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Cardiovascular Evaluation before and after Splenectomy in Children with β Thalassemia

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Cardiac complications represent the leading cause of mortality and morbidity in β thalassemia, with iron overload and high output state being the main precipitating factors. Splenectomy is used in the management of β thalassemia, and its impact on cardiovascular function is an area of controversy with a paucity of data.

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Objective of the Study: To evaluate the effect of splenectomy on cardiovascular function in β thalassemia.
Methodology: This proposed longitudinal observational study was carried out in the Department of Paediatric Surgery in MMCH from January 2017 to April 2018. Patients consent and permission were sought from the medical director to carry out the study on 20 β thalassemia patients who were candidates for splenectomy. Pre- and post-operation changes in hematological and echocardiographic characteristics were apparent using SPSS version 20.
Results: The mean age was of the patients at splenectomy was 8.18±2.59 years. Among the 20 cases 12 (60.00%) were male and 8 (40.00%) were female with the ratio 1.5:1, male predominant. All patients were transfusion dependent thalassemia among them maximum 16 (80%) was severe Hb E/β thalassemia and 4 (20%) was β thalassemia major. Major indication of splenectomy 14(70%) was increased requirement of blood transfusion. Mean 6-monthly pretransfusion hemoglobin was significantly increased after splenectomy from 4.19±0.92 to 8.66±0.73 g/dl ($p<0.001$). Postoperatively, the 6-monthly transfusion requirements were significantly reduced from 14.30±3.18 to 2.15±1.46 units ($p<0.001$), while blood transfusions were discontinued in 4 patients (20%). The mean serum ferritin was not significantly different after surgery ($p>0.05$). All 20 patients were in a high output state, with mean cardiac output being 5.85±1.72 L/min in patients versus 3.6±1.03 L/min in controls ($p<0.001$). Postoperatively, cardiac output was significantly reduced from 5.85±1.72 L/min to 4.99±1.64 L/min ($p<0.05$). Other parameters were not significantly different after surgery ($p>0.05$). Before splenectomy 3(15%) patient clinically developed Heart failure and after splenectomy out of 3 heart failure patients 1(5%) have features of restrictive cardiomyopathy in echocardiogram and 2(10%) have normal findings except high cardiac output.
Conclusion: Splenectomy stabilizes the hemoglobin concentration at higher levels and reduces transfusion needs, reduces high cardiac output and prevent high output failure. Though other cardiac parameters remain unchanged within the first 6 months after splenectomy, it can be assumed that removal of the spleen may contribute to the prevention of further cardiac damage.

Keywords: β thalassemia; splenectomy; cardiovascular; paediatric.

1. INTRODUCTION

Thalassemia is the most common hereditary disorder in the world including Bangladesh [1]. According to WHO reports, approximately 3% of populations are carriers of β thalassemia and 4% are carriers of HbE/β thalassemia in Bangladesh [2]. The basic defect in β thalassaemia is a reduced or absent production of β globin chains with relative excess of α-chains [3]. Free α chains in excess form insoluble precipitates within red cells and their progenitors – erythroblasts in BM are destroyed prematurely (ineffective erythropoiesis); mature red cells in spleen are lysed (hemolysis) [4]. To compensate for the reduced hemoglobin, the synthesis of gamma chains persists after fetal life even beyond 6 months of age. The normal switch mechanism leading to reduction in γ-chain synthesis does not occur and leads to higher fetal hemoglobin $\alpha_2\gamma_2$ (HbF) in postnatal life [5]. Recent advancements in therapeutic options such as transfusion, iron chelation and bone marrow transplantation have brought significant improvement in prognosis for individuals with β thalassemia in the last 20 years. Nevertheless, cardiac disease remains the leading cause of mortality in patients with organ iron deposition [6]. Enlargement of spleen is due to both extra medullary haematopoisis and entrapment of abnormal shape RBC's, excessive destruction of abnormal RBCs & transfusional overload. Splenomegaly further increases transfusional requirement. So, these patients benefit from splenectomy. Splenectomy is indicated when blood transfusion exceed 250ml/kg/year, hypersplenism, abdominal discomfort due to massive splenomegaly and splenic injury [7]. Various studies showed benefits of splenectomy in β thalassemia. [8] reported splenectomy improved the quality of life in form of school going, sports and decreased in abdominal discomfort. Patient's health improved after splenectomy because of improvement in haemoglobin level and decrease in blood transfusion requirement. Effect of splenectomy on iron balance is controversial [9] in his study concluded that Splenectomy improves anemia, but does not reduce iron burden. All guidelines agree that physicians should adopt a guarded approach and restrict splenectomy to certain indications, in view of the observation of an increased risk of venous thrombosis and pulmonary hypertension, alongside overwhelming infections after splenectomy. Splenomegaly due to periods of under-

