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Original Research Article

Splenomegaly and Cholelithiasis in Patients with Thalassemia Major and Thalassemia Intermedia

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Abstract:

Background: Thalassemias are inherited blood disorders, characterized by ineffective erythropoiesis. Incidence of thalassemia syndromes is high in South Asia including India. These patients can be clinically divided into transfusion dependent or non-transfusion dependent. Prevalence of Cholelithiasis and Splenomegaly and their predisposing factors in thalassemia syndromes were being assessed in the present study.

Study design: Cross-sectional observational.

Aim/Objectives: To measure volume of spleen and study prevalence of splenomegaly and cholelithiasis in patients with transfusion-dependent thalassemia major or thalassemia intermedia and factors affecting them.

Methods/ Materials: This study was conducted in the Post Graduate Department of Radio-diagnosis, Government Medical College, Jammu over a period of six months. 100 patients were included and investigated with ultrasonography for gallstones and measurement of splenic volume.

Results: 32 females and 68 males (mean age of 12.6 years) were participants in the study. Mean splenic dimensions were 14.1±6x11.1±4.3x6.2±3.2cms (Length x Width x Height) with mean volume of 507.5±57.6 cm^3. Larger splenic volume was associated with higher mean age, increased frequency of blood transfusion and lower hemoglobin levels. Cholelithiasis was observed in 2%.

Conclusion: Splenomegaly and hypersplenism are common complications in thalassemia, hence routine evaluation for splenic size and volume can predict changes in transfusional requirements. Cholelithiasis is now relatively an uncommon complication among thalassemia patients with more frequent association with older age, large volume blood transfusion and splenectomy, therefore, imaging is usually recommended especially in later age.

Keywords: Thalassemia, Splenomegaly, Cholelithiasis, Blood Transfusion.

Introduction

Hemoglobinopathies are the commonest genetic disorders worldwide. 7% of world population is believed to carry an abnormal haemoglobin gene [1]. About 3 to 5 lakhs babies are born annually with significant haemoglobin disorders [2]. These consist of two major groups- thalassemias and sickle cell syndromes.

Thalassemias are characterised by ineffective erythropoiesis resulting from decreased or absent globin chain production arising from deactivating mutations or deletions in alpha or beta globin genes. Incidence of thalassemia syndromes is high in South Asian countries including India. In fact, India has the largest paediatric population with thalassemia major in the world i.e. 10% of the total thalassemia burden with 10-15000 affected babies born every year [3].

Thalassemia is classified into three main phenotypic categories:

Thalassemia minor or trait,

Thalassemia intermediate (TI)

Thalassemia major (TM)

Among these, TI and TM constitute major burden of disease with requirement of therapeutic interventions particularly lifelong blood transfusions and iron chelation. Based on clinical severity, thalassaemia can be divided into –

Transfusion dependent thalassaemia (TDT)

Non-transfusion dependent thalassaemia (NTDT)

Non-transfusion dependent thalassaemia relatively presents at a later age with a milder spectrum of clinical findings.

Aims / Objectives

The aim of the study was to measure volume of spleen and study prevalence of splenomegaly and cholelithiasis in patients with transfusion-dependent thalassemia major or thalassemia intermedia with an attempt to determine factors affecting these findings.

Methods / Materials

The current study was performed in the Department of Radiodiagnosis, Government Medical College, Jammu. Study design was cross-sectional observational with 100 subjects.

Inclusion Criteria: Diagnosed patients of thalassemia major or intermedia undergoing blood transfusions, registered under the thalassemia unit.

Exclusion Criteria: Post splenectomy and cholecystectomy status.

Prior informed consent was taken from the patient or their attendant. Demographic and clinical information was obtained from medical histories. Abdominal ultrasound was performed using the ultrasonography machine (Mindray DC-70 Exp) with low frequency curvilinear probe.

Longitudinal and transverse planes of gallbladder were evaluated to assess for calculus with adequate fasting.

Spleen was scanned during suspended deep inspiration with patient in supine and/or right posterior oblique position.

Splenic length (A) was measured in longitudinal plane as maximum distance b/w most superomedial and inferolateral points. Splenic width (B) and Splenic thickness/depth (C) were measured in transverse plane as maximum antero-posterior and medio-lateral distance respectively (Figure 1). Splenic volume: length x width x depth x 0.523 (cm^3) [4].

