# Role of serum vitamin A and E in pregnancy

HAN CHEN, NIANFENG QIAN, LIYU YAN and HONGQING JIANG

Haidian Maternal and Child Health Hospital, Beijing 100080, P.R. China

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**Abstract.** Serum levels of vitamin A and E in early, middle and late pregnancy were analyzed to evaluate vitamin nutritional status in pregnancy, and provide guidance for pregnant women about vitamin supplements in pregnancy. In total, 28,023 serum samples were randomly selected from pregnant women in early, middle and late pregnancy between January 2013 and June 2014 in Beijing. High performance liquid chromatography (HPLC) method was used to determine the concentration of serum vitamin A and E in pregnancy. The concentration of serum vitamin A in early, middle and late pregnancy was 0.33±0.08, 0.37±0.09 and 0.33±0.15 mg/l, respectively, total abnormal rate was 25.31%, and deficiency (24.98%) was the main feature. The rate of deficiency in the early pregnancy (38.22%) was greater than that in late pregnancy (35.13%). The serum vitamin E in early, middle and late pregnancy was 9.10±2.47, 14.24±3.66 and 15.80±5.01 mg/l, respectively, total abnormal rate was 5.60%, and excess (5.37%) was the main feature. The excess rate in early pregnancy was at the lowest level (0.50%), and reached the highest level (15.32%) in late pregnancy. The serum levels of vitamin A and E are different during pregnancy. Generally, vitamin A is deficient and vitamin E is in excess. Therefore, monitoring the vitamin A and E levels, and strengthening perinatal education and providing guidance for pregnant women to supply vitamins rationally play important role in guaranteeing maternal and fetal safety.

## Introduction

Vitamin A and E are essential micronutrients in human body, and play very important roles in maternal health and fetal development (1). Vitamin A is an essential nutrient needed in small amounts for the normal functioning of the visual system, it can maintain cell function for growth, normal immune function, hematopoietic system, epithelial integrity, red blood cell production, immunity and reproduction (2), especially during pregnancy. Vitamin A deficiency (VAD) not only increases the risk of miscarriage, night blindness, and pregnancy complication, but also affects the embryonic development. Severe deficiency causes fetal malformations. Excessive vitamin A increases birth defect risks (3).

Vitamin E is an essential vitamin for maintaining the metabolic function of the body and possesses antioxidant and scavenging free radical activities (1). The deficiency of vitamin E in pregnant women leads to placental aging, vascular endothelial injury, incidence of hypertensive disorders of pregnancy, placental abruption, abortion and premature birth (4). While excessive vitamin E in the body affects the absorption and function of other fat-soluble vitamins. However, there are scarce studies analyzing the values of serum vitamin A and E during pregnancy in China. Therefore, there is an urgent need to study serum levels of vitamin A and E in pregnancy.

This study was designed to analyze the serum levels of vitamin A and E in early, middle and late pregnancy, evaluating the vitamin nutritional status in pregnancy in order to provide guidance for pregnant women about vitamin supplements in pregnancy.

## Patients and methods

*Sample collection*. We conducted a quantitative study on the levels of vitamin A and E in 12,340 pregnant women from January 2013 to June 2014 at the Beijing Harmony Health Medical Diagnostics Co., Ltd. (Beijing, China), among which 10,082 cases were primipara and 2,258 cases were pluripara. Those women were 23-40 years of age, healthy, with no high blood pressure, diabetes, chronic kidney disease, congenital heart disease or other internal problems, no thrombotic diseases, such as thrombophilia, antiphospholipid syndrome, no history of long-term drug use, such as aspirin; and were transferred to the general hospital for prenatal examination.

Their average age was 29.96±3.77 years, and their pre-pregnancy BMI ranged from 14.87 to 33.89 kg/m$^2$, with an average of 21.51±3.06 kg/m$^2$. Serum samples were collected from each pregnant woman at their first visit (8-12 weeks of pregnancy), 24-28 weeks and 34-36 weeks of pregnancy. A total of 28,023 serum samples were collected and divided into three groups: group of early pregnancy ($n_{VA}$ = 3,953, $n_{VE}$ = 3,965), group of middle pregnancy ($n_{VA}$ = 9,014, $n_{VE}$ = 9,090) and group of late pregnancy ($n_{VA}$ = 1,002, $n_{VE}$ = 999).

The eligible pregnant women were randomly selected with a stratified sampling method from the prenatal outpatients at

*Correspondence to:* Dr Hongqing Jiang, Haidian Maternal and Child Health Hospital, 33 Haidian South Road, Beijing 100080, P.R. China
E-mail: drjhq91@sohu.com

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class A (grade III) and class B (grade II) hospitals in Haidian, Huairou, Dongcheng, Mentougou, Pinggu, Tongzhou, and Xicheng Districts in Beijing, China.

