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ORIGINAL ARTICLE

Prevalence and Seasonal Variation in Serum 25-Hydroxyvitamin D Concentrations Among Women of Reproductive Age

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SUMMARY

Background: **This study aimed to investigate serum 25-hydroxyvitamin D [25(OH)D] concentrations among women of reproductive age, stratified by age and season, in order to provide information for vitamin D-related health strategies for this population.**
Methods: **A retrospective analysis was conducted on serum 25(OH)D concentrations in women of reproductive age who underwent preconception health examinations at the Physical Examination Department of Haidian District Maternal and Child Health Care Hospital between December 2022 and December 2024. Participants were stratified by age into two groups: advanced maternal age (≥ 35 years) and typical maternal age (< 35 years). Seasonal categorization included spring, summer, autumn, and winter. Intergroup comparisons were performed, and vitamin D nutritional status was classified based on established thresholds.**
Results: **A total of 2,325 women were included in the study. The mean serum 25(OH)D concentration was 34.45 ± 11.07 nmol/L. Vitamin D deficiency was observed in 92.47% of participants, insufficiency in 6.24%, and sufficiency in only 1.29%. Participants in the advanced maternal age group demonstrated significantly higher serum 25(OH)D concentrations compared to those in the normal maternal age group ($p < 0.05$). Seasonal variation in serum 25(OH)D concentrations was observed, with the highest levels recorded during summer and the lowest in spring. Concentrations in summer and autumn were significantly higher than those in winter and spring ($p < 0.05$); however, no significant differences were found between summer and autumn or between winter and spring ($p > 0.05$).**
Conclusions: **A high prevalence of vitamin D deficiency was observed among women of reproductive age in Haidian District, Beijing, with significant variations by age and season. Routine assessment of serum 25(OH)D concentrations is recommended for women planning pregnancy to facilitate timely and appropriate vitamin D supplementation strategies.**
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KEYWORDS

advanced maternal age, vitamin D deficiency, vitamin D insufficiency, women of reproductive age, 25-hydroxyvitamin D

INTRODUCTION

Vitamin D, a fat-soluble secosteroid, is critical for the maintenance of physiological homeostasis. Its principal circulating metabolite, 25-hydroxyvitamin D [25(OH) D], serves as the most reliable indicator of vitamin D status, owing to its relatively high serum concentration, extended half-life, and biochemical stability. Hypovitaminosis D has been recognized as a global public health concern, with an estimated prevalence affecting approximately one billion individuals worldwide [1].

While the role of vitamin D in calcium-phosphate metabolism and skeletal health is well established, an expanding body of evidence suggests that vitamin D deficiency contributes to the etiology and progression of several non-skeletal conditions, including metabolic disorders, such as diabetes mellitus, cardiovascular and cerebrovascular diseases, chronic kidney disease, autoimmune disorders, and neoplasms. Additionally, low maternal serum 25(OH)D concentrations have been associated with adverse pregnancy outcomes, such as increased risks of spontaneous abortion [2], gestational diabetes mellitus [3], pre-eclampsia [4,5], and fetal growth restriction [6].

The preconception period represents a critical window for evaluating serum 25(OH)D concentrations among women of reproductive age, as optimal maternal vitamin D levels are essential for favorable gestational outcomes. Despite documented high rates of vitamin D deficiency in Chinese children and adolescents [7], data specific to women of reproductive age remain limited, both nationally and internationally. Notably, no prior studies have addressed this demographic within the Beijing region.

The present study provides a statistical analysis of serum 25(OH)D concentrations in a cohort of 2,325 women of reproductive age, with stratification by age and season, to characterize patterns of deficiency and inform region-specific, targeted interventions aimed at improving preconception health and mitigating associated risks.

MATERIALS AND METHODS

Patients

A total of 2,325 women of reproductive age who underwent preconception medical evaluations at the Physical Examination Department of Haidian District Maternal and Child Health Care Hospital between December 2022 and December 2024 were included in the study. Based on obstetric criteria defining advanced maternal age as ≥ 35 years, participants were stratified into two groups: the advanced maternal age group (≥ 35 years, n = 271) and the typical maternal age group (< 35 years, n = 2,054).

