Preplanned Studies

Iron Status Among Children Aged 6−17 Years by Serum Ferritin — China, 2016−2017

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Summary

What is already known on this topic?

Iron deficiency (ID) is the most widespread micronutrient deficiency and have several adverse effects on health. Consequences of ID among children include delayed psychomotor development and impaired cognitive performance, which makes it important to monitor the iron status of children.

What is added by this report?

In this study, the serum ferritin (SF) level was 56.6 (95% CI: 56.0–57.2) ng/mL in 65,293 children aged 6–17 years old in the National Nutrition and Health Surveillance in China in 2016–2017. ID prevalence varied significantly in children stratified by sex, age, and regions ranging from 1.0% to 28.1% judged by the standard of SF<15 ng/mL and SF<25 ng/mL. ID prevalence in females aged 12–17 years was the highest among children aged 6–17 years.

What are the implications for public health practice?

Understanding iron status of school children could provide evidence and data for developing policies and strategies for ID and iron deficiency anemia (IDA) control and prevention. Females aged 12–17 years showed high ID prevalence, and iron-rich food interventions are strongly recommended.

Iron deficiency (ID) is the most prevalent micronutrient deficiency worldwide, resulting in adverse health outcomes including anemia, impaired muscle function, poor immune function, delayed psychomotor development, and impaired cognitive performance in children in the short and long term (*1*–*2*).

ID has three progressive stages which include depletion of iron stores (ID), iron deficient erythropoiesis (IDE), and iron deficiency anemia (IDA). Available indicators in different stages contain serum ferritin (SF), soluble transferrin receptor (sTfR), zinc protoporphyrin, transferrin saturation, body iron stores, hemoglobin, reticulocyte hemoglobin, and hepcidin, etc. Each indicator has their own strengths and limitations. SF is the most recommended indicator for determining ID because it reflects a state of iron store in the body and researchers have established a cutoff for iron depletion by using SF (*3*–*4*).

In 2015–2017, China completed its fifth National Nutrition and Health Surveillance and monitored the iron status with large-scale samples. The primary objective of this study was to analyze the prevalence of ID among children aged 6–17 years in China in 2016–2017 to provide guidance to the development of appropriate intervention strategies.

Sampling of participants was based on the protocol for China Nutrition and Health Surveillance of Children and Lactating Women (2016–2017). The details were described in the introduction of China Nutrition and Health Surveys (1982–2017) (*5*). The blood samples in the serum separator tube were promptly centrifuged at 3,000 ×*g* for 15 minutes after venous blood collection and coagulation at room temperature, divided into aliquots of serum, and frozen at −80 ℃ for subsequent assays: SF and high-sensitivity C-reactive protein (hsCRP). SF was measured by electrochemiluminescence immunoassay on Roche Modular e601 automated analyzer; and hsCRP by Roche Tina-quant immunoturbidimetric assay on Hitachi 7600 automatic biochemical analyzer.

All analyses were conducted with SPSS (version 23.0, IBM Corp, Armonk, NY, USA). We log transformed SF to normalize the distribution because SF concentrations were positively skewed. SF distribution was described as geometric means ($\bar{x}_G$) and 95% confidence interval (95% CI) as well as selected percentiles by age and sex subgroups. Concentrations of hsCRP higher than 5 mg/L was considered as the presence of a possible infection or inflammation. ID was defined by the World Health Organization (WHO) recommended standard as SF<15 ng/mL and the National Hygienic Standard WS/T 465-2015 in China as SF<25 ng/mL; both standards were set in the absence of signs of inflammation (*3*,*6*). Independent *t*-tests and chi-squared tests were conducted on continuous variables and categorical variables between subgroups, respectively. Means, percentiles, ID prevalence, and differences between subgroups were analyzed from the method of complex sampling survey. The level of statistical significance was set at $P<0.05$.

In total, 65,293 participants were included after exclusion of hsCRP>5 mg/L, with 32,503 (50.0%) being male and 32,790 (50.0%) being female. The age of all children ranged from 6 to <18 years old with a median age of 11.3 years. The study population distribution was presented in Table 1.

As presented in Table 1, geometric mean SF concentrations were 57.9 (95% CI: 57.0–58.8) ng/mL and 55.5 (95% CI: 54.7–56.2) ng/mL for children aged 6–17 years in urban and rural areas, respectively. The SF concentrations were significantly higher in urban than those in rural areas, while males had a higher levels than that of females ($P<0.05$). The ferritin concentration in female subgroup aged 12–17 years was the lowest among all the subgroups ($P<0.05$).

