vitamin D deficiency has not been studied in depth, and further research is needed.

Conclusion

In summary, the serum vitamin D level and sufficiency rate of pregnant women in this area are low and are affected by multiple factors such as age, season and temperature of pregnant women. Adequate vitamin D levels can reduce the possibility of premature birth and spontaneous abortion by inhibiting inflammatory factors. The role of this study is of great significance for the prevention and treatment of maternal diseases.

Abbreviations

SGA: small for gestational age; VD: Vitamin D; ELISA : enzyme-linked immunosorbent assay

Declarations

Ethics approval and consent to participate

The treatment and grouping of the subjects in this study were informed by pregnant women and were reviewed by the Ethics Committee of Wuxi Maternal and Child Health Hospital. Written informed consent was obtained from a parent or guardian for participants under 16 years old.

Consent for publication

Not applicable.

Availability of data and materials

Data set is available in electronic form which can be accessed upon a reasonable request from the corresponding author.

Competing interests

The authors declare that they have no competing interests.

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Authors’ contributions

ZH and CDZ conceived, designed, wrote, analyzed and interpreted the manuscript. WYR, and JXY collected the data and analyzed and wrote the first draft of the paper. QT and FJY designed, analyzed and critically revised the manuscript for important intellectual content the final paper. All authors have read the manuscript for publication. All authors read and approved the final manuscript.

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Figures

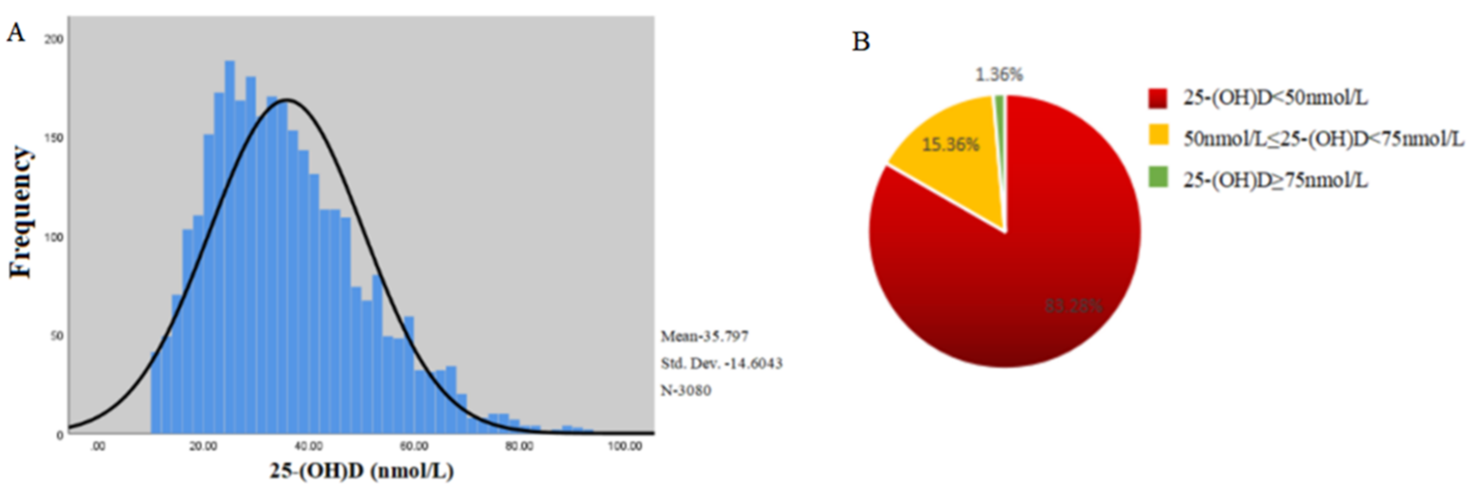

Figure 1

Vitamin D expression in maternal serum A: The frequency distribution map of 25-(OH) D expression. B: Percentage of vitamin D deficiency, insufficiency and adequate samples in pregnant women's samples

