Original Article

Iron Deficient Children and Significance of Serum Ferritin

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Abstract

Objective: To evaluate the significance of serum ferritin in iron deficiency anaemia as compared to other indices.

Methods: Children were selected as anaemic and non-anaemic on the basis of hemoglobin (10g/dl) and transferrin saturation (15%). Red cell morphology, hemoglobin, serum iron, TIBC, transferrin saturation and serum ferritin were determined.

Results: Red cell morphology was of little significance. Haemoglobin, serum iron, transferrin saturation and serum ferritrin were all lower in children. A positive correlation of serum ferritin with age, haemoglobin, serum iron and transferrin saturation and a negative correlation with TIBC was found.

Conclusion: Serum ferritin was more sensitive indicator as compared to serum iron, TIBC, and transferrin saturation (JPMA 55:420;2005).

Introduction

Iron deficiency anaemia, the most commonly recognized form of nutritional deficiency, is prevalent among infants and young children as hypochromic microcytic anaemia.[1] Despite several laboratory procedures available for its detection, mild iron deficiency is frequently undetected by haemoglobin or haematocrit method.[2] Ferritin is the second most important intracellular iron storage protein found in reticuloendothelial system.[3] It functions not only as an intermediate protein during haemoglobin synthesis but also as a storage protein for iron released during haemoglobin denaturation.[4] The levels found in sera of patients with iron deficiency anaemia suggest that the serum concentration of ferritin closely reflect the size of iron stores.[5-7] Serum ferritin has shown a greater sensitivity and predictive value in subjects with uncomplicated anaemia and without anaemia.[8,9] The measurement of ferritin, in addition to being a confirmatory test has particular characteristics of being the only test able to identify risk subjects before they become symptomatic.[10] Serum ferritin is the most accurate test indicating iron status within normal range as well as iron deficiency and excess.[11-16] In a young growing child, who has got a very delicate balance between iron stores, requirement and supply, it is very essential to diagnose iron deficiency at a stage before it results in hypochromic microcytic anaemia.

The objective of this study is to evaluate the significance of serum ferritin in iron deficiency anaemia as compared to other indices.

Subjects and Methods

A cross-sectional study of 100 apparently healthy children with no history of abnormal bleeding, blood transfusion, any extensive surgery or infection visiting Paediatric OPD Lady Reading Hospital, Peshawar for routine check up was performed. Iron deficiency anaemia was considered to be present when, haemoglobin was less than 10 g/dl, transferrin saturation less than 16 percent, TIBC was greater than 400 µg/dl and serum ferritin was less than 10 ng/ml. For the sake of convenience, children were divided in to two groups, 0.5 years to 3 years as group A and above 3 to 12 years as group B. They were examined for red cell morphology, haemoglobin, serum iron, TIBC and ferritin levels.

Five ml of venous blood was collected from all selected children. After thorough mixing 20 µl sample was taken for haemoglobin determination. The remaining blood was centrifuged at 3000 rpm for 5 minutes and clear plasma obtained was stored in appropriate labelled Eppendorph tubes at -20^{0}C for further analysis.

For red cell morphology, blood films were prepared and examined under the light microscope.

Standard kits for hemoglobin by Cyanomethaemoglobin method (Boehringer-Mannheim), Plasma Iron and TIBC (Roche) and Plasma Ferritin by radioimmunoassay (Amersham) were used.

Results

On the basis of transferrin saturation and serum ferritin level, iron deficiency anaemia was more frequent in group A as compared to group B children. Out of a total of 80 anaemic children, 66 (83%) were iron deficient. Compared with non-anaemic children, all anaemic children showed various degrees of red cell morphology. Group A children were highly abnormal than group B. However, no normoblast was seen in any smear of group B children (Table 1).

Table 1. Microscopic Examination of RBC in normal and Iron Deficient Infants and Children.

Group	Total	Normal	Hypochromic	Microcytic	Macrocytic	Anisocytic	Poikilocytic	Target Cells	Normoblast
Normal	20	20 (100)	Nil	Nil	Nil	Nil	Nil	Nil	Nil
Group A	36	2	34	34	13	30	27	16	3
(%)		(5.6)	(94)	(94)	(36)	(83)	(75)	(44)	(8)
Group B	30	12	17	17	4	12	9	4	Nil
(%)		(40)	(57)	(57)	(13)	(40)	(30)	(13)	
Total	66	14	51	51	17	42	36	21	3
(%)		(21)	(77)	(77)	(26)	(64)	(55)	(32)	(5)

Percentage given in parentheses.

Table 2. Hematological parameters Group A and B were Iron deficient of normal and anaemic subjects.

Parameter	Normal		Anaemic		P Value
	Group A n= 10	Group B n=10	Group A n=36	Group B n=30	Anaemic and Control
Haemoglobin (g/dl)	11.0 ± 0.56	12.0 ± 0.54	6.6 ± 1.95	8.0 ± 1.90	<0.005 *
Iron (µg/dl)	83.0 ± 19.0	88.0 ± 15.5	42.0 ±12.2	50.0 ± 12.0	<0.005 *
TIBC (µg/dl)	321.0 ± 47.0	319.0 ± 42.0	452.0 ± 60.0	455.0 ± 40.0	<0.005 *
Transferrin (%)	26.0 ± 7.5	30.0 ± 10.0	10.0 ± 4.0	11.0 ± 2.96	<0.005 *
Ferritin (ng/ml)	42.0 ± 36.0	65.0 ± 62.5	8.0 ± 2.5	9.0 ± 3.5	<0.005 *

* Highly Significant.