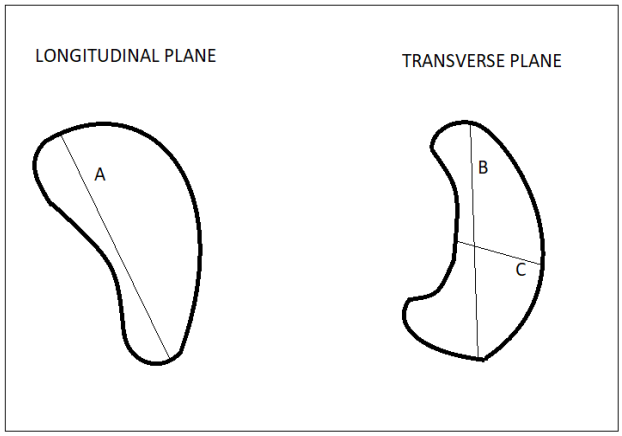


Figure 1: Measurements of spleen.

Results

The study participants included 68 Males and 32 Females. Thalassemia major patients were 94 in number (28 females and 66 males) and Thalassemia intermedia patients were 6 (4 females and 2 males). Majority (45 in number) of patients were below the age of 10 years (Figure 2A).

Range of age for males was 4 to 31years with mean age of 13.2 ±7.1 years. Age of females ranged from 4 to 30 years with mean age of 12.1 ±6.2 years. Age of diagnosis/age at first blood transfusion was between 6 to 18 months for all the patients.

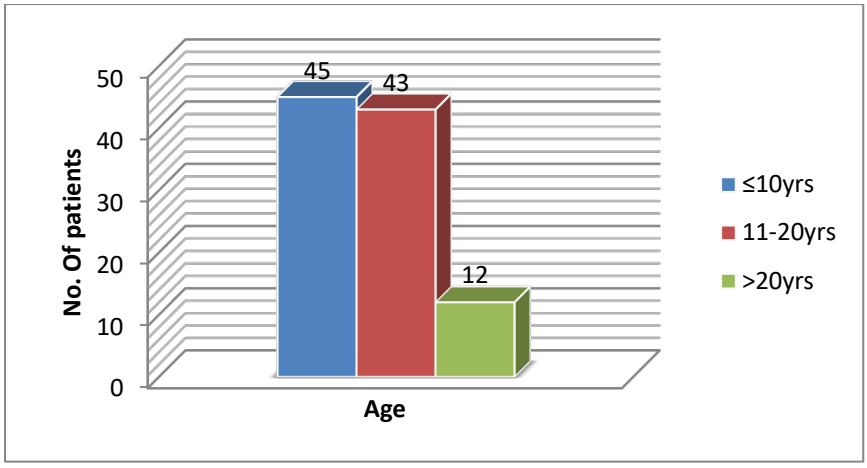
Amount of blood transfused per transfusion was 10ml/kg body weight (packed RBCs). Frequency of blood transfusion was twice a month for majority (86) of thalassemia major patients. 3 patients were receiving blood transfusion once a month, 4 patients thrice a month and one patient recently received four transfusions in a month. Thalassemia intermedia patients (6) were subjected to variable and lesser frequency of transfusion ranging from once a month to once in 2 to 3 months.

Hemoglobin levels ranged from 5.6 to 13 g/dl with mean of 8.5±0.86 g/dl (Figure 2C). Normal Hb levels were observed only in 19% using reference values for different age groups (Newborn: 14-24 g/dL; 0-2 weeks: 12-20 g/dL; 2-6 months: 10-17 g/dL; 6 months-1 year: 9.5-14 g/dL; 1-6 years: 9.5-14 g/dL; 6-18 years: 10-15.5 g/dL; Adult men: 14-18 g/dL; Adult women: 12-16 g/dL) [5].

