

Association between nutritional and physical factors and anemia among schoolchildren aged 5 to 11 years in Beijing

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To the Editor: Previous studies paid less attention on the reasons of anemia in schoolchildren, particularly in a relatively well-off area, which might hamper policy design for anemia control. Thus, the present study would explore the reasons for anemia in schoolchildren aged 5 to 11 years in Beijing based on personal data including dietary intake and serum biomarkers of nutrients.

Data were extracted from a cross-sectional study in 2015, named the Nutrition and Health Surveillance in Schoolchildren of Beijing, whose detailed sampling strategies and methods had been described previously.^[1] The initial study was approved by the institutional review board of the Beijing Center for Disease Prevention and Control (No. 201506). All participants provided written informed consent, including a parental agreement. After applying the exclusion criteria, 4326 participants (study population 1) with social demographic information and anthropometric data, 1969 participants (study population 2) with additional biochemical data, and 554 participants (study population 3) with additional 3 days 24 h-recall dietary information were enrolled in the analyses [Supplementary Figure 1, <http://links.lww.com/CM9/A639>].

Capillary blood hemoglobin (Hb) levels were measured using the Hemocue system (HemoCue Hb201+, Sweden). Anemia was defined as Hb <115 g/L for children aged 5–11 years, and iron deficiency was defined as serum ferritin (SF) < 15 µg/L, according to the 2001 World Health Organization (WHO) recommendations. Iron deficiency anemia (IDA) was defined as the presence of both anemia and iron deficiency (ID) in an individual. Folate deficiency was defined as a serum folate level < 4 ng/mL according to the Chinese criteria, and vitamin B12 deficiency was defined as serum vitamin B12 < 203.25 pg/mL according to the guideline of the National Institute for Health and Care Excellence. Vitamin A deficiency was defined as a

serum retinol concentration <0.7 µmol/L based on the WHO criteria.

Supplementary Table 1, <http://links.lww.com/CM9/A639> showed the characteristics of study population 2. The Hb concentration was 128.9 ± 9.5 g/L, with no significant difference found between boys and girls (128.8 ± 9.4 vs. 129.1 ± 9.5 g/L, $t = -0.8$, $P = 0.40$). The prevalence of anemia was 2.8% ($n = 56$), with boys accounting for 44.6% ($\chi^2 = 0.77$, $P = 0.38$) and rural children accounting for 85.7% ($\chi^2 = 17.10$, $P < 0.01$) of the cases in the anemic group. The prevalence of ID and IDA were 0.7% and 0.2%, respectively. Among the anemic children, only three IDA were found, and no vitamin A, B₁₂ or folate deficiency were detected in biochemical markers. Additionally, the overall prevalence of vitamin A, B₁₂ and folate deficiencies were 0.2%, 0.2%, and 0.6%, respectively. Younger age, rural residence, and no supplement intake were associated with anemia (all $P < 0.05$). In terms of growth status, anemic children were shorter and lighter in comparison with their counterparts (both $P < 0.01$).

To further present the major relevant factors of anemia intuitively, scatter plots were generated to illustrate the distribution of height-for-age Z-score (HAZ), serum ferritin, folate, and vitamin B₁₂ with Hb among anemic children [Supplementary Figure 2, <http://links.lww.com/CM9/A639>]. Only four out of 56 anemic children's HAZ were below -1, and one of the four children had HAZ below -2. Three children below HAZ -1 were 6 years old, but none had nutritional deficiencies. The remaining one with HAZ of -2.14 had a marginal value of serum folate (4.21 ng/mL), and the other two biomarkers (serum ferritin and vitamin B₁₂) were above the corresponding threshold, respectively.

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Table 1: Association between serum biomarkers and hemoglobin by multivariable linear regression* in study population 2 (n=1966†).

Items	β	95% Confidence interval	P value
Sex (ref: boy)	0.608	-0.208, 1.423	0.144
Age	1.517	1.245, 1.788	<0.001
Caregiver's education	0.876	-0.058, 1.810	0.066
Income	-0.195	-0.619, 0.228	0.366
Supplements	-0.159	-1.030, 0.712	0.721
Rural	-0.384	-1.282, 0.514	0.402
HAZ	0.657	0.237, 1.076	0.002
BAZ	0.398	0.026, 0.770	0.036
Ferritin (ng/mL)	0.008	-0.006, 0.022	0.250
sTfR (mg/L)	-0.459	-0.848, -0.070	0.021
Vitamin B ₁₂ (pg/mL)	0.001	-0.001, 0.002	0.451
Folate (ng/mL)	-0.089	-0.221, 0.043	0.188
Vitamin A (μ mol/L)	2.176	0.889, 3.463	0.001
Vitamin D (ng/mL)	0.008	-0.048, 0.064	0.774
Serum zinc (μ mol/L)	0.369	0.107, 0.632	0.006
Total protein (g/L)	0.060	-0.075, 0.196	0.384
Albumin (g/L)	0.152	-0.098, 0.401	0.233
hs-CRP (mg/L)	-0.446	-1.187, 0.296	0.239

*All the list variates were listed as co-variables into multivariable linear regression. †Three children with IDA were excluded. BAZ: BMI-for-age Z-score; HAZ: Height-for-age Z-score; hs-CRP: High-sensitivity C-reactive protein; sTfR: Soluble transferrin receptor.

