RESEARCH PAPER | Medical Science | Volume : 6 | Issue : 6 | June 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 74.50

Chelation Status & Clinical Profile of Thalassemic Children Attending Paediatric Clinics

KEYWORDS: Thalassemia, chelation, serum ferritin

Shyam Choudhari
Chief resident, MD Paediatrics, Department of Paediatrics, Smt Kashibai Navale Medical College, Pune.

M K Behera
HOD, Dept of PaediatricsDepartment of Paediatrics, Smt Kashibai Navale Medical College, Pune.

ABSTRACT *BACKGROUND: Thalassemia is one of the most common hereditary disorders and beta thalassemia major is its severe form. The present study is concerned with the analysis of clinical profile, analysis of liver function and estimation of serum ferritin levels.*

Aim and Objectives: To study clinical profile of thalassemic children, and study serum ferritin levels.

Materials & Method: All registered thalassemic children were included in this study, attending thalassemia clinics in Smt Kashibai Navale Medical College, Pune. Their height, weight, Clinical examination done and size of liver, spleen, hematological , biochemical , LFT and serum ferritin levels estimated.

Result: Thirty children included in study, of which,14 girls(46.6%)and 16 boys(53.3%). Age ranged from 8 months to 9 years with the average age being 3.7 years. Typical haemolytic facies were seen in 16 children (53%). Sixteen children (53.3%) were found to be stunted. Haemoglobin levels ranged from 5 gm%to 9 gm% with average haemoglobin concentration 8 gm%. Consanguineous marriage detected in 8 parents(26.6%).Total number of blood transfusions ranged from 4 to 65 units with average number being 28. Liver was enlarged in all cases except two ranging from 2 cm to 12 cm with average of 4.43cm. Spleen was enlarged in all cases except 6, ranging from 1 cm to 10 cm with average being 3.6cm. SGOT levels were raised in 16 cases (53.3%). SGPT levels raised in 14 cases (46.6%).Serum ferritin levels were raised in all children with average of 3879.5 ng/ml.

Conclusion: Serum ferritin levels were found to be high in all children and they require iron chelation therapy. So in all thalassemia patients serum ferritin levels to be monitored regularly.

INTRODUCTION

India is an ethnically diverse country with an approximate population of 1.2 billion. The frequency of beta-thalassemia trait (βTT) has variously been reported from <1% to 17% and an average of 3.3%[1] Thalassemia is a group of inherited hemoglobin disorders characterized by reduced synthesis of one or more of the globin chains leading to imbalanced globin synthesis which is the major factor in determining the severity of the disease in the thalassemia syndromes. Beta-thalassemia results from a defect in beta globulin chain production and ranges from clinically silent heterogeneous thalassemia minor to severe transfusion-dependent thalassemia major.[2,3] Beta-thalassemia major is a very serious blood disorder since affected individuals are unable to make enough healthy red blood cells and that is why they are totally dependent on blood transfusion throughout their life. Various complications caused by this disease including growth retardation,[4] endocrine dysfunction, hypothyroidism,[6] progressive liver failure[7] and abnormal kidney function. Trace metals, especially iron, are implicated as causative agents in excessive generation of free radicals which are capable of causing oxidative damage to erythrocytes.[8] Iron metabolism in human is unidirectional because of being unable to be eliminated by the excretory route. Therefore, excess of iron is deposited in vital organs such as heart, liver, spleen and endocrine organs.[9,10] Estimation of calcium, sodium, potassium and magnesium is also valuable. Several authors have reported a high incidence of endocrine abnormalities in children, adolescents and young adults suffering from thalassemia. However, the incidence of endocrinopathies varies among different series of the patients. Trace minerals have been shown to have influence on growth and hormones e.g. zinc deficiency is considered a causative factor in osteoporosis and endocrinopathies.[11] The aim of this study is to study the clinical profile, their serum ferritin levels and iron chelation status, evaluate the liver function parameters, and to check their suitability for bone marrow transplantation.

MATERIALS AND METHODS

A total of 30 thalassemia patients (14 girls and 16 boys) were included in this study. Thalassemia patients age ranged between 8 months and 9 years. The clinical examination was done, with special regard to haemolytic facies, hepatomegaly and splenomegaly. As per standard procedure, anthropometric measurement such as height and weight were collected. An integrated questionnaire was employed in order to obtain information on age and education and consanguinity. The data and blood samples were collected.

BIOCHEMICAL ASSAYS

AST and ALT activities were assessed using commercial kits according to manufacturer's instructions. Haematological characteristic were assessed based on laboratory protocol. Serum ferritin was measured using commercial kits according to manufacturer's instructions.

