MAK HILL Publications Research Journal of Medical Sciences

Research Article
doi: 10.59218/makrjms.2023.521.529

Study the Hematological Finding in Thalassemia Major Patients

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ABSTRACT: Thalassemia causes varying degrees of anemia, which can range from significant to life threatening. People of Mediterranean, Middle Eastern, African and Southeast Asian descent are at higher risk of carrying the genes for thalassemia. Thalassemia causes varying degrees of anemia, which can range from significant to life threatening. India is a large Southeast Asian country with a population of over one Billion. An estimated 1-3% of the population are carriers of beta thalassemia, a figure rising up to 17% in some ethnic groups. This is a prospective observational cohort study done in pediatric wards of two hospitals C.R. Gardi Hospital (C.R.G.H.) and associated hospitals from September 2016 may 2018. Main aim of this study is to study the hematological findings in Thalassemia major patients. Out of 60 patients of thalassemia were enrolled and their demographic hematological profile was taken. The mean age was 10.2 years, 75% were males and 81% were Hindus, 40% belonged to upper lower class. Most common clinical features were (97%) icterus followed by (90%) pallor, 80% of thalassemia patients had moderate to severe hepatomegaly. Mean Hb was 8.5±0.9 g dL^{-1}, 67% had severe anemia, Mean MCV level was 73±2 µm3, Mean MCH and MCHC level were 20±2 pg $cell^{-1}$, 28±2 gHb dL^{-1}. Mean ferritin level was 1281.8±219.9 ng dL^{-1}, 45% of thalassemic patients had serum ferritin level between 1000-2000 ng dL^{-1} followed by 39% of patients had serum ferritin level more than 2500 ng dL^{-1}, Mean frequency of blood transfusion 16±2 times a year, 55% of had blood transfusion 5-10 times a year followed by 33% had frequency of blood transfusion 10-15 times a year and only 12% had frequency more than 15 times a year, Mean interval between transfusion 22±2 days, 73% had an interval of 15-25 days between two transfusion. According to 86% had euglycemia and 10% had hyperglycemia when blood sugar was tested randomly. About 90% of thalassemic patients had normal glucose tolerance test followed by 6.5% of thalassemic patients had impaired glucose tolerance test, while 3.3% patients came under diabetic range. About 81% of thalassemic patients had normal serum calcium level while 18% had hypocalcemia, 93% of thalassemic patients had normal serum T4 and TSH level, 1.6% of patients had subclinical hypothyroidism and only 4% of thalassemic patients had overt hypothyroidism. Tablet deferasirox was taken as chelating agent in all thalassemia patients, 51% of which were taking it after 2 years of age, 35% were had started between 1-2 years of age and only 13% started below 1 year of age. The common adverse reaction in thalassemic patients were diarrhea (26.1%), abdominal pain (23%), skin rash (20%), seizures (16%), blurring of vision (3%).

OPEN ACCESS

Key Words
Thalassemia, anemia, population, pediatric, hematological

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Received: 1 July 2023
Accepted: 12 July 2023
Published: 15 July 2023

Citation: Mohit Sharma, Shreya Shrivastava, Sunil Kumar Kasundriya and Amit Kumar Singh 2023. Study the Hematological Finding in Thalassemia Major Patients. Res. J. Med. Sci., 17: 521-529, doi: 10.59218/makrjms.2023.521.529

INTRODUCTION

Thalassemia is an inherited disorder of autosomal recessive gene caused by impaired synthesis of one or more globin chains. The impairment alters production of normal hemoglobin (Hb).

Thalassemia causes varying degrees of anemia, which can range from significant to life threatening. People of Mediterranean, Middle Eastern, African and Southeast Asian descent are at higher risk of carrying the genes for thalassemia[1].

Thalassemia is caused by mutations that decrease hemoglobin synthesis and red cell survival. Thalassemia is caused by decreased or absent production of one type of globin chain, either alpha or beta globin chain. These hematologic disorders range from asymptomatic to severe anemia that can cause significant morbidity and mortality.

It was first recognized clinically by the study of by causas Cooley and Lec.[2], who described a syndrome of anemia with microcytic erythrocytes. Then it was called Cooley's anemia. Later Wipple and Bradford renamed this disease as "Thalassemia". Because it was found in the region of the Mediterranean Sea (thalasa is an old Greek word for sea)[3].

