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Study of Complication in Patients with Beta Thalassemia

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Abstract: ***Background**: Even the life span has prolonged for the last 40 years, increase in frequently seen complications with increasing age negatively affect the life quality of thalassemia patients. **Methods**: In our study, complications encountered in 84 ß-thalassemia patients who were followedup between January 2014 to May 2016 were retrospectively analyzed. 67 patients were followed upwith diagnosis of thalassemia major and 17 with thalassemia intermedia. **Results**: Totally, 56.7% of patients were male and 43.3% were female. Ages varied between 3-17 years with the mean age of 10.3±4.8 years. Mean ferritin level was 2212±1370 ng/mL (41-6263 ng/mL) for 4.5 years. Complications were increased with increasing age. Complication rates were significantly higher among thalassemia major patients compared to thalassemia intermedia patients. There was no statistically significant relationship between complications and mean ferritin levels. The most common complications were endocrine complications (57.7%). Cardiac complications developed in 43.8% of the patients; gastroenterological complications in 19.4%; allergic complications in 10.5 % and infectious complications in 1.5%. **Conclusion**: Organ damage caused by iron overload in the heart and endocrine organs and severely impairs quality of life. Non-invasive imaging techniques have gained importance as serum ferritin levels alone are not sufficient for monitoring body iron load, keeping iron levels in safe, optimum levels, and preventing complications.*

Keywords: ß-thalassemia; thalassemia intermedia;endocrine organs; ferritin

1. Introduction

Thalassemias are hereditary hemolyticanemias with autosomal recessive inheritance characterized by inability to produce one or more globin chains forming hemoglobin molecule [1]. The incidence of ß-thalassemia trait is 2.6 % in India. There are approximately 1,400,000 carriers and 4000 patients in India [2]. Regular blood transfusion and adequate iron chelation therapy are important factors for treatment and follow up of thalassemia patients. Currently, the most common causes of death in these patients are transfusion-related hemosiderosis-induced heart failure and fatal arrhythmias. Osteoporosis, bone pain and bone changes, bile stone formation, increased risk of viral hepatitis, cirrhosis, delayed puberty, growth retardation, developmental delay, diabetes mellitus, and hypothyroidism are the other common complications [3].

The patient does not only suffer from the complications of the disease but also from the ill effects of the frequent treatment. The main mode of the treatment is the blood transfusion[4]. The iron load due to transfusion increases and because of this more of iron is taken up by the soft tissues. The MRI is a reliable source to detect this condition [5].

Osteoporosis and other bony malformations are seen frequently due to increased production of the blood to fight the oxygen lack in the bone marrow. Bossing is seen in majority of cases [6-9]. Growth Retardation will also be seen in majority of cases [10]. The metabolic syndromes may occur especially in puberty due to pituitary malfunctioning which is again basically due to lower oxygen tension in the tissues and hypoxia. [11-13].

In this study, demographic features, clinical and laboratory findings, and complications of ß-thalassemia patients were evaluated retrospectively.

2. Subjects and Methods

In our study, data of 84 ß-thalassemia patients followed between January 2014 and May 2016were retrospectively evaluated. Sixty-seven patients were followed upwith diagnosis of thalassemia major and 17 with thalassemia intermedia. Thalassemia major patientsis treated with regular blood transfusions to maintain pre transfusion hemoglobin (Hb) levels ≥ 9-10g/dL. Thalassemia intermedia patients received erythrocyte transfusion when hemoglobin level was below 7 g/dL. Iron chelation therapy was started forpatients whose ferritin values were above 1000ng/mL and whose age was appropriate for chelation therapy. Desferrioxamine,deferiprone, deferasirox or desferrioxamine and deferipone combinationtherapies were used as iron chelation therapy. Thalassemia major cases whose erythrocyte consumption exceeded 200-250 mL/kg/year and thalassemia intermedia cases who developed hypersplenism or who need increased transfusion underwent splenectomy. Clinical histories, physical examinations, laboratory values [hemoglobin, platelet count, fasting plasma glucose, renal function tests, aspartate aminotransferase (AST), alanine aminotransferase (ALT), bilirubin, calcium, phosphorus, alkaline phosphatase levels, serology for hepatitis B virus, hepatitis C virus, and human immunodeficiency virus, ferritin levels, follicle stimulating hormone, luteinizing hormone, estradiol, testosterone, vitamin D, parathormone levels, thyroid function tests (thyroid stimulating hormone, T3, T4), insulin level] and radiological findings (abdominal and thyroid ultrasonography, bone x rays, T2w magnetic resonance imaging) were evaluated from the patient files. Electrocardiography (ECG), echocardiography (ECHO), and bone mineral densitometry (BMD) results were also evaluated for development of complications.

