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Original Research Article

Study of thalassemia in pediatrics population

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ABSTRACT

Background: Thalassemia is an inherited disorder of AR gene caused by impaired synthesis of one or more globin chains. Study aimed to study of thalassemia in pediatrics population.
Methods: This observational prospective Study done in GMC Shahdol from January 2020 to January 2023 in 60 patients. Children with thalassemia, ≥6 months age and children on regular blood transfusion with or without iron chelation therapy are included and Children with other causes of anemia like nutritional anemia, aplastic anemia, SCA were excluded.
Results: The mean age was 10.2 years, 75% were males. MC clinical features were (97%) icterus followed by (90%) pallor, 80% had moderate to severe hepatomegaly. Mean Hb was 8.5±0.9 gm/dl, 67% had severe anemia, mean MCV level was 73±2 μm^3, Mean MCH and MCHC level were 20±2 pg/cell and 28±2 ghb/dl. Mean ferritin level was 1281.8±219.9 ng/dl, 39% had more than 2500 ng/dl, mean frequency of blood transfusion 16±2 times a year, mean interval between transfusion 22 ±2 days, 10% had hyperglycemia. The 6.5% had impaired GTT, while 3.3% patient's diabetic range. 18% had hypocalcemia, 1.6% had subclinical hypothyroidism and only 4% had overt hypothyroidism. Tablet deferasirox chelating agent in all thalassemia patients. The common adverse reaction was diarrhea (26.1%), abdominal pain (23%), skin rash. Hepatitis C virus infection in 76% and hepatitis B in 48%. Two patients (4%) had decreased LVEF of 35 to 40%.
Conclusions: This study done to evaluate the thalassemic pediatrics patients in whole aspects, which is very important to know about this.

Keywords: Thalassemia, Deferasirox, Chelating agent, Blood transfusion

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 is caused by mutations that decrease Hb 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.

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]

It was first recognized clinically in 1925 by Dr. Causas Cooley, 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).[1]

In people with beta thalassemia, low levels of Hb 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. 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.[2]

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.[3]

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.[3]

Overtime, an influx of iron-containing Hb from chronic blood transfusions can lead to a buildup of iron in the body, resulting in liver, heart, and hormone problems.

Aims and objectives

Aim and objectives were clinical profile, complication and outcome in a thalassemia major child before and after management.

METHODS

Study design

It was an observational and prospective study.

Study duration

Study conducted from January 2020 to January 2023

Study setting

Study carried out at Birsa Munda government medical college, Shahdol, MP.

Inclusion criteria

Children with diagnosis of thalassemia, age group 6 months and above and thalassemia children who are on regular blood transfusion with or without iron chelation therapy were included in study.

Exclusion criteria

Children with other causes of anemia like nutritional anemia, aplastic anemia, sickle cell anemia were excluded.

Sample size was 60

Sample size calculation

To calculate sample size, it was assumed that 50% of patients of thalassemia will have at least one known complication 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.

Ethical approval taken from institutional ethical board

Statistical analysis

The data was entered in Epidata entry (version 3.1) and then transferred to Stata 10.0 (Stata Corp. College station, Texas, 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

In this study 50% of thalassemic patients belonged to 5-10 years of age, 28% of patients belonged to 6 months-5 yrs and 22% belonged to >10 years of age. The 75% of thalassemic patients were males and 25% were females. Male to female ratio 4/1.

Mostly, patients presented with 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%) (Table 1) 50% of thalassemia patients were presented with severe hepatosplenomegaly followed by 30% patients with moderate hepatosplenomegaly and only 20% patients with mild hepatosplenomegaly.

Table 1: Distribution of thalassemia patients according to clinical features.

Clinical features	N (%)
Icterus	58 (97)
Pallor	54 (90)
Facial changes	47 (79)
Loss of appetite	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)

The 67% of thalassemic patient presented with severe anemia and 33% of thalassemic patients with moderate anemia. Mean Hb level:8.2±2 gm/dl. 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. 66% of thalassemic patients had severe hypochromic RBCs and 24% had moderate hypochromia. Mean MCH level: 23±2 pg/cell. 95% of thalassemic patients had severe hypochromic blood and 5% had normal hypochromia. Mean MCHC level: 28±2 gm/dl.

The 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 (Table 2).

Table 2: Distribution of thalassemia patients according to serum ferritin levels (n=60).

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

The 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 (Figure 1). 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.

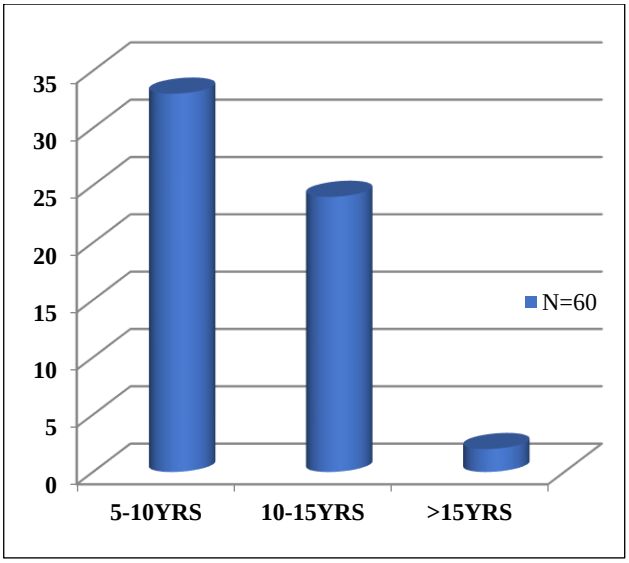

Figure 1: Frequency of blood transfusion in year.