Seasonal categorization was determined based on the calendar month of examination as follows: spring (March - May; n = 758), summer (June - August; n = 590), autumn (September - November; n = 558), and winter (December - February; n = 419).

Participants were excluded if they had a documented history of chronic thyroid or parathyroid disorders, hypertension, diabetes mellitus, chronic hepatic or renal conditions, or if they were receiving vitamin D supplementation during the study period, in order to reduce potential confounding factors.

Study methods

Fasting peripheral venous blood samples (5 mL) were collected in the morning from all participants. Following centrifugation at 3,000 rpm for 10 minutes, the serum was separated for analysis. Serum 25(OH)D concentrations were measured using an enzyme-linked immunosorbent assay (ELISA; IDS, United Kingdom), and absorbance was measured using an RT-6000 microplate reader (Rayto, Shenzhen, China). All assay procedures and instrumentation protocols were conducted strictly in accordance with the manufacturer's instructions, and only reagents within the specified expiration period were utilized.

Assessment of Vitamin D Status

Vitamin D status was classified according to the criteria established in 2011 [8]. Deficiency was defined as serum 25(OH)D < 50 nmol/L, insufficiency as serum 25(OH)D ≥ 50.0 to < 75.0 nmol/L, and sufficiency as 25(OH)D ≥ 75 nmol/L.

Statistical methods

Statistical analysis was performed using SPSS 25.0. Continuous variables with a normal distribution are expressed as mean ± standard deviation ($\bar{x} \pm s$). Intergroup comparisons were conducted using the *t*-test and analysis of variance (ANOVA). Categorical data are expressed as frequency (n) and percentage (%). Statistical significance was set at $p < 0.05$.

RESULTS

Demographic characteristics and serum 25(OH)D nutritional status

Between December 2022 and December 2024, a total of 31,505 women of reproductive age underwent preconception health assessments at the study site. Of these, 2,325 women, aged 22 to 46 years (mean age: 30.82 ± 2.99 years), met the inclusion criteria and had serum 25(OH)D concentrations measured. The mean serum 25(OH)D concentration in this cohort was 34.45 ± 11.07 nmol/L, with individual values ranging from 9.6 to 142.62 nmol/L.

Based on established criteria, 2,150 participants (92.47%) were classified as having vitamin D deficiency, 145 (6.24%) as vitamin D insufficiency, and 30 (1.29%) as vitamin D sufficiency (Table 1).

Comparison of serum 25(OH)D concentrations by age group

Participants were stratified by maternal age. The advanced maternal age group demonstrated a mean serum 25(OH)D concentration of 37.02 ± 14.38 nmol/L, which was significantly higher than the mean level observed in the typical maternal age group, which was 33.97 ±

Table 1. Comparison of serum 25(OH)D concentration in women of reproductive age (n = 2,325).

25(OH)D nutritional status	n	Percentage (%)
Deficient	2,150	92.47
Insufficient	145	6.24
Sufficient	30	1.29
Total	2,325	100.00

Table 2. Comparison of serum 25(OH)D concentrations among different age groups.

Group	n	Serum 25(OH)D concentrations (nmol/L)
Advanced maternal age group	271	37.02 ± 14.38
Typical maternal age group	2,054	33.97 ± 12.24
t	-	3.64
p	-	0.001

Table 3. Seasonal variation in serum 25(OH)D concentrations among women of reproductive age.

Group	n	Serum 25(OH)D concentrations (nmol/L)
Spring group	758	30.67 ± 5.80
Summer group	590	37.45 ± 6.61 *
Autumn group	558	36.61 ± 3.72 *
Winter group	419	30.92 ± 2.85
F	-	27.02
p	-	p < 0.05

The difference between those marked with * and those without * in the table is statistically significant.

12.24 nmol/L ($p < 0.05$) (Table 2). This finding indicates a statistically significant difference in serum vitamin D status between the two age groups.