RESULTS

Total of 30 patients were included in this study attending thalassemia clinics. Out of 30 patients,16 were boys and 14 were girls. The mean age of patients was 3.7 years, ranging from 8 months to 9 years. Consanguineous marriage was detected in parents of 8 patients. Sixteen chil-

Volume : 6 | Issue : 6 | June 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 74.50

dren (53.3%) were found to be stunted, with height for age less than third percentile. Typical haemolytic facies were seen in 16 children. Haemoglobin levels ranged from 5 gm% to 9 gm% with average concentration of 8 gm%. Total number of blood transfusions ranged from 4 to 65 units with average number being 28. Liver was enlarged in all cases except 2 ranging from 2 cm to 12 cm with average of 4.43 cm. Spleen was enlarged in all cases except 6, ranging from 1 cm to 10 cm with average being 3.6cm. SGOT levels were raised in 16 cases(53.3%). SGPT levels raised in 14 cases (46.6%). Serum ferritin levels were ranged from 563 to 10,400 ng/ml with average being 3879.5 ng/ml. Serum ferritin levels were raised in all children. Out of 30 only 8 patients were on regular iron chelation therapy.

Table 1.

Total patients	30
Girls	14 (47%)
Boys	16 (53%)
Consanguinity	8 (26.6%)
Stunting	16 (53%)
No.of blood transfusions	4-65 (Avg 28)
Hepatomegaly	28 (Avg 4.43 cm)
Splenomegaly	24 (Avg 3.6 cm)
SGOT levels	Raised in 16 (53%)
SGPT levels	Raised in 14 (47%)
Sr. Ferritin	Raised in all (avg 3879.5 ng/ml)
Patients on chelation	8 (26.67%)

DISCUSSION

The results obtained in this correlate well with other studies. Growth failure which was seen 53% of patients in simiar studies by Sachdev A et al.[13] Thalassemia is accompanied with metabolic irregulation, iron overload; chronic hypoxia and cell damage. All physiological changes result in ineffective erythropoiesis, haemolysis and anaemia. [14] Most patients are dependent on transfusion for their survival and bone marrow transplantation.

Thalassemia major has a huge impact on quality of life [13]. Iron overload is a major contributor to this problem. The data from present study and others have many implications. Most children with thalassemia would have chances of prolonged survival consequent to the better cardiac and liver functions due to effective chelation. A more effective chelation would lead to a better quality of life due to better growth, skin colour, endocrine functions and energy levels [15].

The serum ferritin level is useful in assessing iron balance trends, but does not accurately predict quantitative iron stores. Measurement of the iron level by liver biopsy is the standard method for accurately determining the iron store. [16]

In or study serum ferritin was raised in all patients ranging from from 563 to 10,400 ng/ml with average being 3879.5 ng/ml similarly observedin many studies by Gomber S et al[15], Michael RD et al16].

Cardiac damage caused by iron overload is the main cause of death in thalassemia. An increased risk of iron induced cardiac disease is observed with liver iron concentration (LIC) values above 15mg of iron per gram of dry weight of liver, and in patients with serum ferritin values above 2500 microgram/liter. The rate of iron loading depends mainly on the rate of blood transfusions, which causes a net iron deposition in the body, of about 15-20 mg/day. In practice, the goal of chelation therapy is to achieve an iron balance by accessing two iron pools, namely intracellular labile iron pool (LIP) and iron from red cell catabolism [17]. Although an increasing number of patients are now treated with bone marrow transplantation, the majority of the patients still depend on regular transfusions. Regular transfusion and chelation therapy have improved the span and quality of their lives.[18]

Higher level of serum AST and ALT in beta-thalassemia patients indicate an abnormal muscle and liver function. These finding are in agreement with the finding of Maher Y. Abdalla et al.[19] There is a positive correlation between serum ALT and AST concentrations and serum ferritin levels. These outcomes are similar to the finding of Maher Y. Abdalla et al.[19] An increase in serum ferritin level in beta-thalassemia patients have been observed in this study, which is consistent with several other studies. [1,15,16] In case of beta-thalassemia patients, absence of beta globin chains lead to accumulation of unpaired alpha globin chains. Excess presence of the alpha globin chains is a primary reason for the cellular oxidative damage and also iron overload.[16] Higher ferritin content was directly linked to the accumulation of reactive iron in the tissues of these patients. Iron overload starts another pathological mechanism leading to oxidative damage of erythrocyte membranes, the so-called "second disease".[20]

Effective pretransplantation iron chelation improves the outcome of bone marrow transplantation as shown in many studies[21,22]

CONCLUSION

Serum ferritin levels were found to be high in most of children, so it should be monitored regularly in all cases of thalassemia. Better counselling and motivation is required for regular iron chelation therapy.

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Volume : 6 | Issue : 6 | June 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 74.50

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