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Original Article

Prevalence of anemia and iron deficiency anemia among elementary school children in Turkey

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Abstract

Aim: The purpose of our study was to determine the rate of anemia and iron store status in Turkish elementary school children.
Materials and Methods: We included 1296 children applied to pediatrics department of a large teaching hospital and evaluated the hemoglobin, iron, unsaturated iron binding capacity and ferritin levels.
Results: The results showed that 9.88% of the children had anemia and 1.62% had iron-deficiency anemia. Despite the normal Hemoglobin (Hb) levels, the ratio of children with low ferritin levels was found to be 36.49%, suggesting that children with normal Hb levels might not be having adequate level of iron stored. The Hb levels were found to be significantly lower in the group of 6- and 7-year old children when compared to other ages.
Conclusion: Being an elementary issue for normal growth and academic success in school, iron status should be closely monitored in school children. Additionally, different age groups have different needs for iron supplementation; therefore contemporary guidelines for the management of anemia in children should be established by authorities.

Keywords: Anemia; children; iron deficiency; iron deficiency anemia

INTRODUCTION

Anemia is one of the major public health issues worldwide. In the last 2015 report on global anemia prevalence, WHO defined the estimated prevalence of anemia as 43% in children corresponding to 273 million patients. According to this report, anemia has a moderate level of significance considering public health in Turkey (1).

The major reason in the etiology of anemia in children is the iron deficiency as a result of high body demand and insufficient nutrition. Hemoglobinopathies, parasitic infections, are among other causes of anemia in the childhood (2). Undiagnosed and/or untreated anemia in the childhood results in psychomotor and mental problems, deteriorated growth and low intellectual and academic capacity in school. Additionally, moderate and severe anemia is related to fatigue during physical activities and brings a burden to the children in play activities and sports (3).

For the diagnosis of anemia, several laboratory tests can be used including complete blood count (CBC), iron and ferritin levels and unsaturated iron binding capacity (UIBC). Additional testing including Hb electrophoresis, receptors of the carrier and storage proteins in the iron metabolism and genetic tests might be needed to further investigate the underlying pathology in the etiology of anemia. According to WHO, Hb concentration is a measure of anemia, and Hb levels lower than 11.5 g/dL is sub-classified in anemia spectrum as mild, moderate and severe. However, Hb levels are not the only determinant of anemia, serum ferritin level below the cut-off ferritin<15 µg/L is accepted to be reflective of depleted iron stores (4).

Since having adequate levels of iron is essential for the normal development and academic achievement of children in school age, we aimed to evaluate the rate of anemia and Hb, iron, UIBC and ferritin levels of children of elementary school age residing in the metropolitan region of Turkey in order to assess the iron status of this age group.

MATERIALS and METHODS

Study Population and Analysis

This is a cross-sectional study, conducted in one of the largest training hospitals in Istanbul, Turkey. Between January-December 2018, children aged between 6-9

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years old who underwent annual check-up, and had simultaneous measurements of Hb, iron, UIBC, ferritin, and CRP were randomly selected from the hospital information system. All of the participants in our study resided in a large metropolitan area. All were Caucasian and of Turkish origin. Health statuses of children were controlled from their medical data and children who have a chronic disease were excluded. Additionally, children with over the limit values (>5 mg/L) of inflammatory marker CRP were excluded. Of the children fitting to our inclusion criteria, a total of 1296 children (548 female, 748 male) were divided into age groups.

The study was approved by the institutional ethical committee. Informed consent was not taken since the study is a cross-sectional data scanning study and the institution this study was held was a teaching hospital.

Serum iron and UIBC levels were measured with spectrophotometric methods, whereas ferritin levels were analyzed with chemiluminescence using Access iron, UIBC and ferritin test reagents (Beckmann Coulter, Inc., USA). Hb values were determined by photometry method using Sysmex XN 3000 analyzer (Sysmex Corp., Japan). The analysis laboratory was a participant of the RIQAS General Clinical Chemistry, Haematology and Immunoassay External Quality Assurance programs (Randox Laboratorıes Ltd., United Kingdom) for the tested parameters, and no deviation in the internal and external quality control results was observed within the study duration.

