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Original Research

Analysis of Differences in the Serum Levels of Various Vitamins During Pregnancy: Effects of Gestational Stage and Age

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Abstract

Background: Pregnant women exhibit an increased demand for nutrients, including vitamins, and a deficiency in vitamins can increase the risk of various pregnancy-related diseases. This study aims to evaluate the vitamin levels in women of different age groups and gestational stages in order to provide targeted dietary guidance and vitamin supplementation strategies. **Methods**: Pregnant women who registered and attended regular prenatal check-ups at Hangzhou Women's Hospital from January to December 2021 were selected as study participants. Ultrahigh-performance liquid chromatography-tandem mass spectrometry (UHPLC-MS/MS) was used to quantitatively determine the concentrations of vitamins A, D, E, K, B1, B2, B9 (folic acid), and B12 in the serum. **Results**: The serum vitamin A, B1, and B9 levels decreased with gestational age in the age-matched group, while the vitamin E level increased slightly ($p < 0.05$). In the advanced-aged group, the levels of vitamins A, B1, B2, and B9 decreased with gestational age, but the levels of vitamins D3, E, K, and B12 slightly increased ($p < 0.05$). In mid-pregnancy, age-matched women had slightly greater serum levels of vitamins E and K than did women in the advanced-aged group (Z = –2.67, p = 0.008; Z = –2.46, p = 0.014). In late pregnancy, significant differences existed in the serum levels of vitamins B2 and B12 between the two age groups (Z = –2.67, p = 0.008; Z = –2.50, p = 0.013). **Conclusions**: Vitamin levels varied by gestational stage and age during pregnancy, suggesting that vitamin supplementation should be individualized and stage-adjusted to improve maternal and child health.

Keywords: age; pregnancy period; vitamins

1. Introduction

Vitamins are a class of small-molecule organic compounds essential for maintaining normal metabolic functions in the human body [1]. They are generally divided into two major categories: fat-soluble vitamins and water-soluble vitamins. Fat-soluble vitamins include vitamins A, D, E, and K, while water-soluble vitamins include B-complex vitamins and vitamin C. Vitamins do not constitute body tissues or provide energy; their nutritional value lies in their roles as coenzymes or cofactors, participating in the body's substance and energy metabolism; they are indispensable nutrients for metabolic regulation and maintaining physiological functions. Although the body's requirement for vitamins is minimal, since these substances cannot be synthesized in the body or are insufficiently synthesized, they must be supplied through the diet. When the body's intake of vitamins from the external environment cannot meet its life-sustaining needs, metabolic disorders occur, leading to illness or even death [2–4].

Pregnancy is a special physiological period in a woman's life, during which changes in metabolism caused by pregnancy increase the body's demand for nutrients, including vitamins. Numerous studies have shown that maintaining good nutritional status during pregnancy is not only essential for ensuring the normal physiological functions of the mother and the smooth delivery of the fetus but also crucial for ensuring the health of the newborn and their health in adulthood [5,6]. Existing clinical data have preliminarily demonstrated the significant role of various vitamins in maintaining the health of pregnant women and fetuses during pregnancy. Vitamin deficiencies can increase the risk of various pregnancy complications in pregnant women, leading to miscarriage, stillbirth, birth defects, preterm birth, and neonatal death [7,8]. Common vitamin deficiencies in pregnant women often include mixed deficiencies [9,10]. Therefore, conducting comprehensive vitamin testing for this special group will provide insights into the levels of various vitamins during pregnancy and provide a basis for recommending rational dietary adjustments or vitamin supplementation.

Liquid chromatography-tandem mass spectrometry (LC-MS/MS) is a mainstream technology for assessing vitamin levels due to its high sensitivity, strong specificity, high accuracy, short analysis time, and ability to simultaneously analyze multiple components of mixtures [11]. Currently, in China, LC-MS/MS technology has been primarily applied to evaluate vitamin levels in the general population, with limited research on pregnant women, focusing only on vitamins A, D, E, K [12,13], and folate [14].