This study was approved by the Ethics Committee of Haidian Maternal and Child Health Hospital (Beijing, China). Signed informed consents were obtained from the patients or the guardians.

*Sampling detection methods*. High performance liquid chromatography (HPLC) was used to quantitatively determine the concentration of serum vitamin A and E (HPLC instrument model: Agilent HPLC 1290; Agilent Technologies, Inc., Santa Clara, CA, USA).

Serum was taken from peripheral venous blood (2 ml), not anticoagulation, and was stored in dark and cool (0-4˚C) environment. Whole blood samples were centrifuged at 2,500 x g at 4˚C for 10 min in a timely manner to obtain serum samples. Protein and impurities were removed, and hexane was added to extract effective components from the serum samples. The supernatant fraction was obtained, dried, and re-dissolved with methanol to detect effective components. Instrument conditions: i) chromatographic columns: Agilent CB; ii) column temperature: room temperature; iii) mobile phase: methanol-pure water; iv) flow rate: VA, 0.5 ml/min; VE, 1.0 ml/min. v) wavelength: VA, 325 nm; VE, 292 nm.

*Sample analysis*. A total of 13,969 samples were used to analyze the serum level of vitamin A, and 14,054 samples were used for serum vitamin E analysis (Table I).

*Reference value*. The normal reference range for serum vitamin A and E was 0.3-0.7 and 5-20 mg/l, respectively. Low test values for vitamin A and E were indicative of nutritional deficiency, while high test values were indicative of nutritional excess.

*Statistical analysis*. Statistical software CHISS (version 2010; Beijing, China) was applied for the data analysis. Comparison between multiple groups was made using one-way ANOVA test followed by a post hoc test (Least Significant Difference). $P<0.05$ was considered to indicate a statistically significant difference. The standard substances were analyzed to establish the standard curve equation. Standard deviation was <15%. Vitamin A and E contents in the quality control and testing samples were calculated based on the standard curve equation. Quality control range was mean ± 2SD, Westgard Multirules were used to determine if the quality control result was qualified, and at least double quality control was used for each batch of samples.

## Results

*Serum vitamin A level in pregnancy*. Serum vitamin A level in pregnancy was 0.36±0.10 mg/l, and according to the stage of pregnancy it was 0.33±0.08, 0.37±0.09 and 0.33±0.15 mg/l in early, middle, and late pregnancy, respectively. The levels in early and late pregnancy were relatively low. The differences were statistically significant ($P<0.05$) (Fig. 1).

There was a total of 25.31% abnormal rate of vitamin A among these pregnant women and most of them were VAD, representing 24.98%. The highest abnormal rate was in early pregnancy, which was 38.35%, the deficiency rate accounted for 38.22% and severe deficiency (<0.2 mg/l) was 2.99%. The second abnormal rate was observed in late pregnancy, which was 35.93%. The deficiency rate accounted for 35.1%, and severe deficiency (<0.2 mg/l) was 29.57%. The differences were statistically significant ($P<0.05$) (Table II).

*Serum vitamin E level in pregnancy*. Serum vitamin E level in pregnancy was 12.9±4.30 mg/l, which was respectively, 9.10±2.47, 14.24±3.66, and 15.80±5.01 mg/l in early, middle, and late pregnancy. The levels in early pregnancy were relatively low. The differences were statistically significant ($P<0.05$) (Fig. 2).

There was a total of 5.60% abnormal rate of vitamin E among these pregnant women and most of them had vitamin

Table I. Serum samples for vitamin A and E analysis (n).

| Groups | Vitamin A | Vitamin E |
|---|---|---|
| Early pregnancy (≤12 weeks) | 3,953 | 3,965 |
| Mid pregnancy (20-24 weeks) | 9,014 | 9,090 |
| Late pregnancy (≥28 weeks) | 1,002 | 999 |
| Total | 13,969 | 14,054 |

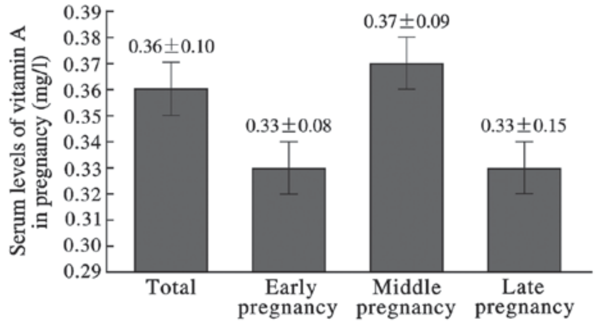


Figure 1. Serum vitamin A level in pregnancy was 0.36±0.10 mg/l. According to the stage of pregnancy the vitamin A levels were 0.33±0.08, 0.37±0.09, and 0.33±0.15 mg/l in early, middle, and late pregnancy, respectively. The levels in early and late pregnancy were relatively low. The differences were statistically significant ($P<0.05$).

