

Comparison of Hematological Parameters Between Splenectomized and Non-Splenectomized Transfusion-Dependent Thalassemia Patients

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ABSTRACT

Background: Thalassemia is a common inherited blood disorder caused by mutations in the hemoglobin gene clusters, leading to defective globin chain synthesis and, in severe cases, transfusion-dependent anemia. The purpose of the study is to evaluate the impact of splenectomy on iron overload by comparing serum ferritin levels between splenectomized and non-splenectomized transfusion-dependent thalassemia patients. **Methods & Materials:** This cross-sectional comparative study at the Department of Transfusion Medicine, Bangabandhu Sheikh Mujib Medical University, Dhaka, included 60 transfusion-dependent thalassemia patients (30 splenectomized, 30 non-splenectomized) to compare hematological parameters, transfusion interval, and serum ferritin. Blood samples were analyzed for complete blood count and peripheral blood film (Sysmex XN-2000) and serum ferritin (Chemiluminescent Immunoassay, Liaison XL). Data were compared using Student's t-test and chi-square test ($p < 0.05$). **Results:** Among 60 transfusion-dependent thalassemia patients, most were 11–20 years old (mean 17.78 ± 6.57 vs 18.87 ± 10.95 years; $p = 0.644$) and male (61.7%; $p = 0.184$). Splenectomized patients had longer transfusion intervals (>4 weeks: 60.0% vs 16.7%; $p = 0.001$), higher MCV, WBC, platelet counts, and serum ferritin (all $p < 0.05$), while peripheral blood film patterns were similar ($p = 0.117$), with severe anemia more common in splenectomized patients. **Conclusion:** Splenectomy in transfusion-dependent thalassemia reduces transfusion frequency and alters hematological parameters but increases iron overload, highlighting the need for careful iron monitoring.

Keywords: Hematology, Splenectomy, Thalassemia.

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INTRODUCTION

Thalassemias represent the most common monogenic disorders worldwide and comprise a group of inherited anemias resulting from mutations within the hemoglobin (Hb) gene clusters. These genetic defects lead to impaired or absent synthesis of one or more globin chain components of the hemoglobin tetramer^[1]. Among inherited disorders characterized by reduced or defective hemoglobin chain production, thalassemia accounts for the highest prevalence^[2]. Although thalassemia occurs across nearly all ethnic groups and geographic regions, their highest distribution is observed within a wide geographic belt extending from sub-Saharan Africa through the Mediterranean region, the Middle East, and the Arabian Peninsula to the Indian subcontinent and Southeast Asia^[3]. It is estimated that approximately 270 million individuals worldwide are carriers of hemoglobinopathies, of whom nearly one-third are carriers of β -thalassemia^[4].

The clinical presentation of thalassemia ranges from relatively mild, nontransfusion-dependent thalassemia (NTDT) to severe transfusion-dependent thalassemia (TDT)^[5]. In patients with TDT, regular red blood cell transfusion remains the cornerstone of management, while iron chelation therapy using desferrioxamine (DFO), deferiprone (DFP), or deferasirox (DFX) is essential to prevent complications related to iron overload^[6]. Children with β -thalassemia major accumulate excess iron soon after becoming transfusion dependent, placing them at increased risk of iron deposition in multiple organs. This progressive iron excess may ultimately lead to significant organ dysfunction if inadequately managed. Splenomegaly in thalassemia patients develops primarily as a consequence of excessive red blood cell destruction and compensatory extramedullary hematopoiesis. A key physiological role of the spleen is the clearance of abnormal or damaged red blood cells from the

circulation^[7]. Enlargement of the spleen results in sequestration and destruction of red blood cells, white blood cells (WBCs), and platelets, and may be associated with abdominal discomfort and pain. In patients with transfusion-dependent thalassemia, the primary indication for splenectomy is hypersplenism, which is characterized by a marked increase in red blood cell transfusion requirements exceeding 200–220 mL/kg/year, clinically significant splenomegaly, and the presence of severe pancytopenia^[8]. The spleen plays a critical role in eliminating abnormal red blood cells from the peripheral circulation. Surgical removal of the spleen may enhance red blood cell survival by reducing splenic destruction, thereby potentially lowering transfusion requirements. However, splenectomy is also associated with alterations in hematological parameters, including thrombocytosis and an increased number of nucleated red blood cells, which may contribute to post-splenectomy complications^[9,10]. In

thalassemic red blood cells, oxidation of globin subunits results in the formation of hemichrome, which binds to the red blood cell membrane. Subsequent degradation of heme leads to the release of toxic non-transferrin-bound iron species, contributing further to cellular damage^[11-13].