transfusion with blood of inappropriately low haemoglobin may be reversible [10]. The long term use of hyper transfusion therapy has made a sea change in the lives of these patients over the last 2-3 decades. However, there has been an observed rise in the occurrence of complications of this therapy due to iron toxicity [11]. Iron overload in thalassemia sufferers especially those treated with multiple blood transfusions can overwhelm the ferritin storage and detoxification capacity. As a result, the process of chelation leads to "free" iron deposition in tissues and blood [12]. Most of the complications of β thalassemia are attributable to iron overload. Complications of iron overload in children include growth retardation and failure or delay of sexual maturation. Later iron overload related complications include involvement of the heart, liver and endocrine glands [13]. Heart complications remain the major cause of mortality in β thalassemia major. The combination of iron mediated toxicity with increased cardiac output is associated with development of heart failure [14]. In heart, the iron leads to impaired function of the mitochondrial respiratory chain, which is clinically manifested by the reduction of cardiac contractility, progressive systolic dysfunction, and development of heart failure [15]. Chronic anemia is responsible for an increase in cardiac output, results from decreased systemic vascular resistance due to decreased blood viscosity and vasodilatation [16]. In several studies, diastolic ventricular dysfunction demonstrated in these patients preceded the onset of systolic impairment [17]. Regular assessment of cardiac function may help to improve the quality of life of these patients and may reduce the morbidity and mortality to a great extent Echocardiography is a non-invasive technique that evaluates cardiac anatomy and function with images and recordings produced by sound energy [13]. Even after significant toxic effects on heart muscle have prevailed, aggressive iron chelation can restore myocardial function to normality [18]. Therefore, regular assessment of iron status is essential for the efficient management of iron overload in β thalassemia patients. Serum ferritin is simple, inexpensive and available method for evaluating iron in thalassemia patients and ferritin is generally associated with the amount of stored iron in the body [19]. This study was conducted in the Department of Paediatric Surgery, Mymensingh Medical College and Hospital from January, 2017 to April, 2018 to evaluate cardiovascular function before and after splenectomy in β thalassemic patient in terms of haematological profile and echocardiographic evaluation of left ventricular function.

The aim of this study was to detect effect of splenectomy on cardiovascular function. This study will certainly serve baseline information for clinicians and other research workers about cardiovascular changes in β thalassemia due to iron overload and increased cardiac output before and after splenectomy, all of which can be easily follow up by echocardiogram and serum ferritin level. As echocardiography is easily available and can detect early cardiac involvement and it be can reverse with adequate iron chelation therapy, after splenectomy the thalassemic patient can be managed properly by regular follow up of iron status by serum ferritin and cardiac status by echocardiogram which will improve life expectancy of these patients.

2. MATERIALS AND METHODS

This study was Longitudinal type of descriptive observational study. Purposive type of non-probability sampling technique was followed for selection of cases. A total number of 20 patients, admitted in department of Paediatric Surgery in Mymensingh Medical College & Hospital, through the outpatient department who fulfill the inclusion criteria were selected in this study. Type of β thalassemia was recorded from past Hb electrophoresis report, if any patient have missing the report, repeat Hb electrophoresis was done to confirm the diagnosis. Indication of splenectomy was determined by evaluating transfusion requirement, splenomegaly and history of mechanical discomfort, past reports of Peripheral blood film and bone marrow examination was reviewed in patient who was diagnosed by a hematologist as suggestive of hypersplenism. All patients were vaccinated against capsulated organisms and after 14 days of vaccination admitted in department of Paediatric surgery, Mymensingh Medical College Hospital (MMCH). After admission all patients were evaluated thoroughly & do all the relevant investigations including echocardiogram. Simultaneously patients were prepared for splenectomy. Blood transfusion was given to maintain Hb% 8-10gm/dl prior splenectomy for each patient. Among 20 patients, 3 patient was present with heart failure who were managed by correction of anaemia very cautiously with packed red cell and diuretics, frusemide 1-2mg/kg intravenous 12 hourly for 2-3days and then oral frusemide 2-3mg/kg in 2 divided dose for 3-4 days with monitoring of urine output and serum electrolytes. Among the 3 heart failure

patients 1 had serum ferritin level >3000ng/dl, intravenous iron chelation for 5days was given in that patient according to guidelines for management of heart failure in β thalassemia patients. After proper counseling of parents and completion of all preoperative preparations, splenectomy was done under general anesthesia. Operative findings and post operative events were documented. Per operative and post operative periods were uneventful. Patients were discharged at 7th or 8th post operative period with advice of post splenectomy antibiotic prophylaxis and follow up schedule. Then patients were followed up at first 15 days after splenectomy and then 1 month interval up to 6 months. During each follow up patients general condition was evaluated and Hb% was done. Serum ferritin & Echocardiogram were done after 6 months of splenectomy. This study was conducted at the Department of Paediatric Surgery, Mymensingh Medical College, Mymensingh, Bangladesh. At January 2017 - April, 2018.

3. OBJECTIVES

General objectives

- To evaluate the effect of splenectomy on cardiovascular function in β thalassemia.

Specific objectives

- To determine the average age of splenectomy indication in β thalassemia.
- To detect blood transfusion requirement and mean pretransfusion hemoglobin level before & after splenectomy in β thalassemia.
- To detect effects of splenectomy on serum ferritin level.
- To determine the effects of chronic anemia and transfusion iron overload on left ventricular dimensions, systolic & diastolic function and cardiac output.
- To determine the effects of splenectomy on the left ventricular dimensions, systolic & diastolic function and cardiac output.