Optimal vitamin levels during pregnancy are not only essential for maintaining normal physiological functions and ensuring smooth delivery but also crucial for the health of newborns. Numerous clinical practices have shown that pregnant women require more vitamin intake than prepregnant women, and the requirements for vitamin types and intake amounts vary during different stages of pregnancy [15]. Ultrahigh-performance liquid chromatography-tandem mass spectrometry (UHPLC-MS/MS) is utilized in this study to determine the serum concentrations of various vitamins (vitamins A, D, E, K, B1, B2, B9 (folic acid), and B12) in pregnant women belonging to different age groups during mid- and late pregnancy. The aim of this study was to investigate the effects of different gestational stages and ages on the serum levels of various vitamins during pregnancy. This research provides clinical evidence for targeted dietary guidance and vitamin supplementation, aiming to achieve personalized and rational vitamin supplementation.

2. Materials and Methods

2.1 Study Participants

This cross-sectional study was conducted in Hangzhou city (population greater than 10,000,000), the capital of Zhejiang Province, which is among the most developed areas on the southeastern coast of China and has a high level of medical care. The annual number of births from 2018 to 2020 was greater than 13,000 in Hangzhou Women's Hospital. A total of 193 pregnant women who were registered at our hospital between January and December 2021 were selected. A total of 339 serum samples from mid- and late pregnancy were collected. The ages of the pregnant women ranged from 24 to 44 years. The inclusion criteria were as follows: (1) singleton pregnancy; (2) no preexisting medical conditions before pregnancy; (3) at least one serum vitamin level measurement completed during follow-up; (4) discontinued intake of multivitamin mineral tablets for at least 8 weeks; (5) the daily dosage of folic acid tablets was controlled between 0.4–0.8 mg, and the daily dosage of vitamin D was kept within 250 IU; and (6) receive one prenatal nutrition consultation during the second trimester. The exclusion criteria were as follows: (1) major organic disease; (2) incomplete prenatal testing or lack of follow-up records; and (3) history of adverse pregnancy outcomes, such as pregnancies affected by neural tube defects, Down syndrome, stillbirths, or neonatal deaths.

The grouping criteria were as follows: (1) Age group: age-matched group: $>$20 years old and $<$35 years old; advanced-aged group: $\geq$35 years old. (2) Gestational week groups: mid-pregnancy: 22 to 26 weeks; late pregnancy: 34 to 38 weeks.

2.2 Methods

2.2.1 Serum Collection and Sample Pretreatment Methods

(1) Serum collection method: 5 mL of peripheral blood was collected from pregnant women using disposable vacuum blood collection tubes (containing a blood coagulation activator). The tubes were gently shaken and allowed to stand at room temperature in a light-protected environment for 30 minutes. The tubes were centrifuged at 3000 rpm for 10 minutes at 4 °C. The supernatant was transferred to clean EP tubes and immediately stored at –20 °C until further processing.

(2) Pretreatment method for fat-soluble vitamins (A, D, E, K):

The standard reference materials used were as follows: vitamin A (Sigma-Aldrich (St. Louis, MO, USA), purity $\geq$98.0%, high-performance liquid chromatography (HPLC) grade), 25(OH)D2/D3 (Sigma-Aldrich, purity $\geq$98.0%, HPLC grade), vitamin E (Sigma-Aldrich, purity $\geq$99.0%, HPLC grade), and vitamin K (Sigma-Aldrich, purity $\geq$97.0%, HPLC grade).

A total of 100 µL of each serum sample was precisely pipetted, 70 µL of internal standard solution was added, the mixture was vortexed for 30 seconds, 500 µL of n-hexane (Merck KGaA (Darmstadt, Germany), HPLC grade) was added, the mixture was vortexed for 1 min and centrifuged at 11,000 rpm for 15 min at 4 °C, after which the upper layer was evaporated at room temperature under a stream of nitrogen. The residue was reconstituted in 150 µL of 70% methanol-water solution, vortexed for 30 seconds, and centrifuged at 11,000 rpm for 5 minutes, after which the supernatant was analyzed.

