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Research Paper

Iron status of thalassemic Children in South Rajasthan

Medical Science

KEYWORDS : thalassemia, iron overload, ferritin.

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ABSTRACT

Background-Thalassemias are a group of inherited autosomal recessive disorders caused by defects in the synthesis of one or more of the hemoglobin chains, cause hemolysis and impair erythropoiesis. . Repetitive blood transfusion leads to iron overload which adversely affect the function of liver, heart and endocrine glands.

Objective- The aim of this study was to evaluate the status of iron in β-thalassemia major children with means of ferritin, transferrin, TIBC and % TS.

Methods-The analyzed group consisted 50 subjects and 50 controls further divided in two age groups i.e. I and II. Ferritin was measured by ferrozine method.

Results-Thalassemic subjects have significantly higher iron, ferritin, % TS and reduced levels of TIBC and transferrin.

Conclusions- Evaluation of ferritin in thalassemic children help in monitoring, the level of iron obtained by repetitive blood transfusions and there for the damage of a number of organs. In spite of chelation therapy ferritin was found to be elevated several folds in subjects.

Introduction

Beta –thalassemia major is an autosomal recessive disease that leads to a severe hemolytic anemia in early infancy (1,2). Depletion or impaired synthesis of β-globulin chain result in an imbalanced production of globulin chains towards higher production of α-chain (3). Studies have shown that the overall prevalence of β-thalassaemia in India is 3-4% with an estimate of around 8,000 to 10,000 new births with major disease each year (4).

The progressive iron overload observed in β-thalassemia major patients is the side effect of ineffective erythropoiesis, increased gastrointestinal absorption of iron , lack of physiological mechanism for excreting excess iron , lack of physiological mechanism for excreting excess iron and multiple blood transfusions which results in hemochromatosis. Even elevated body iron load is observed in milder form of thalassemia (5).

Iron overload is a consequence of chronic transfusion therapy that adversely affects the function of the heart, liver and endocrine glands (6).In these patients; iron deposition in parenchymal tissues begins within 1 year of starting the regular transfusion (7). A unit of red blood cells transfused contains approximately 250 mg of iron and a patient who receives 25 units per year, accumulates 5 grams of iron per year in the absence of chelation (8).

The accumulation of iron in the liver, heart and multiple endocrine glands results in severe damage to these organs, with variable endocrine organ failure (9,10).Iron stores in the body exist primarily in the form of ferritin. In the body, small amounts of ferritin are secreted into the plasma. The concentration of this plasma (or serum) ferritin is positively correlated with the size of the total body iron stores in the absence of inflammation (11). As iron loading progresses, the capacity of serum transferrin, the main transport protein of iron, to bind and detoxify iron may be exceeded. Thereafter, the non-transferrin-bound fraction of iron within plasma may promote generation of free hydroxyl radicals, propagators of oxygen-related damage (12). The iron burden on the body can be estimated by means of serum ferritin, iron and TIBC levels. Effective management of iron overload in thalassaemia requires monitoring both for iron toxicity and the effects of excessive chelation (13). The estimation of serum ferritin levels is the most commonly employed test to evaluate iron overload in β-Thalassaemia Major. A target ferritin of approximately 1000 mg/l is generally recommended standard practice in thalassaemia major (TIF Guidelines, 2000).

The aim of this study was to evaluate the iron status in β-thalassemia major children with means of iron, ferritin, transferrin, TIBC and % TS.

Materials and Methods

This study was conducted in Department of Biochemistry Jhalawar Hospital and medical college, Jhalawar. A total of 50 clinically diagnosed β- thalassemia major children (1-14 years) were randomly selected irrespective of their gender, which were on regular blood transfusion therapy. 50 healthy age matched controls were selected and for the sake of convenience, patients and controls were divided in two age groups i.e. Age group I. 1-3years and Age group II. 4-14 years. Written consent was taken from parents/ guardians. The work was approved by ethical committee of Jhalawar Hospital and Medical College.

Exclusion and Inclusion criteria- Patients with a confirmed diagnosis of β- thalassemia major between 1-14 years were selected, who were on blood transfusion and iron chelation therapy. Exclusion criteria included (1).Thalassemia trait or intermedia (2). History of Jaundice due to viral hepatitis (3). History of splenectomy (4). Positive screening test for hepatitis C or B.

Experimentals - Blood was collected in EDTA vial for hematological estimations and in plain vial for estimation of other parameters in sera.

CBC was done on automated cell counter. Iron, TIBC, total protein and albumin, were estimated by using commercial logotech diagnostic kits on autoanalyzer. Ferritin was estimated by sandwich immunoluminometric assay using Maglumi ferritin (CLIA) Kit and transferrin by ELISA. The value of % TS was calculated using the formula-

$$\% \text{ TS} = \frac{\text{Serum iron concentration}}{\text{TIBC}} \times 100$$

Mean and SD were calculated and student's t-test (unpaired) was used to compare the two groups. $p<0.05$ was considered statistically significant.

