Original Article

Latent iron deficiency in non-anaemic children under five years of age

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Abstract

Introduction: The most common nutritional deficiency in world is iron deficiency. The iron deficiency is the most common cause of anemia due to nutritional deficiency and is seen most commonly in children under five years of age.

Objective: To determine the frequency of iron deficiency in non-anemic children under five years of age.

Materials and Methods: A descriptive cross-sectional survey was conducted in pediatrics department of PAEC, General Hospital Islamabad, from August 2020 to February 2021. A total of 145 non-anemic children, ages 2-59 months were enrolled through non-probability consecutive sampling in this study. The complete blood count and C-reactive protein were sent for laboratory tests to rule out infection/inflammation. In children with normal hematocrit (30-40%) and CRP (≤ 6), serum ferritin levels were sent. Those children in whom serum ferritin levels were ≤12ng/ml was regarded as cases of latent iron deficiency. SPSS version 23 was used for data entry and analysis. Age and gender for effect modifiers were controlled by stratification. The chi square test was used for post stratification. The value of $p \leq 0.05$ was considered significant.

Results: The mean age of the patients was 3.20±5.41 years. Among all children, 69 (47.6%) were boys and remaining 76 (52.4%) were girls. Out of 145 children, 62 (42.8%) were iron deficient whereas 83 (57.2%) were non-iron deficient. The male to female ratio of iron deficiency was 1:1.3. The prevalence of iron deficiency among infants was 46%, followed by toddlers 42% and preschoolers 41%. The mean serum ferritin level was 22.96±2.21 ng/ml. The mean hematocrit was 33.84±2.68. The statistical analysis showed that there was an insignificant association between iron deficiency and age groups of children ($p \geq 0.5$).

Conclusion: The study concluded that the iron deficiency in children is very common, especially in infants. Screening of iron deficiency in children under five years of age seems to be a very important task for better child care.

Keywords: Anemia, Iron-Deficiency; Child, Preschool; Malnutrition.

Introduction

The most common micronutrient deficiency is iron deficiency (ID) worldwidely.[1] According to WHO, ID is the most common form of malnutrition in the world affecting around 2 billion people worldwide, accounting for 25% of the world's population.[2] According to global estimates, 50% of anemia is because of iron deficiency. Iron is necessary for development of immune system of body. ID have been linked to poor cognition, and impaired motor and psychomotor development.[3] ID ranges between 25-80% in preterm babies during infancy. ID has a worldwide prevalence of 4% in infants ≤ 6 months, 12% in infants 6-12 months and 6.6 to 15.2% in toddlers. In a Nigerian study, 27.5% of non-anemic children under five years of age were iron deficient.[4,5]

In Pakistan, ID is a critical health problem as its prevalence among Pakistani population is between 30-69%. ID, in children ≤ 5yrs of age ranges between 65-78% in Pakistan.[6] Childhood ID is especially dangerous due to the increased mortality and its permanent impact on mental development, which can lead to irreversible loss of productivity in adult health.[5]

The most common symptom of iron deficiency is anemia, the terms iron deficiency (ID) and iron deficiency anemia (IDA) are used interchangeably.[7] Risk factors of anemia include low iron diet, low iron absorption due to phytates and phenolic compounds in the diet and high demands like growth spurts, improper feeding patterns, low birth weight infants, history of recurrent upper respiratory tract infection, diarrhea, trauma, surgery, worm infestation. Nutritional IDA is common in children between 6 months to 2 years, low maternal education, large family size, prolonged breastfeeding, low maternal iron status are the causes.[8]

Preventive measures include preventing premature birth, delayed cord clamping, breast feeding exclusively up to 6 months, providing solid foods in addition to breast milk during different diets, avoidance of cow's milk, iron enriched formula milk, using iron rich solid foods, proper maternal education.[9] Iron status can be evaluated by various tests including total iron binding capacity (TIBC), serum transferrin saturation/levels, iron staining of bone marrow and serum ferritin levels. Serum ferritin level is the surrogate marker of iron stores of the body and single best test done for diagnosis.[10] According to WHO, ferritin levels below 12ng/ml have been considered as depleted iron stores. The non-anemic children were identified who have hematocrit levels between 30-40%.[11]

The rationale of this study was to document prevalence of iron deficiency in non-anemic children of the most vulnerable age group and to screen them for presence of its latent form. Because of the huge burden of disease both worldwide and locally, routine screening for the presence of ID is consideration to prevent its long-lasting deleterious effects and to prevent its progression to even more detrimental IDA and its consequences. The objective of the study was to determine the frequency of iron deficiency in non-anemic children under five years of age.