(3) Pretreatment method for water-soluble vitamins (B1, B2, B9, B12):

The standard reference materials used were vitamin B1 (Sigma-Aldrich, purity $\geq$98.0%, HPLC grade), vitamin B2 (Sigma-Aldrich, purity $\geq$99.0%, HPLC grade), vitamin B9 (Sigma-Aldrich, purity $\geq$98.0%, HPLC grade), and vitamin B12 (Sigma-Aldrich, purity $\geq$98.0%, HPLC grade).

A total of 100 µL of serum sample was precisely pipetted, 300 µL of internal standard methanol solution (Merck KGaA, HPLC grade) was added, the mixture was vortexed for 1 minute, and the mixture was centrifuged at 11,000 rpm for 15 minutes at 4 °C. The upper layer was evaporated under a stream of nitrogen, the residue was reconstituted in 150 µL of 10% methanol-water solution, the mixture was vortexed for 30 seconds, the mixture was centrifuged at 11,000 rpm for 5 minutes, and the supernatant was analyzed.

2.2.2 Serum Vitamin Detection Method

UHPLC-MS/MS was utilized to evaluate the vitamin levels.

The main instrument used was a Waters ACQUITY UPLC tandem mass spectrometer (Milford, MA, USA) (KySciReda).

2.2.3 Statistical Analyses

Data analysis was performed using SPSS 22.0 statistical software (IBM Corp., Armonk, NY, USA). Continuous variables with normal distribution were presents as mean

Table 1. Comparison of prenatal vitamin usage between the age-matched group and the advanced-aged group.

		Age-matched group [n (%)]	Advanced-aged group [n (%)]	Pearson χ^2	p
Discontinue multivitamin mineral	8–11 weeks	79 (85.9)	85 (84.2)	0.11	0.740
	≥12 weeks	13 (14.1)	16 (15.8)		
Folic acid	0.4 mg	63 (68.5)	66 (65.3)	0.21	0.644
	0.8 mg	29 (31.5)	35 (34.7)		
Vitamin D	100–125 IU	55 (59.8)	59 (58.4)	0.04	0.847
	200–250 IU	37 (40.2)	42 (41.6)		

Table 2. Comparison of serum levels of various vitamins in pregnant women in the age-matched group at different gestational stages.

	Mid-pregnancy (n = 92)	Late pregnancy (n = 67)	Mann-Whitney	
			Z Statistic	p
VitD2 (ng/mL)	0.38 (0.19, 0.69)	0.29 (0.15, 0.43)	–1.81	0.070
VitD3 (ng/mL)	21.37 (14.26, 31.67)	23.01 (15.20, 31.01)	–0.31	0.759
VitA (ng/mL)	0.40 (0.35, 0.49)	0.34 (0.31, 0.40)	–3.95	<0.001
VitE (μg/mL)	14.12 (12.81, 16.74)	15.80 (13.62, 18.43)	–2.25	0.025
VitK (ng/mL)	0.78 (0.37, 1.32)	0.70 (0.34, 1.52)	–0.28	0.778
VitB1 (ng/mL)	1.79 (1.40, 2.55)	1.34 (1.06, 1.67)	–4.46	<0.001
VitB2 (ng/mL)	6.21 (3.90, 9.24)	6.37 (3.91, 10.18)	–0.40	0.691
VitB9 (ng/mL)	21.32 (11.52, 31.35)	13.27 (8.70, 24.64)	–2.13	0.033
VitB12 (ng/mL)	0.15 (0.13, 0.17)	0.14 (0.12, 0.20)	–0.33	0.738

± standard deviation (SD); non-normal variables were reported as median (interquartile range); and categorical variables in numbers and percentages (%). Nonnormally distributed data were compared using the Mann–Whitney U test, while normally distributed data were compared by independent samples Student's test. The inter-group comparison of categorical data was conducted using the Pearson chi-square test. A significance level of $p < 0.05$ was considered to indicate statistical significance.