Beta-thalassemia includes three main forms: Thalassemia major variably referred to as "Cooley's Anemia" and "Mediterranean Anemia", Thalassemia intermedia and Thalassemia minor also called "beta-thalassemia carrier", "beta-thalassemia trait" or "heterozygous beta-thalassemia".

Beta thalassemia is a disorder that reduces the production of hemoglobin. Hemoglobin is the iron-containing protein in red blood cells that carries oxygen to cells throughout the body.

In people with beta thalassemia, low levels of hemoglobin lead to a lack of oxygen in many parts of the body. Affected individuals also have decreased red blood cells (anemia), which will manifest as pale skin, weakness, fatigue and serious complications.

It is estimated that 1.5% of the world's population are carriers of β-thalassemia with an estimated 60,000 new carriers born each year[4]. Southeast Asia accounts for about 50% of the world's carriers while Europe and the Americas jointly account for 10-13% of the world carriers[5].

India is a large Southeast Asian country with a population of over one Billion. An estimated 1-3% of the population are carriers of beta thalassemia, a figure rising up to 17% in some ethnic groups[6,7].

In India, prevalence of Thalassemia is very high in Punjabis, Sindhs, Gujaratis, Bengalis, Parsee, Lohana and certain tribal communities and in Northern, Western and Eastern part, while it is much less in the south of India[8].

About 6,000 children are born with thalassemia major each year, more than 30% of birth with a major thalassemia syndrome in South East Asia[7].

Overtime, an influx of iron-containing hemoglobin from chronic blood transfusions can lead to a buildup of iron in the body, resulting in liver, heart and hormone problems. The aims and objective of this study is to study the clinical features, complications in Beta-thalassemia patient and outcome from Ujjain district and so that timely intervention can be done to prevent complications.

Aims and objectives: This is a prospective observational cohort study done in pediatric wards of two hospitals C.R. Gardi Hospital (C.R.G.H.) and associated hospitals, from September 2016 May 2018. Main aim of this "study is to study the hematological finding in Thalassemia major patients''.

MATERIALS AND METHODS

Study design: Observational and prospective Study Study duration: September 2016 may 2018.

Study setting: The study was conducted in pediatric wards of two hospitals C.R. Gardi Hospital (C.R.G.H.) and associated hospitals.

Study participants

Inclusion criteria:

- Children with diagnosis of thalassemia
- Age group 6 months and above
- Thalassemia children who are on regular blood transfusion with or without iron chelation therapy

Exclusion criteria: Children with other causes of anemia like nutritional anemia, aplastic anemia, sickle cell anemia.

Sample size: To calculate sample size it was assumed that 50% of patients of Thalassemia will have at least one known complications thus to detect at least 50% of complication with a difference of +/-20% around the assumed complications rate of 50% with a power of 80 two sided alpha 0.05 estimated minimum sample size is 103.

Data collection: Children who fulfill the inclusion criteria for the study will be selected. After proper clinical examination and preliminary investigation, the child will be subjected to clinical outcome and complication. The data will collect on proper proforma.

The data thus collected will be subjected to statistical analysis.

Pre and post transfusion hemoglobin and serum ferritin level, complete hemogram, Hb electrophoresis, peripheral blood smear, urine urobilinogen are done as a part of standard care for thalassemia patients.

Serum ferritin level will be estimated by chemiluminescent immunometric assay[6].

Haemoglobin estimation will be done by Beckmen Coulter machine using cyanmethemoglobin automated method.

Statical analysis: The data was entered in Epidata Entry (version 3.1) and then transferred to Stata 10.0 (Stata Corp. College Station, Texas and USA) software for statistical analysis. Frequency and percentages are presented for categorical data. Chi square test was used for measuring association between different categories. Binary logistic regression were applied and calculate odd ratio. A *P*-value less than or equal to 0.05 was considered significant. T-test was used for comparing the mean duration of stay.

RESULTS

About the -50% of thalassemic patients belonged to 5-10 years of age, 28% of patients belonged to 6 months -5 years and 22% belonged to >10 years of age. According to -75% of thalassemic patients were males.

About the -81% of thalassemic patients belonged to hindu religion and 19% belonged to population. About -40% of thalassemic patients belonged to upper lower class, 38% patients belonged to lower class, 12% of patients belonged to lower middle class and only 10% patients belonged to upper middle class.

