Vitamin A status and its hematological correlates among preschool children in Beijing, China

doi: 10.6133/apjcn.202209/PP.0002
Published online: September 2022

Running title: Vitamin A & anemia in Beijing preschool children

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ABSTRACT

Background and Objectives: Vitamin A is vital for the growth and health of children. This study aimed to estimate the current vitamin A status and the prevalence of vitamin A deficiency (VAD) among preschool children and explore the correlation between serum vitamin A concentration and changes in hematological parameters. **Methods and Study Design:** The study included 697 children aged 1-6 years, presenting for routine checkups at the Department of Pediatrics, Peking University Shougang Hospital, Beijing, from April 2017 to December 2020. We obtained the complete laboratory test data of 630 children. **Results:** The mean serum vitamin A concentration among preschool children was 0.29±0.08 mg/L, with a median of 0.29 mg/L. The proportion of children with VAD and marginal VAD (MVAD) was 9.84% and 43.49%, respectively. The highest prevalence of VAD and MVAD was in the 3- to 4-year age group. Compared with the normal vitamin A serum concentration group, other groups had lower mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, and higher red blood cell distribution width. The mean serum vitamin A concentration among anemic children was significantly lower (0.27±0.07 mg/L) than among those children who were not anemic (p<0.05). **Conclusions:** VAD constitutes a public health problem in northern China. The prevalence of VAD is highest, and the serum vitamin A concentration was the lowest among preschool children aged 3-4 years. Vitamin A serum concentration was associated with red blood cell indices. We should attach more importance to those children aged 3-4 years.

Key Words: Vitamin A status, Vitamin A deficiency, hematological indices, preschool children, China

INTRODUCTION

Vitamin A is a key micronutrient for child health and affects growth and immune function.[1,2] Inadequate vitamin A intake has a direct impact on eye health and vision and can lead to night blindness, corneal xerosis, abnormal hematopoietic function, and growth retardation in children.[3-6] According to a recent systematic review in China, vitamin A deficiency (VAD) remains a public health concern nationwide, especially in rural districts.[7]

Undernutrition impacts hematopoietic and lymphoid organs.[8] Vitamin A status is related to some hematological parameters. Indian children who did not receive foods with plentiful vitamin A tended to be anemic.[9] Many studies have examined a close connection between vitamin A supplementation, iron status improvement and hemoglobin concentrations

increase.[10-13] Vitamin A supplementation benefited neutrophilic phagocytic function in Venezuelan children.[11] Vitamin A stores contributed to the numbers and function of natural killer cells in a Bangladeshi study.[14]

We have assessed the prevalence of VAD and its association with anemia among preschool children as a public health problem in Beijing, northern China.

MATERIALS AND METHODS

Study area

This study in Shijingshan District, covers an area of 84 km^2, one of the smaller districts of Beijing. It has a population of 570000, and population density of 6648 people/km^2. The economic growth rate in this district is higher than the average for the whole city. Its distribution of health resources is better than the median for the entire city. Commonly available foods include rice, beef, mutton, eggs, fresh vegetables, and fruits produced in the local countryside.

Study population

Some 697 children aged 1-6 years, presenting for routine checkups at the Department of Pediatrics, Peking University Shougang Hospital, Beijing, from April 2017 to December 2020, were studied. Children who had a history of hematological malignancies, chronic diarrhea, or hepatobiliary diseases were excluded. The research protocol was approved by the Ethics Committee of Peking University Shougang Hospital. Children and their parents had advanced information about the proposed research, and parents provided written consent.

Blood sampling and laboratory testing

Peripheral blood was collected by venipuncture. An automatic hematology analyzer (XN-4000; Sysmex, Japan) was used to measure the routine blood parameters. Hematological indices included white and red blood cell counts, Hb, hematocrit, mean corpuscular volume (MCV), mean corpuscular Hb (MCH), mean corpuscular Hb concentration (MCHC), red blood cell distribution width (RDW), platelets, plateletcrit, mean platelet volume, and platelet distribution width. Serum vitamin concentration was measured by HPLC (LC-20AD; Shimadzu, Japan).

Definitions

The normal reference range for serum vitamin A concentration was 0.3-0.7 mg/L.VAD was regarded as <0.2 mg/L (<0.7 μmol/L), and marginal vitamin A deficiency (MVAD) between 0.2 mg/L and 0.3 mg/L (0.7-1.05 μmol/L).[15] Anemia was diagnosed when Hb was <110 g/L at 0.50-4.99 years and was <115 g/L at 5.00-11.99 years, in accordance with World Health Organization (WHO) criteria.[16]

Statistical analysis

SPSS version 22 (IBM Corp, Armonk, NY, USA, 2013) was used for data analysis. Continuous variables are presented as mean ± standard deviation. Differences between proportions were assessed with the chi-squared test. Differences between study groups were assessed by the independent samples t-test. Categorical and continuous variables were analyzed using the one-way ANOVA test. Statistical significance was set at $p<0.05$.