3. Results

3.1 General Information of the Participants

This study included 92 participants in the age-matched group, aged 24 to 34 years (29.01 $\pm$ 2.38). In the age-matched group, 92 serum samples were collected during mid-pregnancy, while 67 serum samples were collected during late pregnancy. There were 101 participants in the advanced-aged group aged 35 to 44 years (37.26 $\pm$ 1.89). In the advanced-aged group, 101 serum samples were collected during mid-pregnancy, while 79 serum samples were collected during late pregnancy.

All participants ceased the intake of multivitamin mineral tablets for at least 8 weeks upon enrollment. Throughout the entire pregnancy, the daily dosage of folic acid was maintained between 0.4–0.8 mg, and the daily intake of vitamin D supplementation did not exceed 250 IU. The specific supplementation details of vitamins during pregnancy for the age-matched group and advanced-aged group are presented in Table 1, with no statistically significant differences observed ($p > 0.05$).

3.2 Comparing Serum Levels of Different Vitamins in Pregnant Women of the Same Age Group across Various Gestational Stages

Compared to those in late pregnancy, pregnant women in the age-matched group showed statistically significant differences in the serum levels of vitamins A, E, B1, and B9 (folate) during mid-pregnancy (Z = –3.95, $p < 0.001$; Z = –2.25, p = 0.025; Z = –4.46, $p < 0.001$; Z = –2.13, p = 0.033). Specifically, vitamin A, B1, and B9 levels decreased with gestational age, while serum vitamin E levels slightly increased. In the advanced-aged group, except for vitamin D2, the serum levels of other vitamins (vitamins D3, A, E, K, B1, B2, B9, and B12) were significantly different (Z = –2.00, p = 0.045; Z = –3.27, p = 0.001; Z = –3.82, $p < 0.001$; Z = –3.43, p = 0.001; Z = –2.95, p = 0.003; Z = –3.50, $p < 0.001$; Z = –4.51, $p < 0.001$; Z = –2.27, p = 0.023). Specifically, the serum levels of vitamins A, B1, B2, and B9 tended to decrease, while the serum levels of vitamins D3, E, K, and B12 slightly increased (refer to Tables 2,3).

3.3 Comparison of Serum Levels of Various Vitamins in Pregnant Women among Different Age Groups at the Same Gestational Stage

During mid-pregnancy, the serum concentrations of vitamin E and vitamin K in the age-matched group were slightly greater than those in the advanced-aged group, and the differences were statistically significant (Z = –2.67, p = 0.008; Z = –2.46, p = 0.014). However, there were no sta-

Table 3. Comparison of serum levels of various vitamins in pregnant women in the advanced-aged group at different gestational stages.

	Mid-pregnancy (n = 101)	Late pregnancy (n = 79)	Mann–Whitney	
			Z Statistic	*p*
VitD2 (ng/mL)	0.35 (0.20, 0.60)	0.33 (0.20, 0.55)	–0.29	0.770
VitD3 (ng/mL)	22.95 (17.64, 28.25)	27.37 (19.13, 33.20)	–2.00	0.045
VitA (ng/mL)	0.40 (0.34, 0.47)	0.35 (0.28, 0.42)	–3.27	0.001
VitE (µg/mL)	13.39 (11.95,15.07)	15.10 (13.41,17.89)	–3.82	<0.001
VitK (ng/mL)	0.47 (0.25, 0.97)	0.84 (0.42, 1.34)	–3.43	0.001
VitB1 (ng/mL)	1.73 (1.36, 2.21)	1.51 (1.15, 1.84)	–2.95	0.003
VitB2 (ng/mL)	6.46 (4.13, 11.56)	4.26 (2.35, 7.25)	–3.50	<0.001
VitB9 (ng/mL)	23.44 (15.65, 29.94)	13.49 (10.37, 20.39)	–4.51	<0.001
VitB12 (ng/mL)	0.14 (0.12, 0.20)	0.16 (0.14, 0.21)	–2.27	0.023

Table 4. Comparison of serum levels of various vitamins in the age-matched group and advanced-aged group during mid-pregnancy.

