Original Paper

Frequency of Hypoferritinemia, Iron Deficiency and Iron Deficiency Anemia in Outpatients

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Abstract

The prevalence rates of hypoferritinemia (IDec/one abnormal indicator), iron deficiency (IDef/two abnormal indicators) and iron deficiency anemia (IDA) in children who were referred to the outpatient clinics of the Department of Pediatrics for the first time within 1 month were investigated. Exclusion criteria were iron therapy before and during the study period and a history of chronic illness. Acute-phase reactants, such as erythrocyte sedimentation rate and C-reactive protein levels, were measured in all cases indicative of infectious diseases. Blood samples were obtained from each study patient admitted to the outpatient clinics during the study period. The hospital charts were later further evaluated, and samples of patients with any current illness known to interact with the iron status of the patient were discarded, and patients were contacted to supply new samples about 1 month after treatment of the infection. Thus, in patients with indications of an infection, samples obtained 1 month after treatment were assessed. The children (n = 557) were divided into four age groups: those aged 4 months to 2 years (group I), 2–6 years (group II), 7–12 years (group III) and 12–18 years (group IV). Children with a decrease in serum ferritin levels without anemia (IDec), and those with lower ferritin, transferrin saturation (TS) and serum iron (SI) concentration (IDef) were evaluated. IDA was diagnosed if hemoglobin (Hb) concentrations were lower than those adjusted for age, ferritin <12 ng/ml and TS ≤16% and if SI was decreased. IDec, IDef and IDA were detected in 26, 11.1 and 12.7% of the patients, respectively. Only 50.1% of the patients visiting the outpatient clinics were found to be normal. The rates of IDec (28.9%), IDef (21.9%) and IDA (26.2%) were highest in group I. IDec had the highest percentages in all groups. In group I, the rates of IDec, IDef, and IDA were 37.2, 66.1 and 69%, respectively. SI concentration was abnormal in 77.1% of the cases in group I (4 months to 2 years of age). Half of the patients referred to the outpatient clinics were suffering from abnormalities related to lower SI concentrations. Close monitoring and treatment of iron deficiency is advised especially in early childhood.

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Introduction

Iron deficiency is the most frequently encountered nutritional deficiency and ranks first among the etiologic factors of childhood anemia [1, 2]. The frequency of iron deficiency anemia (IDA) seen in children is gradually de-

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creasing in developed countries. However, in developing countries it remains common [3–5] and is still frequently observed in infancy, school age and adolescence. It is associated with deleterious effects, such as growth and developmental retardation, gastrointestinal alterations, impaired immune responses, reduced cognitive functions, behavioral changes and intolerance to exercise [6–8].

In this study, we aimed to determine the types and frequency of iron deficiency that parents did not care and/or recognize in children between 4 months and 18 years of age who presented for various reasons to the outpatient clinics of the Department of Pediatrics of Elazig.

Patients and Methods

Children between 4 months and 18 years of age who were referred to the outpatient clinics for the first time during 1 month were enrolled in this study. Informed consent was obtained from the parents, and the Ethics Committee of the Medical Faculty of the Fırat University approved the study protocol. Exclusion criteria were iron deficiency treatment before or during the study period and any history of chronic illness. Since the iron status was determined according to our laboratory criteria, a new diagnosis of chronic illness did not have any impact on our results. Acute-phase reactants, such as erythrocyte sedimentation rate and C-reactive protein levels, were measured in all the cases suggestive of infectious disease. Blood samples were obtained from each patient admitted to our outpatient clinics during the study period; their hospital charts were later further evaluated, and samples of patients with any current disease known to interact with the iron status were discarded, and patients were contacted to supply new samples about 1 month after treatment of infection. If this new visit resulted in the diagnosis of a disease that was not noticed during the previous examination on admission, they were excluded at that stage. Control values of all the children hospitalized for serious acute infections, which were obtained 1 month after patient discharge, were included in the analysis. Fecal samples of patients with iron deficiency were examined microscopically and samples were tested for occult blood.

