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Post total splenectomy outcome in thalassemia patients

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ABSTRACT

Introduction: Splenectomy in thalassemia patient is indicated in the transfusion-dependent patient when hypersplenism increases blood transfusion requirement, prevents adequate control of body iron with chelation therapy and increased risk for infection.
Method: This study was retrospective study aims to evaluate the outcome of splenectomy in pediatric thalassemia patients and its related factor. A total 34 thalassemia patient with post total splenectomy patients was included in this study.
Result: Mean age was 20.7 ± 6.5 years old with majority mild malnutrition (61.8%) and the majority of spleen size Schaffner 6-7 (73.5%). The duration between thalassemia diagnosis and total splenectomy was 6-7 years. Statistical analysis showed significant decreased of mean blood transfusion volume from 4691.4 cc per year to 3764.2 cc per year ($p = 0.048$), decreased mean blood transfusion volume from 219.6 cc per Kg Body Weight (BW) per year to 125.5 cc per Kg BW per year ($p<0.001$) and decreased of blood transfusion frequency from 12-14 times per year to 6-8 times per year ($p<0.001$). There is only one case subcutaneous emphysema as complication after splenectomy.
Conclusion: Overall, this study showed total splenectomy improve the outcome of thalassemia with hypersplenism with low rate of complication.
Keywords: splenectomy, pediatric thalassemia, outcome.

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INTRODUCTION

Thalassaemia represents a heterogeneous group of inherited diseases characterised by the lack or reduced production of haemoglobin β-chains. The typical pathophysiology bedrock is increased destruction of red blood cells by reticuloendothelial system, in particular by the spleen, resulting in its enlargement (splenomegaly).[1]

Splenectomy is indicated in the transfusion-dependent patient when hypersplenism increases blood transfusion requirement and prevents adequate control of body iron with chelation therapy. An enlarged spleen—without an associated increase in transfusion requirement—is not necessarily an indication for surgery. Patients with hypersplenism may have moderate to enormous splenomegaly, and some degree of neutropenia or thrombocytopenia may be present.[2,3]

Splenectomy is known to be associated with short and long term complications such as infections, hypercoagulability and thromboembolism. Recurrence of anemia may occur due to the presence of splenunculi which enlarge following splenectomy. Therefore it is necessary to detect and remove them during surgery.[2]

If a decision to perform surgery is made, partial or full splenectomy is the option. Partial splenectomy is a complicated surgery utilized to preserve some splenic function. It should be reserved for infants requiring splenectomy. Full splenectomy can usually be performed by laparoscopic technique. However, open procedure is necessary in cases of marked splenomegaly.[4]

MATERIAL AND METHODS

This retrospective cross-sectional descriptive study aims to evaluate the outcome of splenectomy in pediatric thalassemia patients and its related factor. This study was conducted in Thalassemia Center of Pediatric Department and Pediatric Surgery Division, Faculty of Medicine, University of Indonesia Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia. Period of study from January 1993 – December 2009.

The subject criteria are Thalassemia patient underwent splenectomy from January 1993 – December 2009 and Thalassemia diagnosis made by Hemoglobin electrophoresis examination. Splenectomy performed by open surgical technique. Left subcostal incision was made to open the abdomen, peritoneum was opened in the line of incision and splenic artery and vein were

Table 1. Subject Demographics

Characteristic	N	%
Age (mean ± SD)	20.7 ± 6.5	
Sex		
Male	16	47.1
Female	18	52.9
Nutrition Status		
Normal	12	35.3
Mild malnutrition	21	61.8
Severe malnutrition	1	2.9
Liver size		
3	2	5.9
4	10	29.4
5	5	14.7
6	9	26.5
7	2	5.9
8	2	5.9
9	2	5.9
10	2	5.9
Spleen size (Schuffner grade)		
5-6	4	11.8
6-7	25	73.5
7-8	5	14.7
Family Thalassemia history		
Yes	6	17.6
No	28	82.4
Type of Thalassemia		
HBE	18	52.9
Beta	16	47.1

