Assessment of Hemosiderosis in Thalassemia major patients attending a Superspeciality hospital

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Abstract

Background: Beta Thalassemia major is a hereditary haemolytic anaemia which is treated by blood transfusions on a regular basis. The objective of this study was to evaluate the hematological parameters and estimate the iron overload by estimating the serum ferritin in transfusion dependent thalassemia major patients.

Methods: This cross sectional study was carried out in Department of Pathology, Jawaharlal Nehru medical college, Belagavi, Karnataka, India. All the patients admitted in the Department of Pediatrics between age group of 10 years and above during the study period were included in the study. The exclusion criteria were patients with abnormal liver functions, presence of infections at the time of sample collection and any haemoglobinopathy other than Beta thalassemia major. Estimation of Serum ferritin was done by Direct Chemiluminescence principle using Advia Centaur XP Immunoassay system. The data was analysed using SPSS version 20.

Results: Mean serum ferritin was 3786 ±2382 ng/mL. The mean serum ferritin in females was 4411 ±1299 ng/mL and in males was 3636± 2572 ng/mL. The mean serum ferritin in Non-Chelated patients group was 4505 ±2633 ng/mL which is much higher as compared to mean serum ferritin in Chelated patients group 2479± 963 ng/mL.

Conclusion: The high level of serum ferritin of thalassemia major patients noted in this study supports the rationale for regular follow-up of transfusion dependent thalassaemic patients with respect to iron overload to ensure proper management of hemosiderosis associated complications.

Key words: serum ferritin; thalassemia major; iron overload; hemosiderosis

Introduction:

Beta Thalassemia major is a hereditary haemolytic anaemia which is treated by blood transfusions on a regular basis. It is seen more frequently than expected in our country due to high consanguineous marriage and birth rates. The overall prevalence of Beta thalassemia in India is 3-4% and around 8,000 to 10,000 children are born with Thalassemia major disease per year.[1] Iron overload is a important and frequent complication of thalassemia which leads to vital organ damage and increased rates of mortality. Iron deposition in parenchymal tissues starts within one year of beginning the regular blood transfusions in these patients.[2] 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 serum ferritin positively correlates with the quantity of total body iron stores in the absence of inflammation. Chronic blood transfusions inevitably lead to iron overload as humans cannot actively remove excess iron. The cumulative effects of iron overload lead to significant morbidity and mortality, if untreated.[3] One unit of red blood cells transfused has approximately 250 mg of iron[4], while the body cannot excrete more than 1 mg of iron per day. A patient who receives 25 units per year, accumulates 5 grams of iron per year in the absence of chelation[5]. There is also increased intestinal iron absorption which is seen in these patients. Capacity of serum transferrin, which is the main transport protein

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of iron, to bind and detoxify iron may be exceeded as the iron loading progresess. Later, the non-transferrin-bound fraction of iron within plasma may promote production of free hydroxyl radicals, which are promoters of oxygen-related damage.[6] Excess iron is severely toxic to all cells of the body and can cause serious and irreversible organic damage which results in liver cirrhosis, diabetes, hypogonadism and heart disease.[7] There is direct correlation between fibrosis of the liver and the age of patient, the liver iron concentration and number of blood units transfused.[8]Serum ferritin, Serum Iron and Total Iron Binding Capacity (TIBC) levels can estimate the iron burden on the body. Proper management of iron overload in thalassemia requires careful watch, over both iron toxicity and effects of excessive chelation therapy.[9]

According to Thalassemia International Federation Guidelines it is recommended to maintain serum ferritin of approximately 1000 ng/dl in thalassemics. Iron chelator DFO mesylate is best available chelator which improves the quality of life and prolongs the life of thalassemics.[10,11] But the disadvantage is that it is expensive and needs daily parenteral infusions which leads to reduced compliance to therapy. Hence in developing countries, oral chelator which is cheap would be better alternative which includes Deferasirox. This drug was approved by the FDA for blood transfusional hemosiderosis in children aged above two years.[9]

The objective of this study was to evaluate the hematological parameters and estimate the iron overload by estimating the serum ferritin in transfusion dependent thalassemia major patients attending the superspeciality hospital. This is the first study being done in this part of the country.