Results

Red cell indices and parameters of iron profile of control and thalassemic subjects for age group I are given in table-1 and for age group II in table-II.

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Table (1):Comparison of measured parameters between control and thalassemic subjects in age group I(1-3 years)

Parameters	Control (n=22) Mean±SD	Thalassemia (n=22) Mean±SD	p-value
Hb	11.78±0.30	6.43±1.76	<0.0001
MCV	82.23±4.70	76.50 ±8.53	0.0161
MCH	29.01±3.13	23.18 ±2.83	<0.0001
RDW	12.56±0.66	20.60±3.93	<0.0001
Total protein	7.16±1.56	6.50±0.35	0.1606
Albumin	4.47±0.32	3.77±0.54	<0.0001
Iron	72.27±21.33	157.00±46.17	<0.0001
TIBC	307.77±35.51	180.83 ±10.74	<0.0001
%TS	23.80±7.22	87.03±25.23	<0.0001
Ferritin	47.14 ±8.29	1725.17±521.19	<0.0001
Transferrin	162.82 ±12.58	148.42±14.41	0.0048

Table (2): Comparison of measured parameters between control and thalassemic subjects in age group II (4-14 years)

Parameters	Control (n=28) Mean±SD	Thalassemia (n=28) Mean±SD	p-value
Hb	12.57±0.47	5.96±1.31	<0.0001
MCV	84.85±5.12	77.00 ±6.07	<0.0001
MCH	29.66 ±2.66	23.11 ±2.07	<0.0001
RDW	12.36±0.65	19.33± 5.27	<0.0001
Total protein	7.72±0.40	6.66±0.35	<0.0001
Albumin	4.56 ±0.31	3.86 ±0.45	<0.0001
Iron	75.71±20.42	140.62±53.52	<0.0001
TIBC	318.22±29.60	178.54±13.91	<0.0001
%TS	24.23±7.49	78.38 ±26.97	<0.0001
Ferritin	51.46±7.99	1813.62 ±627.01	<0.0001
Transferrin	165.64±13.80	143.62 ±11.46	<0.0001

A highly significant reduction (p<0.0001) was observed in hemoglobin level in thalassemic subjects as compared to control in both age groups with significant decrease in MCV and MCH. The observed mean ± SD of iron for control and thalassemic subjects was 72.27+21.33 and 157.00+46.17 in age group I and in age group II it was 75.71+20.42 and 140.62+53.52 respectively. A Significantly reduction in TIBC and transferrin was observed for both age groups with decreased calculated value of %TS. The level of ferritin in thalassemic subjects was found to be elevated several folds in age group I and II with mean ± SD of 1725.17 ± 521.19 and 1813.62 ± 627.01 as compared to control 47.14 ± 8.29 and 51.46 ± 7.99, respectively.

Discussion

Beta-thalassemia major is one of major public health problems in India. It is estimated that there are about 65,000-67,000 beta-thalassemia patients in India with around 9,000-10,000 cases being added every year(14).The inevitable consequence of regular life-saving transfusions in thalassemia major is the accumulation of excess iron within tissues. This causes progressive organ damage and dysfunction which, without treatment, can lead to an increase in morbidity and mortality (15). Serum ferritin determination is widely accepted as a simple method for following iron load in patients with primary hemochromatosis (16)

In this study, reduced total protein and albumin indicates a poor nutritional status in subjects. The observed high level of iron and ferritin may be due to a number of reasons, including repetitive blood transfusions, peripheral hemolysis, increased intestinal iron absorption as well as ineffective erythropoiesis (17, 18, 19). Ferritin is a positive acute phase protein, level of which may elevate in infection or inflammation. In the absence of inflammation or liver disease, high serum ferritin concentration indicate iron overload (20).

Transferrin concentration and total iron binding capacity (TIBC) are currently used to assess iron status for clinical purposes, TIBC is considered as a measure of transferrin concentration in serum or plasma. Although correlation between TIBC and transferrin is generally considered as good, conversion factors between the two analysts found in literature show large difference. Due to binding of iron to other plasma proteins (mainly albumin), TIBC methods generally overestimate the iron binding capacity of transferrin (21).

Transferrin is a negative APP and low concentrations are present in inflammation. In thalassemia due to failure to incorporate iron into erythrocytes instead of a deficiency of iron, the transferrin concentration may be normal or low but the protein is highly saturated with iron (22).In response to elevated iron and reduced TIBC the obtained values of %TS was found to be elevated in thalassemic subjects.

Conclusion

The lifelong dependency of thalassemic subjects on blood transfusions results in iron overload and a significant damage to a number of organs. High level of serum ferritin in patients supports the rationale for regular follow-up of transfusion dependent thalassaemic patients for ferritin, to monitor the side effects of transfusion.

Recommendations

Routine measurements of serum ferritin levels and reevaluation of the current protocol of chelation therapy is needed to protect the damage of a number of organs in thalassemic subjects, due to repetitive blood transfusions in early childhood.

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