Table 1 shows various clinical features with which patients presented icterus (97%), pallor (90%), facial changes (79%), loss-of-appetite (60%), lethargy (60%), skin-pigmentation (58%), breathlessness (33%), skeletal changes (30%), diarrhea (27%), fever (14%), oliguria (12%) respiratory distress (17%), hematemesis (16%), dark colored urine (11%), vomiting (7%), edema (2%)

About to the -50% of thalassemia patients were presented with severe hepatosplenomegaly followed by 30% patients with moderate hepatosplenomegaly and only 20% patients with mild hepatosplenomegaly (Fig. 1).

Table 2 shows that 46% of thalassemic patients presented between -1SD and -2SD followed by 20% thalassemic patients presented between -3SD and -2SD followed by 20% thalassemic patients between less than <-3SD and only 14% thalassemic patients between -1SD and MEDIAN. Mean height was 105.77 cm (SD±13.79).

Table 3 shows that 67% of thalassemic patient presented with severe anemia and 33% of thalassemic patients with moderate anemia. Mean hemoglobin level 8.2±2 g dL^{-1}.

Table 4 shows that 65% of thalassemic patients had severe microcytic RBCs and only 35% 0f thalassemic patients had moderate microcytic RBCs Mean MCV level: 73±2 μm^3.

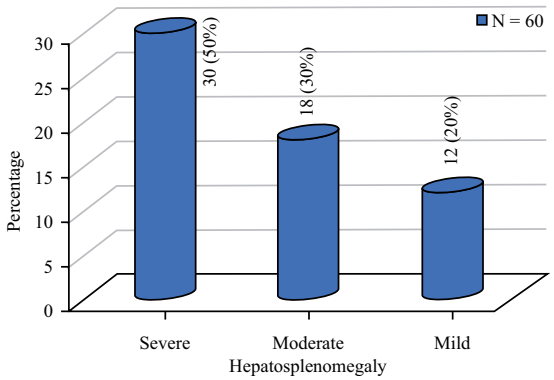

Fig. 1: Hepatosplenomegaly

Table 1: Distribution of thalassemia patients according to clinical features

Parameters	Values
Clinical features	N = 60
Icterus	58 (97%)
Pallor	54 (90%)
Facial changes	47 (79%)
Loss of apeptite	36 (60%)
Lethargy	36 (60%)
Skin pigmentation	35 (58%)
Fatigue	22 (37%)
Breathlessness	20 (33%)
Skeletal changes	18 (30%)
Diarrhea	16 (27%)
Fever	14 (23%)
Oliguria	12 (20%)
Respiratory distress	10 (17%)
Hematemesis	10 (16%)
Dark colored urine	7 (11%)
Vomiting	4 (7%)
Edema	1 (2%)

Table 2: Distribution of thalassemia patients according

Parameters	Values
Anthropometry	N = 60
Between -1SD&-2SD	28 (46%)
B/W -3SD &-2SD	12 (20%)
<-3SD	12 (20%)
B/W -1SD&median	8 (14%)
Total	60

Table 3: Distribution of thalassemia patients according to hemoglobin levels

Age	Moderate	Severe
<1	1 (1.6)	2 (3.3)
2-3	6 (10)	7 (11.6)
4-6	2 (3.3)	12 (20)
7-9	4 (6.6)	3 (5)
>9	7 (11.6)	16 (27)
Total	20 (33)	40 (67)

Table 4: Distribution of thalassemia patients according to blood MCV levels

Age	Moderate	Severe
<1	2 (3.3)	1 (1.6)
2-9	9 (15)	27 (45)
>10	10 (16.6)	11 (18.5)
Total	21 (35)	39 (65)

Table 5: Distribution of thalassemia patients according to MCH levels

Age	Moderate	Severe
<1	1 (2)	2 (3.3)
2-9	10 (16.6)	26 (43)
>10	9 (15)	12 (20)
Total	20 (24)	40 (66)

Table 5 shows that 66% of thalassemic patients had severe hypochromic RBCs. Mean MCH Level: 23±2 pg $cell^{-1}$.