The 10% 0f thalassemic patients were presented with hyperglycemia, 4% of thalassemic patients with hypoglycemia and 86% of patients were euglycemia. The 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. 18% of thalassemic patients had hypocalcemia and mean serum calcium level: 8.20±2 mg/dl.

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 3). The 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 3: Distribution of thalassemia patients according to serum thyroid levels (n=60).

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

Most common adverse drug reaction found was Diarrhea (26%), followed by abdominal pain (23%) skin rash (20%) seizure (16%) and in only 3% of patients blurring of vision was found (Figure 2). In this study 76% of thalassemia patients had hepatitis c virus infection and 52% of thalassemic patients had hepatitis B virus infection. 4% of thalassemia patients were had decreased left ventricular ejection fraction (LVEF).

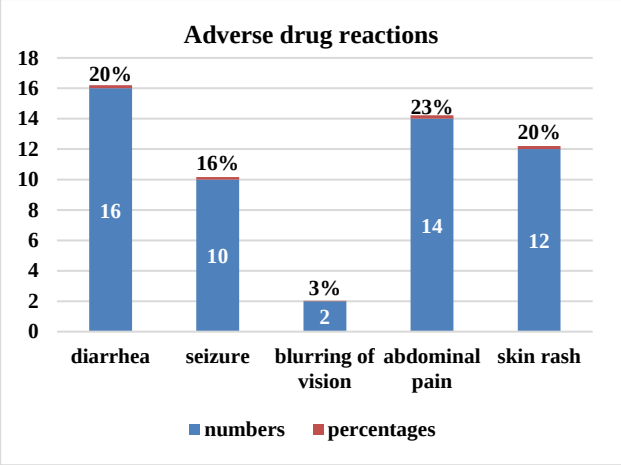

Figure 2: Adverse drug reaction.

DISCUSSION

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 in Iran done on 50 Thalassemia major children out of which 66% were (n=33) were males and 34% (n=17) were females. In Present study group comprised of patients ranging between 6 months to 18 years with a mean age of 10.20±3 years.

Mean heamoglobin in present study was 6.244 (±1.66) gm/dl which is much lower than most of studies done. In study by Keikhaei et al at Ahwaz Jondishpour university of medical sciences, Ahwaz, Iran mean Hb was (8.5±0.9) gm/dl.[5]

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 Chattopadhyay et al at N. R. S. medical college, Kolkata found that hepatomegaly was the most common presenting complaint among 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%).

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 Kumar et al 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%).[6]

In present study 67% of thalassemic patient presented with severe anemia and 33% of thalassemic patients with moderate anemia. The 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. 65% of thalassemic patients had severe microcytic RBCs and only 35% 0f thalassemic patients had moderate microcytic RBCs, mean MCV value was 73±2 μm^3. The 95% of thalassemic patients had severe hypochromic anemia and mean MCHC value was 28±2 gHb/dl.

In present study 55% of thalassemia patients had frequency of blood transfusion 5-10 times per year followed by 33% 10-15 times per year and only 12% patients more than 15 times per year. Similar study done by Shah et al 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.[7]

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 Shah et al 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.

In present study 49% of thalassemic patients had ferritin levels between 1000-2500 ng/ml followed by 39% of thalassemic patients more than 2500 level ng/ml and only 12% of thalassemic patients had ferritin level less than 1000 ng/ml.

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 Thako et al 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 thalassemic 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.[8]

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. 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.

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 Thako et al 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%).[8]

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/caretakers 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 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 Gadappa et al at department of paediatrics, Smt. Kashibai Navale medical college and general hospital, Pune.[9] 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.

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. 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 lowT4). Similar study done by Farideh Mogharab et al 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.[10]

In present study 18% of thalassemic patients had hypocalcemia with mean serum calcium 8.3±0.8 mg/dl. Similar study done by Shah et al at Kabir medical college, Peshawar-Pakistan found that frequency of hypocalcemia was 49%.[11] Hyperphosphatasemia was associated with 53% of hypocalcemic patients (Hypoparathyroidism was suspected in 26 patients). Mean serum calcium was 8.46±0.94 mg/dl while mean phosphate level was 5.33±0.77 mg/dl 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.

In present study, n=46 (76%) of thalassemia patients had hepatitis C virus infection and n= 29(48%) of thalassemic patients had hepatitis B virus infection**.**

In my study, 4% of thalassemic patients on echocardiography had decreased LVEF and 86% patients of thalassemia had normal ejection fraction (≥60%). Similar study done by Chate et al at department of pediatrics, LTMMC and GH, Sion, Mumbai, Maharashtra found that out of 32 thalassemic patients LVEF on 2-D echocardiography was ≥60% in all the 32 patients.

Limitations

This study is limited due to small sample size and single center study. Due to lack of funding and men power this is limited duration of study.

CONCLUSION

In this study we found that male patients are more thalassemic than female. Icterus, pallor and hepatomegaly are the most common sign and symptoms. Anemia is mostly severe type and mean Hb was 8.5±0.9 gm/dl ranges. Mean MCV level, mean MCH and MCHC level were significantly decreased. Around 39% of patients had serum ferritin level more than 2500 ng/dl, more than half of the patients had blood transfusion 5-10 times a year, mean interval between transfusion 22±2 days ,73% had an interval of 15 to 25 days between two transfusion. 10% patients had hyperglycemic, 6.5% of thalassemic patients had impaired glucose tolerance test, while 3.3 % patients came under diabetic range. 18% had hypocalcemia, 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. The common adverse reaction was diarrhea, abdominal pain, skin rash, seizures, blurring of vision. Hepatitis C virus infection was found in ¾ patients

and hepatitis B surface antigen (HBsAg) was positive in half of the thalassemia patients.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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