Materials and Methods

After approval from Institutional Review Board ---removed \for blind review---from August 2020 to February 2021. Written informed consent was taken from parents/guardians of all enrolled children. A total of 145 children (WHO sample size calculator was used for sample calculation; whereas, the following parameters were used the population proportion was 24.4% with CI 95% and absolute precision was 7%),[5] both gender, ages between 2 to 59 months, with history of pica, learning and behavioral disorders, breath-holding spells, poor school performance, febrile seizures, cow milk intake, and hematocrit 30%-40% and CRP between 1-6mg/L were enrolled through non-probability consecutive sampling for this study. Children with co-morbidities including malnutrition, infection/inflammation, congenital heart diseases, chronic renal/liver failure and hemoglobinopathies like thalassemia, sickle cell anemia, G6PD deficiency were excluded from the study.

The following procedure was done for data collection; a questionnaire was developed to determine the appropriate social characteristics, complete history of chronic illness, drug including iron, history of transfusions, dietary, current or recent infection, symptoms seen in iron deficient patients, worm infestation and physical examination for pallor, stigmata of chronic illnesses, signs of inflammation and malnutrition.

Serum samples were sent to same hospital setting laboratory for complete blood picture (CBC) to look for hematocrit and C-reactive protein (CRP) to look for infection/inflammation. Two milliliters of blood were taken from patients and then centrifuged to separate serum to measure ferritin levels. A 2-step immune-metric technique was used; involved reaction of

ferritin in the sample serum with biotinylated antibody in the first step. The antigen-antibody complex was captured by streptavidin coated on the well. Second step was reaction of the complex with horseradish peroxidase (HRP)-labeled antibody conjugate. This was measured by a luminescent reaction and its amount was directly proportional to the concentration of ferritin. All this was done using VITROS ECI/ECiQ immunodiagnostic systems.[5,8] The CBC, CRP and ferritin levels were done in the hospital free of cost. For statistical analysis the data was entered in SPSS version 23. Descriptive analysis was used for measuring mean, standard deviation for numerical variables like age. Iron deficiency was measured as frequency and percentage. Age and gender for effect modifiers were controlled by stratification. The chi square test was used for post stratification. The value of $p \leq 0.05$ was considered significant.

Results

A total of 145 patients with iron deficiency were recruited for the study; 47.6% (n=69) were boys and 52.4% (n=76) were girls. Also, the mean age of the patients was 3.20±5.41 years with minimum 2 months and maximum 59 months of age (Table 1). The male to female ratio of iron deficiency was 1:1.3. The mean serum ferritin level was 22.96±2.21 ng/ml. The mean hematocrit was 33.84±2.68 (Table 1). The prevalence of iron deficiency in children under 5 years of age is 42.8% (Table 2).

Descriptive statistics (percent frequencies) between gender, age and iron deficiency were studied and post stratification chi square was applied (Table 3).

Table 1: Descriptive analysis of demographics and serum analysis, n=145

Age (mean)	3.20±5.41 years		
Gender (frequency and percent)	Male	69	47.6%
	Female	76	52.4%
Iron deficiency ratio	1:1.3		
Age in brackets (frequency and percent)	02-12 months	39	26.9%
	13-23 months	50	34.5%
	24-59 months	56	38.6%
Serum ferritin levels (mean)	22.96±2.21 ng/ml		
Hematocrit (mean)	33.84±2.68		

Table 2: Descriptive statistics of iron status, n=145

Iron status	Frequency	Percentage
Iron deficient	62	42.8%
Non-iron deficient	83	57.2%