Determination of Anemia

In our study, we used the cut-off points as suggested by WHO for the children of age 5-11 years (5). According to their criteria, we defined Hb concentrations lower than 11.5 g/dL as anemia, whereas children with 11.0-11.4 g/dL Hb concentration is sub-classified as mild, and Hb concentrations between 8.0 and 10.9 g/dL were accepted as moderate anemia. Hb level is lower than 8.0 g/dL was accepted as severe anemia.

Determination of iron Status

For the determination of the iron status of children, serum ferritin measures lower than 15 ug/L were accepted as having depleted iron stores (4). Children with simultaneous hemoglobin and ferritin levels below defined ranges were categorized as having iron deficiency anemia (IDA).

Statistical Analysis

Data are expressed as mean±standard error of the mean (SEM). Statistical analyses were done using the MedCalc statistical analyzer (MedCalc Software, Belgium). Comparisons of two groups were done using Student's t-tests. The ratios of conditions (non-anemia, mild anemia, moderate anemia) between the age groups were compared using the X2 test. Spearman's correlation test was performed for the relationship between Hb, iron and ferritin levels in each age group. The results were evaluated using a significance value of $p<0.05$.

RESULTS

Hb, iron, UIBC, and ferritin levels of all subjects included in the study are shown in Table 1. The rate of anemia in the studied children was 9.88% (128/1296), and none had severe anemia (Table 2). The rate of anemia between 6-7-year old children versus 8-9-year old children found to be statistically significant (6 vs 8-year old p=0.022, 6 vs 9-year old p=0.0035, 7 vs 8-year old p=0.0011, 7 vs 9-year old p=0.0001).

Table 1. The values of hematological parameters of the study group

Age; number	Hb (g/dL)			Iron (µg/dL)			UIBC (µg/dL)			Ferritin (µg/L)		
	Mean	SEM	95% CI	Mean	SEM	95% CI	Mean	SEM	95% CI	Mean	SEM	95% CI
6; 310	12.59	0.04	12.51 -12.67	72.30	2.01	68.34-76.26	296.16	3.51	289.25-303.07	22.32	1.17	20.00-24.64
7; 295	12.74	0.04	12.65 -12.83	72.68	2.02	68.70-76.65	302.67	4.20	294.39-310.95	22.84	1.02	20.83-24.86
8; 337	12.84	0.04	12.76- 12.93	74.96	1.99	71.05-78.87	302.09	3.72	294.78-309.40	22.57	0.84	20.90-24.23
9; 354	12.87	0.04	12.79- 12.96	73.11	1.79	69.59-76.63	304.91	3.23	298.55-311.28	23.19	0.84	21.53-24.85

Ferritin levels were normal in 65.51% of the children (823/1296) and depleted iron stores were determined in 36.49% (473/1296). The differences between frequencies of low ferritin levels among different age groups were found to be nonsignificant (Table 3). Among those with anemia, 16.40% (21/128) had low ferritin levels, which lead the overall ratio of IDA to be 1.62% in our whole study group.

The age-dependent mean levels of Hb, iron, and UIBC of children with depleted iron stores were shown in Table 4. The Hb values were found to be significantly different between six years old versus 8 and 9-year old children ($p<0.001$). The mean levels of iron, UIBC, and ferritin of children grouped according to the presence and severity of anemia were shown in Table 5.

Iron levels were found to be statistically significant between the children without anemia and with moderate anemia, as well as between the children with mild and moderate anemia ($p<0.001$). No statistically significant differences were found between the groups in terms of

UIBC and ferritin levels. The ratio of anemia and IDA were similar when the children were divided into groups in terms of gender.