Table 6: Distribution of thalassemia patients according to blood MCHC levels

Parameters	Values
Age	N = 60
Normal (32-36)	3 (5%)
Abnormal (hypochromic)	57 (95%)
Total	60

Table 7: Distribution of thalassemia patients according to serum ferritin levels

Parameters	Values
Serum ferritin	N = 60
<1000	8 (12%)
1000-2500	29 (49%)
>2500	23 (39%)
Total	60

Table 8: Distribution of thalassemia patients according to interval between transfusion (days)

Parameters	Values
Interval between transfusions (days)	N = 60
15-25 days	44 (73%)
25-35 days	10 (16%)
35-45 days	6 (11%)
Total	60

Table 9: Distribution of thalassemia patients according to random blood sugar levels

Parameters	Values
Blood sugar	N = 60
Euglycemia	52 (86%)
Hyperglycemia	6 (10%)
Hypoglycemia	2 (4%)
Total 60	

Table 10: Distribution of thalassemia patients according to glucose tolerance test

Parameters	Values
Glucose tolerance test (GTT)	N = 60
Impaired glucose tolerance	4 (6.5%)
Diabetic	2 (3.3%)
Normal	54 (90%)
Total	60

Table 6 shows that 95% of thalassemic patients had severe hypochromic blood. Mean MCHC level: 28±2 g dL^{-1}.

Table 7 shows that 49% of thalassemic patients had ferritin levels between 1000-2500 followed by 39% of thalassemic patients more than 2500 levels and only 12% of thalassemic patients had lesser than 1000 levels. Mean ferritin level: 1281±219 ng dL^{-1}.

About to -55% of thalassemia patients had frequency of blood transfusion 5-10 times per year followed by 33% of patients between 10-15 times per year and only 12% patients more than 15 times per year. Mean frequency of blood transfusion 16±2 times a year.

In this study 73% of thalassemia patients were transfused blood between 15-25 days followed by 16% of patients were transfused between 25-35 days and only 11% of patients were transfused blood between 35-45 days. Mean interval between transfusion 22±2 days (Table 8).

Table 9 shows that 10% 0f thalassemic patients were presented with hyperglycemia, 4% of thlassemic patients with hypoglycemia and 86% of patients were euglycemia.

Table 10 shows that 90% of thalassemic patients had normal glucose tolerance test followed by 6.5% of thalassemic patients which had impaired impaired glucose tolerance test. Only 3.3% of thalassemic patients had glucose tolerance test in diabetic range.

Table 10: Distribution of thalassemia patients according to glucose tolerance test

Parameters	Values
Glucose tolerance test (GTT)	N = 60
Impaired glucose tolerance	4 (6.5%)
Diabetic	2 (3.3%)
Normal	54 (90%)
Total	60

Table 11: Distribution of thalassemia patients according to serum calcium levels

Parameters	Values
Serum calcium	N = 60
Normal	49 (81%)
Hypocalcemia	11 (18%)
Total	60

Table 12: Distribution of thalassemia patients according to serum thyroid levels

Parameters	Values
Level	N (60)
T4 and TSH (normal)	56 (93%)
T4 normal and TSH increase	1 (1.6%)
T4 decrease and TSH increase	3 (4.4%)
Total	60

Table 13: Distribution of thalassemia patients according to age of onset of drug chelating agent (deferasirox)

Parameters	Values
Age of on set	N = 60
<1	8 (13%)
1-2	21 (35%)
>2	31 (51%)
Total	60

Table 14: Distribution of thalassemia patients according to adverse drug reaction

Parameters	Values
Adverse drug reaction	N = 60
Diarrhea	16 (26%)
Abdominal pain	14 (23%)
Skin rash	12 (20%)
Seizure	10 (16%)
Blurring of vision	2 (3%)
Total	60

Table 11 shows that 18% of thalassemic patients had hypocalcemia and mean serum calcium level: 8.20±2 mg dL^{-1}.

Table 12 shows that out of 60 thalassemic patients 93% of thalassemic patients had normal thyroid followed by 5.4% patients had subclinical hypothyroidism and only 1.6% thalassemic patient had overt hypothyroidism.

Table 13 shows that 51% of thalassemia patients started deferasirox more than 2 years of age, 35% of patients started deferasirox between 1-2 year while 13% of patients started deferasirox less than 1 year of age.

Table 14 shows that most common adverse drug reaction found was Diarrhea (26%), followed by abdominal pain (23%) followed by skin rash (20%) followed by seizure (16%) and in only 3% of patients blurring of vision was found.

About 76% of thalassemia patients had hepatitis c virus infection. So, 52% of thalassemic patients had hepatitis b virus infection.