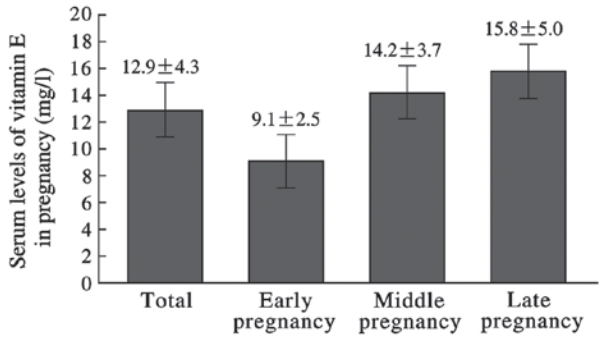


Figure 2. Serum vitamin E level in pregnancy was 12.9±4.30 mg/l. According to the stage of pregnancy the vitamin E levels were 9.10±2.47, 14.24±3.66, and 15.80±5.01 mg/l in early, middle, and late pregnancy, respectively. The levels in early and late pregnancy were relatively low. The differences were statistically significant ($P<0.05$).

Table II. Detection of serum levels of vitamin A in pregnancy.

| | Deficiency, n (%) | | | | | |
|---|---|---|---|---|---|---|
| Groups | (<0.2 mg/l) | (0.2-0.3 mg/l) | Normal, n (%) (0.3-0.7 mg/l) | Excess, n (%) (>0.7 mg/l) | Total (n) | Total abnormal rate (%) |
| Early | 118 (2.99) | 1,393 (35.24) | 2,437 (61.65) | 5 (0.13) | 3,953 | 38.35 |
| Mid | 95 (1.05) | 1,531 (16.98) | 7,354 (81.58) | 34 (0.38) | 9,014 | 18.42 |
| Late | 296 (29.57) | 56 (5.59) | 642 (64.14) | 8 (0.80) | 1,002 | 35.93 |
| Total | 3,489 (24.98) | | 10,433 (74.69) | 47 (0.33) | 13,969 | 25.31 |

Table III. Detection of serum levels of vitamin E in pregnancy.

| Groups | Deficiency, n (%) (<5 mg/l) | Normal, n (%) (5-20 mg/l) | Excess, n (%) (>20 mg/l) | Total (n) | Total abnormal rate (%) |
|---|---|---|---|---|---|
| Early | 30 (0.76) | 3,915 (98.74) | 20 (0.50) | 3,965 | 1.26 |
| Mid | 2 (0.02) | 8,505 (93.56) | 583 (6.41) | 9,090 | 6.43 |
| Late | 0 (0.00) | 846 (84.68) | 153 (15.32) | 999 | 15.32 |
| Total | 32 (0.23) | 13,266 (94.39) | 756 (5.37) | 14,054 | 5.60 |

E excess, representing 5.37%. The lowest abnormal rate was among women in early pregnancy, which was 1.26%. The deficiency rate accounted for 0.76%, and the excess rate was 0.5%. The abnormal rate increased during pregnancy, and the highest rate was observed among women in late pregnancy, which was 15.32%. All these abnormal cases were vitamin E excess. The differences were statistically significant (P<0.05) (Table III).

## Discussion

VAD is considered a major nutritional concern in poor societies, especially in lower income countries. The main underlying cause of VAD, as a public health problem, is a diet that is chronically insufficient in vitamin A that can lead to lower body stores and fail to meet physiological needs (5,6). Preschool age children and pregnant women are the high-risk groups of VAD.

Previous studies have found that maternal VAD can have an adverse effect on embryonic development, resulting in poor fetal growth and several congenital defects, such as cryptophthalmos and anophthalmos, heart defects, central nervous system abnormalities, retardation of skeletal development and malformation (7,8). Between 1995 and 2005, the global VAD rate (serum retinol content <0.7 $\mu$mol/l) was 15.3%, among which Asia was the most serious, with a deficiency of Vitamin A of 18.4%, with that in China being 22.8% (9). The results of the study on the nutritional status of vitamin A in Chinese cities from 2010-2012 showed that the deficiency of vitamin A in pregnant women was 7.4%, and the lack of vitamin A in large cities was 11.5% (10).