RESULTS

Vitamin A status of preschool children

We obtained the complete laboratory test data of 630 children in the cohort. The mean serum vitamin A concentration among preschool children was 0.29±0.08 mg/L, with a median of 0.29 mg/L (Figure1). The proportion of children with VAD and MVAD was 9.84% and 43.49%, respectively (Figure 2).

The mean age of the group was 2.2±1.3 (range: 1.0–5.9) years, and 45.2% (285/630) of the children were female. Vitamin A serum concentration did not differ significantly between boys and girls. Girls had a higher prevalence of VAD than boys, but boys had a higher prevalence of MVAD than girls ($p<0.05$). A significantly higher vitamin A serum concentration was noted in the group aged 1-2 years, compared with the group aged 3-4 years ($p<0.05$). The prevalence of VAD and MVAD was significantly different between the different age groups ($p<0.05$) (Table 1), and the highest prevalence of VAD and MVAD was seen in the 3- to 4-year age group.

Serum vitamin A concentration and hematological indices

The relationships between serum vitamin A concentration and hematological indices are summarized in Table 2. Vitamin A serum concentration was associated with red blood cell indices ($p<0.05$). Compared with those with normal vitamin A serum concentration, others

had a lower MCV, MCH, MCHC, and higher RDW. There were no significant differences between serum vitamin A concentration and other hematological parameters.

Association between serum vitamin A and anemia

Overall, 61 (9.7%) of the 630 children were anemic. The mean serum vitamin A concentration among anemic children was 0.27±0.07 mg/L, which was significantly lower than that of children who were not anemic (p<0.05) (Table 3).

DISCUSSION

The prevalence of VAD and MVAD was 9.84% and 43.49%, respectively among preschool children, in this study. According to the WHO guidelines, 17 it is considered a mild public health problem. We noted better vitamin A status in the Shijingshan region, compared with two other studies in China, which reported prevalence of VAD as 12.2% and 19.61%.[18,19] As mentioned above, there are recognizable advantages of living in the Shijingshan district. Therefore, for years, more attention has been paid to children's nutritional status and health science education in this district. Nevertheless, there is a difference between our findings and the reported prevalence of VAD and MVAD (5.16% and 24.29%, respectively) in a Chinese systematic review, 7 which probably indicates a potential for improvement in vitamin A status in the district we studied.

The prevalence of VAD was highest, and serum vitamin A concentration was lowest in the aged 3-4 years age group, inconsistent with previous studies,[4,7,19] where VAD declined with increasing age. WHO recommends high-dose vitamin A supplements in infants and children aged 6 to 59 months to reduce morbidity and mortality.[20] However, VAD could be reduced by replacing the high-dose periodic capsule distribution programs with frequent low-dose vitamin A intakes.[21] Chinese children are required to be administered supplementary vitamin A and drops daily from several days after birth until 3 years. Daily vitamin A supplementation recommended is 1500 IU for infants and 2000 IU for toddlers, which probably accounts for the lowest prevalence of VAD being among the group aged 1-2 years. The high prevalence of VAD in the group aged 3-4 years might be due to a change in living conditions after entering kindergarten and frequent exposure to infections. Thus, to monitor the health of children aged 3-4 years may ensure that they receive a nutritionally adequate and varied diet, measures to improve immune function and reduce the risk of infection. Animal foods (such as milk, eggs, animal viscera) and dark vegetables and fruits (pumpkin, carrots, broccoli, spinach, mangoes, and oranges) are rich in vitamin A or its precursors. Parents can biodiversify the preschool

child's dietary pattern to these ends. Vitamin A food fortification or routine vitamin supplementation may play a role in vitamin A deficiency prevention and anemia alleviation in older children in China, but a dietary approach should ultimately be more sustainable and beneficial for general health.

Several studies have found that serum vitamin A is not identifiable different by gender [4,7] However, in our study, the prevalence of VAD in girls was higher than that in boys, while the prevalence of MVAD was higher in boys compared to that in girls. Though our findings were not entirely consistent with previous studies, data were limited, and altogether sex did not appear to confer difference vitamin A status.