DISCUSSIONS

In present study out of 60 children 75% (n = 45) were males and 25% (n = 22) were females. It is comparable to the study done by Karimi et al. (2009) in Iran done on 50 Thalassemia major children out of which 66% were (n = 33) were males and 34% (n = 17) were females. A similar study done by Taher *et al*.[9] included 104 thalassemia major patients out of which 63% (n = 75) were male and 37% (n = 39) were female. In a study done by Ozyouk 61% were males and 39% were females out of the total 49 patient.

The prevalence of β-thalassemia trait varies between 3-17% because of consanguinity and caste and area endogamy. 4 Every year, ten thousand children with β-thalassemia major are born in India, which constitutes 10% of the total number in the world.5 HbE thalassemia is common in north-east parts of India.

In Present study group comprised of patients ranging between 6 month to 18 years with a mean age of 10.20+/-3 years. Similar observation Arora study at Lady Harding Medical College, New Delhi, studied 30 children and 20 matched controls. The mean age of study group 11.83+/-1.91 years (range 9-17 years) and that of control group 12+/-2.17 years (range 9-17 years) was comparable. Chui *et al*.[10] in an Arab hospital studied 17 children aged 6-17years (average 11.2 years). In Sollaino *et al*.[11] studied study group had a range of 7.5-18 years with mean a mean age of 12.5 (+/-3.5 years).

Mean heamoglobin in present study was 6.244 (+/-1.66) g dL^{-1} which is much lower than most of studies done. In study by Bijan at Ahwaz Jondishpour University of medical Sciences, Ahwaz, Iran mean hemoglobin was (8.5+/-0.9) g dL^{-1}. In study by Breuer *et al*.[12] found mean heamoglobin of patient was (9.87+/-1.45 g dL^{-1}). A similar study done by Kanj *et al*.[13] mean hemoglobin was (8.8+/-1.1) g dL^{-1}. In a study done by Brittenham *et al*.[14] mean hemoglobin was (9.3+/-1) g dL^{-1} this reason behind such a low mean value of hemoglobin was because parents stay away from hospital, ignorance and literacy.

In present study various clinical features with which patients presented were icterus (97%), pallor (90%), facial changes (79%), loss-of-appetite (60%), lethargy (60%), skin pigmentation (58%), breathlessness (33%), skeletal changes (30%), diarrhea (27%), fever (14%), oliguria (12%) respiratory distress (17%), hematemesis (16%), dark colored urine (11%), vomiting (7%), edema (2%). Similar study done by Kaustubh Chattopadhyay et al at N.R.S. Medical College, Kolkata found that hepatomegaly was the most common presenting complaint among the study population (66.3%), followed by jaundice (53.9%), splenomegaly (47.5%), thalassemic facies (53.2%) and Growth retardation (23.6%).Skin pigmentation (16.5%), Ascites (3%) and edema (3%).

The pathogenesis of growth failure in thalassemia is multifactorial and is mainly due to transfusional iron overload and resulting endocrinopathies (GH deficiency, hypothyroidism, diabetes), nutritional deficiencies and intensive use of chelating agents particularly deferrioxamine. Other etiologies particularly in sub optimally treated children are increased metabolism, chronic anemia and hypoxia. The anterior pituitary is particularly sensitive to iron associated free radical oxidative stress. Even a modest amount of iron deposition in anterior pituitary by MRI can interfere with its function. Dysregulation of the GH insulin like growth factors axis leads to growth hormone deficiency and growth deceleration. (Hematology blood transfusion)[15].

All children with Beta thalassemia major >10 years should undergo standing and sitting height every 6 months, bone age, growth hormone stimulation, insulin like growth factor (IGF) -1 level and IGF-BP3 level.

Frequent blood transfusion should be considered in patients with growth failure with reassessment for tapering or withdrawal when a sustained clinical benefit is achieved. Thalassemia a global health problem[16,17].

In present study 50% of thalassemia patients presented with severe hepatosplenomegaly followed by 30% patients with moderate hepatosplenomegaly and only 20% patients with mild hepatosplenomegaly. Similar study done by Santosh Kumar at Department of Pediatrics, MGM Medical College and LSK Hospital, Kishanganj, Bihar found Out of 211 patients hepatomegaly was the most common clinical finding among the study population (57.8%), followed by splenomegaly (54.9%).

In present study 67% of thalassemic patient presented with severe anemia and 33% of thalassemic patients with moderate anemia.

In present study 66% of thalassemic patients had severe hypochromic anemia and 34% of thalassemic patients had moderate hypochromic anemia, mean MCH value was 23±2 pg $cell^{-1}$.

