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A Study of Serum Ferritin Levels in Hospitalized Children Suffering From Anemia: A Hospital Based Study

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Abstract
Background: *Iron deficiency is the commonest form of malnutrition worldwide and according to the World Health Organization affects 43% of the world's children. In children it is frequently caused by dietary deficiency, because milk has low iron content. It is develops when there is inadequate iron for hemoglobin synthesis and is the result of imbalance between iron assimilation and iron loss.*
Method: *This prospective hospital based study was conducted on 100 children between 6 months to 5 years, admitted in pediatrics department of Rural tertiary care hospital, Mullana. Children with Thalassemia, malignancy, and bleeding disorders were excluded. 2 ml of venous blood anti-coagulated with EDTA was taken and complete blood counts (Hb, TLC, DLC, Platelet count, Red cell indices), peripheral blood film and S.ferritin estimation was done.*
Results: *Serum ferritin had a mean value of 40.676 ng/ml (min: 0.1ng/ml; max 246.6ng/ml) It was 31.86 ng/ml for age group 6-24 months, 52.35 ng/ml for 25-36 months and 55.035 ng/ml for age group 37-60 months, showing rising trends of serum ferritin with age. Mean hemoglobin of the children is 8.84gm/dl (with minimum being 2.4gm/dl and maximum 10.9 gm/dl), median being 9.45g/dl. Microcytic Hypochromic anemia was seen in 72% children while Normocytic and Normochromic anemia was seen in 28% of children.*
Conclusion: *Peripheral blood film and RBC indices although aid to diagnose the type of anemia, where resources permit serum ferritin estimation should be done as is the only sensitive test to diagnose iron deficiency anemia in initial stages. This results in prevention of the children to progress from iron deficiency (depleted iron store) to the iron deficiency anemia and its morbid consequences.*
Keywords: *Serum ferritin, Iron deficiency anemia, Microcytic-Hypochromic, anemia.*

Introduction

Anemia is a widespread public health problem associated with an increased risk of morbidity and mortality, especially in pregnant women and young children[1].Anemia is defined as decrease in the red blood cells (RBC) volume or a reduction of hemoglobin concentration below the range of values occurring in healthy person[2]. In pediatric age group it is the most common hematological disorder. Iron deficiency anemia is the commonest nutrient deficiency in India with prevalence about 75% in children under the age of 5 years,[3] in children it is frequently caused by dietary deficiency, because milk has low iron content. It is develops when there is inadequate iron for hemoglobin synthesis and is the result of imbalance between iron assimilation and iron loss.[4]The cutoff values of serum ferritin were revised in 1993 and it was reported that ferritin levels < 12 µg/L under 5 years of age, <15 µg/L above 5 years of age and <30 µg/L in the presence of infection reflect the depleted iron stores[5].

The concentration of plasma ferritin is positively correlated with size of total body iron stores in absence of inflammation. Under steady state condition, serum ferritin levels correlate with total body iron stores; thus, the serum ferritin the is most convenient laboratory test to estimate iron stores[6]. The value are different in different age group. serum ferritin levels are elevated in acute and chronic inflammations, liver disorders and other chronic disorders[7]. The hemoglobin concentration that is used to define anemia is commonly assessed and used as a proxy for iron status, but this indicator is neither a sensitive nor specific measure of iron deficiency[8].

In a growing infant, who has got a very delicate balance between iron stores, high requirements and limited supply, it is very important to diagnose iron deficiency at a stage before it result in iron deficiency anemia.

As per WHO anemia defined as reduced hemoglobin levels to less than 11g/dl in children aged 6 months to 60 months[9].Iron deficiency anemia was defined as Hb values less than WHO thresholds (<11g/dl) with the presence of presence of two or more of the following parameters; mean corpuscular volume (MCV) less than 70 fl, serum ferritin below 30 ng/ml, and transferrin saturation (TSAT) less than 16%.[10]

The present study was carried out to know the serum ferritin levels and correlation between serum ferritin and other hematological parameters (Hb, MCV, MCHC, PBF etc) in hospitalized children suffering from anemia.

Material & Methods

This was ahospital based study carried out at department of Pediatrics, Maharishi Markandeshwar institute of medical sciences and Research, Mullana, Ambala Haryana over a period of two year from December 2014 to November 2016.

This study was conducted on 100 children in the age group of 6 months to 60 months who were hospitalized in pediatrics ward for some other illness, but incidentally were found to have anemia (hemoglobin <11g/dl). The details regarding Age, Sex, social class, family income, occupation, education of the parents was collected. Children suffering from Thalassemia, bleeding disorders and leukemia were excluded. Ethical committee of our institute had given approval for this study. Informed consent was obtained from parents.IDA was defined as Hb values less than 11g/dl with the presence of mean corpuscular volume (MCV) less than 70 fl and serum ferritin below 30 ng/ml (in presence of infections).