Table 2. The ratio of children with and without anemia

Age	ANEMIA		
	Non-Anemia (11.5 g/dL)	Mild (11-11.4 gdL)	Moderate (8-10.9 g/dL)
6	273 (87.22%)	24 (7.66%)	13 (5.12%)
7	249 (84.4%)	24 (8.13%)	22 (7.47%)
8	313 (92.87%)	14 (4.15%)	10 (2.98%)
9	333 (94.06%)	13 (3.67%)	8 (2.27%)
Total	1168 (90.12%)	75 (5.78%)	53 (4.1%)

When 200 children were randomly selected for each age group, Spearman's correlation test showed a positive relationship between Hb and serum iron levels for 6-, 7- and 8-year old children, and between ferritin and iron levels for 9-year old children.Correlation coefficiencies and p values are depicted in Figure 1. When the children were divided into gender-specific groups, positive correlations were still present in the 6-, 7- and 8-year old children groups.

Table 3. The ratio of children with low and normal levels of serum Ferritin

Age	Depleted iron stores (Ferritin<15 µg/L)	Normal levels of Ferritin (Ferritin≥15 µg/L)
6	127 (40.96%)	183 (59.04%)
7	108 (36.61%)	187 (63.39%)
8	117 (34.71%)	220 (65.29%)
9	121 (34.18%)	233 (65.82%)
Total	473 (36.49%)	823 (63.51%)

Table 4. The values of hematological parameters of the children with serum Ferritin levels <15 µg/L

Age	Hb (g/dL)			Iron (µg/dL)			UIBC (µg/dL)		
	Mean	SEM	CI	Mean	SEM	CI	Mean	SEM	CI
6	12.18	0.07	12.04-12.32	67.59	2.80	62.02-73.15	321.91	5.74	310.53-333.29
7	12.40	0.08	12.22-12.57	71.11	3.06	65.03-77.18	332.16	6.84	318.60-345.72
8	12.58	0.07	12.43-12.73	73.39	3.12	67.20-79.58	320.42	5.88	308.76-332.09
9	12.52	0.08	12.35-12.68	67.40	2.87	61.71-73.09	327.08	4.64	317.87-336.28

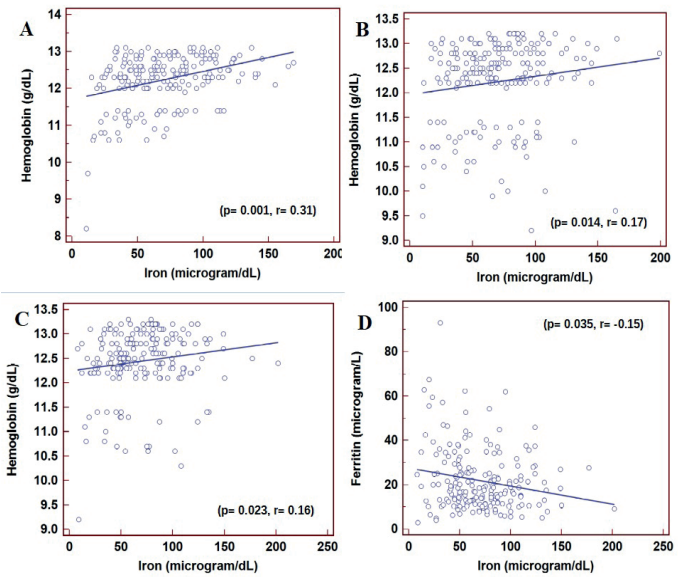

Figure 1. Correlation graphs of parameters according to age groups. P values and correlation coefficiencies were depicted on each figure. A. Correlation graph of Hemoglobin and iron levels in 6-year old children.B. Correlation graph of Hemoglobin and iron levels in 7-year old children.C. Correlation graph of Hemoglobin and iron levels in 8-year old children.

