

Impact of splenectomy on quality of life of children with β -thalassemia

Abstract

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Context: About 10,000 babies with β -thalassemia major are born every year in India, posing a major healthcare burden on the country. In clinically symptomatic individuals, monthly blood transfusions, chelation therapy and splenectomy are the mainstay of therapy at present. **Aims:** To objectively assess the impact of splenectomy on quality of life (QOL) of children with β -thalassemia presenting with symptomatic hypersplenism. **Settings and Design:** This is a prospective study of thalassaemic children referred to pediatric surgical unit of a tertiary care hospital located in Maharashtra, India between January 2010 and December 2012. **Materials and Methods:** Of 360 cases registered at the thalassaemia unit of the center during above defined period, 50 cases (35 males and 15 females) between 5 and 16 years underwent splenectomy. QOL was assessed objectively by means of the composite QOL index calculated by summing-up the responses to a 10-item, 4-point disease specific response scale devised, especially for purpose of the present study; preoperatively and 2 years postoperatively and comparison between the two was carried out. This is the first ever study of this kind. **Statistical Analysis Used:** Chi-square test was used for statistical analysis in the present study. **Results:** The mean preoperative QOL index of 13.5 rose to 31.3 (over a scale of 40) 2 years following splenectomy. The "P value" calculated by comparison between the preoperative and postoperative composite QOL index is >0.001 that is, statistically significant. **Conclusions:** Splenectomy has a definite role in the management of children with β -thalassemia, presenting with hypersplenism. Objective assessment of QOL indicates mean elevation of QOL index by 17.8, thus emphasizing significant impact of splenectomy on the overall QOL of these children.

Key words: Child, Composite Quality of Life (QOL) Index, Packed Red Blood Cell (PRBC) Transfusion Requirement, Splenectomy, β -Thalassemia

INTRODUCTION

Thalassemia is one of the most common monogenic disorders in India. Approximately 7500-12,000 babies with β -thalassemia major are born every year in the country.^[1] Because of the magnitude of the disease and health-care burden it poses, it has been covered as part of various National Programs by the Government of India. The Pediatrics Department at our hospital runs an eight-bedded thalassaemia unit since June 2000. About 80-100 new cases are registered every year. Children with features of hypersplenism [Figure 1] and increased packed red blood cell (PRBC) transfusion requirement are referred to the pediatric surgical unit for splenectomy. Open splenectomy is performed with utmost care [Figure 2] and only when clearly indicated. Regular follow-up assessments are done following splenectomy. Our goal is to provide continued care, optimum quality of life (QOL) within constraints of available resources and complication-free long-term survival. The present study aims to objectively assess this goal. It has been measured by means of a specially devised scale to calculate the composite QOL index pre and postoperatively in children with β -thalassemia having symptomatic hypersplenism. This is first ever study of this kind.

MATERIALS AND METHODS

It is a prospective study of thalassaemic children referred to the pediatric surgical unit of a tertiary care hospital located in Maharashtra between January 2010 and December 2012. Of 360 cases

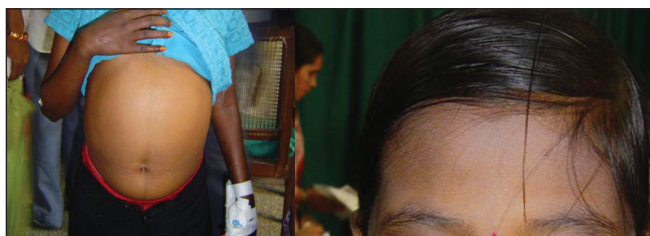


Figure 1: Child with β -thalassemia. Note massively enlarged spleen and the typical "Thal" facies

registered at the (pediatric) thalassemia unit of the hospital during above defined period, 55 cases with hypersplenism and increased PRBC transfusion requirement underwent complete open splenectomy. Five patients above 16 years were excluded from the study. Remaining 50 children were between 5 and 16 years. There were 35 males and 15 females. Two children were HIV positive.