Although splenectomy is commonly performed to reduce transfusion requirements in transfusion-dependent thalassemia patients, its impact on iron overload remains unclear. Previous studies have reported inconsistent effects of splenectomy on serum ferritin levels and transfusion burden, and direct comparisons between splenectomized and non-splenectomized patients are limited. This lack of consistent evidence highlights the need for further evaluation. The purpose of the study is to evaluate the impact of splenectomy on iron overload by comparing serum ferritin levels between splenectomized and non-splenectomized transfusion-dependent thalassemia patients.

OBJECTIVE

- To evaluate the impact of splenectomy on iron overload by comparing serum ferritin levels between splenectomized and non-splenectomized transfusion-dependent thalassemia patients.

METHODS & MATERIALS

This cross-sectional, comparative study was conducted at the Department of Transfusion Medicine, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, from December 2021 to October 2022. A total of 60 transfusion-dependent thalassemia patients were included, comprising 30 splenectomized and 30 non-splenectomized individuals, who were selected based on specific inclusion and exclusion criteria for the

comparison of hematological parameters between splenectomized and non-splenectomized transfusion-dependent thalassemia patients.

Inclusion criteria:

- Transfusion-dependent thalassemic patients aged above 5 years
- Both male and female patients
- Splenectomized thalassemic patients who were dependent on regular transfusions and had received at least 10 transfusions prior to surgery
- Non-splenectomized thalassemic patients (with hypersplenism or splenomegaly) receiving regular blood transfusions for at least 2 years

Exclusion criteria:

- Thalassemic patients aged below 5 years
- Thalassemic patients not dependent on regular blood transfusions
- Thalassemic patients without splenectomy, hypersplenism, or splenomegaly
- Patients with bleeding disorders due to causes other than thalassemia
- Thalassemic patients or their guardians unwilling to provide informed consent

The study focused on demographic variables (age and sex), clinical data (transfusion interval), and laboratory parameters including hemoglobin, hematological indices (MCV, MCH, MCHC, RDW, HCT, WBC, platelet count), serum ferritin, and peripheral blood film findings. After obtaining ethical approval

from the Institutional Review Board (IRB) of BSMMU, demographic and clinical information was collected using a semi-structured questionnaire and review of medical records.

For laboratory evaluation, 5 mL of venous blood was collected under aseptic conditions from each participant. Serum ferritin levels were measured by Chemiluminescent Immunoassay (CLIA) using the automated analyzer Liaison XL at the Department of Biochemistry and Molecular Biology, BSMMU. Complete blood count and peripheral blood film analyses were performed using Fluorescence Flow Cytometry (FFC) on the Sysmex XN-2000 autoanalyzer at the Department of Laboratory Medicine, BSMMU. All collected data were recorded in case record forms and compiled into a master chart for analysis.

Continuous variables were expressed as mean \pm standard deviation, and categorical variables were presented as frequency and percentage. Comparisons between splenectomized and non-splenectomized groups were made using Student's t-test for continuous variables and chi-square test for categorical variables. A p-value less than 0.05 was considered statistically significant. Ethical approval was obtained from the IRB of BSMMU. Informed written consent was obtained from all participants or their guardians after explaining the purpose of the study, procedures, confidentiality, voluntary participation, and the right to withdraw at any time. The study was conducted under direct supervision, and all laboratory analyses were performed in accredited departments following standard protocols. The results of this study are intended for publication in peer-reviewed journals and may guide clinicians in optimizing the management of transfusion-dependent thalassemia patients.