Inclusion criteria

- β thalassemia with huge splenomegaly causing mechanical discomfort.
- β thalassemia with blood transfusion requirement more than 250 ml/kg/year of packed red cells or more than 400 ml/kg/year of whole blood.
- β thalassemia with hypersplenism.
- Age range: 5-12 years.

Exclusion criteria

- Age <5 year
- β thalassemia with known congenital heart disease & other comorbidities.

Procedure of Data Collection: In each case after obtaining written consent of the parents/ guardians in the consent form information from history, clinical examination was recorded in predesigned data collection sheet. After that all information were gathered systematically and put into the same data collection sheet including all investigation findings, management & follow up findings (Appendix-I).

Statistical analysis: Statistical analysis was performed with statistical package for social sciences (SPSS) version 20.0. Comparisons were performed by chi-square test for categorical variables, paired student's t-test for quantitative variables. P value less than 0.05 were considered statistically significant.

4. RESULTS

This longitudinal type of descriptive observational study was carried out in the Department of Paediatric Surgery, Mymensingh Medical College Hospital during the period of January 2017 to April 2018. Total 20 patients were included in this study among them 12 were male and 8 were female with the ratio of male: female 1.5:1. The age ranges from 5 year to 12 years with the mean age of 8.18±2.59 years. All patients were selected purposively with β thalassemia having indication of splenectomy. All patients were evaluated by hematological profile and echocardiogram parameter. Echocardiographic data were compared before and after splenectomy and preoperative data were compared with control group from other study.

The following observations were noted.

Table 1. Age distribution No of patient (N = 20)

Age (in years)	No. of patients	Percentage
5-6	6	30.0
7-8	6	30.0
9-10	3	15.0
11-12	5	25.0
Total	20	100.00
Mean ± SD		**8.18±2.59**

Table 1 shows maximum patient 6 (30.00%) in age group (5-6) years and 6 (30.00%) in age group (7-6) years. The mean age was 8.18±2.59 years.

Table 2. Sex distribution No of patient (n = 20)

Age in years	Sex			
	Male		Female	
	No	%	No	%
5-6	3	15	3	15
7-8	4	20	2	10
9-10	2	10	1	5
11-12	3	15	2	10
Total	12	60.00	8	40.00

Chi-square test, P=0.937 NS
d.f. 3, χ2 = 0.417
NS = Not significant, p > 0.05

Table 2 Shows among the 20 cases 12 (60.00%) were male and 8 (40.00%) were female. Sex ratio of Male: Female = 1.5: 1 (p>0.05).

Table 3 Shows postoperatively mean 6-monthly pretransfusion hemoglobin level was significantly increased to 8.66±0.73 g/dl from 4.19±0.92 (p<0.001).6-monthly transfusion requirements were significantly reduced postoperatively from 14.30±3.18 to 2.15±1.46 units (p<0.001) and mean serum ferritin levels were not significantly different after surgery (p>0.05).

Table 4 Shows All 20 patients were in a high output state, with mean cardiac output being 5.85±1.72 L/min in patients versus 3.6±1.03 L/min in controls (p<0.001). Other parameters were also significantly higher in patients compared to healthy (p<0.01).

Table 5 Shows cardiac output (5.85±1.72 L/min vs 4.99±1.64 L/min) was significantly reduced after splenectomy (p<0.05) and other parameters were not significantly different after splenectomy (p>0.05).

Table 6 Shows Mean EF (%), E/A ratio, PASP (mm of Hg) were within normal values and difference between before and after splenectomy was not significant (p>0.05).

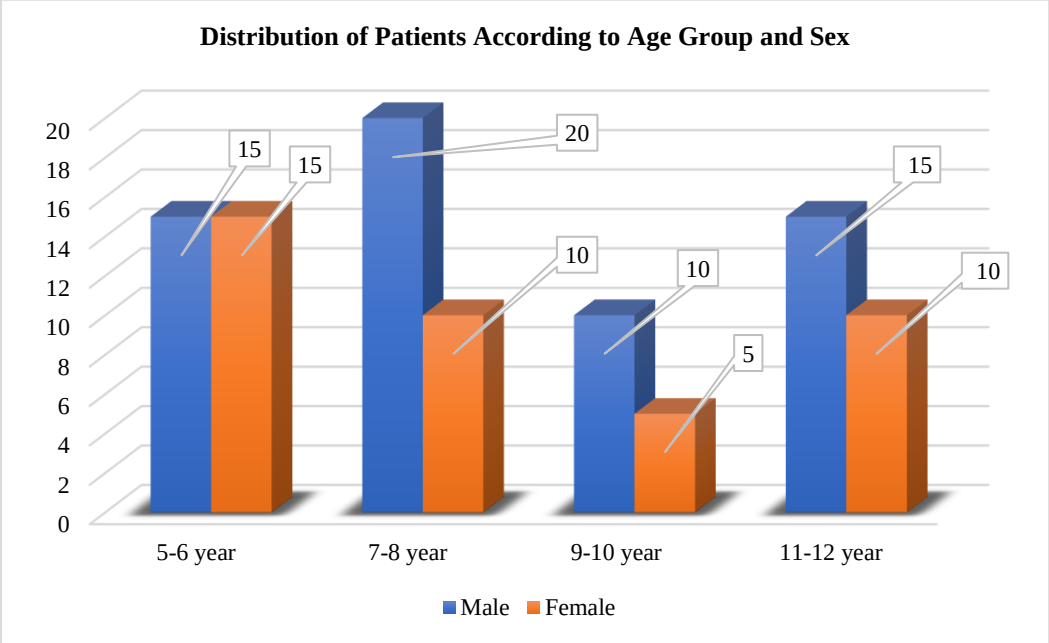


Fig. 1. Column Chat Showed Distribution of Patients According to Age Group and Sex