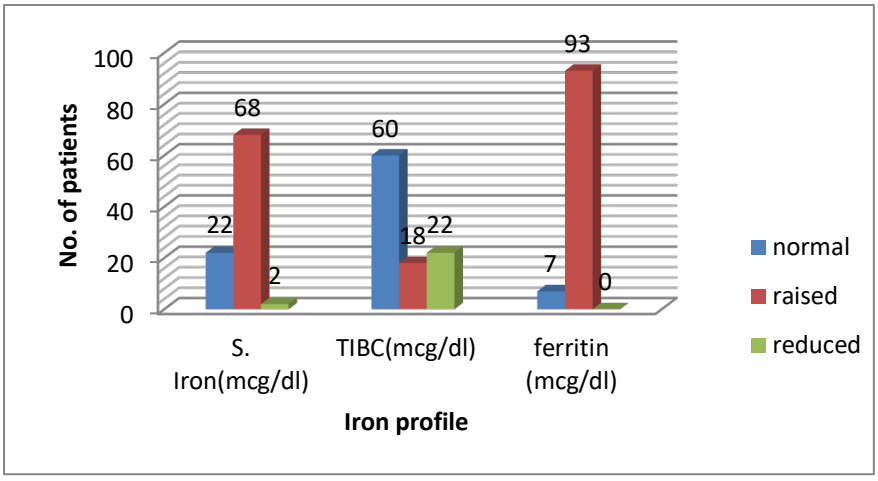
Mean Serum iron and ferritin levels were raised measuring 234.6 µg/dl (range: 51 to 662 µg/dl) and 4040.48±1453 µg/ml (range: 129-5354µg/dl) respectively. Mean total iron binding capacity (TIBC) was normal m/s 390.5 µl/dl (range: 135 to 1826 µl/dl) (Figure 2B) (Reference values: S

iron:60-170mcg/dl; TIBC:240 to 450 mcg/dl; S ferritin: Males:324-336 Females:11-307 mcg/dl) [6].

Iron chelators (deferasirox or deferiprone) were being administered to all the patients with variable frequency and duration.



A



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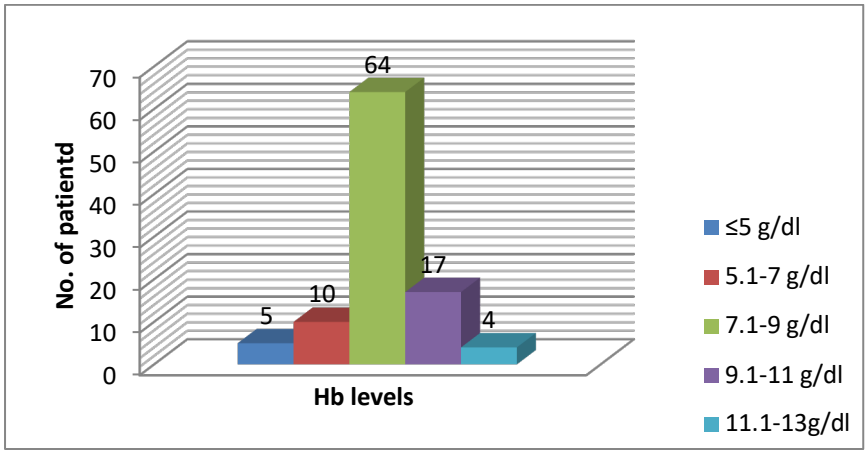


C

Figure 2: Age distribution (A); Iron profile (B) and Haemoglobin levels (C) in study group of Thalassemia patients.

Mean splenic dimensions measured were: Length- 14.1±6 cms (range: 6.1 to 27 cms); Width-11.1±4.3 cms (range: 6.5 to 15 cms) and Thickness- 6.2±3.2 cms (range: 3.5 to 13 cms) with mean splenic volume of 507.5±57.6 cm^3. According to reference splenic size/volume [7] for variable ages of the patients, splenomegaly was observed in 82% of the patients with massive splenomegaly in 14.7 % of these (Figure 3).

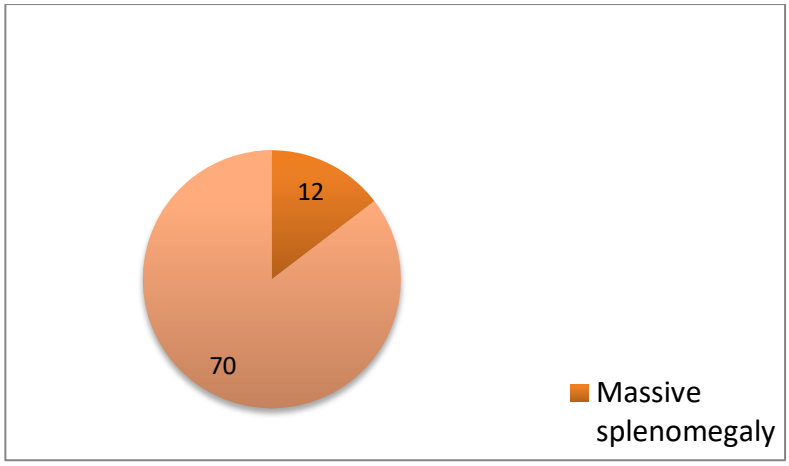


Figure 3: Massive splenomegaly among study group of thalassemia patients with splenomegaly.