Mean serum vitamin A concentration among anemic children was 0.27±0.07 mg/L, lower than that of non-anemic children. This accorded with previous reports, which demonstrate positive correlations between Hb and serum retinol concentrations among schoolchildren.[22-24] In our study, serum vitamin A concentration was correlated with red blood cell indices. Compared with the normal serum vitamin A group, other groups had a lower MCV, MCH, MCHC, and a higher RDW. Microcytic anemia which occurs in infants and toddlers, as judged by and MCV, MCH, and RDW need distinction from each other by cause of microcytosis.[25] Despite vitamin A being a recognized factor in the pathogenesis of anemia,[26,27] iron deficiency is its major etiology in developing countries. The anemia caused by iron deficiency is typically microcytic and hypochromic.[25] Vitamin A deficiency is considered to alter the iron status and metabolism, resulting in ineffective erythropoiesis.28 Vitamin A may also contribute to the pathogenesis of anemia via biologic mechanisms such as modulation of erythropoiesis, immune function, and as a result of the anemia of infection.[27] Thus, the serum vitamin A concentration might affect erythrocyte indices both directly and indirectly.

The present study has limitations. It has no information about iron metabolism in relation to vitamin A status and no indices of inflammation, when inflammation is a notable contributor to anemia. The retrospective study design has meant that various likely confounders have not been considered so that the multivariable analyses of interest and importance to account for socio-demography, have not been conducted. Most importantly, the background diet is not available. Intestinal helminthiasis, the most prevalent cause of iron deficiency worldwide has not been assessed. Hereditary anemia such as thalassemia and G6PD deficiency has not been excluded.

In conclusion, VAD is associated with anemia in the city of Beijing in northern China, particularly in 3-4 years old preschool children, to whom greater public health nutritional attention needs to be paid.

ACKNOWLEDGEMENTS

The authors thank Xue-Mei Wang for her help in providing data from a previous study and Shou-Kui Hu for the preparation of this manuscript. Finally, the authors thank all the staff members of Beijing Harmony Health Medical Diagnostics Co., Ltd, without whom, data registration and this study would not have been possible.

CONFLICT OF INTEREST AND FUNDING DISCLOSURE

The authors declare that they have no conflict of interest.

This study (GCCRC202105) was supported by Peking University Shougang Hospital Scientific Research and Development Funds.

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Table 1. Vitamin A serum concentration of children aged 1 to 6 years

Variables	Total (n=630)	Child sex		*p* value	Age group (years)			*p* value
		Female (n=285)	Male (n=345)		1-2 (n=471)	3-4 (n=126)	5-6 (n=33)	
VA (mg/L) (mean±SD)	0.29±0.08	0.29±0.08	0.29±0.07	0.689†	0.30±0.08‡	0.27±0.08‡	0.28±0.07	<0.001§
Prevalence of VAD, n (%)	62 (9.84)	36 (12.6)	26 (7.5)	0.013¶	38 (8.1)	20 (15.9)	4 (12.1)	0.004¶
Prevalence of MVAD, n (%)	274 (43.49)	108 (37.9)	166 (48.1)		194 (41.2)	64 (50.8)	16 (43.5)	

SD: standard deviation; VA: vitamin A; VAD: vitamin A deficiency; MVAD: marginal vitamin A deficiency.
†Independent sample t-test.
‡Comparing the groups aged 1-2 years and 3-4 years by independent sample t-test, $p<0.05$.
§One-way ANOVA test.
¶Chi-square test.

Table 2. Relationship between serum vitamin A concentrations and hematological parameters (mean ± SD)

Hematological parameters	Normal (n=294)	MVAD (n=274)	VAD (n=62)	*F*	*p* value†
WBC ($\times10^9$/L)	9.0±2.3	9.0±2.9	9.0±3.5	0.008	0.992
RBC ($\times10^{12}$/L)	4.68±0.32	4.72±0.33	4.67±0.42	1.361	0.257
Hb (g/L)	127±9	125±9	126±13	2.325	0.099
HCT (%)	37.5±2.3	37.3±2.4	37.6±3.4	0.274	0.760
MCV (fL)	80.1±3.5	79.1±4.2	80.4±3.7	5.467	0.004
MCH (pg)	27.2±1.3	26.6±1.8	27.0±1.8	8.844	<0.001
MCHC (g/L)	339±9	336±12	335±12	9.197	<0.001
RDW (%)	12.9±1.2	13.3±1.5	13.0±1.0	6.660	0.001
PLT ($\times10^9$/L)	302±79	295±84	293±80	0.679	0.508
PCT (%)	0.29±0.07	0.28±0.08	0.28±0.07	0.341	0.711
MPV (fL)	9.6±0.8	9.7±0.9	9.7±0.8	0.780	0.459
RDW (fL)	10.3±1.4	10.4±1.6	10.4±1.7	0.846	0.430

MVAD: marginal vitamin A deficiency; VAD: vitamin A deficiency; WBC: white blood cell; RBC: red blood cell; HCT: hematocrit; MCV: mean corpuscular volume; MCH: mean corpuscular hemoglobin; MCHC: mean corpuscular hemoglobin concentration; RDW: red blood cell distribution width; PLT: platelets; PCT: plateletcrit; MPV: mean platelet volume; PDW: platelet distribution width; SD: standard deviation.
†One-way ANOVA test.