Table 3. Patient's Hematological profile before and after splenectomy No of patients (n = 20)

	Before splenectomy	After splenectomy	t-value	P value
Mean 6-monthly Pre-transfusion hemoglobin (g/dl) [a]	4.19±0.92	8.66±0.73	23.038	0.000**
6-monthly transfusion requirement (units)	14.30±3.18	2.15±1.46	19.978	0.000**
Serum ferritin (ng/ml)	1346.25±616.40	1722.60±858.96	1.815	0.085[NS]

[a] *Mean values of the last 6 months prior to and the first 6 months after splenectomy Paired Student's 't' test*
*** P< 0.001(Highly significant); NS (Not significant)*

Table 4. Echocardiographic parameters- Preoperative Left ventricular diameters and mass and cardiac output compared with control from other study No of patients (n=20)

	Controls (from other study)	Before splenectomy	t-value	P value
IVSTd (mm)	6.44±1.02	7.82±2.32	2.630	0.012*
IVSTs (mm)	9.84±1.32	11.00±2.13	2.400	0.021*
LVIDd (mm)	33.8±7.4	43.82±8.08	5.523	0.001**
LVIDs (mm)	17.8±5.8	26.23±5.45	6.875	0.000**
LVPWTd (mm)	3.99±0.49	7.84±2.07	8.213	0.000**
LVPWTs (mm)	4.13±0.48	11.61±2.69	12.339	0.000**
LV MASSd (gm)	57.2±12.3	100.30±51.21	3.763	0.001**
CO (L/min)	**3.6±1.03**	**5.85±1.72**	**5.727**	**0.000****

Paired Student's 't' test
*** P< 0.001(highly significant)*

Table 5. Echocardiographic parameters - Left ventricular diameters and mass and cardiac output before and after splenectomy No of patients (n=20)

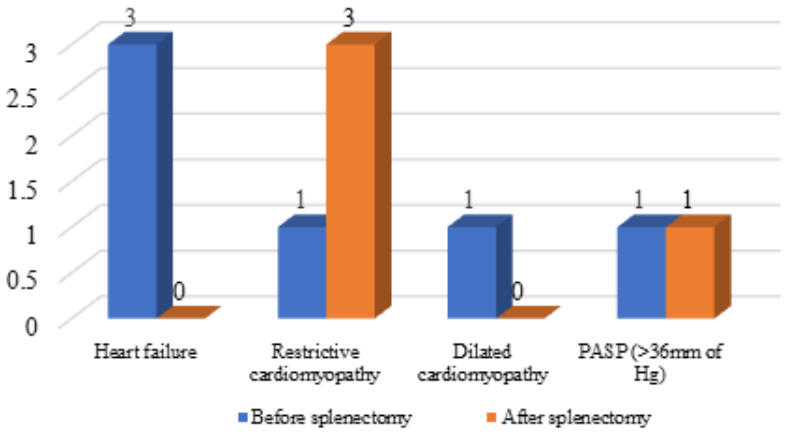
	Before splenectomy	After splenectomy	t-value	P value
IVSTd (mm)	7.82±2.32	11.00±13.78	1.013	0.324^{NS}
IVSTs (mm)	11.00±2.13	11.09±1.81	0.141	0.89^{NS}
LVIDd (mm)	43.82±8.08	43.14±6.45	0.995	0.332^{NS}
LVIDs (mm)	26.23±5.45	24.61±5.90	2.016	0.058^{NS}
LVPWTd (mm)	7.84±2.07	7.50±1.78	0.685	0.502^{NS}
LVPWTs (mm)	11.61±2.69	10.84±1.58	0.984	0.337^{NS}
LV MASSd (gm)	100.30±51.21	89.25±26.44	1.320	0.203^{NS}
CO (L/min)	**5.85±1.72**	**4.99±1.64**	**2.529**	**0.020***

Paired Student's 't' test
*** P< 0.001(highly significant); NS (Not significant)*

Table 6. Echocardiographic parameters - for systolic dysfunction (EF), diastolic dysfunction (E/A ratio) & pulmonary hypertension (PASP) No of patients (n=20)

	Normal values	Before splenectomy	After splenectomy	t-value	P value
EF (%)	>55	68.65±7.71	67.93±6.89	0.553	0.586^{NS}
E/A ratio	1-2	1.59±0.35	1.63±0.39	1.215	0.239^{NS}
PASP (mm of Hg)	≤36	28.40±9.13	29.15±9.30	1.958	0.065^{NS}