In present study 65% of thalassemic patients had severe microcytic RBCs and only 35% 0f thalassemic patients had moderate microcytic RBCs, mean MCV value was 73±2 µm3.

In present study 95% of thalassemic patients had severe hypochromic anemia and mean MCHC value was 28±2 gHb dL^{-1}.

Is characterized by reduced Hb level (<7 g dL^{-1}), mean corpuscular volume (MCV) >50 <70 fl (femtoliters) and mean corpuscular Hb (MCH) >12

<20 pg. In peripheral blood smear affected individuals show RBC morphologic changes (microcytosis, hypochromia cells) and nucleated RBC (i.e., erythroblasts). The number of erythroblasts is related to the degree of anemia and is markedly increased after splenectomy. Thalassemia intermedia is characterized by Hb level between 7 and 10 g dL^{-1}, MCV between 50 and 80 fl and MCH between 16 and 24 pg (Deyde VM et-al, Hematological disorder)[18].

In present study 55% of thalassemia patients had frequency of blood transfusion 5-10 times per year followed by 33% of patients between 10-15 times per year and only 12% patients more than 15 times per year. Similar study done by Neeraj at NHL Municipal Medical College, Ahmedabad found that 36% of thalassemic patients had blood transfusion more than 15 times per year, 34% of thalassemic patients had blood transfusion between 5-10 times per year and only 28% of thalassemic patients had transfused blood more than 10 times per year.

In present study 73% of thalassemia patients were transfused blood between 15-25 days followed by 16% of patients were transfused between 25-35 days and only 11% of patients were transfused blood between 35-45 days. A Similar study done by Neeraj shah et al (2010) at NHL Municipal Medical College, Ahmedabad found that 42% of thalassemic patients were transfused blood between 15-25 days followed by 38% of thalassemic patients had transfused blood between 25-35 days and only 20% of thalassemic patients transfused blood between 25-35 days.

Severe anemia with hemoglobin <7 g% for more than 2 weeks is widely accepted as an indication to start blood transfusion[19]. The goal should be aimed to maintain a pre-transfusional Hb level of 9-10 gdL^{-1} and a post-transfusion Hb level of 13-14 gdL^{-1}. Such regime generally prevents growth impairment, organ damage and bone deformities. Care should be taken to avoid faster transfusion exceeding 5 mL kg^{-1} hrs^{-1} and amount of transfused RBC should not exceed 15-20 mL kg^{-1} day^{-1}. The frequency of transfusion is usually every 2-4 weeks (an overview of Thalassemia).

In present study 49% of thalassemic patients had ferritin levels between 1000-2500 ng mL^{-1} followed by 39% of thalassemic patients more than 2500 level ng mL^{-1} and only 12% of thalassemic patients had ferritin level less than 1000 ng mL^{-1}. Similar study done by Saraya, at Department of Pediatrics and Computer Center, AIIMS Delhi studied Serum ferritin levels in 64 patients with beta homozygous thalassemia (BHT), 120 patients with beta heterozygous thalassemia and 46 normal subjects. Incidence of iron overload seen in 32 Beta heterozygous thalassemia cases was similar in untransfused and transfused cases. Among heterozygotes thalassemia patients, iron stores were depleted in 24 (20%) patients, mostly females 70.8 and 29.2% of males.

The iron burden on the body can be estimated by means of serum ferritin, iron and TIBC levels. The estimation of serum ferritin levels is the most commonly employed test to evaluate iron overload in β-thalassemia major. The association between serum ferritin and levels of body iron are well-established and the test is easy to perform compared with other tests for iron overload. (Iron chelation status in young children with Thalassemia)[20]. In present study 51% of thalassemia patients started chelating agent by Deferasirox more than 2 years of age, 35% of patients started deferasirox between 1-2 year while 13% of patients started Deferasirox at less than 1 year of age. Similar study done by Dhaval conducted a study on Efficacy and Safety of Deferasirox in Pediatric Patients of Thalassemia at a Tertiary Care Teaching Hospital B.J. Medical college and Civil hospital Ahmedabad found that 64% of thalasssemic patients started deferasirox more than 2 years of age, 26% of thalassemic patients started deferasirox between 1-2 years of age and only 10% started deferasirox less than 1 year of age.