RESULTS

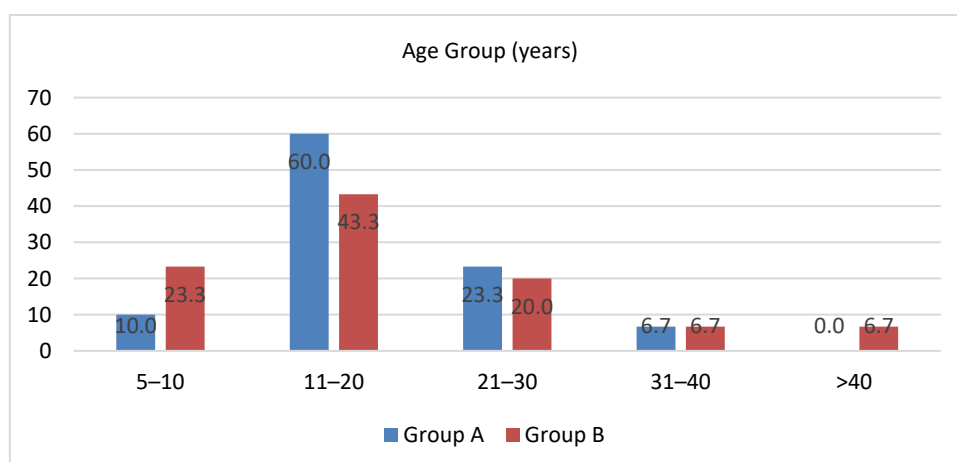


Figure 1 Age Distribution of the Study Population ($n = 60$).

The majority of patients were aged 11–20 years, with 18 (60.0%) in the splenectomized group and 13 (43.3%) in the non-splenectomized group. Patients aged 21–30 years comprised 7 (23.3%) and 6 (20.0%) of the splenectomized and non-splenectomized groups, respectively. Fewer patients were aged 5–10 years (10.0% vs

23.3%), 31–40 years (6.7% in both groups), and >40 years (0% vs 6.7%). Mean age was 17.78 ± 6.57 years in the splenectomized group and 18.87 ± 10.95 years in the non-splenectomized group, with no statistically significant difference ($p = 0.644$) *Figure 1*.

Males predominated in both groups,

comprising 21 (70.0%) in the splenectomized group and 16 (53.3%) in the non-splenectomized group. Females accounted for 9 (30.0%) and 14 (46.7%) of the splenectomized and non-splenectomized groups, respectively. However, The difference in sex distribution was not statistically significant ($p = 0.184$) *Table I*.

Table I
Sex Distribution of the Study Population ($n = 60$).

Sex	Group A (n = 30)	Group B (n = 30)	Total (n = 60)	p-value
Male	21 (70.0)	16 (53.3)	37 (61.7)	0.184
Female	9 (30.0)	14 (46.7)	23 (38.3)	

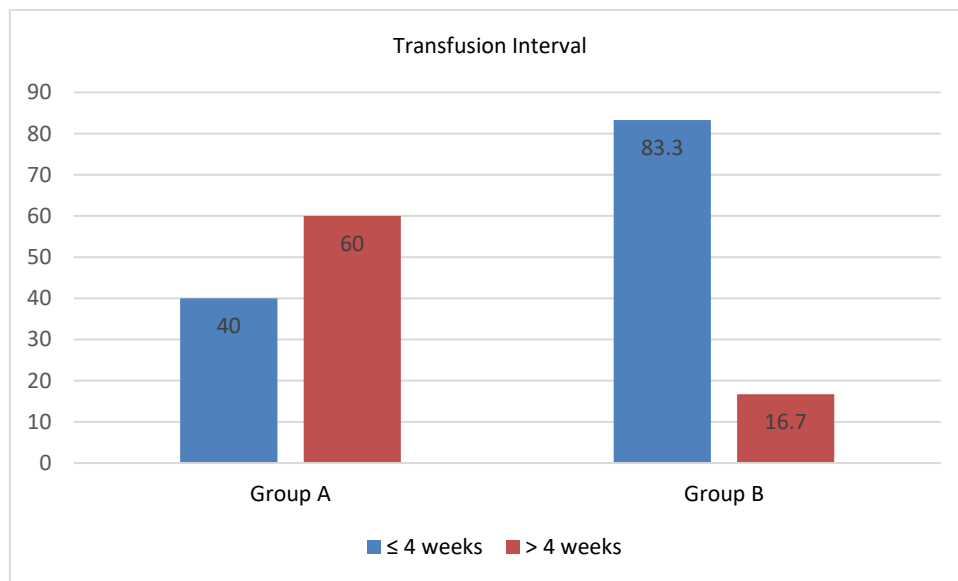


Figure 2 Transfusion Interval Distribution of the Study Population ($n = 60$).