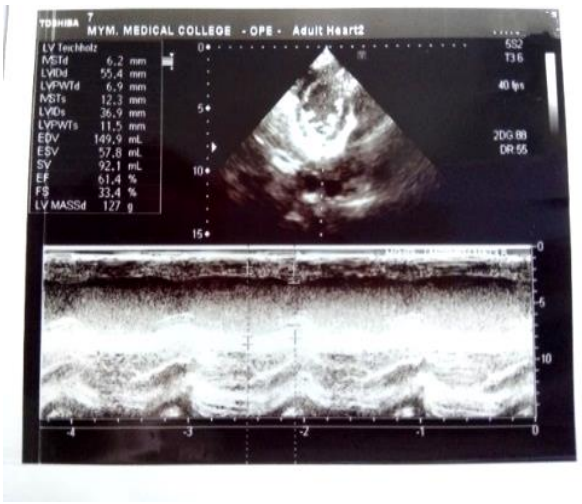
Paired Student's 't' test NS (Not significant)



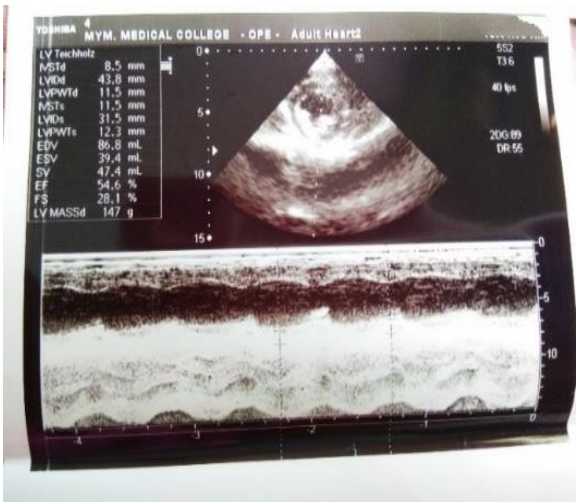
3(15%) Patient clinically developed HF

Restrictive cardiomyopathy was encountered in 3 (15%), remain asymptomatic

Fig. 2. Distribution of cardiac impairment before and after splenectomy (N=20)

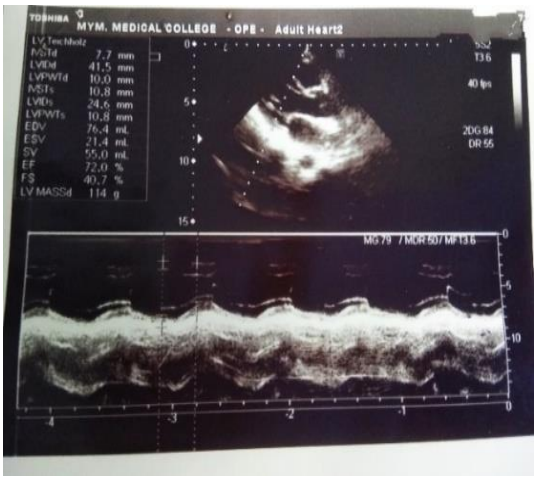


Case-4: Echocardiogram after splenectomy (Stroke volume 47.4 ml/min)

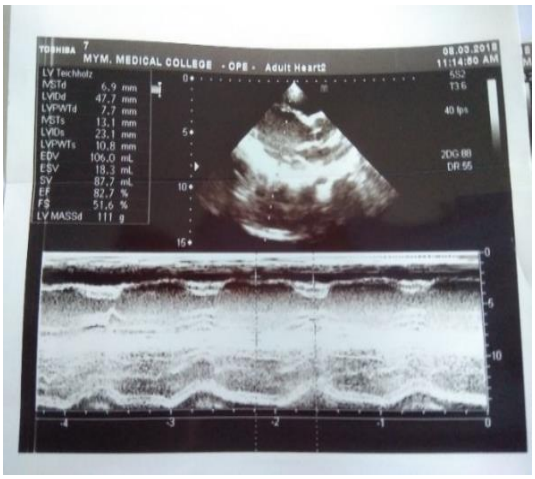


Case-4: Echocardiogram before splenectomy (Stroke volume 92.1ml/min)

Photograph 1. Shows Echocardiogram before and after splenectomy of Case-4

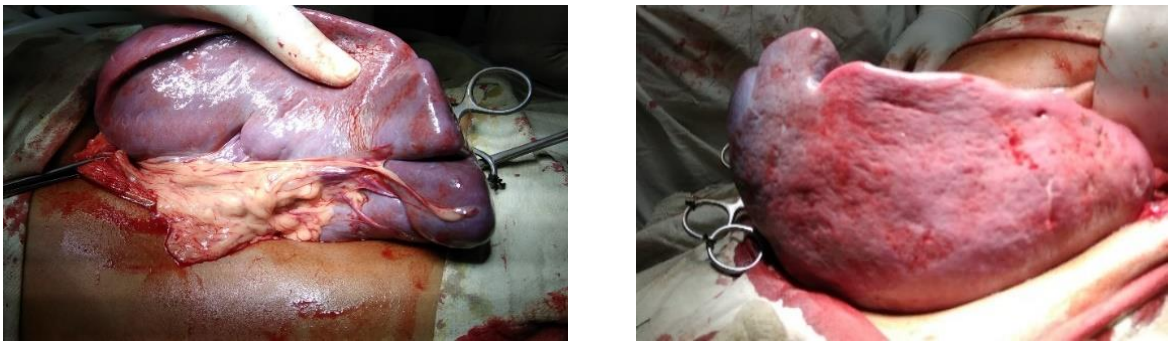


Case-10: Echocardiogram before splenectomy (Stroke volume 87.7ml/min)