Table 2. Splenectomy in Thalassemia

Characteristic	N	%
Duration of operation (hour)		
1	2	5.9
1.25	1	2.9
1.5	6	17.6
2	20	58.8
2.5	3	8.8
2.75	1	2.9
3	1	2.9
Blood loss (ml) (Median/Range)	200 (50 – 2000) ml	
Temperature instability		
Yes	3	8.8
No	31	91.2
Comorbidities		
Heart Failure	1	2.9
Hepatitis C	2	5.8
Restrictive Pulmonary Disease	3	8.8
Neurogenic Bladder	1	2.9
Pulmonary Tuberculosis	3	8.8
None	24	70.6

identified and ligated. The spleen was retracted to ligate splenocolic, lienorenal and splenophrenic ligaments between ligatures. Stomach was retracted, short gastric arteries identified and ligated at gastrosplenic ligament, Finally, gastrosplenic ligament is also incised between ligatures. Spleen was removed and haemostasis achieved with particular attention to splenic hilum, diaphragmatic surface and colonic surface.

Data obtained from each subject include: Medical history, age; sex; Body Weight (BW), nutrition status, liver size, pre-operation spleen size, transfusion frequency, volume of blood transfusion before and after splenectomy and blood counts before and after splenectomy and operation report. The data analysed using SPSS, Wilcoxon test and paired sample t-test were used to compare blood parameter outcome in thalassemia patient, all value considered significant if $p<0.05$.

RESULTS

The mean age of the 34 patients was 20.7 years old and 6.6 years of standard deviation. There were 16 (47.1 %) males and 18 (52.9 %) females. Nutritional status showed 12 patients (35.3 %) with normal status, 21 mild malnutrition (61.8 %) and 1 severe malnutrition (2.9 %). All of the subjects showed liver enlargement with various sizes from 3 – 10 cm. The spleen size was classified using Schaffner Grade: 4 patients (11.8 %) with grade 5-6, 25 patients (73.5 %) with grade 6-7 and 5 patients (14.7 %) with grade 7-8. Majority of patients (82.4 %) have no family history of thalassemia (Table 1). Data regarding operation duration, blood loss during operation, and comorbidities were shown in table 2. Splenectomy significantly decreases frequency of blood transfusion compared to before splenectomy condition (p=0.001) (Table 3).

The annual transfusion frequency to maintain a target haemoglobin of 9 g/dl decreased significantly after splenectomy in all subject (p=0.0001). The total volume of annual blood transfusion requirement pre-surgery was 4,691.4 ml/year which decreased significantly to 3,764.2 ml/year (p=0.048) and mean annual blood transfusion requirement pre-surgery was 219.6 ml/kg/year, which decreased significantly to 125.5 ml/kg/year (p=0.001) post-surgery (Table 4).

The pre-splenectomy hemoglobin level ranged from 4.8 to 11.1 g/dl with mean 6.6 g/dl and significantly increased to 7.7 g/dl with ranged from 5.2 – 9.1 g/dl after splenectomy (p = 0.001). The pre splenectomy platelet counts ranged from 38,900 – 994,000 cells/mm^3 (mean 222,500 cells/mm^3) whereas 24 h post splenectomy, counts ranged from 277,300 – 996,000 cells/mm^3 (mean 664,000 cells/

mm^3) which significantly increased (p=0.001). This results also accompanied with significant increase of mean white blood counts (p=0.001) and not significant increase of ferritin level (p = 0.109) (Table 4).