The cases were divided into four age groups: 4 months to 2 years (n = 187), and 2–6 (n = 166), 6–12 (n = 168) and 12–18 years of age (n = 36). Venous blood was drawn from all the patients at the time of referral. Every sample was analyzed for hemoglobin (Hb) concentration, hematocrit (Hct), erythrocyte indices (mean corpuscular volume, mean corpuscular hemoglobin and mean corpuscular hemoglobin concentration) and red cell distribution width using an ADVIA 120 blood counter. Serum iron (SI) levels and total iron binding capacity were measured with an Olympus AU 600 autoanalyzer. Serum ferritin was analyzed using an Immulyte 2000 (BioDPC) autoanalyzer using the chemiluminescence method. Then transferrin saturation (TS) was calculated.

Hb concentrations below the values adjusted for age groups (4 months to 2 years, <10.5 g/dl; 2–6 years, <11.5 g/dl; 6–12 years, <12 g/dl; and 12–18 years, <12 g/dl) were considered as indicators of Hb deficiency. Since the aim of this study was to determine the iron status and its ratio of change in children referred to our outpatient clinics, impaired iron status was defined using multiple criteria, to avoid the impact of other causes of anemia (i.e. anemia of chronic illness). Normal Hb, SI and TS levels in the presence of lower ferritin (<12 ng/ml) values signified hypoferritinemia (IDec/one abnormal indicator). Iron deficiency (IDef/two abnormal indicators) was considered in case of normal Hb but lower SI, TS (<16%) and ferritin (<12 ng/ml) values. IDA was diagnosed in cases of decreased Hb, SI, TS (<16%) and ferritin (<12 ng/ml) values [9].

For statistical evaluations, χ^2 and Student's t tests were performed on the data using a software program (SPSS). $p < 0.05$ was considered to be statistically significant.

Results

Five hundred and fifty-seven children were evaluated (mean age 7.8 ± 3.2 years): 278 girls (49.9%) and 279 (50.1%) boys. For the group with normal SI levels, mean age was 6.7 ± 4.1 years, being 4.8 ± 3.9 years in the IDec group, 2.4 ± 2.4 years in the IDef group, and 3.0 ± 3.8 years in the IDA group. Significant differences in mean age were detected in patients with IDA, IDec and normal SI levels, and between the IDef group and the groups with normal SI levels and the IDec group. The difference in mean age between the IDec group and the remaining three groups was also statistically significant ($p < 0.01$).

The distribution of the patient population according to age was as follows: group 1, n = 187 (33.6%); group II, n = 166 (29.8%); group III, n = 168 (30.2%), and group IV, n = 36 (6.5%). IDec, IDef and IDA were detected in 145 (26%), 62 (11.1%) and 71 (12.7%) cases, respectively. Only 279 (50.1%) patients did not show any evidence of IDec, IDef or IDA. IDec (28.9%), IDef (21.9%) and IDA (26.2%) most frequently occurred in group I. In this age group, only 22.9% of the cases had normal serum values. The distribution of the iron deficiency status according to gender was also assessed. IDec was more common in girls (53.8%), while IDef and IDA were seen prominently in boys (71 and 62%, respectively). The hematologic values of the cases are presented in table 1.

Iron-deficient nutrition was remarkably higher (81.3%) in the IDA group than in the other groups. The incidences of excessive tea consumption (61.7%), pica (1.8%), the presence of parasitosis (7.4%) and occult blood in feces (2.3%) were also assessed.