Case-10: Echocardiogram after splenectomy (Stroke volume 55.0 ml/min)

Photograph 2. Shows Echocardiogram before and after splenectomy of Case-10



Photograph 3. Per operative picture of spleen (Case-3), (Case-15)

5. DISCUSSION

β thalassemia is the most common inherited haemolytic anaemia presenting with chronic anaemia and its consequences affecting both male and female. In this study among the 20 patients 12 were male and 8 were female with the ratio 1.5:1(p>0.05). Definite male preponderance has been noted by various other authors. Porecha et al., [7] reported male-to-female ratio approximately 7:3, Al-Salem et al., [20] mentioned male to female ratio 10:1, Akhtar et al.,) [8] reported male to female ratio about 6:1. In this study, Age ranges from 5-12 years with the mean of 8.18±2.59 years which is consistent with other study done by Easa, [21] the mean age of patients at splenectomy was 8.75+4.32 years for β thalassemia major patients. Porecha et al., [9], Bhosale et al., [22] and Akhtar et al., [8] also showed mean age at splenectomy was 9 years. Ammar et al., [9] and Al-Salem et al., (2016) [20] reported 6.68 ± 2.54 years and 8 years respectively. All the patient was transfusion dependent β thalassemia among them 16 (80%) were severe HbE/β thalassemia and rest 4(20%) were β thalassemia major which is consistent with study done by Mannan et al., [2] who reported most of the β thalassemia patient in our country is HbE/ β thalassemia. Among the 20 cases major indication of splenectomy was increased requirement of blood transfusion 14 (70%), huge splenomegaly causing mechanical discomfort 5(25%), and hypersplenism 1(5%). Porecha et al., [9] reported the major indication for splenectomy was higher blood transfusion requirement and Akhtar et al., [8] reported major indication of splenectomy were hypersplenism. Various study showed that removal of the spleen improves the hemoglobin concentration and substantially reduces the transfusion needs. Akhtar et al., [8] reported blood transfusion requirements per year were decreased after splenectomy. Pecorari et al., [23] reported splenectomy reduces the transfusion requirement to half of the presplenectomy stage. Bhosale, et al., [22] found at a mean follow-up of 3 years, all children continue to reap the benefits of splenectomy, their transfusion requirement remains low than the preoperative requirement, Hb levels were maintained at a higher range >8 gm%. Aessopos et al., [24] reported in their study mean 6-monthly hemoglobin level of all patients was significantly increased postoperatively from 8.1±0.6 to 9.2±0.4 g/dl (p<0.001) and 6-monthly transfusion requirements were significantly reduced from 28±5 to 22±4 units (p<0.001) in thalassemia major patients, while in thalassemia intermedia patients' transfusion needs reduced by approximately 21% and discontinued in 80% patients.

In this study hematological assessment shows the mean 6-monthly hemoglobin level of all patients was significantly increased after splenectomy from 4.19±0.92 g/dl to 8.66±0.73 g/dl (p<0.001). Postoperatively 6-monthly transfusion requirements were significantly reduced from 14.30±3.18 to 2.15±1.46 units (p<0.001), while blood transfusions were discontinued in 4 (20%) patients. So, this study rationalized the other international studies. The mean preoperative serum ferritin concentration was 1346.25±616.40ng/ml and postoperatively 1722.60±858.96 ng/ml which was not statistically significant (p>0.05). This result is similar with the study by Aessopos et al., [24]. As anaemia was significantly improved after splenectomy in all patients in this study and blood transfusion as well as transfusional iron intake was reduced it was expected that serum ferritin level will decrease but not decreased, this may be due to spleen is also a storage site of iron and slow downtrend of serum ferritin level. Akhtar et al., [8] reported average ferritin level was reduced after splenectomy and cost of iron chelation also reduced. Another study by Easa, [21] reported

the higher level of serum ferritin in splenectomized patients than non splenectomized patients despite the decrease of frequency of blood transfusion. In this study no patient was on iron chelation therapy before splenectomy except one who present with heart failure and serum ferritin level was more than 3000 ng/ml, intravenous iron chelation was given in that patient for management of heart failure and after splenectomy 5 patients were started oral iron chelator as their serum ferritin level was more than 2500 ng/ml but no features of heart failure. Although the role of splenectomy on iron balance is controversial, an aggravating effect of splenectomy on hemosiderosis has been suggested by some authors. Ammar et al., (2014) [9] in his study stated splenectomy improves anemia, but does not reduce iron burden. 25. Latif et al., [25] reported significantly higher serum ferritin levels in splenectomized patients with HbE/β thalassemia than in the non splenectomized ones. Thrombocytosis is frequently encountered after splenectomy. In this study preoperatively complete blood count was done in each patient where platelet count among 20 cases was in range of 1,20,000 - 1,50,000/cu mm. After splenectomy on first postoperative period platelet count was done in each patient and found in range of 2,24,000-4,52,000/cu mm, which indicate platelet count was increased after splenectomy but none of the patient had platelet count >5,00,000/cu mm and no patient developed any features of thrombosis like chest pain, abdominal pain or deep vein thrombosis.