Table 2 described the percentile distribution of SF concentrations in age and sex subgroups, which were widely arranged and varied among subgroups.

The prevalence of ID for children was shown in Table 3. Overall, the prevalence of ID in children aged 6–17 years, as defined by SF<25 ng/mL and SF<15 ng/mL, was 11.2% and 4.9% in this weighted population, respectively. According to ID judged by the cut-off value of 25 or 15 ng/mL for SF concentration, the prevalence of ID was significantly different in the subgroups by age, sex, or regions ($P<0.05$). Children aged 12–17 years had a higher incidence of ID than children aged 6–11 years ($P<0.05$). Males had a lower ID prevalence than females ($P<0.05$). The prevalence of ID in urban areas was significantly different with that in rural areas ($P<0.05$).

DISCUSSION

This study explored the status of SF and ID based on SF among children aged 6–17 years in China. This is the first survey on iron status among a large, nationally representative children samples in China.

SF is the best indicator to reflect the body iron store and could be measured by standardized laboratory assays as well as established cut-offs, but SF is considered as an acute-phase protein. Inflammation, infection, and liver disease could impact SF levels and bring deviations for iron status of the body. The WHO recommends using one or two acute phase proteins to reflect the state of inflammation in the body. CRP is a sensitive indicator that rises rapidly in the early stages of infection (*3*). In the study, hsCRP was used to screen children for the presence of infection or inflammation. Children with elevated hsCRP concentrations (>5 mg/L) were excluded from the analysis. The geometric mean concentrations of SF

TABLE 1. Serum ferritin levels for children aged 6–17 years — China, 2016–2017 (ng/mL).

Age group (years)	Total			Urban			Rural		
	n	$\bar{x}_G$	95% CI	*n*	$\bar{x}_G$	95% CI	*n*	$\bar{x}_G$	95% CI
6–17									
Total	65,293	56.6	56.0–57.2	30,960	57.9	57.0–58.8	34,333	55.5§	54.7–56.2
Male	32,503	66.4	65.5–67.2	15,404	69.4	68.0–70.7	17,099	63.8§	62.8–64.9
Female	32,790	47.3*	46.5–48.0	15,556	47.2*	46.1–48.4	17,234	47.3*	46.3–48.2
6–11									
Subtotal	36,596	60.4	59.8–61.1	17,423	62.0	60.9–63.1	19,173	59.3§	58.5–60.2
Male	18,223	60.5	59.6–61.5	8,665	62.2	60.7–63.8	9,558	59.3§	58.1–60.6
Female	18,373	60.3	59.4–61.3	8,758	61.7	60.2–63.3	9,615	59.3§	58.2–60.5
12–17									
Subtotal	28,697	53.1	52.2–54.0	13,537	54.8	53.5–56.2	15,160	51.3§	50.2–52.5
Male	14,280	72.7†	71.3–74.2	6,739	75.8†	73.7–78.1	7,541	69.6†§	67.8–71.4
Female	14,417	37.6*†	36.7–38.6	6,798	38.5*†	37.2–40.0	7,619	36.7^{*b§}	35.5–37.9

Abbreviation: CI=Confidence Interval; $\bar{x}_G$=geometric means.

* *P*-value <0.05 for differences between male and female at same age group.

† *P*-value <0.05 for differences between children 6–11 years and 12–17 years.

§ *P*-value <0.05 for differences between urban and rural areas.

TABLE 2. Median and selected percentiles of serum ferritin concentrations for children aged 6–17 years in China in 2016–2017 (ng/mL).