Seasonal variation in serum 25(OH)D concentrations

Analysis of seasonal trends revealed significant variation in serum 25(OH)D concentrations among the seasonal subgroups. The highest mean concentration was recorded during the summer months, with a mean of 37.45 ± 6.61 nmol/L, which was significantly greater than the levels observed in both the winter (30.92 ± 2.85 nmol/L) and spring (30.67 ± 5.80 nmol/L) groups ($p < 0.05$).

Similarly, the autumn group exhibited a mean serum 25(OH)D concentration of 36.61 ± 3.72 nmol/L, significantly higher than that observed in the winter and spring groups ($p < 0.05$). No statistically significant differences were observed between the summer and autumn groups or between the winter and spring groups ($p > 0.05$) (Table 3).

DISCUSSION

Vitamin D is an essential fat-soluble micronutrient with diverse physiological functions, including regulation of calcium-phosphorus homeostasis and immune modulation. Primary sources of vitamin D include cutaneous synthesis via ultraviolet B (UVB) radiation and dietary intake [9]. Following absorption or dermal production, vitamin D undergoes sequential hydroxylation - first in hepatic mitochondria, forming 25(OH)D and, subsequently, in the renal proximal tubules via 1α-hydroxylase to produce the biologically active form, 1,25-dihydroxyvitamin D (1,25(OH)$_2$D) [10].

Circulating 25(OH)D exists as two isoforms - vitamin

D_2 (ergocalciferol) and vitamin D_3 (cholecalciferol) - which differ in potency, with vitamin D_3 exhibiting greater efficacy in promoting calcium absorption. In the epidermis, UVB exposure converts 7-dehydrocholesterol (7-DHC) to vitamin D, which binds to vitamin D-binding protein (DBP) for hepatic transport. Dietary vitamin D is absorbed in the intestine with lipids in the form of chylomicrons and subsequently binds to DBP or lipoproteins for systemic distribution and metabolism. The final active metabolite, $1,25(OH)_2D$, exerts hormone-like properties and binds to nuclear vitamin D receptors (VDRs), regulating gene transcription involved in calcium metabolism, cellular proliferation, differentiation, immune regulation, and apoptosis.

The biological activity of $1,25(OH)_2D$ is 500 - 1,000 times greater than that of 25(OH)D; however, its short half-life (6 - 8 hours) and susceptibility to parathyroid hormone-mediated regulation limit its clinical utility as a biomarker. In contrast, 25(OH)D has a longer plasma half-life (~3 weeks) and remains relatively stable, unaffected by fluctuations in calcium, phosphorus, or parathyroid hormone levels. As a result, it is the preferred biomarker for evaluating vitamin D status. Adequate serum 25(OH)D concentrations are essential for proper skeletal development and mineralization and are also associated with immunological, reproductive, and antineoplastic functions.

Beyond its classical role in bone and mineral metabolism, vitamin D demonstrates immunomodulatory properties and reproductive relevance. VDR expression has been documented in ovarian, uterine, and placental tissues. Altered expression of VDR at the maternal-fetal interface has been associated with adverse pregnancy outcomes, including recurrent pregnancy loss [2]. Emerging evidence suggests that vitamin D sufficiency may support embryo implantation and pregnancy maintenance, whereas inadequate 25(OH)D concentrations are linked to obstetric complications such as spontaneous abortion, gestational diabetes mellitus, preeclampsia, intrauterine growth restriction, and preterm birth [11,12].

The diagnostic criteria for vitamin D status in the 2011 Endocrine Society guideline [8] are also applicable in China. Vitamin D deficiency and vitamin D inadequacy were common in lactating women in China [13]. Similarly, a 2013 study by Song et al. documented a 90% deficiency rate among pregnant women in Beijing [14]. In Beijing, a 2009 study of adolescent girls (mean age: 15 years) reported a vitamin D deficiency rate of 89.2%, with a mean serum 25(OH)D concentration of 33.0 nmol/L - significantly lower than values reported in southern China [15].