3. Statistical Analysis

Data were analyzed using SPSS version 20.0. Categorical variables were given as number and percent, numerical variables were reported as mean ± standard deviation and

median. The difference between groups in terms of categorical variables was evaluated by using qui-square test. P valve 0.05 or less considered as a statistical significant.

4. Results

A total of 84 ß-thalassemia patients including 46 (54.7%) boys and (45.2%) girls with the age range of 3-19 years were evaluated retrospectively. Sixty-seven of the patients were followed up with diagnoses of thalassemia major and 17 with thalassemia intermedia. Of thalassemia major patients, 34 (50.7%) were boys and 33(42.2%) were girls. Of thalassemia intermedia patients, 12 (70.5%) were boys and 5 (29.4%) was a girl. The mean age of the patients was 10.3±4.8 years (range: 3-19 years).

Mean ferritin level was 2212±1370 ng/mL (41-6263 ng/mL) for 4.5 years. Complications were increased with increasing age. Complication rates were significantly higher among thalassemia major patients compared to thalassemia intermedia patients. There was no statistically significant relationship between complications and mean ferritin levels.

Parenteral desferrioxamine, oral deferiprone or deferasirox were used for iron chelation therapy. Type of chelation therapy is given in Table 1. Twenty nine patients with thalassemia major and 8 patients with thalassemia intermedia underwent splenectomy. Fifteen (17.8%) patients underwent hematopoietic stem cell transplantation.

Table 1: Type of chelation therapy for thalassemia major patients

Chelator	*n*	*Percentage*
Desferrioxamine+Deferiprone	32	47.7
Deferasirox	26	38.8
Desferrioxamine	09	13.4
Total	67	100

Table 2: Complication on different system

Complication		*Patients in %*
Cardiac complication (43.8%)	Increase in left ventricle wall thickness	12.3
	Diastolic dysfunction	8.5
	Systolic dysfunction (EF<%55)	11
	Heartfailure	5
	Pericardial effusion	4
	Dilated cardiomyopathy	1
	Left ventricle enlargement	1
	Left atrium enlargement	1
Endocrine (57.7%)	Osteoporosis	19.5
	Growthretardation-short stature	16.3
	Hypothyroidism	11.4
	Delayedpuberty-ypogonadism	6.52
	Diabetes mellitus	4.0
Allergic action (10.5%)	Transfusion-related	5
	Chelation-related	5.5
Gastroenterological (19.4%)	Constantlyelevated transaminases	17.9
	Bile stone	1.5
Infectious (1.5%)	Chronic hepatitis B	1.5

The second leading complications were cardiac complications (43.8%). Cardiac iron load was studied with T2w MRI in 18 out of 67 thalassemia major patients. Severe involvement (<8 msec) was detected in one patient, moderate involvement (8-14 msec) was detected in 2 patients and mild involvement (14-20 msec) was detected in 8 patients. Four patients were normal (>20 msec). Cardiac complications are shown in Table 2. There was no statistically significant relationship between mean ferritin levels and cardiac complications (p> 0.05).

Gastroenterological complications were seen in 19.4% of the patients. Patients were evaluated in terms of constant transaminase elevation, bile stone formation and hepatic failure. Constant transminase elevation was detected in 17.9% of the patients, temporary transaminase elevation was detected in 50.7%, and bile stone was detected in 1.5% of the patients. No patients developed hepatic failure. Transaminase elevation was statistically significant in the patients whose mean ferritin level was >2500 ng/mL (p< 0.05).

HBV infection was detected in 1.5% of all patients. There were no patients positive for HCV or HIV. A rare complication of thrombosis-related cerebrovascular event and left hemiplegia was observed in one patient with ß-thalassemia major. This patient had both protein C and S deficiency.

5. Discussion

The major Haemoglobin called HbA is present in the Human in a quantity of about 85 to 90 percent in children above one year of age. A minor component HbA2 is also present in negligible amounts. The major component in foetal life is HbF of which only traces are seen after one year. Each Haemoglobin molecule has two alpha chains and two beta chains which are associated with one another in HbA. The alpha chain is constant component and delta chain replaces the beta chain in the HbA2 and gamma globulin chain replaces the beta chain in the HbF.

Thalassemias are inherited disorders of haemoglobin synthesis that results from the alteration in the rate of globin chain production. A decrease in the rate of production of this globulin results Haemoglobin synthesis abnormalities. Because two types of chains are involved and this pairing results in the formation of haemoglobin in a ratio of 1:1 any deviation from the normal results in accumulation of the unused part of the haemoglobulin which again results in the early destruction of the red blood corpuscles.

Thalassemia should be considered as a differential diagnosis with hypochromic, microcytic anemia that has not responded to iron supplementation. Children with Beta major variety usually demonstrate no symptoms until about six months, when beta chain are needed to pair with alpha chain to form HbA and indirectly results in gamma to turn off. This is called switching process. If this switching mechanism is impaired severe pallor and hepato – splenomegaly can be seen due to rapid destruction of the RBCs. Icterus is usually seen in mild to moderately. Liver may start dysfunctioning due to iron overload. Symptoms of severe anaemia and and heart murmurs to failure can be appreciated.