	Age-matched group (n = 92)	Advanced-aged group (n = 101)	Mann–Whitney	
			Z Statistic	*p*
VitD2 (ng/mL)	0.38 (0.19, 0.69)	0.35 (0.20, 0.60)	–0.09	0.929
VitD3 (ng/mL)	21.37 (14.26, 31.67)	22.95 (17.64, 28.25)	–0.61	0.543
VitA (ng/mL)	0.40 (0.35, 0.49)	0.40 (0.34, 0.47)	–0.90	0.371
VitE (µg/mL)	14.12 (12.81, 16.74)	13.39 (11.95,15.07)	–2.67	0.008
VitK (ng/mL)	0.78 (0.37, 1.32)	0.47 (0.25, 0.97)	–2.46	0.014
VitB1 (ng/mL)	1.79 (1.40, 2.55)	1.73 (1.36, 2.21)	–1.08	0.280
VitB2 (ng/mL)	6.21 (3.90, 9.24)	6.46 (4.13, 11.56)	–1.05	0.294
VitB9 (ng/mL)	21.32 (11.52, 31.35)	23.44 (15.65, 29.94)	–0.76	0.448
VitB12 (ng/mL)	0.15 (0.13, 0.17)	0.14 (0.12, 0.20)	–0.35	0.728

tistically significant differences in the serum levels of other vitamins between the age-matched group and the advanced-aged group ($p > 0.05$) (Table 4).

In late pregnancy, there were statistically significant differences in the serum levels of vitamin B2 and vitamin B12 between the age-matched group and the advanced-aged group ($Z = –2.67$, $p = 0.008$; $Z = –2.50$, $p = 0.013$), with significantly higher levels of vitamin B2 observed in the age-matched group. However, there were no statistically significant differences in the serum levels of other vitamins between the age-matched group and the advanced-aged group ($p > 0.05$) (Table 5).

4. Discussion

4.1 Analysis of Differences in the Serum Levels of Various Vitamins at Different Gestational Stages within the Same Age Group

The majority of pregnant women must improve the quality of their diet, as even with dietary supplements, more than 20% of participants are at risk of inadequate intake of one or more micronutrients [16]. Folic acid supplementation is widely recommended before pregnancy and throughout the first 12 weeks to prevent neural tube defects (NTDs), such as spina bifida and anencephaly [17–19]. It is generally advised for all individuals of child-bearing potential to consume 0.4–0.8 mg (400–800 µg) of folic acid per day [20–22]. Those who have had a previous pregnancy affected by an NTD should consider a higher dosage, typically 4 mg per day [23]. Other risk factors that warrant targeted measurement and possibly enhanced folic acid supplementation strategies include certain genetic conditions, such as mutations in folate-related enzymes (e.g., methylenetetrahydrofolate reductase [MTHFR]) [24]; medical conditions, such as diabetes [24]; bariatric surgery [25], which affects nutrient absorption; and the use of medications that interfere with folate metabolism, such as antiepileptic drugs [26]. A recent recommendation suggested screening for vitamin D deficiency before pregnancy or during early pregnancy [27]. Our study indicated that compared to those in mid-pregnancy, the serum levels of vitamins A, B9, and B1 in pregnant women in the age-matched group decreased with increasing gestational age, while the serum vitamin E level slightly increased. In contrast, pregnant women in the advanced-aged group showed a decreasing trend in the serum levels of vitamins A, B1, B2, and B9, while the serum levels of vitamins D3, E, K, and B12 had a slight increase, with statistically significant differences. As pregnancy progresses to late pregnancy, with the growth and development of the fetus, there was a greater demand for vitamins A, B1, and B9 (folate) in the age-matched group and for vitamins A, B1, B9 (folate), and

Table 5. Comparison of serum levels of various vitamins in the age-matched group and advanced-aged group during late pregnancy.