The introduction of the iron chelator deferoxamine greatly ameliorates the effects of iron toxicity but long-term cardiac mortality has been very disappointing[21,22]. There is strong evidence that long-term deferoxamine chelation does not effectively prevent myocardial siderosis in a majority of patients[23]. Deferiprone, the first approved oral chelator has been shown in randomized controlled trials to be effective monotherapy at 100 mg kg^{-1} day^{-1} in treating mild to moderately severe myocardial iron loading (myocardial T2×8-20 ms), significantly improving both myocardial iron and ejection fraction and the combination of deferiprone at 75 mg kg^{-1} day^{-1} with deferoxamine is likewise effective[7,24]. However greater total iron clearance is seen with combined treatment, which suggests that it might be useful for severe myocardial siderosis (T2×<10 ms)[19,25,26].

The conventional treatment at many centers for severe myocardial siderosis with heart failure is long-term, continuous, high-dose intravenous deferoxamine. Several small studies have confirmed that this approach is effective and reversal of cardiomyopathy is possible. Combined chelation therapy in this situation might be effective, yet prospective trials examining the treatment of severe cardiac siderosis are lacking.

Since the body has no effective means of effectively removing iron, the only way to remove excess iron is to use iron chelators. The major step forward in improving survival and reducing

complications was the introduction of the chelating agent deferoxamine, used as a subcutaneous infusion. Two oral chelators, deferiprone and deferasirox have recently become available, making therapy easier and more efficacious. Compliance, although improved by the switch to oral therapy, still presents a problem and is the major obstacle to effective prevention of iron overload. The orally active chelators seem to be more effective in gaining access to the chelatable iron pool of cardiomyocytes, binding labile iron and attenuating reactive oxygen species formation 46. Other study showed that the combination therapy is associated with lower risk of mortality.

In present study various adverse drug reactions found were Diarrhea (26%), followed by abdominal pain (23%) followed by Skin rash (20%) followed by seizure (16%) and in only 3% of patients blurring of vision was found. Similar study done by Dhaval conducted a study on Efficacy and Safety of Deferasirox in Pediatric Patients of Thalassemia at a Tertiary Care Teaching Hospital B.J.Medical college and Civil hospital found that a total of 117 ADRs were observed in 52 patients from 19498 doses, most common being diarrhea (46%), raised serum creatinine (28%), raised hepatic enzymes (26%), abdominal pain (26%) and skin rashes (24%).

Diarrhea was most common drug adverse reaction in present study. Diarrhea in these patients can be because of a faulty drug administration technique causing improper drug dispersion. Emphasis should therefore be laid on educating the patient/care takers at each visit to ensure better drug compliance and to reduce the incidence of adverse reactions such as diarrhea.

In present study, hyperglycemia was found in 10% of thalassemic patients and hypoglycemia in 4% of thalassemic patients and 86% of thalassemic patients were euglycemic. Using oral glucose tolerance test 90% of thalassemic patients had normal glucose tolerance test followed by 6.5% of thalassemic patients who had impaired glucose tolerance and only 3.3% of thalassemic patients had Glucose tolerance test in diabetic range. Similar study done by Swati Mohan Gadappa et al at Department of Paediatrics, Smt. Kashibai Navale Medical College and General Hospital, Pune. In their study Found that out of 25 children 16% of thalassemic patients had impaired Glucose Tolerance and 84% of thalassemic patients had normal glucose tolerance. Similar study by Ashraf at Department of pediatrics Hamad Medical Centre Qatar found that out of 16 thalassemic children 25% patients had impaired fasting blood glucose concentration followed by 6.25% thalassemic patient had blood glucose level in diabetic range and 12.5% thalassemic patient had impaired glucose tolerance (IGT) (BG >7.8 and <11.1 mmol L^{-1}). Glucose intolerance in adolescence and diabetes mellitus later in life are also frequent complications mainly due to iron overload, chronic liver disease and genetic predisposition[26]. The effect of iron overload on glucose metabolism is probably due to iron deposition in liver and pancreas causing increased insulin resistance or decreased insulin production leading to glucose intolerance and further diabetes mellitus.