In this study preoperative left ventricular diameters and mass were significantly higher in all patients compared to controls. All 20 patients were in a high output state, with mean cardiac output being 5.85±1.72 L/min in patients versus 3.6±1.03 L/min in controls ($p<0.001$). After splenectomy cardiac output was reduced from 5.85±1.72 L/min to 4.99±1.64 L/min) which is statistically significant ($p<0.05$). Other parameters of left ventricular diameters and mass were not significantly different after splenectomy ($p>0.05$). As cardiac output is increased in β thalassemia due to compensatory reaction to chronic anaemia, by improving anaemia after splenectomy cardiac output become reduced but changes in other parameters were not significantly improved, may be due to short period of follow up. This is similar with the study by Aessopos et al., [24]. Mean values of EF (%), E/A ratio, PASP (mm of Hg) were within normal range before and after splenectomy. But altered E/A ratio was encountered in 4 patient (1 before splenectomy, 3 after splenectomy), mild decreased EF (54%) found in 1 patient before splenectomy which was improved after splenectomy (it become 60%), increased PASP (57mm of Hg) was encountered in 1 patient before splenectomy, and which was not significantly altered after splenectomy. Aessopos et al., [24] encountered pulmonary hypertension in 7 of 32 patients (21.9%). Pal et al., [26] reported no systolic dysfunction, EF in all patient >50% in their study which is consistent with this study. Bhosale et al., [22] done two-dimensional echo on all of their cases before splenectomy and found many of them had EF between 50% to 60% and after splenectomy on mean follow-up of 3 years 2-D echo has shown stabilization of cardiac function in few of their children. Cardiac complication is the leading cause of mortality and morbidity in thalassemia and heart failure is the main cause of death in this patient. In this study among the 20 cases total 3 (15%) patient clinically developed heart failure before splenectomy and 17(75%) patients have no features of HF. Out of 3 heart failure patients 1(5%) have features of restrictive cardiomyopathy in echocardiogram and 2(10%) have normal findings except high cardiac output. Patients with heart failure were managed properly as per guidelines and after correction of heart failure splenectomy was done. After splenectomy during 6 months follow up period no patient developed any features of heart failure. In β thalassemia both dilated and restrictive cardiomyopathy can occur but restrictive pattern is more common due to deposition of iron. In this study among the 20 patient's restrictive cardiomyopathy was found in 4 (20%) (1 before and 3 after splenectomy) dilated cardiomyopathy in 1(5%) before splenectomy. Among this 5 patients, 1(20%) restrictive cardiomyopathy patient developed symptomatic heart failure before splenectomy, whereas 4(80%) remain asymptomatic through the study period. It was observed that all the restrictive cardiomyopathy patients have high serum ferritin level >2500ng/ml.

This study reveals post-splenectomy haemoglobin level is increased and maintained, simultaneously reduce transfusional requirement but serum ferritin level does not altered. Cardiac output decreased from high state after splenectomy but all other parameters were not improved but no further deterioration occurred within follow up period. According to the current study, children with β thalassemia can benefit from splenectomy in that anemia is likely to be

corrected, transfusion needs are likely to be reduced and there will be a decrease in cardiac output but cardiovascular assessment will have to be done frequently given a lingering risk.

6. LIMITATIONS OF THE STUDY

- Sample size is small and purposive.
- It is a single centered study.
- Follow up period is short for evaluation of cardiac changes.

7. CONCLUSION

Splenectomy stabilizes the hemoglobin concentration at higher levels and reduces transfusion needs, reduces high cardiac output and prevents high output failure. Though other cardiac parameters remain unchanged within the first 6 months after splenectomy, it can be assumed that removal of the spleen may contribute to the prevention of further cardiac damage. Splenectomy does not affect serum ferritin level significantly within first 6 months though it reduces transfusional iron intake. Echocardiography is widely available, relatively inexpensive, simple, non-invasive way of assessing early cardiac alterations in β thalassemia patients and marked improvement in survival of these patients can be achieved by monitoring of cardiac function with this simple test. Regular assessment of cardiac function may help to reduce the morbidity and mortality to a great extent.

8. RECOMMENDATIONS

Splenectomy should not be delayed when indicated. Yet, even after decades of experience, long-term outcomes of splenectomy on cardiac status have not been established. So, it is recommended to study on a large sample over long period of time in this regard. Echocardiography is recommended for an early detection and long-term monitoring of cardiac dysfunction in β thalassemia patients before and after splenectomy on regular basis and proper iron chelation therapy according to serum ferritin level is also recommended to improve the life expectancy of these patients.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

CONSENT

As per international standards or university standards, patient(s) written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

The Ethical Review Committee (ERC) of Mymensingh medical college approved the protocol prior to commencement of the study in November, 2016. After starting of Institutional Review Board in Mymensingh Medical College, the IRB again approved the protocol and give certificate in 13th January, 2018.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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APPENDIX-I

DATA COLLECTION SHEET

1. Case serial no:

2. Hospital reg. no.:

3. Ward/Bed:

4. Date of data collection:

5. Particulars of the patients:

Name:	Informer:
Age:	Address:
Sex:	Date of admission :
Father's name :	Date of discharge :
Mother's name:	Contact number :