Among the study population, 60.0% of splenectomized patients received transfusions at intervals greater than 4 weeks, compared to only 16.7% of non-splenectomized patients. Conversely, 40.0% of splenectomized patients and 83.3% of non-splenectomized patients

received transfusions at intervals of 4 weeks or less. The difference was statistically significant ($p = 0.001$) *Figure 2*.

There was no significant difference in hemoglobin, MCH, MCHC, RDW, or hematocrit between the groups. Splenectomized patients had significantly

higher MCV (75.64 ± 6.93 vs 69.99 ± 8.89 fL; $p = 0.008$), WBC count (12.24 ± 5.35 vs $9.31 \pm 3.88 \times 10^3/\mu\text{L}$; $p = 0.019$), and platelet count (556.0 ± 255.91 vs $210.34 \pm 116.15 \times 10^3/\mu\text{L}$; $p < 0.001$) compared to non-splenectomized patients (*Table II*).

Table II
Hematological Parameters in Splenectomized and Non-Splenectomized Transfusion-Dependent Thalassemia Patients ($n = 60$).

Hematological Variable	Group A (n = 30)	Group B (n = 30)	p-value
Hb (g/dL)	7.26 ± 1.57	6.78 ± 1.83	0.285
MCV (fL)	75.64 ± 6.93	69.99 ± 8.89	0.008
MCH (pg)	23.31 ± 2.94	25.21 ± 12.99	0.441
MCHC (g/dL)	30.83 ± 2.83	30.93 ± 2.15	0.874
RDW	26.13 ± 6.07	27.93 ± 5.87	0.248
HCT	25.21 ± 9.95	26.79 ± 24.45	0.744
WBC ($10^3/\text{L}$)	12.24 ± 5.35	9.31 ± 3.88	0.019
Platelet ($10^3/\text{L}$)	556.0 ± 255.91	210.34 ± 116.15	<0.001

Splenectomized patients had significantly higher serum ferritin levels than non-splenectomized patients. Half of the splenectomized patients (50.0%) had

ferritin levels >5000 ng/mL, compared to 13.3% in non-splenectomized patients. Mean ferritin was 5843.98 ± 4162.00 ng/mL in splenectomized patients and $3253.32 \pm$

2247.28 ng/mL in non-splenectomized patients ($p = 0.004$) *Table III*.

Table III
Comparison of Serum Ferritin Levels Between Splenectomized and Non-Splenectomized Patients ($n = 60$).

Serum Ferritin (ng/mL)	Group A (n = 30)	Group B (n = 30)	Total (n = 60)	p-value
<1000	1 (3.3)	4 (13.3)	5 (8.3)	0.004
1000–2500	6 (20)	8 (13.3)	14 (23.3)	
2500–5000	8 (26.7)	15 (50)	23 (38.3)	
>5000	15 (50)	4 (13.3)	19 (31.7)	
Mean \pm SD (ng/mL)	5843.98 \pm 4162.00	3253.32 \pm 2247.28	—	0.004

Peripheral blood film findings were comparable between the groups, with no statistically significant difference ($p =$

0.117). Moderate anemia predominated in non-splenectomized patients, while severe

anemia was more frequent among splenectomized patients (Table IV).

Table IV
Peripheral Blood Film Patterns in Splenectomized and Non-Splenectomized Patients ($n = 60$).