Cholelithiasis was observed in 2% of patients (thalassemia major). Multiple small calculi were noted with diameter measuring 5-7 mm (Figure 5). All patients with cholelithiasis were above 20 years of age with higher frequency (thrice a month) of blood transfusion.

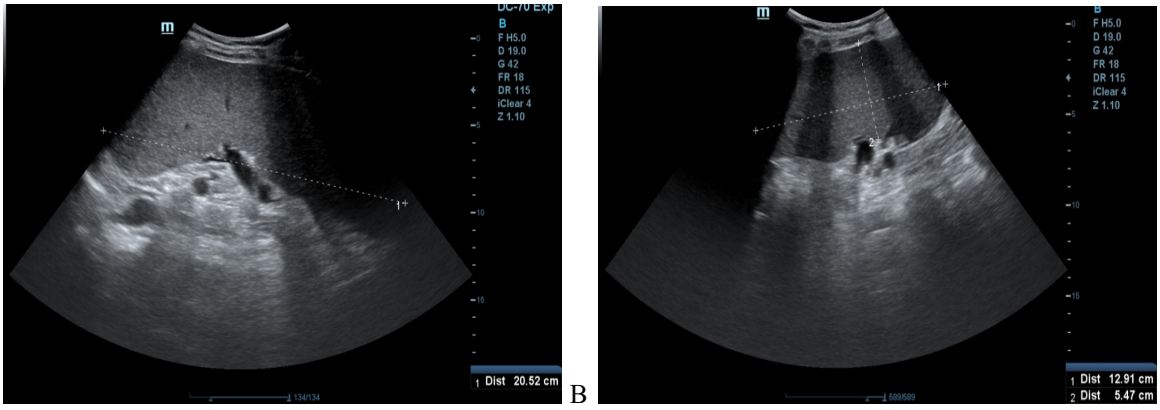


Figure 4: Splenomegaly. Longitudinal plane (A) and transverse plane (B).

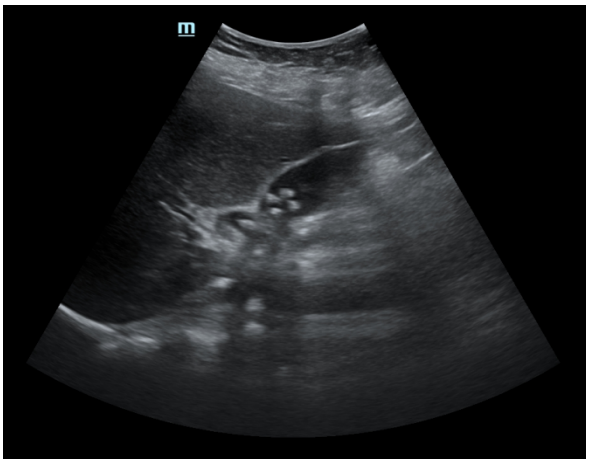
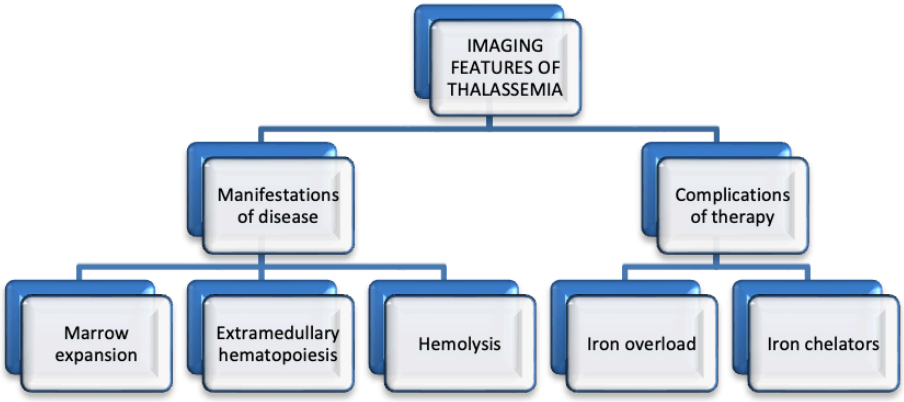