Materials and Methods

This cross sectional study was carried out in Department of Pathology, Jawaharlal Nehru medical college, Belagavi, Karnataka, India over a period of one year from January 2014 to December 2014. Ethical clearance was obtained from the Institutional Ethics Committee and informed consent was taken from the patients. All the patients admitted in the Department of Pediatrics between age group of 10 years and above during the study period were included in the study. The exclusion criteria were patients with abnormal liver functions, presence of infections at the time of sample collection and any haemoglobinopathy other than Beta thalassemia major. Socio-demographic data, relevant clinical history and clinical examination was collected. Under sterile conditions, about 3 mL of blood was collected through venipuncture. Estimation of Serum ferritin was done by Direct Chemiluminescence principle using Advia Centaur XP Immunoassay system. The data obtained was entered in datasheet and data was analysed using SPSS version 20. Categorical data was expressed in terms of rates, ratios and percentage. Continuous data was expressed as Mean ± standard deviation, median and range.

Results

The clinical examination and hematological profile of 31 patients was done. The commonest age group was 10 to 12 years comprised of 58.06% of the patients followed by 13-15 years age group (29.03%). Majority of the patients were on chelation therapy (71.43%). Mean age was 12.45 ± 2.38 years. Median age was 12 years as shown in Table 1. The youngest patient was 10 years and oldest was 18 years**.** There are 26 male patients and 5 female patients with male to female ratio was 5:1 as shown in Table 2. Physical examination revealed splenomegaly and hepatomegaly were present among the patients. Splenomegaly was the most common clinical finding among the study population, followed by hepatomegaly Mean serum ferritin of all 31 patients was 3786 ±2382 ng/mL with a range from 343-10710 ng/mL. The mean serum ferritin in Females was 4411 ±1299 ng/mL with range of 2664 to 6107 ng/mL. Mean serum ferritin in males was 3636± 2572 ng/mL with a range of 343 to 10710 ng/mL Hence, in our study mean serum ferritin was higher in females as compared to males. The mean serum ferritin in Non-Chelated patients group was 4505 ±2633 ng/mL which is much higher as compared to mean serum ferritin in Chelated patients group 2479± 963 ng/mL as shown in Table 3. Hence,iron chelation is definitely effective in preventing complications of iron overload.

Discussion

The commonest hemolytic anemia in India is Thalassemia. The major cause of late morbidity and mortality in patients with thalassemia major is transfusional hemosiderosis. Prevention of hemosiderosisis is possible by iron chelation therapy which will reduce the concentration of serum ferritin. This will be effective in preventing iron induced tissue injury which in turn prolongs life expectancy. There is a drastic improvement in recent years in management of thalassemia patients. These improvements are due to safer blood transfusions, availability of oral and parenteral iron chelators and newer imaging techniques that allow specific organ assessment of the degree of hemosiderosis.[12] Reticuloendothelial cells are the first location for deposition of iron which is followed by parenchymal iron deposition in liver and heart. Cardiac failure and hepatocellular failure

are the result of iron depostion. Hence, timely and frequent evaluation of the hemoisderosis is utmost important in management.[13] This evaluation needs a non-invasive and quantitative method for measuring body iron stores which is also safe, accurate, easily available and cost effective. The iron status of the body in overload conditions can be assessed by parameters like serum ferritin, liver biopsy, CT and T2 MRI assessment of liver and cardiac iron, in combination with echocardiography and endocrine function assessment.[14] Each of these parameters has a different role. Serum ferritin measurement is easy to perform test even though it offers variable results but is one the best predictor of hemosidersis. [15] The liver is the major site of iron overload is liver as it contains 70% of body iron content. Hence, liver iron correlates directly with total body iron in transfusional hemosiderosis. Best and most accurate method to directly asses iron overload is liver iron concentration[16]. Indirect method is using serum ferritin level measurement is which was readily available and cost effective hence was performed in our centre. A target ferritin of approximately 1000 ng/l is generally recommended standard practice in thalassemia major and the patients having values below 2500 ng/l on two-thirds of occasions had less risk of cardiac complications than patients who failed to maintain this level.[17]