Peripheral Blood Film (PBF) Result	Group A (n = 30)	Group B (n = 30)	Total (n = 60)	p-value
Mild microcytic hypochromic anaemia with target cells and nucleated cells	3 (10.0)	2 (6.7)	5 (8.3)	0.117
Moderate microcytic hypochromic anaemia, anisopoikilocytosis, target cells	16 (53.3)	9 (30.0)	25 (41.7)	
Severe microcytic hypochromic anaemia, anisopoikilocytosis, target cells, fragmented cells, teardrop cells	11 (36.7)	19 (63.3)	30 (50.0)	

DISCUSSION

Transfusion-dependent thalassemia (TDT) is a severe inherited anemia that often necessitates regular red blood cell transfusions to maintain adequate hemoglobin levels and prevent complications. Splenectomy is frequently performed in these patients to reduce transfusion requirements and manage hypersplenism, but its impact on hematological parameters and iron overload remains incompletely understood. The findings of this study demonstrate that splenectomized patients have higher mean corpuscular volume, white blood cell and platelet counts, as well as significantly elevated serum ferritin levels compared to non-splenectomized patients. These results highlight the dual impact of splenectomy—altering hematological indices while potentially exacerbating iron overload—underscoring the need for careful post-splenectomy monitoring and optimized chelation therapy in TDT patients.

In the present study, the majority of patients were aged 11–20 years. The mean ages of 17.78 ± 6.57 years in the splenectomized group and 18.87 ± 10.95 years in the non-splenectomized group, with no statistically significant difference was observed between groups ($p = 0.644$). This age distribution indicates that transfusion-dependent thalassemia predominantly affects children and adolescents, which is consistent with previous literature. Bhattacharjee et al. reported a median age at splenectomy of 12 years (range 5–34) in a retrospective cohort of TDT patients, noting that most procedures occurred during childhood or adolescence, reflecting the early onset of complications necessitating splenectomy^[14]. Similarly, Caocci et al. found a median age at splenectomy of 12 years (range 1–32) in adult TDT patients^[15],

confirming that splenectomy is commonly performed at a relatively young age in thalassemia populations. These findings collectively support the observation that the bulk of TDT patients, regardless of splenectomy status, are relatively young, which aligns with the age distribution reported in our study.

In the present study, males predominated in both groups, comprising 21 (70.0%) in the splenectomized group and 16 (53.3%) in the non-splenectomized group, while females accounted for 9 (30.0%) and 14 (46.7%), respectively. The difference in sex distribution between the two groups was not statistically significant ($p = 0.184$), indicating a comparable gender pattern among splenectomized and non-splenectomized transfusion-dependent thalassemia patients. This finding aligns with the results reported by Azeez et al., who observed that among 60 thalassemia major patients, 33 (55%) were male and 27 (45%) were female, with no significant sex-related differences between splenectomized and non-splenectomized groups^[16]. These observations suggest that sex does not appear to influence the likelihood of undergoing splenectomy in transfusion-dependent thalassemia populations and that male predominance in these cohorts may reflect general demographic patterns rather than disease- or treatment-specific factors.

In the present study, splenectomized patients demonstrated significantly longer transfusion intervals compared with non-splenectomized patients, with 60.0% of splenectomized individuals receiving transfusions at intervals greater than 4 weeks versus only 16.7% of non-splenectomized patients ($p = 0.001$). Conversely, the majority of non-splenectomized patients (83.3%) required transfusions at intervals of 4 weeks or less.

These findings indicate that splenectomy is associated with reduced transfusion dependence, reflecting improved red blood cell survival and decreased peripheral destruction. Similar observations have been reported by Osataphan et al., who found that splenectomy in transfusion-dependent thalassemia patients significantly reduced the need for transfusions and, in many cases, enabled conversion from transfusion-dependent to non-transfusion-dependent status^[5]. Likewise, Bhosale et al. noted a reduction in both transfusion requirement and frequency following splenectomy in β -thalassemia patients^[17], supporting the finding of a greater proportion of longer transfusion intervals among splenectomized patients in the current study. These concordant results underscore the clinical benefit of splenectomy in prolonging transfusion intervals and reducing transfusional burden in thalassemia populations.