Figure 5: Cholelithiasis; Multiple small intraluminal calculi in gall bladder

Discussion

Thalassemia is usually diagnosed early in life. It should be suspected in a child with microcytic anaemia if the history or laboratory findings are inconsistent with iron deficiency. Patients are generally asymptomatic till 6 months of age due to presence of HbF at birth and subsequent predominance of HbA around 6 months.

The Mentzer index (mean corpuscular volume/red blood cell count) of less than 13 suggests thalassemia and more than 13 suggests iron deficiency [8]. Haemoglobin electrophoresis is diagnostic [9].



General osseous manifestations include diffuse osteoporosis, medullary space expansion and thinning of cortical bone [10]. Initial trabecular thinning occurs with subsequent coarsening. Growth retardation and skeletal deformity occur more frequently in transfusion dependent thalassemia.

Extramedullay Haematopoiesis (EMH) may be classified as paraosseous or extraosseous. Extraosseous EMH most commonly affect the liver and spleen, resulting in hepatosplenomegaly or pseudotumours. EMH can also occur in- Lymphnodes, kidneys, CNS, adrenals, mesentery, paratracheal region, thymus, heart, breasts, prostate, and broad ligaments.

Iron overload occurs secondary to repeated transfusions and increased intestinal absorption and includes: parenchymal deposition in liver, reticuloendothelial- liver, spleen, Renal or mixed.

Desferrioxamine toxicity leads to rickets-like features [11]. Deferiprone toxicity produces subchondral bone flattening and thickened articular synovium/cartilage [12].

Splenomegaly is a long known common finding in thalassemia major as well as intermedia due to the high rate of hemolysis (red blood cell destruction). The hyperactivity of the spleen results in splenomegaly. The enlarged spleen is often accompanied by an enlarged liver. Splenomegaly may also increase rejection in low risk matched related donor bone marrow transplant for thalassemia [13] .

In our study the volume of the spleen was significantly larger (507.5±57.6 cm^3) as opposed to normal (80.29 +/- 25.88) [14]. Clinically, spleen was palpable in 18% of patients. Relative larger splenic volumes were found in patients who were inconsistent with recommended transfusion frequency and iron chelation. Hb levels were relatively lower in these patients. Strict transfusion and chelation protocols are practiced to control the disease. Splenectomy is considered beneficial for children with thalassemia and hypersplenism because it reduces their transfusion requirements and subsequent iron overload and improves Hb levels [15].

Thalassemia patients are susceptible to cholelithiasis due to hemolysis and ineffective erythropoiesis. Cholesterol is the major constituent of gallstones. Splenectomy, advancing age and larger volume blood transfusion represent risk factors for cholelithiasis [16]. Despite the milder clinical severity and lower frequency of transfusions, ratio of cholelithiasis has been higher in thalassemia intermedia patients than thalassemia major [17], however, In our study none of the thalassemia intermedia patients demonstrated cholelithiasis while 2 thalassemia major patients (both females aged> 20 years) were diagnosed with the same. Higher mean blood transfusion volume (15ml/kg) and relatively higher pre-transfusion Hb levels (>9g/dl) were noted in these patients with cholelithiasis.

Conclusion

Thalassemia presents with spectrum of multimodality imaging findings in both treated and undertreated thalassemia disorders. Splenomegaly is a common finding which can be controlled with strict transfusion and chelation protocols, hence routine evaluation for splenic size and volume can predict changes in transfusional requirements. Although there is potential reduction in transfusional iron loading after splenectomy, this must be weighed against long-term consequence of asplenia. Cholelithiasis are now relatively uncommon and risk factors include older age, larger volume of blood transfusion and post-splenectomy, therefore, imaging is usually recommended especially in older patients. If a thalassemia patient is proceeding to splenectomy, concomitant cholecystectomy can be considered.

Abnormalities secondary to iron chelation are also now more commonly observed. Chelation regimes should be adjusted periodically to avoid

underchelation leading to increased iron toxicity or overchelation with increased chelator toxicity.

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