Table 1. The distribution of the iron deficiency status and the hematologic values of the cases according to age groups and gender

	Hypoferritinemia (IDec/one abnormal indicator)				IDef/two abnormal indicators				IDA			
	4 m–2 y n = 53	2–6 y n = 38	6–12 y n = 46	12–18 y n = 8	4 m–2 y n = 41	2–6 y n = 3	6–12 y n = 17	12–18 y n = 1	4 m–2 y n = 51	2–6 y n = 6	6–12 y n =10	12–18 y n = 5
Hb, g/dl	11.4±0.8	12.9±1.1	12.1±1.1	13.2±0.6	11.3±0.6	11.9±1.2	12.5±0.9	12.6±00	9.6±1.1	10.7±1.5	10.5±1.4	10.6±1.1
MCV, fl	72.1±7.3	78.3±3.1	74.4±8.6	79.1±5.4	68.1±8.6	75.1±6.1	72.2±5.2	83.8±0.0	64.4±8.2	64.5±8.9	67.8±6.5	62.2±6.1
F, ng/ml	21.3±12.9	27.8±18.5	25.5±23.1	16.3±8.5	11.3±11.3	26.7±6.7	11.7±6.6	8.3±0.0	6.8±5.8	14.6±6.7	8.8±5.7	4.2±1.5
TS, %	7.9±0.2	8.0±0.3	13.4±0.5	5.9±0.1	7.6±0.2	5.0±1.0	12.9±0.5	12.3±0.0	5.9±0.1	3.1±0.5	11.2±0.7	3.9±0.1
Iron deficiency, %												
Total	28.9	27.7	22.0	22.2	21.9	10.2	1.8	2.8	26.2	6.1	4.2	13.9
F/M	38.9/61.1	63.0/37.0	59.5/40.5	75.0/25.0	22.0/78.0	41.2/58.8	66.7/33.3	0.0/100	38.8/61.2	40.0/60.0	28.6/71.4	40.0/60.0
Female	53.8				29.0				38.0			
Male	46.2				71.0				62.0			

Means ± SD. m = Month; y = year; MCV = mean corpuscular volume; F = Ferritin (ng/ml); TS = transferrin saturation (%); F/M = female/male.

Discussion

Iron is an important micronutrient required for body functions. It is necessary for all types of cells and organisms. It is also required for mental, motor and emotional development, normal learning processes, social activities, positive mood changes, cognitive functions, immune maturation, hormonal metabolism, working capacity and reproduction. Data on the prevalence of IDA in various populations are valuable because they contribute to the evaluation of this common and significant health problem in a global perspective. IDA is an important healthcare problem in poorly developed and developing countries where its rates have been reported to vary between 7 and 51% [10, 11]. The prevalence of IDA should be determined in an unselected population. In Turkey, studies performed in various age groups and at various socioeconomic levels found rates between 7.8 and 93% [12, 13]. To treat IDA, a diet supplemented with iron is mandatory. If iron deficiency is diagnosed and treated at an early stage of the disease, then cognitive deficits will not last permanently [14–18].

In the liver, iron concentrations are highest during the first 2 years of life. They markedly decrease during childhood. Children of higher socioeconomic status have richer iron stores [19]. In India, nutritional anemia was detected in infants (65%), children between 1–6 years of age (60%) and adolescent girls (88%). Among nutritional anemias, IDA was the most common form of anemia [20]. In Nigeria, 67% of the infants between 9 and 15 months of age showed Hb levels <10 g/dl [21]. In 77.1% of all our ambulatory cases between 4–24 months of age, unfavorable changes in SI concentrations were detected. IDA reached its highest percentage (26.2%) in this age group. In other age groups, the incidence of IDA varied between 4.2 and 13.9%. In our study, the rates of IDec and IDef were significantly higher in group I (4 months to 2 years of age). IDec and IDef may affect concentration, learning skills, growth development and mortality long before the onset of anemia [1, 22, 23]. IDec, IDef and IDA were detected in 26, 11.1 and 12.7% of our cases, respectively. It can be seen that in 37.1% of our cases iron stores had waned before the development of IDA. If iron deficiency is recognized and treated at an early stage, adverse effects on the nervous system are prevented [20]. Serum lead levels, which rise in cases of iron deficiency, also have neurotoxic effects [24]. Particularly in iron-deficient preschool children, physical development can be improved if iron deficiency is treated. Treatment of small children with IDA has a substantial impact on the psychomotor development within 5–11 days of therapy. In order to determine the frequency of IDec, IDef and IDA, it may be appropriate to obtain blood samples in children of preschool age and especially during early childhood [25]. Therefore, we tried to determine SI levels long before the onset of IDA. The incidence of IDA was calculated to be 5.1% in 2- to 12-year-old children in Elazig province, in contrast to the 29.3% reported in a study conducted 3 years ago. In children aged 2–6 years, the frequency of IDA was 6.1%, and the corresponding incidence was 32% in this study. The rate of IDA in 4- to 24-month-old children was 26.2%, while the incidence in the patient population as a whole was found to be 12.7%.