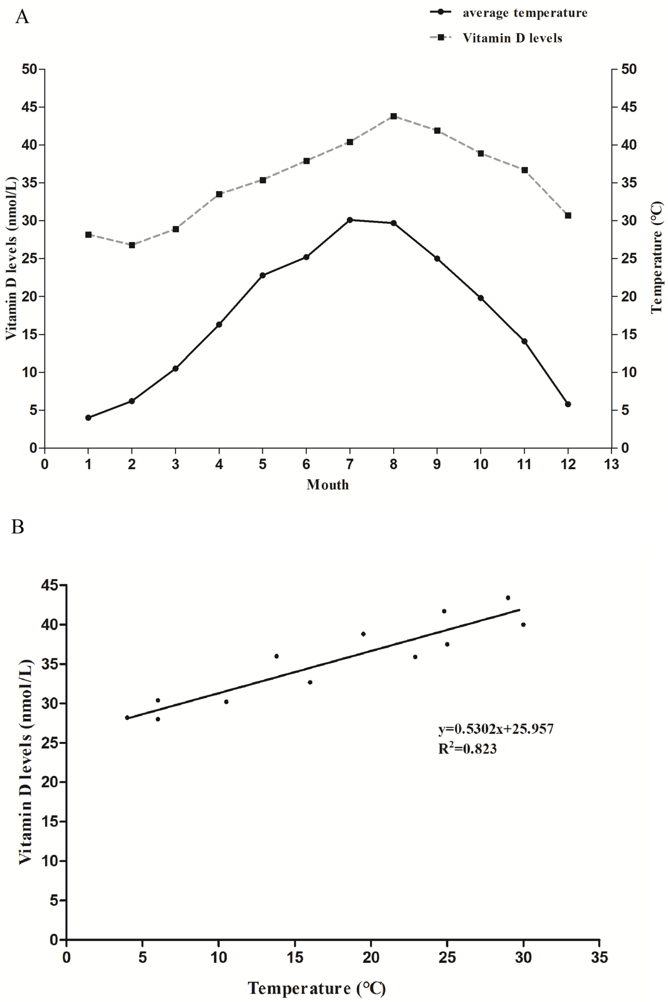

Figure 2

Linear regression analysis of the effect of temperature on serum vitamin D levels in pregnant women A: The vitamin D levels in serum and temperature changes in pregnant women with the month B: Linear Regression Analysis of Vitamin D Level and Temperature in Pregnant Women serum