The study revealed that the pregnant women in Beijing mainly had VAD. The total rate of VAD was 24.98%, which accounted for 35.13% in late pregnancy, and severe deficiency (<0.2 mg/l) rate was 29.57%. However, other studies in the region of developing countries showed that VAD was found among 20% (in Egypt), 15.8% (in Nigeria) and 18.8% (in Bangladesh) of pregnant women (11-13). Our study showed that the serum levels of vitamin A in early and late pregnancy were quite low. This might be related to the health status of pregnant women, reaction of pregnancy, hormone levels, regional differences, and many other factors. Firstly, traditionally, botanical food has higher proportion (80%) in the diet structure of Chinese women than animal foods, especially animal liver which is rich in vitamin A. Besides, progesterone level gradually increases during pregnancy and reaches the peak in late pregnancy. Progesterone can accelerate vitamin A in liver and fat tissues to release into blood (14). Since the progesterone level is relatively low in early pregnancy, there is a lower serum vitamin A level. Moreover, vitamin A is fat-soluble and its absorption and utilization is closely associated with that of fat. Because of the pregnancy reaction, there is a decrease in food intake of vitamin A and fat, and a limited storage in blood, liver, and fat tissues leading to less vitamin A releasing to blood. The concentration of vitamin A is related to the concentration of retinol biding protein (RBP). In the early stage of pregnancy, RBP concentration is low. So, the serum level of vitamin A declines accordingly (2). Low levels of vitamin A in late pregnancy may be affected by the significant growth in fetal weight and nutrition demand.

Currently, WHO recommends routine vitamin A supplementation during pregnancy or at any time during lactation in areas with endemic VAD (where night-blindness occurs). In pregnancy, extra vitamin A is required for growth and tissue maintenance in the foetus, for providing it with some reserves and for maternal metabolism. Pregnant women have a basal requirement of 370 $\mu$g/day, maximum dose of 3,000 $\mu$g/day and recommended daily allowance (RDA) of 770 $\mu$g/day (15,16). Based on the findings mentioned above, physicians should pay close attention to the nutritional status of pregnant women, and monitor vitamin A serum level in different pregnancy stages, especially in early and late pregnancy (2). Upon test reports, physicians can provide personalized dietary guide for patients. Those pregnant women whose vitamin A is too low should intake animal food with rich vitamin A, as well as vegetables. For pregnant women who intake enough food with vitamin A, physicians should teach them how to convert between different types of food and to diversify their food recipes (14). For those who intake excessive vitamin A, physicians should help them to achieve reasonable diets. By accepting personalized dietary guidance and ensuring an optimized nutrition intake during pregnancy the possibilities of fetal abnormalities and congenital defects caused by intaking insufficient vitamin A can be lower (10).

Vitamin E is the necessary micronutrient for maintaining the body's normal metabolism and function, with the features of antioxidant and radical scavenging (1). Pregnant women have a fast metabolism, an increase of the production of free radicals, and an increase of lipid peroxidation. So, low vitamin E levels can lead to excessive free radicals, resulting in aging of placenta, vascular endothelial injuries, increasing the incidence of hypertensive disorders in pregnancy (4,17-19). It may also damage the membrane of fetal membrane cells, increasing the risk of premature rupture of fetal membranes (6). Vitamin E has anticoagulant activity, excessive vitamin E can have an impact on blood clotting in the fetus, increasing the risks of high levels of bilirubin and nuclear jaundice for newborn babies (20). In addition, excessive vitamin E has an antagonistic effect on other fat-soluble vitamins in the blood of pregnant women, preventing the absorption and functions of other vitamins (21).

The findings of this study showed that women had the lowest serum level of vitamin E in early pregnancy while the highest in late pregnancy. Vitamin E was present in excess (5.37%). As gestational age increased, the excess rate of vitamin E reached the peak of 15.32% in late pregnancy. Except for some factors including hormone levels and general health condition, intaking excessive vitamin E from food and drug supplementation may be the main reason (22). Therefore, physicians should pay close attention to monitor the changes in vitamin E level in pregnancy and provide proper nutrition guidance, especially emphasizing on rational vitamin E supplement.

In conclusion, good nutritional status during pregnancy not only can guarantee the normal physiological functions and keep mothers healthy, but is also crucial for fetal development and delivery. By detecting the serum levels of vitamin A and E among pregnant women in Beijing and evaluating their vitamin nutritional status, the study has value in guiding the vitamin supplements of pregnant women. In practice, we can reduce the possibility of fetal abnormalities and congenital defects by emphasizing perinatal education and nutrition supplement guidance, strengthening the monitoring of vitamin status, and developing early prevention and intervention strategies.

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## Availability of data and materials

All data generated or analyzed during this study are included in this published article.

## Authors' contributions

HC and HJ designed the study and performed the experiments; HC, NQ, LY and HJ were responsible for the acquisition of the data; HC and NQ analyzed the data; HC and HJ prepared the manuscript. All authors read and approved the final manuscript.

## Ethics approval and consent to participate

This study was approved by the Ethics Committee of Haidian Maternal and Child Health Hospital (Beijing, China). Signed informed consents were obtained from the patients or the guardians.

## Patient consent for publication

Not applicable.

## Competing interests

The authors declare that they have no competing interests.

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