Mean value of haemoglobin in anaemic children of group A and B compared to normal was much lower and was highly significant (Table 2). A significant difference of serum iron of normal and anaemic children of group A and group B was observed (Table 2). However, highly significant difference between serum iron of anaemic group A and B children was also found (Table 2).

The increase in mean TIBC of anaemic children group A and B was highly significant. Comparing the two age group children there was no significant difference in TIBC level in either normal or anaemic children (Table 2).

A significant decrease in mean transferrin saturation of anaemic group A and anaemic group B children was seen (Table 2). Again mean transferrin saturation of normal group A was not significantly different however, a significant difference was found between the transferrin saturation level of anaemic group A and anaemic group B children (Table 2).

There was no significant difference in the serum ferritin between the normal and anaemic subjects but a highly significant difference of serum ferritin between the normal and anaemic of group A and group B was present (Table 2).

Table 3. Data Showing Significance of Serum Ferritin as Index of Iron Stores Compared with Other Tests.

Tests Performed	Patients	Total Cases	Specificity (%)		Sensitivity (%)	
TIBC	Iron Deficient	66	12	(18)	54	(82)
	Total Anaemic	80	22	(28)	58	(73)
Transferrin Saturation	Iron Deficient	66	3	(5)	63	(95)
	Total Anaemic	80	13	(16)	67	(84)
Serum Ferritin	Iron Deficient	66	0	(0)	66	(100)
	Total Anaemic	80	12	(15)	68	(85)

In anaemic children the sensitivity of serum ferritin was 85% and specificity 15%. It was less than the normal value of 15 ng/ml in all iron deficient children (Table 3). Correlation of serum ferritin with age, haemoglobin, serum iron, TIBC, transferrin saturation was tested by Karl Pearson correlation coefficient. There was positive correlation of serum ferritin with age (r=0.13). The changes in ferritin concentrations were positively correlated with

Table 4. Results Showing Correlation of Serum Ferritin with Age and other Hematological Parameters.

Parameters	Control n=20	Anaemic n=66
Age	r = 0.33*	r = 0.13*
Hb	r = 0.27*	r = 0.27**
Iron	r = -0.10*	r = 0.23**
TIBC	r = -0.02*	r = -0.03*
Transferrin	r = 0.03*	r = 0.19*

*Non Significant; **Significant

haemoglobin (r = 0.27), serum iron (r = 0.23) and transferrin saturation (r = 0.19) in anaemic patients (Table 4).

Discussion

In iron deficiency anaemia, hemoglobin, transferrin saturation and ferritin become abnormal and decrease in iron stores is reflected by falling serum ferritin.[7] The decrease in serum iron and increase in TIBC, is difficult to document. The blood smear is rarely helpful in diagnosing iron deficiency until anaemia has become severe. All the above tests except ferritin, either lack specificity or are not suitable for application on large-scale population studies. Lower iron status of our population is due to racial, environmental, parasitic and dietary factors.[15-17] Among the dietary factors the most important ones are low heme-proteins in diet and high phytate content of the wheat flour.[18] The evaluation of body stores in differential diagnosis of anaemia is an important factor. Iron deficiency was found to be the commonest cause of anaemia in both groups in our study.

Further more hemoglobin, PCV, transferrin saturation and MCHC indices only become abnormal when iron stores have been completely exhausted.[19] Study revealed that nutritional iron deficiency anaemia was less prevalent in higher age group than younger age group children.

Hypochromia, microcytosis, macrocytosis, anisocytosis, poikilocytosis and target cells were observed among the most normocytic, normochromic children. Red cell morphology was not a reliable indicator of iron deficiency anaemia. The disturbed red cell morphology was seen only when the iron deficiency anaemia was severe in our study. A significant increase in haemoglobin levels with the advancement of age was also observed.[6] Age has no effect on TIBC it was similar in all ages for healthy persons after 2 years of age.[5,7] Transferrin saturation has shown better results in anaemic as well as in control subjects in comparison with red cell morphology, serum iron and TIBC. There was a significant difference between transferrin saturation of normal and iron deficient anaemic subjects.

In this study, serum ferritin was the only reliable and sensitive haematological parameter for diagnosis of iron deficiency anaemia and estimation of iron stores in normal and anaemic individuals. It was more precise and sensitive as compared to serum iron, TIBC and transferrin saturation for detection of iron stores in normal and iron deficient subject[3,5,7], which was less than normal value of 15 ng/ml in all iron deficient children was in good agreement with others.[3,5,7,8] In inflammatory and other conditions there is blockage to reutilization of reticuloendothelial storage iron (ferritin), thus there is a low level of haemoglobin, decreased serum iron, decreased transferrin saturation and high level of serum and tissue ferritin.[7] Second most specific parameter was transferrin, which was less than 16 percent in 95 percent of iron deficient anaemic cases and above 16 percent in 5 percent cases. Moreover, MCHC and TIBC[6] are regarded as least sensitive of the indices in diagnosis of iron deficiency anaemia. In the present work, a positive correlation of serum ferritin with age has also been reported by other investigators.[6] The correlation of different indices is consistent with other studies.[5,6]

Serum ferritin was more sensitive indicator as compared to serum iron, TIBC, and transferrin saturation.

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