2 ml of venous blood anti-coagulated with EDTA was taken and complete blood counts (Hb, TLC, DLC, Platelet count, Red cell indices)were estimated using automated cell counter method using SYSMEX automated hematology analyser B226 04/2009 Japan. Peripheral blood film was read by a pathologist and on the basis of morphology of RBC, peripheral blood film (PBF) was labeled as Microcytic hypochromic and Normocytic normochromic type.

Estimation of Serum Ferritin

Method: Chemiluminescence immunoassay (Lilac Acculite CLIA)

Principle: The essential reagents required include high affinity and specific antibodies, with different and distinct epitope recognition, in excess and native antigen. In this procedure, the immobilization takes place during the assay at surface of an opaque chemiluminescent reaction cell through the interaction of streptavidin coated on the opaque reaction cell exogenously added biotinylated monoclonal antibody coupled to the analyte of interest. upon mixing monoclonal biotinylated antibody, the enzyme labeled antibody and test serum containing the native antigen and the antibody, without competition, to form a soluble sandwich complex.

The statistical analysis was carried out using the SPSS 21.0. Data was summarized using descriptive statistics. continuous variables were presented as mean and standard deviation(SD) while categorical variables as number and percentage, Chi-square test and "t" test were performed to compare the relationship among two or more categorical variables. When comparing the means of more than two groups, one-way ANOVA test was conducted. A p value of < 0.05 was taken as statistically significant.

Results

Out of 100 children who were included in the study 45% were diagnosed to have lower respiratory tract infections, 30% with acute gastro enteritis and rest 25% with global developmental delay with cerebral palsy. All the children taken in the study had anemia with Hb levels <11g/dl. Mean hemoglobin of the children is 8.84gm/dl (with minimum being 2.4gm/dl and maximum 10.9 gm/dl), median being 9.45g/dl.Table:1 shows the hematological parameters noted in children with anemia.

Serum ferritin had a mean value of 31.86ng/ml for the age group 6-24 months, 52.35ng/ml for 25-36 months and 55.03ng/ml for age group 37-60 months, showing a rising trend of serum ferritin with age(p value 0.060) (Table-2).

Mean age in serum ferritin <30 ng/ml of the children is 23.97 and those with serum ferritin ≥30 ng/ml is 31.16 months. The mean hemoglobin in serum ferritin <30 ng/ml is 8.625 gm/dl and that in the group of serum ferritin ≥30 ng/mlis 9.114 showing greater prevalence of iron deficiency of iron deficiency anemia in younger age group (Table-3).

Out of 56 hypoferritinemia (<30 ng/ml)cases 46 had mean corpuscular hemoglobin concentration (MCHC) in range of 20-30 g% and 10 had normal values. MCHC values had a significantly corelation with serum feritin levels (Table-4).

Out of 100 children 92% had microcytic (MCV<70fl) type of RBC and 8% had normocytic RBC, and no statistical significant correlation were found between serum ferritin levels and mean corpuscular volume (Table-5).

On the basis of red cell morphology, microcytic hypochromic anemia was seen in majority of cases (72 %) followed by Normocytic normochromic anemia in 28 % of cases. Iron deficiency anemia with microcytic-hypochromic PBF was seen in 45% and without microcytic-hypochromic PBF was seen in 56% of children (Fig-1).

In present study results shows 10 (50%) out of 20 children suffering from mild anemia and hypoferritinemia showed microcytic-michromic PBF, however the rest of 10 had no peripheral blood film changes. However in moderate anemia out of 25 hypoferritinemia cases, 24 showed the PBF changes and only 1 child with hypoferritinemia did not show any morphological changes in RBC. This support the high sensitivity of serum ferritin in picking up IDA cases suffering from mild anemia. (Table-6).

Children were also grouped on the basis of socio economic status according to modified kuppuswamy classification 2014 showing 36% in lower class, 32% each in both middle and upper class, However no statistical significant correlation were found between mean serum

ferritin value and socioeconomic status(p value 0.607) (Table-7).

All the children taken in the study had anemia with Hb levels <11g/dl. Iron deficiency anemia was confirmed in children with Microcytic hypochromic PBF and serum ferritin levels below 30ng/ml (cut off value by WHO in children with infection). The overall prevalence of IDA in our study was 45%.