Complete blood count and peripheral smear is sufficient to suspect the disease. In thalassemia major and intermedia the

haemoglobin level ranges from 2 to 7Gm/Dl. MCV and MCh are lowered. Reticulocytic count is seen to be elevated due to continuous stress of replacement of the RBCs.

Genetic counselling is needed for the whole family to prevent the birth in thalassemia major and pre – natal testing can be done to test the patients. Carriers are easy to screen. Prenatal diagnosis and genetic counselling are to be conducted to ward of the unnecessary burdens that the patients family has to suffer.

The main mode of treatment is the blood transfusion. Patients with thalassemia require medical treatments for monitoring the complications of the disease as well as the complications of the transfusion therapy. Blood transfusion should be initiated at an early age when the child is asymptomatic. The iron deposition in the tissues is one more unnecessary complication of massive iron load. The excess iron from the body has to be removed by chelation therapy and this has dramatically increased the life expectancy. After multiple transfusions the patients tend to have reactions. These complications can be minimized by leucocyte filters during transfusions or using leucocyte depleted packed cells.

The major complications of the blood transfusions are those related to transmission of infections especially blood borne infections like hepatitis.

In this study a demographic pattern of the disease has been studied and reported.

6. Conclusion

A total of 84 ß-thalassemia patients including 46 (54.7%) boys and (45.2%) girls with the age range of 3-19 years were evaluated retrospectively. Sixty-seven of the patients were followed up with diagnoses of thalassemia major and 17 with thalassemia intermedia. Of thalassemia major patients, 34 (50.7%) were boys and 33 (42.2%) were girls. Of thalassemia intermedia patients, 12 (70.5%) were boys and 5 (29.4%) was a girl. The mean age of the patients was 10.3±4.8 years (range: 3-19 years).

References

[1] Weatherall DJ. Disorders of globin synthesis: The thalassemias. In: Lichtman MA, Beutler E, Kipps TJ, Seligsohn U. Williams Hematology, 7th ed. Newyork: McGraw-Hill Book Company; 2006: 633-667
[2] T.C. Sa¤l›kBakanl›¤› AÇSAP GenelMüdürlü¤ü. Hemoglobinopatikontrol program›: Canatan D, Ayd›nok Y. Talasemivehemoglobinopatiler, Tan› veTedavi. RetmaMatbaa Ltd, Antalya; 2007: 29.
[3] Cunningham MJ, Sankaran VG, Nathan DG, Orkin SH. The Thalassemias. In: Orkin SH, Nathan DG, Ginsburg D, Look AT. Nathan and Oski'sHematology of Infancy and Childhood, 7th ed. Philadelphia: Sounders Elsevier; 2009:1015-1109
[4] Olivieri NF, Brittenham GM. Iron chelating therapy and the treatment of thalassemia.Blood89: 739-761,1997.
[5] Maggio A, Capra M, Pepe A, et al. A critical review of non invasive procedures for the evaluation of body ironburden in thalassemia major patients. PediatrEndocrinol Rev 6: 193-203, 2008.
[6] Molyvda-Athanasopoulou E, Sioundas A, Karatzas N, et al. Bone mineral density of patients with thalassemiamajor: four-year follow-up. Calcified Tissue International 64: 481-484, 1999.
[7] Borgna-Pignatti C, Cappellini MD, De Stefano P, et al. Survival and complications in thalassemia. Ann NYAcadSci 1054: 40-47, 2005.
[8] Angastiniotis M, Pavlides N, Aristidou K, et al. Bone pain in thalassemia: assesment of DEXA and MRI findings. J PediatrEndocrinolMetab 11: 779-784, 1998.
[9] Jensen CE, Tuck SM, Agnew JE, et al. High incidence of osteoporosis in thalassemia major. J PediatrEndocrinolMetab 11: 975- 977, 1998.
[10] Cario H, Stahnke K, Sander S, Kohne E. Epidemiological situation and treatment of patients with thalassemia major in Germany: results of the German multicenter beta-thalassemia study. Ann Hematol 79: 7-12, 2000.
[11] Low LC. Growth, puberty and endocrine function in beta-thalassaemia major. JPediatrEndocrinolMetab10: 175- 184, 1997. 12.
[12] Saka N, Sukur M, Bundak R, et al. Growth and puberty in thalassemia major. J PediatrEndocrinolMetab 8:181-186, 1995.
[13] Aydinok Y, Darcan S, Polat A, et al. Endocrine complications in patients with beta-thalassemia major. JTrop Pediatr 48: 50-54, 2002.