Additionally, an assessment of disparity of dietary factors between non-anemic and anemic participants was conducted with study population 3 [Supplementary Table 2, <http://links.lww.com/CM9/A639>]. No significant differences in dietary intakes were found between two groups. Younger age, living in the rural area, smaller height, and weight were significantly associated with anemia (all $P < 0.05$).

To comprehensively understand the potential influencing factors of anemia, Hb was set as a dependent variable, and multivariable linear regression was performed with serum biochemical data [Table 1] without three IDA participants who had relatively clear reason for anemia. The results revealed that age, HAZ, BMI-for-age Z-score (BAZ), serum vitamin A, and zinc were positively associated with Hb, while soluble transferrin receptor was negatively associated with Hb (all $P < 0.05$). However, the associations of vitamin A and zinc with anemia did not exist anymore in dietary intake regression analysis, and the age and BAZ remained significantly related to Hb [Supplementary Table 3, <http://links.lww.com/CM9/A639>]. Furthermore, to confirm our thought, study population 1 was divided into three layers according to age tertiles for stratified analysis [Supplementary Table 4, <http://links.lww.com/CM9/A639>]. As expected, height, weight, and Hb increased dramatically with age (all $P < 0.05$), and regression results showed that age ($\beta=1.501$, $P<0.001$), sex ($\beta=0.579$, $P=0.038$), HAZ ($\beta=0.814$, $P<0.001$), BAZ ($\beta=0.301$, $P=0.008$), and rural area ($\beta=-1.014$, $P=0.001$) were the independent factors associated with Hb.

In conclusion, with the exception of a small number of children with IDA, most anemia cases could not be

attributed to common nutritional deficiencies, such as folate, vitamin A and vitamin B₁₂. Multivariate analyses revealed that lower Hb concentration was associated with younger age and lower HAZ or BAZ. Results suggested that the growth status represented by age or HAZ/BAZ might be the potential cause of lower Hb values.

In the present study, iron intake does not seem to influence body iron storage since dietary iron levels were similar between anemic and non-anemic students. The traditional Chinese diet was dominated by plant-based food, however, using the China Health and Nutritional Survey data, He *et al*^[2] illustrated that a plant-based diet was not primarily responsible for poor iron status. Furthermore, haem iron intake did not always support a good iron status in Chinese adults. The evidence pointed out that who had less iron intake would not always had ID consistently. In addition, lower Hb value was not majorly contributed by ID adherently in schoolchildren as the previous study hinted,^[3] which was confirmed in the present study.

In this study, the prevalence of anemia gradually decreased with age, and the means of Hb concentrations demonstrated a steady increase as age increases [Supplementary Table 4, <http://links.lww.com/CM9/A639>]. The age-related change described herein was attributable to the natural physical growth development, wherein most children with anemia at baseline in 2015 were not anemic after two years in 2017 [Supplementary Table 5, <http://links.lww.com/CM9/A639>]. Our results showed that children with anemia were shorter and lighter than those without anemia. However, considering their overall nutritional status and severity of anemia, we believe that anemia was not the reason as to their stunted growth status. It was more likely that they were relatively younger with a slight delayed physical development. In a cluster-randomized clinical trial conducted in Côte d'Ivoire involving children aged 12 to 36 months with a high prevalence of IDA, the prevalence dropped to from 33.0% to 18.7% in the control group after 9 months without any intervention.^[4] These results indicated that with growth development, IDA might regress naturally in a certain number of children. In the present study, we demonstrated a positive association between age and Hb even after adjusting for all other confounders, which implied a physiologically lower Hb concentration in younger children.^[5] In addition to a meta-analysis which concluded that Hb concentration was related to length for age standardized Z score in children aged below 5 years,^[6] our research sheds light on the situation of 5 to 11-year-old schoolchildren.

A major strength of the present study is the full-scale individual-level data on the nutritional risk factors for anemia in schoolchildren in Beijing. However, the lack of data on menstruation, helminths, malaria, and genetic factors of Hb subtypes limited the analysis of all possible risk factors for anemia. Finally, the present study used cross-sectional data that limited causal inference.

In conclusion, the major factors influencing Hb in Beijing schoolchildren aged 5 to 11 years included their age and growth status. Based on the generally low prevalence of anemia in the present population, those who were anemic

might recover with aging and proper physiological development. Public policies should focus on comprehensive lifestyle intervention including balanced diet to promote schoolchildren's physical development and growth. Tracking the trends of Hb levels and growth status is recommended for the anemic individual treatment.

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Conflicts of interest

None.

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