Table 1 Statistical characteristics of various hematological parameters

	Hb(g/dl)	TLC(cells/cumm)	MCH	MCV	MCHC	Serum ferritin(ng/ml)
Mean	8.840	10426.00	22.048	67.887	28.086	40.676
Median	9.450	9950.00	22.650	69.500	28.900	24.500
Std deviation	1.9383	3984.227	4.4119	10.5078	3.9422	45.8751
Range	8.5	27200	21.4	50.1	18.4	246.6
Minimum	2.4	2800	12.4	42.6	17.3	0.1
Maximum	10.9	30000	33.8	92.7	35.7	246.7

Table 2 Age wise distribution of mean serum ferritin in pediatric patients suffering from anemia

Age (months)	Serum ferritin Mean(ng/ml)	N(no of cases)	Std deviation(SD)	p value (ANOVA)
6-24	31.86	60	37.8238	>0.05(0.06)
25-36	52.35	17	64.3263	
37-60	55.03	23	45.7339	
TOTAL	40.61	100	45.8751	

Results of above table showing a rising trend of serum ferritin with age (p value 0.060)

Table 3 Mean hemoglobin and Age compared to serum ferritin levels <30ng/ml in children

Serum ferritin levels	No of cases	Mean hemoglobin (g/dl)	Mean age(months)
<30 ng/ml	56	8.625	23.97
≥30ng/ml	44	9.114	31.6

Table 4 Comparison of Mean corpuscular hemoglobin concentration (MCHC) of RBCs with serum ferritin levels

MCHC Group (g%)	Serum ferritin < 30ng/ml	Serum feritin ≥ 30ng/ml	Total	p value (Chi-square))
Normal (>30)	10	20	30	<0.05** (0.003))
	33.3%	66.7%	100%	
Low mean corpuscular hemoglobin concentration (20-30)	46	24	70	
	65.7%	34.3%	100%	
Total	56	44	100	
	56%	44%	100%	

** statistically significant

The above table results showing statistically significant correlation between serum ferritin and MCHC of RBCs.

Table 5 Correlation betwwen mean corpuscular volume (MCV) of RBCs with serum ferritin levels in childen suffering from anemia

MCV Group (fl)	Serum ferritin < 30ng/ml	Serum feritin ≥ 30ng/ml	Total	p value (continuity correction)
Microcytic RBC (<70fl)	53	39	92	>0.05(0.467)
Normocytic RBC (>70fl)	3	5	8	
TOTAL	56	44	100	

The above tabulated results showing no statistical significant correlation found between serum ferritin and Microcytic RBCs.

Table 6 Comparison between children suffering from hypoferritinemia and peripheral blood film findings with severity of anemia

Hemoglobin (g/dl)	Serum ferritin <30ng/ml) With Microcytic Hypochromic PBF	Serum ferritin <30ng/ml) with out PBF changes	Total cases with serum ferritin <30 ng/ml
Mild(10-10.9)	10	10	20
Moderate (7-9.9)	24	01	25
Severe (<7)	11	-	11
Total	45	11	56

This table shows the sensitivity of serum ferritin in picking up iron deficiency anemia in case of mild anemia who still have no morphological changes in their PBF towards microcytic hypochromic pictures.

Table 7 Correlation between Socio-economic status and mean serum ferritin levels in children

Socio-economic status (as per modified kuppuswamy Classification 2014)	Serum ferritin (mean ng/ml)	No cases	Std deviation	p value
Lower	34.617	36	44.853	>0.05 (0.607)
Middle	45.128	32	54.201	
Upper	43.041	32	37.984	
Total	40.607	100	45.875	

The mean values of serum ferritin for lower, middle and upper socioeconomic status are tabulated above and have no statistical significant results in mean values.