In the present study, vitamin D deficiency was identified in 92.47% of 2,325 women of reproductive age undergoing preconception evaluation, with only 6.24% and 1.29% classified as insufficient and sufficient, respectively. These findings indicate a higher prevalence of deficiency than previously documented, underscoring the severity of this public health issue in northern China. Vitamin D deficiency poses significant risks to bone metabolism and skeletal health, primarily manifested as osteoporosis and increased fracture susceptibility. Recent epidemiological surveys revealed that the prevalence of vertebral fracture was 10.5% among men and 9.7% among women in China [16]. Several region-specific factors may contribute to the high prevalence of vitamin D deficiency in this cohort. Limited UVB exposure due predominantly indoor occupations, a sedentary urban lifestyle, and seasonal reductions in ambient UV radiation, particularly during winter and spring, are key contributing factors in Haidian District, Beijing. The urban infrastructure, high-rise buildings, and demanding academic and professional environments further reduce opportunities for sunlight exposure. Additionally, dietary patterns common in northern China typically include lower intake of vitamin D-rich foods, contributing to reduced bioavailable vitamin D.

Although aging is generally associated with diminished cutaneous vitamin D synthesis and bioavailability, higher serum 25(OH)D concentrations were found among participants of advanced maternal age compared to their younger counterparts. This difference may be explained by behavioral factors. Younger participants may have been more likely to maintain indoor-centric lifestyles, limit outdoor activity on both weekdays and weekends, and employ sun-protection strategies - such as the use of sunscreen, parasols, and wide-brimmed hats - resulting in decreased endogenous vitamin D production.

Seasonal analysis of serum 25(OH)D concentrations revealed a peak during the summer months, followed by autumn, with the lowest values observed in spring. This pattern aligns with established seasonal variations in solar irradiance at northern latitudes. Beijing, located north of the Tropic of Cancer, experiences maximum UVB exposure in summer as the solar declination angle reaches its northernmost point. Although daylight increases in spring, the physiological delay in vitamin D levels - attributable to the ~3-week half-life of circulating 25(OH)D - likely accounts for the springtime nadir observed in this study. The absence of a statistically significant difference between spring and winter groups further supports this hypothesis.

The high prevalence of vitamin D deficiency identified in this cohort highlights the need for targeted public health strategies to improve vitamin D status among women of reproductive age in northern China. Given that approximately 80 - 90% of endogenous vitamin D is synthesized through UVB exposure [17], public health interventions should prioritize strategies to enhance safe sun exposure and dietary intake among this population.

Women planning pregnancy are strongly encouraged to assess serum 25(OH)D concentrations during the preconception period and initiate supplementation as needed to optimize maternal and perinatal outcomes. Individuals engaged in office-based occupations may benefit from specific guidance to increase midday sun exposure, particularly during winter and spring, such as uti-

lizing open outdoor spaces away from shaded or built-up environments. Additionally, incorporation of vitamin D-rich foods, such as animal liver, deep-sea fish, egg yolks, and fortified dairy products, may further support nutritional adequacy.
Routine monitoring of serum 25(OH)D levels and individualized supplementation regimens should be integrated into preconception health programs to reduce the risk of deficiency-associated complications, including miscarriage, gestational diabetes, hypertensive disorders of pregnancy, and fetal growth abnormalities.
There were some limitations in the present study. First, ELISA for 25(OH)D quantification was used instead of the mass spectrometric method due to budgetary constraints, and we will prioritize mass spectrometry method in future studies. Second, measuring parathyroid hormone (PTH) levels is crucial to verify whether vitamin D deficiency induces secondary hyperparathyroidism. In our follow-up studies, we will systematically assess serum PTH concentrations to validate this potential pathophysiological linkage. Third, this retrospective study was limited by the lack of data on participants' dietary intake, sun exposure, and lifestyle behaviors, precluding multivariate analysis of contributing factors. Future studies should incorporate structured questionnaires to enable comprehensive assessment of determinants influencing vitamin D status among women of reproductive age in urban northern China.

Declaration of Interest:
None.

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