Age group (years)	$P_{2.5}$	P_5	P_{10}	P_{25}	P_{50}	P_{75}	P_{90}	P_{95}	$P_{97.5}$
Total									
6–17									
Total	9.8	15.2	23.4	38.7	59.9	89.6	131.8	166.3	203.9
Male	17.9	23.1	30.3	45.0	66.5	100.3	147.7	188.3	225.7
Female	7.0	10.3	16.9	32.2	52.5	79.2	112.4	137.3	165.4
6–11									
Subtotal	19.1	24.0	30.5	43.1	61.4	86.1	119.3	146.1	179.4
Male	19.3	24.1	30.5	43.3	61.2	84.9	119.7	148.2	187.8
Female	18.8	23.9	30.4	43.0	61.7	87.2	118.7	142.6	171.0
12–17									
Subtotal	7.2	10.7	17.1	33.4	58.0	93.9	144.1	181.2	221.8
Male	16.7	21.8	30.1	47.6	75.1	118.2	171.5	212.7	251.8
Female	5.2	7.3	11.0	22.7	42.7	68.9	102.7	131.2	160.6
Urban									
6–17									
Total	9.2	14.5	22.5	38.3	61.4	95.5	141.0	181.0	220.7
Male	17.6	22.8	30.3	45.6	69.5	108.2	159.1	206.1	246.3
Female	6.5	9.7	15.6	31.2	52.7	81.4	118.6	146.2	177.8
6–11									
Subtotal	18.2	23.4	30.0	43.3	63.1	90.8	125.9	158.7	197.5
Male	18.5	23.5	30.5	43.3	62.4	91.0	127.6	168.7	206.1
Female	17.8	23.3	29.6	43.2	63.6	90.8	125.0	153.3	189.1
12–17									
Subtotal	7.0	10.7	17.2	33.7	59.6	100.1	152.3	193.5	236.1
Male	16.8	22.3	30.3	48.5	79.6	124.8	181.0	224.7	262.5
Female	5.2	7.1	11.2	22.9	43.5	71.4	111.6	142.0	170.4
Rural									
6–17									
Total	10.5	16.0	24.0	39.1	58.9	85.1	122.6	153.0	184.4
Male	18.1	23.4	30.3	44.4	64.3	93.1	138.3	172.9	205.2
Female	7.4	10.8	17.9	33.2	52.4	76.9	105.9	129.0	152.5
6–11									
Subtotal	19.9	24.5	30.8	43.0	60.1	83.5	113.8	138.6	166.7
Male	20.1	24.5	30.5	43.3	60.1	81.9	114.4	140.5	168.9
Female	19.7	24.5	31.1	42.7	60.1	85.0	113.6	136.8	161.4
12–17									
Subtotal	7.4	10.7	17.1	33.2	56.4	88.1	134.5	171.6	206.1
Male	16.3	21.4	29.8	46.7	71.6	109.6	161.1	198.4	231.6
Female	5.2	7.4	10.8	22.4	41.9	66.3	95.4	118.0	141.5

were 57.9 (57.0–58.8) ng/mL and 55.5 (54.7–56.2) ng/mL for children aged 6–17 years in urban and rural areas, respectively. Males aged 12–17 years had a higher level of SF than those aged 6–11 years. The results are in line with the findings from a previous study (7). Since their dietary iron absorption is

TABLE 3. Iron deficiency prevalence for children aged 6–17 years — China, 2016–2017 [% (95% CI)].

Age group (years)	SF<25 ng/mL			SF<15 ng/mL		
	Total	Urban	Rural	Total	Urban	Rural
6–17						
Total	11.2(10.8, 11.6)	11.8(11.2, 12.4)	10.6(10.1, 11.2)§	4.9(4.6, 5.2)	5.4(4.9, 5.8)	4.5(4.1, 4.9)§
Male	6.1(5.7, 6.6)	6.3(5.7, 7.0)	5.9(5.4, 6.6)	1.6(1.4, 1.9)	1.8(1.5, 2.2)	1.4(1.2, 1.8)
Female	16.9(16.2, 17.6)*	18.0(16.9, 19.0)*	16.0(15.0, 17.0)*§	8.6(8.1, 9.2)*	9.3(8.5, 10.2)*	7.9(7.3, 8.7)*§
6–11						
Subtotal	5.5(5.1, 5.9)	6.0(5.4, 6.6)	5.2(4.6, 5.8)	1.3(1.1, 1.5)	1.5(1.3, 1.9)	1.1(0.8,1.4)
Male	5.5(5.0, 6.1)	6.0(5.3, 6.8)	5.2(4.4, 6.1)	1.2(0.9, 1.5)	1.5(1.1, 2.0)	1.0(0.6, 1.5)
Female	5.5(4.9, 6.2)	6.0(5.1, 7.0)	5.2(4.4, 6.1)	1.4(1.1, 1.7)	1.6(1.2, 2.2)	1.2(0.9, 1.6)
12–17						
Subtotal	16.7(16.0, 17.4)	16.4(15.5, 17.4)	16.9(16.0, 17.9)	8.4(7.9, 8.9)	8.4(7.7, 9.1)	8.4(7.7, 9.2)
Male	6.7(6.1, 7.4)†	6.6(5.7, 7.6)	6.9(6.0, 7.8)†	2.0(1.7, 2.4)†	2.0(1.6, 2.7)	2.0(1.6, 2.6)†
Female	27.6(26.4, 28.8)*†	27.1(25.4, 28.8)*†	28.1(26.4, 29.8)*†	15.4(14.4, 16.4)*†	15.2(13.9, 16.7)*†	15.5(14.1, 17.0)*†