In present study, out of 60 thalassemic patients 93% of thalassemic patients had normal thyroid function followed by 5% patients had subclinical hypothyroidism (normal T4 and high TSH) and only 1.6% thalassemic patients had overt hypothyroidism (high TSH and low T4). Similar study done by Rahul Government Medical College, Surat, Gujarat found that Thyroid function as indicated by the level of thyroid hormones was impaired in 10 out of 100 patients (10%) all 10 patients (10%) had subclinical hypothyroidism (normal T4 with high TSH), no case of secondary hypothyroidism (high TSH, T4) was found. Similar study done by Farideh Jahrom University of Medical Sciences, Jahrom, Iran found that Thyroid hormone level was normal in 106 of 112 total examined patients (94.6%) and only 6 patients (5.4%) suffered from hypothyroidism.

The most common form of thyroid dysfunction seen in thalassemia is primary hypothyroidism. Nonetheless, the frequency of hypothyroidism shows a discrepancy depending on the region, quality of management and treatment protocols. Different studies suggest that thyroid dysfunctions appear with a frequency of 13-60% in thalassemic patients after 10 years of age regardless of difference in the rate of prevalence, largely as in the form of subclinical hypothyroidism[27].

In present study 18% of thalassemic patients had hypocalcemia with mean serum calcium 8.3±0.8 mg dL^{-1}. Similar study done by Salva at Kabir Medical College, Peshawar Pakistan found that frequency of hypocalcemia was 49%. Hyperphosphataemia was associated with 53% of hypocalcemic patients (Hypoparathyroidism was suspected in 26 patients). Mean serum calcium was 8.46±0.94 mg dL^{-1} while mean phosphate level was 5.33±0.77 mg dL^{-1} in the subjects.

Hypocalcemia occurring in β-thalassemia major is attributed to hypoparathyroidism mainly. Low parathyroid hormone levels lead to excessive calcium loss in urine, decrease bone remodeling and decreased intestinal absorption of calcium 15. Hypocalcemia is a common biochemical abnormality which may be asymptomatic in mild cases or present as acute life threatening crisis. Chronic hypocalcemia complications are mainly those of bone disease. In addition, severe hypocalcemia can result in cardiovascular collapse, hypotension which does not respond to fluids and

dysrhythmias. Neurological complications of low serum calcium are acute seizures, tetany, basal ganglia calcification, parkinsonism, hemiballismus and choreoathetosis.

CONCLUSION

Out of 60 patients of thalassemia were enrolled and their demographic hematological profile was taken. The mean age was 10.2 years, 75% were males and 81% were Hindus, 40% belonged to upper lower class.

Most common clinical features were (97%) icterus followed by (90%) pallor, 80% of thalassemia patients had moderate to severe hepatomegaly. Mean height was 105.77±14 cm, Mean Hb was 8.5±0.9 mg dL^{-1}, 67% had severe anemia, Mean MCV level was 73±2 μm^3, Mean MCH and MCHC level were 20±2 pg $cell^{-1}$, 28±2 gHb dL^{-1}.

Mean ferritin level was 1281.8±219.9 ng dL^{-1}, 45% of thalassemic patients had serum ferritin level between 1000-2000 ng dL^{-1} followed by 39% of patients had serum ferritin level more than 2500 ng mg dL^{-1}, Mean frequency of blood transfusion 16±2 times a year, 55% of had blood transfusion 5-10 times a year followed by 33% had frequency of blood transfusion 10-15 times a year and only 12% had frequency more than 15 times a year, Mean interval between transfusion 22±2 days, 73% had an interval of 15-25 days between two transfusion, 86% had euglycemia and 10% had hyperglycemia when blood sugar was tested randomly.

About 90% of thalassemic patients had normal glucose tolerance test followed by 6.5% of thalassemic patients had impaired glucose tolerance test, while 3.3% patients came under diabetic range.

About 81% of thalassemic patients had normal serum calcium level while 18% had hypocalcemia, 93% of thalassemic patients had normal serum T4 and TSH level, 1.6% of patients had subclinical hypothyroidism and only 4% of thalassemic patients had overt hypothyroidism.

Tablet deferasirox was taken as chelating agent in all thalassemia patients, 51% of which were taking it after 2 years of age, 35% were had started between 1-2 years of age and only 13% started below 1 year of age.

The common adverse reaction in thalassemic patients were diarrhea (26.1%), abdominal pain (23%), skin rash (20%), seizures (16%), blurring of vision (3%). Hepatitis C virus infection was found in 76% and hepatitis B surface antigen (HBsAg) was positive in 48% of thalassemia patients.

Two patients (4%) out of 60 thalassemic patients had decreased left ventricular ejection fraction of 35-40%.

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