Table 5. The values of hematological parameters of the children subgrouped according to presence or absence of anemia

Non-Anemia	Mean	SEM	CI
Iron (g/dL)	73.71	2.39	68.99-78.42
UIBC (g/dL)	302.92	4.51	294.01-311.83
Ferritin (g/L)	21.92	0.98	19.99-23.85
Mild Anemia			
Iron (g/dL)	63.02	3.59	55.86-70.18
UIBC (g/dL)	305.13	6.52	292.13-318.13
Ferritin (g/L)	21.77	1.78	18.22-25.32
Moderate Anemia			
Iron (g/dL)	49.52	4.77	39.95-59.10
UIBC (g/dL)	320.96	10.14	300.61-341.31
Ferritin (g/L)	21.30	2.37	16.53-26.07

DISCUSSION

Anemia is one of the biggest public health concerns in the world. Being the mostly observed type of nutritional deficiency worldwide, iron deficiency is the major cause of anemia in children of all ages (6). Iron deficiency in the

childhood may be caused as a result of consumption of smaller amounts of iron-containing foods, malabsorption of iron through the intestines and simultaneous intake of iron chelators in the same meal resulting in decreased absorption (7). Since iron is required for hemoglobin synthesis, deteriorated oxygen transport to the tissues as a result of anemia results in adverse outcomes in the childhood, such as poor cognitive and motor development, decreased immune response to microorganisms and even agitation and behavioral problems. Taken together, all these symptoms are related to low academic performance in the school (8).

The purpose of our study was to determine the frequency of iron deficiency and iron deficiency anemia in children aged 6 to 9 years, who referred to our hospital for their annual check-up. Children between 6-9 years are in the elementary school age according to regulations in Turkey.

Among 1,296 children meeting the criteria for inclusion, we detected the frequency of anemia as 9.88%. When the serum ferritin levels were analyzed, the ratio of children with depleted iron stores was 36.49%. 1.62% of children with both low Hb and ferritin levels were defined as having IDA.

Being one of the major public health issues, the Turkish Municipality of Health started a screening and treatment program for the children with anemia and IDA. In the frame structure of this program, iron supplements were provided for children between 4-24 months old. While the frequency of anemia and IDA decreased following the program, the presence of anemia in children over two years old is still an important concern. According to WHO report "Worldwide prevalence of anemia 1993–2005", the prevalence of anemia in pre-school age children was 32.6 in Turkey (9). A more recent 2011 report revealed 30% anemia prevalence in Turkish pre-school age children (1). The frequency of school-age children was not analyzed within these reports since this group was not among the major risk groups for anemia. However, according to the 1993-2005 data report, the global prevalence of anemia in school-age children was 25.4%, corresponding to one out of every four school-age children. In a study on 15-17 years old Turkish children, the overall prevalence of anemia and IDA was found as 5.9% and 2.2%, respectively (10).

Another study scanned Turkish school children aged between 7 and 14 years found the prevalence of IDA as 9.4% and of iron deficiency (ID) as 28.5%. In the same study, the frequency of IDA was 6.6% and ID was 29.9% in children aged 7-11 years (11). In a study by Akın et al., the ratio of IDA was 3.29% (12). Taken together, differing rates of anemia and IDA in children might be caused from various reasons. Firstly, the definition of IDA differs in studies. For instance, while some authors claim that Hb levels lower than 11 g/dL together with ferritin levels lower than 15 mg/L is adequate for IDA diagnosis, some studies add the evaluation of RDW and MCHC values in order to strengthen the diagnosis (2,13,14). Additionally, the age range in studies might be very wide, including elementary school children and adolescents in the same study. Therefore, since every age group in the childhood has different nutritional needs and different metabolic processes affecting iron status, classification of children into narrower sub-groups might be more efficient for a better understanding of their hematologic status.