Table 3. Association between serum vitamin A concentrations and anemia

Status	n	VA (mg/L) (mean±SD)	*p* value†	Prevalence of VAD (n (%))	*p* value†
Anemic	61	0.27±0.07	0.036	6 (9.8)	0.999
Non-anemic	569	0.29±0.08		56 (9.8)	

VA: vitamin A; VAD: vitamin A deficiency; SD: standard deviation.
†Independent sample t-test.

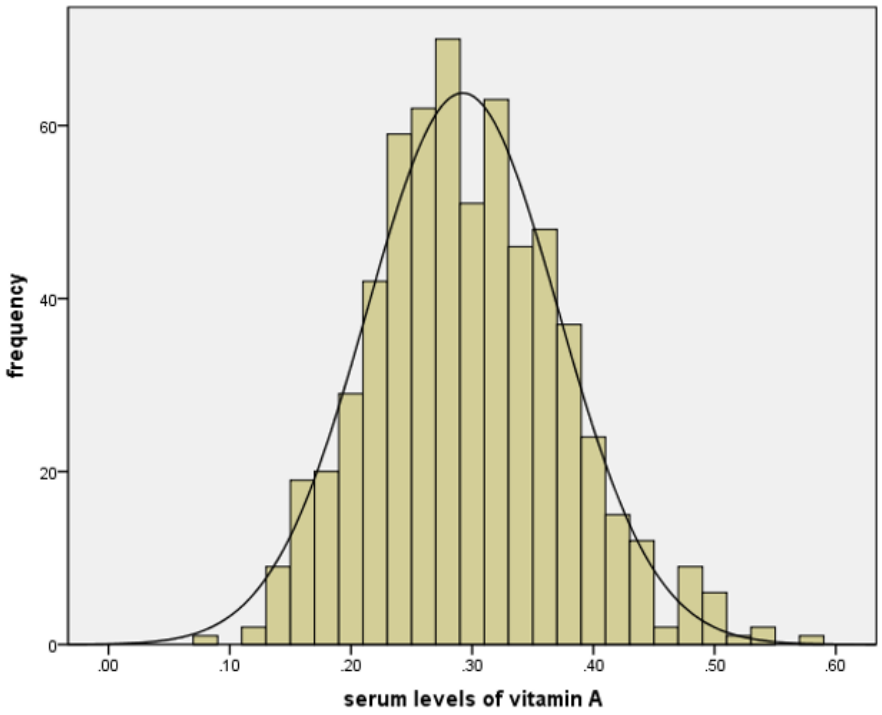

Figure 1. Frequency distribution of serum concentration of vitamin A among children aged 1-6 years. (n=630; serum concentration of vitamin A: 0.29±0.08 mg/L [mean ± standard deviation]).

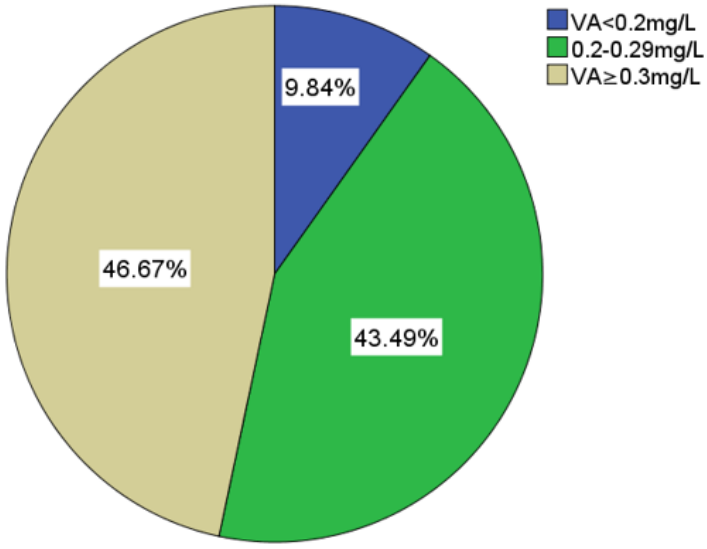

Figure 2. The corresponding proportion of children with various vitamin (VA) concentrations.