Since the incidence of IDec can be underestimated in patients with mild infections due to increased serum levels of ferritin, which also functions as an acute-phase re-

actant, cases with serious infections were excluded from this study. The finding that the incidence of IDec was lower than expected may be explained by the time blood was sampled, i.e. 1 month after treatment of infections. In these cases, there may be mild infections causing an increase in serum ferritin levels without much effect on the erythrocyte sedimentation rate and C-reactive protein values. Only 50.1% of the patients who were referred to the clinics for any reason had normal SI concentrations. SI concentrations of the remaining 49.9% varied greatly.

Health problems related to the iron status were observed mostly in patients aged 4–24 months. The combined incidence of IDec, IDef and IDA peaked in patients aged 4–24 months. Compared with IDef and IDA, the incidence of IDec was higher irrespective of gender in this group. Except for IDec, IDef and IDA were nearly twice as common in boys. When the patient population was taken as a whole, IDec was more commonly (53.8%) seen in girls, whereas IDef (71%) and IDA (62%) were more prevalent in boys. IDec was higher (75%) in girls aged 12–18 years. IDef (78%) was more prevalent in 4- to 24-month-old boys, while the incidence of IDA was higher (71.4%) in boys 6–12 years of age.

The incidence of IDec was much higher and the incidence of IDA lower in all age groups. The low socioeconomic status of our country is considered responsible for the high rates of patients with impaired iron status observed in our study population. High numbers of malnourished children in poor families, repeated infections, and delayed or improper access to the health services due to lack of health insurance are among the factors responsible for these high rates [3–5, 11]. The workload imposed by daily activities and other responsibilities of the parents in addition to their economic problems cause delays in noticing the symptoms and seeking medical help for children with an impaired iron status. The presence of different socioeconomic classes in the Turkish population might account for the discrepancies in the results on the iron status ratios reported in the literature [12, 13]. Therefore, our study population consisted of lower middle-class patients.

IDec was mostly observed in girls (53.8%), while IDef and IDA were seen predominantly in boys (71 and 62%, respectively). Contrary to previous studies, impaired iron status was unexpectedly higher in boys than girls. This may be attributed to sociocultural attitudes of families making them more sensitive to health problems of boys and more likely to seek medical help.

Pica denotes an abnormal state of appetite or craving for a substance that is not fit for food for a duration of at least 1 month. In this study, the incidence of pica was found to be 1.8%, while a previous study reported an incidence of 2.4% [25]. In our cases dirt eating (geophagia) was the most common form of pica.

In agreement with our study, recent studies have shown a high rate of IDA in Turkey [12, 13], and the national policy on prophylactic iron supplementation free of charge for pregnant women and babies up to 12 months has been started in the past year. Future studies will reflect the impact of this policy on the iron status of Turkish children.

Highly variable SI levels during childhood have unfavorable effects on growth and development. In 77.1% of cases aged 4–24 months, SI concentrations were not within normal ranges. Half of the ambulatory patients appeared to experience problems related to iron deficiency. This issue, which is disregarded or unheeded by the families, appears to be an important public healthcare problem in patients referred for a wide range of health problems. Therefore, during early childhood, close monitoring of the iron status of children is important to be able to initiate early treatment if necessary.

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