	Age-matched group (n = 67)	Advanced-aged group (n = 79)	Mann–Whitney	
			Z Statistic	*p*
VitD2 (ng/mL)	0.29 (0.15, 0.43)	0.33 (0.20, 0.55)	–1.48	0.138
VitD3 (ng/mL)	23.01 (15.20, 31.01)	27.37 (19.13, 33.20)	–1.65	0.099
VitA (ng/mL)	0.34 (0.31, 0.40)	0.35 (0.28, 0.42)	–0.03	0.976
VitE (µg/mL)	15.80 (13.62, 18.43)	15.10 (13.41, 17.89)	–0.68	0.498
VitK (ng/mL)	0.70 (0.34, 1.52)	0.84 (0.42, 1.34)	–0.66	0.507
VitB1 (ng/mL)	1.34 (1.06, 1.67)	1.51 (1.15, 1.84)	–1.34	0.179
VitB2 (ng/mL)	6.37 (3.91, 10.18)	4.26 (2.35, 7.25)	–2.67	0.008
VitB9 (ng/mL)	13.27 (8.70, 24.64)	13.49 (10.37, 20.39)	–0.31	0.755
VitB12 (ng/mL)	0.14 (0.12, 0.20)	0.16 (0.14, 0.21)	–2.50	0.013

B2 in the advanced-aged group. Therefore, the supplementation dose of vitamins in late pregnancy should be moderately increased or obtained through dietary adjustments. This study demonstrated that vitamin D did not exhibit a decreasing trend, which may be related to the supplementation of vitamin D3 during pregnancy.

4.2 Analysis of Differences in Serum Vitamin Levels between Different Age Groups at the Same Gestational Stage

In this study, it was shown that during mid-pregnancy, the serum levels of fat-soluble vitamins E and K in the age-matched group were slightly greater than those in the advanced-aged group. Vitamin E is a natural antioxidant that not only maintains the balance between oxidation and antioxidation in the body, effectively reducing the toxic effects of free radicals but also regulates the degradation and synthesis of fetal membranes, thereby maintaining their integrity. Previous studies have indicated that during pregnancy, due to increased metabolism, low levels of vitamin E can lead to the accumulation of excessive free radicals and damage fetal membrane cells, which may result in premature rupture of membranes and increase the risk of hypertension during pregnancy and delivery [28]. A randomized controlled study suggested that the use of vitamins C and E in women with preterm premature rupture of membranes (PPROM) was associated with a longer latency period before delivery [29]. Some research has also indicated that vitamin E deficiency might be a risk factor for preeclampsia [30]. Supplementing with vitamin E during mid-pregnancy could have a protective effect against preeclampsia by alleviating overall blood pressure [31]. However, in our study, there were no statistically significant differences between the age-matched group and the advanced-aged group in terms of the incidence of pregnancy-induced hypertension or premature rupture of membranes ($p > 0.05$). A multicenter randomized trial of women at high risk of preeclampsia in low-nutrition populations in developing countries conducted by the World Health Organization showed that supplementation with vitamins C and E did not prevent preeclampsia [32]. High-dose supplementation with vitamin E may also reduce birth weight. As a coenzyme, vitamin K is involved in the synthesis of specific proteins related to blood clotting and bone metabolism. Liu *et al*. [33] reported that giving pregnant women vitamin K1 before 35 weeks of gestation significantly improved the activity of vitamin K-dependent coagulation factors II, VII, and X, thereby significantly reducing the incidence of intraventricular hemorrhage and periventricular hemorrhage in premature infants. Vitamin K deficiency in pregnant women can lead to difficulty in stopping bleeding and impaired blood coagulation and may cause bleeding in newborns. Research also indicates that low dietary intake of vitamin K is associated with decreased bone density in women [34,35] and may increase the risk of hip fractures [36]. Considering the hazards of vitamin E and K deficiency, pregnant women in the advanced age group may need to supplement vitamin E and K appropriately during mid-pregnancy, more than those in the age-matched group.