Although there are different indexes using the parameters in CBC for the diagnosis of hematological conditions CBC alone is not sufficient to diagnose the etiology of anemia. Thus, additional testing is required in order to widen the view into each individual's hematological status. Hb electrophoresis is widely used in Turkey since this country is on the Mediterranian region where different types of hemoglobinopathies are frequently observed. Among Hb electrophoresis, iron, ferritin, UIBC, transferrin saturation, and soluble transferrin receptor levels are measured to determine the iron status. With the help of new automatized hematology analyzers, different reticulocyte indices might be used in order to investigate the etiology in the erythropoietic level.

However, biochemical parameters are affected by various factors. Being an acute phase reactant, ferritin, the storage form of iron is observed in increased levels in the status of inflammation. Thus, higher ferritin levels should be confirmed in terms of the presence of inflammatory response within the organism. There are studies suggesting that ferritin might be used as a marker of iron status only when iron stores are depleted, and ferritin levels are below the reference range (15).

Since anemia and IDA are known to be occurring as a result of low intake of iron-containing foods and evaluated as a nutrition dependent issue, the prevalence of IDA is correlated with low income and socioeconomic status. Our study group consists of children belonging to low-middle income families who applied to the pediatrics departments of a large public hospital in Istanbul, Turkey. Despite their socioeconomic status, the low rate of anemia and IDA in our study group might be a result of frequent follow-up during the childhood, and administration of free iron supplements to the children of all ages by the public authorities. Being in a region with a large number of individuals having different types of hemoglobinopathies, Hb status of Turkish patients is an emerging concern in terms of public health. Additionally, parasitic infections are observed in low frequency in the large metropols, thus the ration of children with anemia and IDA might be higher in rural regions. However, most of the parasite types known to cause anemia in childhood are not present in Turkey.

A positive correlation between Hb and iron levels in the children of 6, 7 and 8 years old, and between iron and ferritin levels in children of eight years old might be caused from the nutritional needs of different age groups. For instance, although mean Hb levels seem similar between

age groups, the ratio of anemia in the six and seven-year old group was significantly higher than eight and nine-year old group. This finding suggests that six- and seven-year old children are more prone to anemia as a result of rapid growth if iron supplementation is not provided at an adequate level. Furthermore, six-year old children are at their first year of schooling in a regular basis, their nutritional habits might be deteriorated due to long school days and classes at early hours in the morning. Similarly, the absence of correlation between Hb and iron levels and any other parameter might be a result of increased use of iron for different cellular processes in a rapid growth phase.

There are some limitations to our study. Firstly, our results represent the group of children, who applied for an annual check-up to a certain hospital in Istanbul, Turkey. Therefore, different groups of children who applied to different hospitals might yield different results. Additionally, we did not gather information regarding weight, height, dietary habits, iron supplement use, socioeconomic status of the children. Other markers of hematological evaluation such as transferrin, soluble transferrin receptor were not included in the study. We also do not have information regarding the inflammatory status of the children for the group with higher ferritin levels. However, children with CRP levels out of the reference range were excluded.

The strong sides of our study were that the sample population represents the elementary school children aged 6-9 years old in a large metropol of Turkey. Additionally, serum iron, ferritin, and UIBC levels were evaluated in order to assess anemia as well as the Hb levels. We also divided the subjects into subgroups according to ages aiming to define the anemia ratios in different age groups.

CONCLUSION

This work highlights the need that hematological parameters should be followed up closely with the help of laboratory analysis in children of growing age. Despite the low rate of anemia and IDA in our study group, there are still studies exhibiting higher rates of anemia and IDA in Turkish children coming from different socioeconomic environments and rural regions. Since 6- and 7-year old children had a larger rate of anemia compared to different age groups, extra nutritional and supplemental effort should be provided for children in the first years of school life. While iron supplements are used, it should be kept in mind that being also an oxidant molecule, periodic monitoring of iron levels may be required (16, 17). Furthermore, Hb levels within reference limits are not sufficient to handle a child as non-anemic, thus ferritin levels should be analyzed in order to evaluate the status of iron stores.

Competing interests: The authors declare that they have no competing interest.

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