DISCUSSION

The splenomegaly is known to occur in major thalassemia patients causing excessive destruction of abnormal RBCs and excessive iron overload deposition in liver and heart.[7] Splenomegaly further increases transfusion requirement hence these patients are benefited from splenectomy.[4,5] The struggle against thalassemia has dramatically increased against the past few years across the world. Advance modalities of treatment include bone marrow transplantation, peripheral blood stem cells transplantation, cord blood stem cells transfusion, gene therapy and stimulation of fetal hemoglobin.[6,8,9]

Several studies have demonstrated a fall in the transfusion requirement to<150 ml/kg/y immediately after splenectomy.[10,11] In the present study the annual total volume of blood transfusion (p=0.048), mean volume of blood transfusion (p = 0.001) and transfusion frequency (p=0.001) decreased significantly. This is similar to the study conducted by Cohen et al. which showed that transfusion requirements remained stable after the predictable fall in the first year post-surgery, thus reducing hospital visits and improving quality of life.[11] Porecha et al. demonstrated a fall in transfusion requirements post-splenectomy along with better quality of life due to improved haemoglobin in Indian thalassemias.[4]

Splenectomy results in a hypercoagulable state by permitting the circulation of greater numbers of red cells with altered membranes, and an increase in the number of platelets. Thrombocytosis develops in 75 % of splenectomised patients, and in 15 % it reaches 1,000,000 cells/mm^3 or more, platelet levels typically peak between 1 wk and 4 mo after splenectomy.[12] In our series there was a significant rise in platelet counts (p=0.001). That thalassemia patients are at an increase of thrombotic complications has been known for many years and it has been recently confirmed by an extensive study conducted in the Mediterranean area and Iran.[8] Certain haemostatic anomalies found in thalassemia patients suggest the existence of a chronic-hypercoagulable state. Thalassaemic red blood cells, in fact, facilitate thrombin formation as a consequence of the altered asymmetry of the membrane phospholipids with enhanced exposure of phosphatidylserine.[13]

The role of splenectomy in worsening iron overload is uncertain. In our case, the mean ferritin level after splenectomy was increased over 3 times from pre splenectomy level (p = 0.109). It is often suggested that the spleen could represent a safe reservoir for the transfused iron and that splenectomy would, therefore, favour a more massive accumulation of iron in the liver. However, the iron content of the spleen, at splenectomy, is low, amounting to no more than one fifth to one-tenth of the liver iron content.[14,15]

Table 3. Pre and Post Splenectomy Blood Transfusion Frequency

Frequency of blood transfusion	n	%	p-value
Pre-Splenectomy			
8-10	1	2.9	
10-12	4	11.8	
12-14	29	85.3	
Post-Splenectomy			0.001
2-4	2	5.9	
4-6	6	17.6	
6-8	18	52.9	
8-10	6	17.6	
10-12	2	5.9	

Table 4. Pre and Post Splenectomy effect in blood transfusion and blood counts

	Pre Splenectomy Mean (Min-Max)	Post Splenectomy Mean (Min-Max)	p-value
Blood Transfusion			
Total Volume per year (ml)	4,691.4 (1,407.5 – 12,700)	3,764.2 (575 – 7350)	0.048[a]
Total Volume/BW/year (ml)	219.6 (64.7 – 375)	125.5 (11.1 – 247.5)	0.001[b]
Blood Counts			
Hemoglobin (gr/dl)	6.6 (4.8 – 11.1)	7.7 (5.2 – 9.1)	0.001[a]
White blood	9,8 (1,2 – 108) x 10^3	68 (14.2 – 182.5) x 10^3	0.001[a]
Platelets	222.5 (38.9 – 994) x 10^3	664.3 (277.3 – 996) x 10^3	0.001[a]
Ferritin	1,887.7 (212.5– 3753)	7,755 (1371-18480)	0.109[a]

Note: [a]Wilcoxon test; [b]Paired T test

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CONCLUSIONS

The splenectomy in thalassemia patients has its benefits and risks. The main goal is to improve the patient's quality of life which closely related to the needs of blood transfusion and its related complications. The splenectomy showed promising results to decreased blood transfusion frequency and improved overall blood profile.

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ETHICAL CONSIDERATION

All study procedure has been approved by Ethical Committee Faculty of Medicine, Universitas Syiah Kuala-Zainoel Abidin General Hospital, Banda Aceh-Indonesia.

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