In our study, about half of the patients were aged between 10 to 12 years (58.06%). The mean age was 12.45 ± 2.38 years and median age was 12 years with younger patients being 10 years and oldest being 18 years. The mean age observed in the present study was close to that of Chern et al.[18] (14.8 ± 6.9 years) and comparable with the other study from Tehran (15.20 ± 3.1 years). Najafipour F et al in Iran reported mean age was 15.62 ± 4.44 years.[12] In another study by Khalifa et al[13] showed age range of patients to be 10-30 years as compared to the present study where the age range is 10-18 years. Clinical features of Beta thalassemia are usually manifested in younger age group and become more severe with advancing age**.** In the present study majority of the patients (83%) were males with male to female ratio of 5:1. Similarly, study done by Khalifa et al[13] showed majority of patients were males. The sex distribution pattern observed in the present study was similar to other studies from Kolkata.[19] According to a study conducted by Neeraj et al on 142 beta-thalassemia major patients aged 3 years or more receiving regular blood transfusions at a transfusion centre in Western India, 53.5% were undertransfused (mean Hb <10 gm%), 67% of the patients were taking some form of chelation therapy but out of them only 2% were adequately chelated[16].

In our study 71.43% patients were on chelation therapy which is much higher as compared to other studies.

Normal values of serum ferritin for men and women are 12-300 ng/mL and 12-150 ng/mL, respectively[20]. The values in our study are higher compared with similar regional and international studies. In various studies done by Choudhry VP et al[21], Lucas et al[22], Riaz et al[23] and Koreti et al[14], their mean ferritn levels were much higher compared to our study where mean ferritin of patients was 3786 µg/l. However, in various other studies by Bandyopadhyay et al[24], Shah et al[25], Nadeem Ikran et al[17], Al Jaouni et al[26], Rehman M et al[27] and Cunningham et al[28] the mean serum ferritin were lower as compared to our study as shown in Table 4.

Mean serum ferritin of all patients was markedly raised 3786 ±2382 ng/mL with mean serum ferritin higher among females (4411±1299 ng/mL) as compared to males which had serum ferritin of 3636±2572 ng/mL. Similarly ferritin was markedly increased in Non-chelated group (4505±2633 ng/mL) as compared to chelated group of patients (2479±963 ng/mL) as shown in Table 3. Thus it can be concluded from the present study that serum ferritin concentration which is considered to be a marker for liver iron concentration, was found to be increased in all the Beta thalassemia major patients.

A study was done by Lucas et al[25] on 48 thalassemia pateints using chelation with deferiprone. The mean serum ferrtin before the start of chelation was 5743 ng/mL which later reduced to 3558 ng/mL after completion of chelator therapy which indicates the importance of reducing iron toxicity. Our study showed similar results where the patients in chelated group had lower serum ferritn as compared to non -chelated group.

The following measures would be optimum for the thalassemia care. Programs that provide acceptable care, including transfusion of safe blood and supportive therapy including chelation, must be established. Estimation of serum ferritin must be done regularly to assess iron overload so as to facilitate chelation therapy if required. Screening of thalassemia major patients for biochemical abnormaities and other complications must be started at appropriate age as per the guidelines is recommended. Thalassemia International Federation also recommends regular monitoring of these patients with blood counts, liver function tests and serum ferritin at regular interval to prevent complications.

Conclusion

There is a strong need to create awareness among patients about the consequences of hemosiderosis in their body. The high level of serum ferritin of thalassemia major patients noted in this study supports the rationale for regular follow-up of transfusion dependent thalassaemic patients with respect to iron overload to ensure proper management of hemosiderosis associated complications. Proper chelation could improve the quality of life of these patients.

Acknowledgements:

We thank the patients and their parents for co-operating in this study. We also thank all the support from the Department of Pathology and Pediatrics of our Institution in conducting this study. We also acknowledge Mr. Shrikant V. Virgi, Incharge of KLES Blood bank and technical and teaching staff of KLES Blood Bank and Hospital for all the support in conducting this study.

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Conflict of interest: Nil

Source of funding: Nil

Date of submission: July 10th 2020

Date of acceptance: December 9th 2020