Table 3: Relationship between gender, age and iron deficiency, n=145

Variables		No. of patients	Iron deficiency		p-value
			Iron deficient	Non-iron deficient	
Gender	Male	69	27 (39.0%)	42 (61.0%)	0.400
	Female	76	35 (46.0%)	41 (54.0%)	
Age brackets	02-12 months	39	18 (46.2%)	21 (53.8%)	0.878
	13-23 months	50	21 (42.0%)	29 (58.0%)	
	24-59 months	56	23 (41.0%)	33 (59.0%)	

Discussion

In this study 145 children with iron deficiency status were studied. Most of the children 38.6% were 24-59 months of age and female gender was predominant with 52.4% proportion compared to male who were 47.6% and the prevalence rate of iron deficiency was 42.8%. In the study conducted by Eckowchi et al the overall prevalence of iron deficiency was found out to be 27.5%.[8] Kisiangani study showed iron deficiency of 20.8%.[12] In a study by Verga, prevalence of ID at 12 months was 5.7%.[13]

In Pakistan, prevalence of ID is between 30-69% where 40-50% preschool children and 69% of children ≤ 2 years have ID.[6] US data indicates a prevalence of 9% for ID and 3% for IDA in 1-3yrs children. Similarly, European studies found out a prevalence of 5-20% for ID and 3-9% for IDA in the similar age groups.[14,15] American Academy of Pediatrics has given a conclusive plan for worldwide screening for anemia in this age group. Worldwide screening for ID and IDA also includes assessment of the predisposing factors that lead to the development of these conditions like low birth weight, prematurity, lead exposure, breastfeeding exclusively ≥ 04 months without iron supplementation, whole milk or whole-grain foods that do not include iron-reinforced cereals or naturally rich foods, dietary problems, poor growth and low socioeconomic status. Selective screening can be done if any of these risk factors are present at any age.[16]

In this study, children with hematocrit in the normal range (30-40%), normal hemoglobin and CRP and no evidence of any chronic illness were studied. Whereas, in a prospective study conducted by Eckwochi et al children with hematocrit level were 30 and above (30-40%).[8] In our study, the prevalence of iron deficiency in children 02-12 months of age was 29%, in age group 13-23 months, it was found out to be 33.9%, and in age group 24-59 months had a prevalence of iron deficiency of 37.1%. The statistical difference was insignificant (p = 0.878). In a study conducted by Eckwochi et al the prevalence of ID in infants 02-12 months was 29.2%, in toddlers 13-23 months 24.4%, and in preschoolers 24-59 months 27.9%. The statistical difference was insignificant (0.997).[8] In a study conducted in Ibadan, Nigeria, by Owa et al included 6-24 months children and showed that 29.2% iron deficiency.[17]

Our study revealed mean serum ferritin levels of 22.96±2.21 ng/ml and mean hematocrit level was 33.84±2.63. Whereas, in the study by Eckwochi et al the mean serum ferritin was 54.9 (0.2-454) ng/ml and the mean hematocrit was 35.[8] In this study, prevalence of ID in all age groups was high insignificant (p = 0.878), similar to that shown by Eckwochi et al study (p = 0.741).[8]

This study revealed that 46% females were iron deficient and 39% males were iron deficient, suggesting that further studies showed be carried out to reach to the cause of this age discrepancy in the prevalence of iron deficiency among male and females of the same age group.

This study found out the prevalence of major element (iron) deficiency in children to emphasize the importance of the early iron supplementation that can prevent ID, but this study has some limitations too; firstly, serum ferritin was the investigation of choice and its easy availability cannot be ensured in every healthcare setup and it is an acute phase protein and can give false results. Secondly, the study was done in a single centre therefore, its results cannot be generalized. Thirdly, the time duration of the study was short which is insufficient in which a large population could not have been studied for generalization of results. Furthermore, other parameters of the population should also have been discussed and other nutrient deficiencies could have been studied along this study. The age group chosen could have been extended to cover older children too.

Conclusion

The study concluded that the iron deficiency in children is very common, especially in infants. Screening of iron deficiency in children under five years of age seems to be a very important task for better child care. Early identification of the iron deficiency, prevention of the conditions that lead to it, early iron supplementation and prophylaxis, along with its early treatment, prevents all the complications of ID in childhood.

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