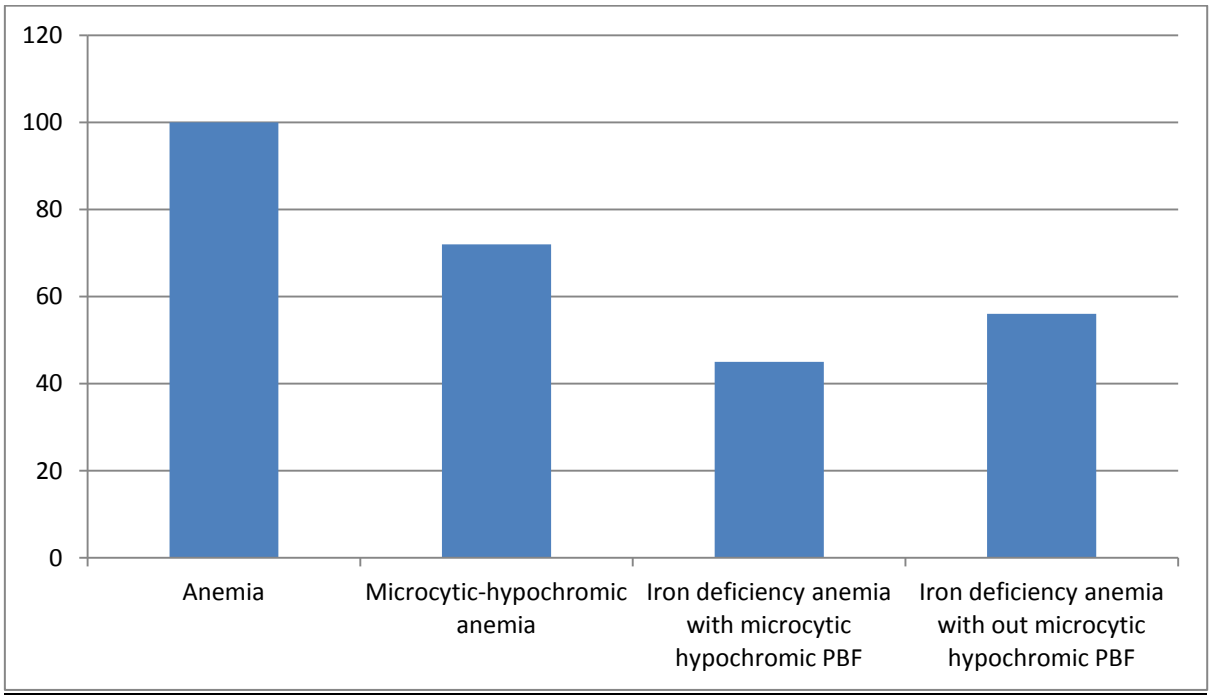

Figure 1 Distribution ofanemia on the basis of Hemoglobin <11g/dl, Peripheral blood film changes and serum ferritin level <30 ng/ml.

Discussion

Iron deficiency is the most widespread and common nutritional disorder in the world inspite of the efforts to decrease the frequency. The prevalence varies in different parts of the world with higher rates in the developing countries[11]. WHO recommends prophylactic supplementation of iron at a dosage of 2 mg/kg/day to all children between 6 and 23 months of age, especially where the diet does not include fortified foods, or

prevalence of anemia in children approximately 1 year of age is severe[12].

There are many studies with prevalence of anemia in the community, but there are few studies conducted to know the prevalence of true iron deficiency anemia among the hospitalized children.

Akin F et al in their study on iron deficiency anemia among hospitalized children in Konya, Turkey concluded low serum ferritin value reflect depleted iron stores.[13] Kadavir MR et al in their study showed a statistical significant correlation of low serum hemoglobin and low serum ferritin levels (p value <0.05)[14].

In iron deficiency anemia, hemoglobin, serum ferritin, transferrin saturation become abnormal and decrease in iron stores is reflected by falling serum ferritin. Zanella A et al 24 in their study on sensitivity and predictive value of serum ferritin and free erythrocyte protoporphyrin of iron deficient. Mei et al 2005[15] and O' Meara et al 2011[16] concluded that currently the central parameters for determination of significant iron deficiency as well as therapeutic response is serum ferritin.

In 2005 Abdus Sattar Khan and Said Alam Shah conducted a study in Peshawar in Pakistan and come a conclusion that serum ferritin was more sensitive indicator compared to serum Iron, TIBC and serum transferrin saturation in diagnosis of iron deficiency anemia[19]. Similar results were found in our study.

In the study of K.S Phiri conducted on patients with severe anaemia in a high infection pressured area, they found mean ferritin levels to be 729.2 µg/L and suggested that it was necessary to change the cutoff limit of ferritin from 30 to 273 µg/L in order to improve its diagnostic efficiency[17]. The mean ferritin level of our patients was 40.676 ng/ml (min. 0.1; max.: 246.7). 44% of our subjects had a ferritin level above 30 ng/ml with other parameters indicating iron deficiency anemia.

The prevalence of Iron deficiency anemia on the basis of serum ferritin level <30ng/ml and microcytic hypochromic peripheral blood film among our study cases is 45%. this is less than 66% prevalence in under 5 years children studied, by Hanumante NM at al in 2008.[3] and NNMB-National Nutrition Monitoring Bureau 2003.[18]

Conclusion

Peripheral blood film and RBC indices although aid to diagnose the type of anemia, where resources permit serum ferritin estimation should be done as is the only sensitive test to diagnose iron deficiency anemia in initial stages. This results in prevention of the children to progress from iron deficiency (depleted iron store) to the iron deficiency anemia and its morbid consequences. Therefore before start the iron therapy serum ferritin estimation is mandatory in all hospitalized children suffering from anemia.

Declaration

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Conflict of interest- none

Ethical approval- done

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