In this study, splenectomized transfusion-dependent thalassemia patients exhibited significantly higher mean corpuscular volume (MCV: 75.64 ± 6.93 vs 69.99 ± 8.89 fL; $p = 0.008$), white blood cell count (12.24 ± 5.35 vs $9.31 \pm 3.88 \times 10^3/\mu\text{L}$; $p = 0.019$), and platelet count (556.0 ± 255.91 vs $210.34 \pm 116.15 \times 10^3/\mu\text{L}$; $p < 0.001$) compared with non-splenectomized patients, while hemoglobin, MCH, MCHC, RDW, and hematocrit showed no statistically significant differences. These findings are consistent with previous studies demonstrating the hematologic impact of splenectomy in thalassemia. Tripodi et al. reported significantly elevated leukocyte and platelet counts in splenectomized patients relative to non-splenectomized counterparts^[18], reflecting reduced peripheral destruction and sequestration of blood cells after splenectomy, which

parallels the higher WBC and platelet counts observed in our study. Similarly, Mohamed AAF et al. documented a significant increase in both platelet and total leukocyte counts following splenectomy, supporting our observation of elevated counts in the splenectomized cohort^[19]. The increase in MCV observed in our study may also reflect improved red blood cell survival and altered erythropoiesis post-splenectomy, further highlighting the physiological hematologic changes associated with spleen removal in transfusion-dependent thalassemia patients. In the present study, splenectomized transfusion-dependent thalassemia patients exhibited significantly higher serum ferritin levels compared to non-splenectomized patients, with half of the splenectomized individuals (50.0%) exceeding 5000 ng/mL and a mean ferritin of 5843.98 ± 4162.00 ng/mL versus 3253.32 ± 2247.28 ng/mL in the non-splenectomized group ($p = 0.004$). These findings are consistent with previous reports highlighting increased iron overload in splenectomized thalassemia patients. Pootrakul et al. observed significantly higher serum ferritin levels in splenectomized β -thalassemia/Hb E patients compared with non-splenectomized patients^[20], reflecting enhanced iron accumulation following splenectomy. Similarly, Casale et al., in a retrospective analysis of transfusion-dependent thalassemia major patients, reported that ferritin concentrations were markedly elevated in the splenectomized group during the presplenectomy period^[10], emphasizing the association between spleen removal and higher iron burden, even though levels may decline over the long term. These studies support our results, indicating that splenectomy contributes to greater iron accumulation and underscores the importance of careful iron monitoring and chelation management in this patient population.

In this study, peripheral blood film examination revealed that microcytic hypochromic anemia with varying degrees of anisopoikilocytosis and target cells was prevalent among both splenectomized and non-splenectomized transfusion-dependent thalassemia patients. Moderate anemia predominated in non-splenectomized patients (30.0%), whereas severe anemia with features such as fragmented cells and teardrop cells was more frequent among splenectomized patients (36.7%), although the difference was not statistically significant ($p = 0.117$). These findings are in line with previous observations by Shehata et al., who reported that splenectomized thalassemia patients often exhibit increased circulating nucleated red blood cells (NRBCs) and reticulocytes^[21], reflecting more pronounced ineffective erythropoiesis

and abnormal red cell morphology post-splenectomy. The higher proportion of severe anemia features in the splenectomized group in our cohort may be attributed to the loss of splenic filtration, which normally removes abnormal and fragmented erythrocytes, thereby allowing these cells to persist in peripheral circulation. Overall, our results support the notion that splenectomy influences peripheral blood film patterns by increasing the prevalence of severe morphologic abnormalities in transfusion-dependent thalassemia patients.

LIMITATIONS

The study had several limitations:

- The study was conducted at a single tertiary care center, which may limit the generalizability of the findings.
- Participants were selected using non-random, convenience sampling, introducing the possibility of selection bias.
- Long-term outcomes following splenectomy could not be evaluated due to the cross-sectional study design.
- Advanced modalities for assessing iron overload, such as magnetic resonance imaging or liver biopsy, were not employed; instead, serum ferritin was used as a cost-effective surrogate marker, which may not fully reflect total body iron stores.

CONCLUSION

Splenectomy is commonly performed in transfusion-dependent thalassemia patients to reduce red blood cell destruction and transfusion requirements. In this study, splenectomized patients showed longer transfusion intervals and higher white blood cell and platelet counts compared to non-splenectomized patients, reflecting improved hematologic stability post-splenectomy. However, they also exhibited significantly higher serum ferritin levels, indicating increased iron overload. Peripheral blood film findings were largely similar between groups, although more severe anemia features were observed in splenectomized patients. These results suggest that while splenectomy can reduce transfusion burden and modify hematological parameters, careful monitoring and management of iron accumulation remain crucial.

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