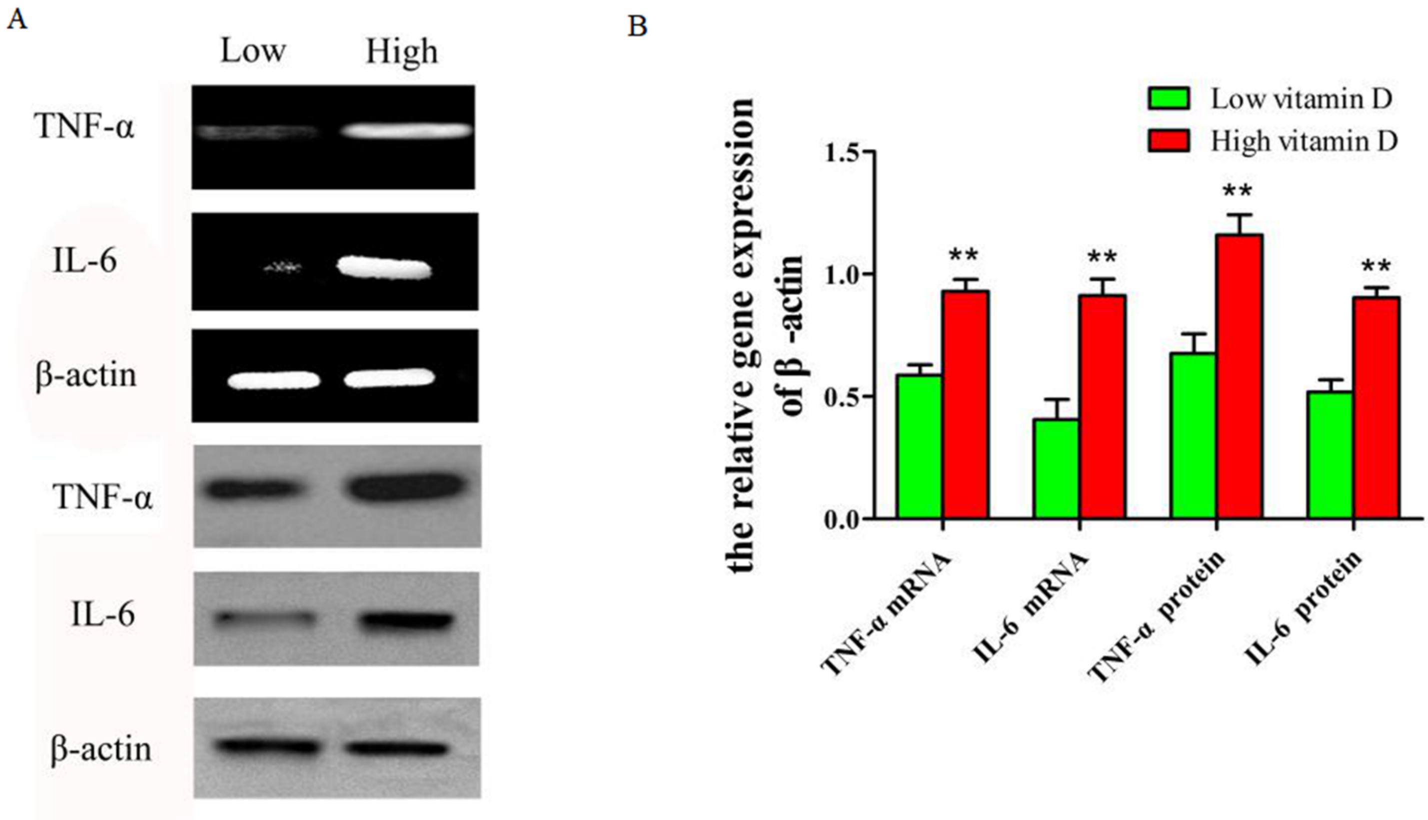

Figure 3

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Jiang W, Wu J, Huang M, Wang S, Muyiduli X, Si S, Shen Y, Chen Z, Yu Y (2019) The interaction between prepregnancy BMI and gestational vitamin D deficiency on the risk of gestational diabetes mellitus subtypes with elevated fasting blood glucose. Clinical Nutrition. doi:10.1016/j.clnu.2019.10.015 19. Robertson C, Lucas RA, Le Gresley A (2019) Scope and limitations of nuclear magnetic resonance techniques for characterisation and quantitation of vitamin D in complex mixtures. Skin Research and Technology. doi:10.1111/srt.12773 20. Medhat E, Rashed L, Abdelgwad M, Aboulhoda BE, Khalifa MM, El-Din SS (2019) Exercise enhances the effectiveness of vitamin D therapy in rats with Alzheimer's disease: emphasis on oxidative stress and inflammation. Metabolic Brain Disease. doi:10.1007/s11011-019-00504-2 figure legends Fig 1. Vitamin D expression in maternal serum A: The frequency distribution map of 25-(OH) D expression. B: Percentage of vitamin D deficiency, insufficiency and adequate samples in pregnant women's samples Fig 2. Linear regression analysis of the effect of temperature on serum vitamin D levels in pregnant women A: The vitamin D levels in serum and temperature changes in pregnant women with the month B: Linear Regression Analysis of Vitamin D Level and Temperature in Pregnant Women serum Fig 3.Vitmine D could inhibit the expression of TNF-α and IL-6 mRNA and protein A: The expression of TNF-α and IL-6 mRNA were analyzed by RT-PCR; The expression of TNF-α and IL-6 proteins were analyzed by Western blot; B: The expression levels were semi-quantified by densitometric measurements, normalized with β-actin internal control;** $P < 0.01$ vs.Low vitmine D group