Abbreviation: SF=serum ferritin.
* Chi-squared test *P*-value <0.05 for differences between male and female at same age group;
† Chi-squared test *P*-value <0.05 for differences between children 6–11 years and 12–17 years.
§ Chi-squared test *P*-value <0.05 for differences between urban and rural areas.

increasing during body growth, young men may increase levels of stored iron and result in increased SF until reaching normal level. The study also found that SF levels in males were higher than that in females.

SF threshold of 15 ng/mL ensures the specificity of the diagnostic ID, but the sensitivity was relatively low. Yu D et al. conducted a meta-analysis of the threshold value of SF for ID determination, and the conclusion was that the diagnostic accuracy and comprehensive efficiency of SF were increased if the threshold value of SF was 25 or 30 ng/mL (*8*). The findings were supported by other studies (*9*). In this study, the prevalence of ID among children aged 6–17 years was estimated to be 4.9% in China according to WHO recommendation. When ID was defined as SF< 25 ng/mL, which might be more sensitive in detecting early depletion of body iron stores, the percentage increased from 4.9% to 11.2%. According to the results in the 2010–2012 National Nutrition and Health survey, based on cutoffs of 25 ng/mL and 15 ng/mL for SF, the results showed that ID prevalence among 472 children aged 6–11 years in big cities were 2.3% and 0.6%, respectively; among 543 children aged 6–11 years in poverty rural areas were 6.1% and 1.5%, respectively; among 450 children aged 12–17 years in big cities were 9.1% and 3.6%, respectively; and among 602 children aged 12–17 years in poverty rural areas were 10.3% and 4.3%, respectively (*10*). In the survey, resampling for measuring iron indicator was conducted based on the samples from the big cities and poverty rural areas, respectively, and the sample size was small, in addition, the method used for SF was an immunoturbidimetry assay. In the present study, a representative large-scale sample was involved and the method for SF determination was electrochemiluminescence immunoassay with the advantages of high sensitivity and stability. Therefore, the results and trends were not compared between 2010–2012 and 2016–2017.

ID results from long-term imbalance caused by inadequate dietary iron intake, poor iron absorption or utilization, increased iron requirements, or chronic blood loss. Lin XM et al. analyzed the iron nutrition status of 1,012 school-age children aged 7–13 years in Beijing's mountainous areas and found that 26.5% school-age children had SF below 30 ng/mL (*11*). In the present study, except for girls aged 12–17 years, ID prevalence of other children was low. In China, socioeconomic conditions were improving and many nutrition intervention programs targeting poor children were implemented in recent years (*12*–*13*). In 2011, the Nutrition Improvement Program for Rural Compulsory Education Students (NIPRCES) was launched by the State Council (*12*). In rural boarding schools, NaFeEDTA-fortified soy sauce has been used to improve the iron deficiency and anemia status for students in some rural areas (*13*). As a result, children in rural areas have improved iron intake because of education, dietary diversification, and iron-fortified food consumption. The level of iron stores was lower in female aged 12–17 years, which may be related to the high iron requirements in this period. In addition, the iron loss in menstruation and bad dietary habits for keeping slim could also contribute.

This study was subject to some limitations. First, α1-acid glycoproteins (AGP) was a marker to reflect the state of inflammation in the body, which responds to inflammation later, but duration longer than CRP. In chronic or subclinical infections, AGP may be more appropriate for determining the inflammatory status of the body. In our study, AGP was not included. Second, sTfR and hemoglobin are good indicators for determining IDE and IDA. In the future, more studies including SF, sTfR, and Hb should be conducted to comprehensively assess the iron status of children.

In conclusion, understanding iron status of school children could provide evidence and data for developing policies and strategies for ID and IDA control and prevention. The prevalence of ID varies significantly in children by sex, age, and regions ranging from 1.0% to 28.1% based on SF below 15 ng/mL and 25 ng/mL. Females aged 12–17 years showed high ID prevalence, and iron-rich food interventions are strongly recommended.

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