In this study, during late pregnancy, statistically significant differences were observed in the serum levels of the water-soluble vitamins B2 and B12 between the age-matched and advanced-aged groups.

The serum B2 levels were significantly greater in the age-matched group, while the serum vitamin B12 levels were significantly greater in the advanced-aged group. Vitamin B2 is a component of many important coenzymes in the body. These enzymes, which are necessary for the metabolism of proteins, sugars, fats, energy utilization, and composition, promote growth and development, protect the eyes, and maintain skin health, transferring hydrogen during metabolic processes of substances in the body. The coenzyme vitamin B2 can also affect mitochondrial function, oxidative stress, and vasodilation related to preeclampsia, protecting the fetus from the effects of hypoxia. Pregnant women deficient in vitamin B2 may experience inflammation of the mouth, lips, tongue, eyes, skin, etc., and the number of individuals with deficiency symptoms increases as pregnancy progresses, which is also reflected in the advanced-aged group. A study in Okinawa, Japan, revealed that maternal intake of folate, vitamin B6, and vitamin B2 during pregnancy may prevent poor social behavior, hyperactivity problems, and emotional problems, respectively, in children [37].

Adequate vitamin B12 is essential for maintaining normal hematopoietic and neurological function. Maternal vitamin B12 deficiency has been shown to be closely related to low birthweight infants and may increase the risk of neural tube defects in fetuses [38]. In addition, since folate, vitamin B6, and vitamin B12 are closely related to homocysteine metabolism, the accumulation of homocysteine is related to various abnormal or harmful changes in the body. Elevated levels of homocysteine and folate deficiency during pregnancy, as well as vitamin B12 deficiency, may be risk factors for preeclampsia and future cardiovascular risk. Extremely high maternal plasma folate and B12 levels at birth are associated with an increased risk of autism spectrum disorders in children, with B12 concentrations $\geq$536.8 pmol/L increasing the risk by 2.5 times (95% confidence interval (CI): 1.4, 4.5) [39]. Higher maternal red blood cell folate and vitamin B12 levels in early pregnancy are significantly associated with gestational diabetes [40]. Adequate vitamin B12 status in early pregnancy is associated with a lower risk of gestational diabetes [41]. There is high-quality evidence supporting the increased risk of neural tube defects and low birth weight infants with low maternal vitamin B12 levels during pregnancy, moderate-quality evidence supporting the increased risk of gestational diabetes, the impact on offspring cognitive function, and the risk of diabetes [42]. Maternal vitamin B12 deficiency during pregnancy is also associated with a greater risk of preterm birth (adjusted risk ratio = 1.21, 95% CI: 0.99, 1.49) [43].

Both vitamin deficiency and excess may lead to adverse pregnancy outcomes, so it is believed that supplementation with vitamins in different age groups during pregnancy should follow individualized principles. Pregnant women in the advanced-aged group may require more vitamin B2 supplementation during mid-pregnancy, while those in the age-matched group may need more vitamin B12 supplementation during late pregnancy.

5. Conclusions

There are differences in the serum levels of various vitamins during different gestational stages and among different age groups during pregnancy, indicating that vitamin supplementation throughout pregnancy should be adjusted according to age and gestational stage to improve maternal and child health.

Availability of Data and Materials

The minimal anonymized dataset necessary to replicate these study findings was kept as a Supporting Information file.

Author Contributions

PH designed the study and collected the data, while FZ analyzed the data and drafted the manuscript. Finally, PH critically reviewed the manuscript for important intellectual content. Both authors read and approved the final manuscript. Both authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was conducted in accordance with the International Code of Ethics for Biomedical Research Involving Human and Helsinki Declaration, and the study protocol was approved by the Ethical Review Committee of Hangzhou Women's Hospital in China, approval number [20201201]. The participants recruited for this study volunteered to participate and signed written informed consent forms.

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.31083/j.ceog5107152.

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