6. Presenting complaints:

7. History of present illness:

8. Past history:

9. Treatment history:

- ✓ Duration of blood transfusion:
- ✓ Frequency of blood transfusion :
- ✓ Quality of blood transfused: Whole fresh blood/Packed red cell
- ✓ History of taking iron chelation therapy :
- ✓ Any other treatment history :

10. Family history:

Consanguinity:
Father:
Mother:
Other sibling:

11. Immunization history:

12. Socio-economic history:

13. General Physical Examination:

Appearance:	Respiratory rate:
Body built:	Temperature:
Nutrition :	Blood pressure:
Anaemia:	JVP:
Jaundice:	Weight :
Cyanosis:	Height :
Edema:	Thyroid gland :
Dehydration:	Accessible lymph nodes :
Pulse:	Skin condition :

14. Systemic examination:

A. Abdomen examination:

A) Inspection
Size & shape:
Distension :
Umbilicus :
Visible peristalsis :
Hernial orifices :

B) Palpation	**C) Percussion**
Temperature :	Percussion note:
Tenderness :	**D) Auscultation**
Deep palpation -	Bowel sound :
Liver:	Any bruit :
Spleen : Size:	
Kidney:	
Urinary bladder :	

B. Cardio vascular System examination:

Precordium:

(a) Inspection:

Shape of the chest:

Any visible impulse/apex beat:

(b) Palpation:

Apex beat:

Thrill:

(c) Auscultation:

Heart sound:

Added sound:

15. Other Systemic Examination:

Lungs: Bilateral basal crepitation present/absent:

16. Type of β thalassemia:

Hb electrophoresis report:

17. Indication of Splenectomy :

Blood transfusion requirement/kg/year:

H/O mechanical discomfort:

Review of past medical records suggestive of Hypersplenism (if any):

Peripheral blood film (if any):

Bone marrow examination report (if any):

18. Investigations:

A. Laboratory tests:	
Complete blood count :	PBF:
Serum bilirubin:	HBs Ag:
S.SGPT:	S.ferritin :
PT :	Serum creatinine:
B. Imaging study:	
Chest X-ray P/A view:	
Echocardiogram :	

19. Pre-operative preparation:

- ✓Pre-operative blood transfusion to maintain Hb level >8gm/dl
- ✓Management of Heart failure or any other complication before splenectomy
- ✓Nothing per oral 6 hours before the operation

20. Operation note:

- ✓Date of operation:
- ✓Anesthesia:
- ✓Per-operative findings:
  - Spleen condition:
  - Gall stone present/absent:
  - Any accessory spleen:

21. Postoperative management:

- ✓ Nothing per oral for 24-36 hours
- ✓ Nasogastric suction
- ✓ Antibiotics
- ✓ Analgesic
- ✓ **At 1st post-operative day :**
  Hb% -
  Total platelet count-

22. Any post-operative complication:

23. Post-operative follow-up:

Follow-up first visit 2 weeks after splenectomy and then 1-month interval to the out-patient department of paediatric surgery over 6months postoperatively.

Visit	**Hb level (gm/dl)**	**Blood transfusion require(units) or not**	**Others**
1st visit 2wks after splenectomy			**PBF** (if needed):
2nd visit 1 month after splenectomy			
3rd visit 2 months after splenectomy			
4thvisit 3 months after splenectomy			
5th visit 4 month after splenectomy			
6th visit 5 month after splenectomy			
7th visit 6 month after splenectomy			**Echocardiogram:** **S. ferritin(ng/ml):**

24. Calculation of Mean 6-monthly pretransfusion hemoglobin 6 months period preceding splenectomy and 6 months period following splenectomy

SL No.	**Pretransfusion hemoglobin level (gm/dl)** in 6 months period preceding splenectomy (from past medical records)	**Pretransfusion hemoglobin level (gm/dl)** in 6 months period following splenectomy (from follow up schedule)
Avearage		

25. 6-months transfusion requirements before and after splenectomy

Variable	**6-months period preceding splenectomy** (from past medical records)	**6-months period following splenectomy** (from follow up schedule)
Transfusion requirement(units)		

26. S. ferritin level (ng/ml) before and 6 months after splenectomy

Variable	**Before splenectomy**	**6 months after splenectomy.**
S. ferritin level (ng/ml)		

27. Echocardiogram findings: Before splenectomy& 6 months after splenectomy:

A. Left ventricular dimensions and mass before and 6months after splenectomy:

Variables	**Before**	**After**
IVSTd (mm)		
LVIDd (mm)		
LVPWTd (mm)		
IVSTs (mm)		
LVIDs (mm)		
LVPWTs (mm)		
LV MASSd (g)		

B. Left ventricular stroke volume and calculation of Cardiac output by SV×HR before and 6months after splenectomy

Variables	**Before splenectomy**	**6 months after splenectomy**
SV (ml)		
HR (beats/min)		
CO=SV×HR (ml/min)		
CO (L/min)		

C. Parameters for LV systolic function (EF), diastolic function (E/A ratio) and pulmonary hypertension (PASP) before and 6months after splenectomy

Variables	Before splenectomy	6 months after splenectomy
EF (%)		
E/A ratio		
PASP(mm of Hg)		

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