On initial presentation/referral to the thalassemia unit of our hospital, confirmation of diagnosis of β -thalassemia was done by hemoglobin (Hb) electrophoresis. Complete baseline work-up of the child was carried out. It included:

- Hematological investigations: Hb, complete blood count, mean corpuscular hemoglobin (MCH), mean corpuscular volume, MCH concentration; blood grouping; complete liver function tests, renal function tests, bleeding time, clotting time, prothrombin time, etc.
- Serological investigations: Detection of HIV, hepatitis B surface antigen, hepatitis C virus antibodies
- Serum ferritin, calcium and phosphorus levels
- Radiological investigations: Ultrasonography of abdomen, two-dimensional echocardiogram (ECHO)
- Work-up for tuberculosis: Chest X-ray, mantoux test, erythrocyte sedimentation rate, sputum examination

Depending upon severity of symptoms, that is, breathlessness, fatigue, edema feet, vomiting etc., they were admitted at intervals of 15-20 days and received triple saline washed PRBC transfusions, since even the smallest volume of plasma or white blood cells provokes antibody formation. The children are on iron chelation therapy.

Children with following criteria were referred for splenectomy

- PRBC transfusion requirement $>250-300$ ml/kg/year²¹
- Respiratory embarrassment (mechanical discomfort) from massive splenomegaly even with lesser transfusion requirement, that is, >200 ml/kg/year
- Symptomatic hypersplenism

Vaccination (polyvalent pneumococcal, meningococcal and hemophilus influenzae) was completed 2-4 weeks prior to splenectomy and complete work-up as above was repeated. Detailed parental counseling was done. They were explained about the fact

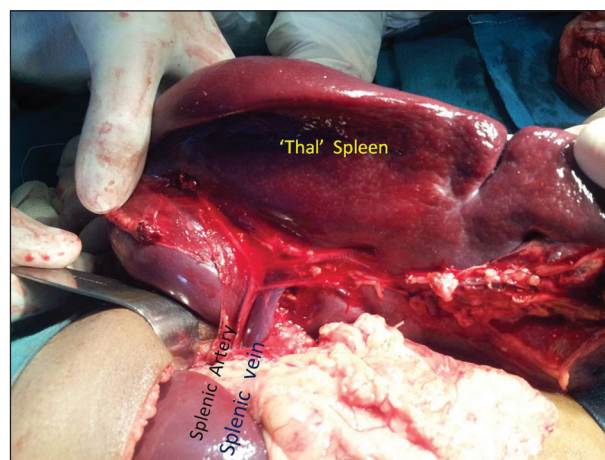


Figure 2: Intra-operative photograph showing near complete mobilization. Spleen with main splenic artery and vein

that thalassemia is a life-long disease and splenectomy is not curative but would offer only limited benefits to the child. Splenectomy was done by open technique through transverse left upper quadrant incision. Following splenectomy, the children were put on Penidure (intramuscular Benzathine Penicillin) prophylaxis 3-5 Lac units at three weekly intervals and prophylaxis was continued for 5 years.

For the purpose of the present study, we took into account 10 different specific measures (items) applicable to day-to-day activities of these children, affecting their life as a whole. Measures were identified so as to cover children across a broad age range, and included a provision for completion by different respondents (child only, parent only, or both) and physical parameters measured by the interviewer. Measures testing the affective, cognitive and psychomotor domains were included. Few measures tested are in general more or less subjective such as the general perception of health, capacity to play, dyspnea, sleep pattern, bodily pain and group activities with peers. However, with the present scoring system employed [Table 1], they were put forth objectively; and the responses therein were recorded and inferred objectively. The other measures tested were totally objective like Hb drop before transfusion, number of hospitalizations per year (school absentees per year), height percentile for age and weight percentile for age. They cover physical functioning, scholastic performance (occupational role), interpersonal relationships with peers and psychological functioning. Initially, with the aim to formulate a standard protocol, all children attending the thalassemia OPD were interviewed. The interview and scoring was carried out by three different residents, who interviewed the children along with the parents and examined the child on separate occasions and scoring was done by each one of them separately. The measures were objectively recorded over the scale of 1-4 (score of four means the best possible situation in these children and score of one means the most severe involvement). The composite QOL index was calculated by adding-up the score of each item to yield a total score for the individual. Scores range from 10

to 40, higher scores indicating higher QOL. The interview time was 10-15 min. Following this initial exercise, the protocol was critically assessed and validated by our statistician. It has been found to have a good internal consistency and very low inter-rater variance (variability) of 0.05-0.07. The standardized protocol/scale [Table 1] has been followed for consequent interviews of the study population.

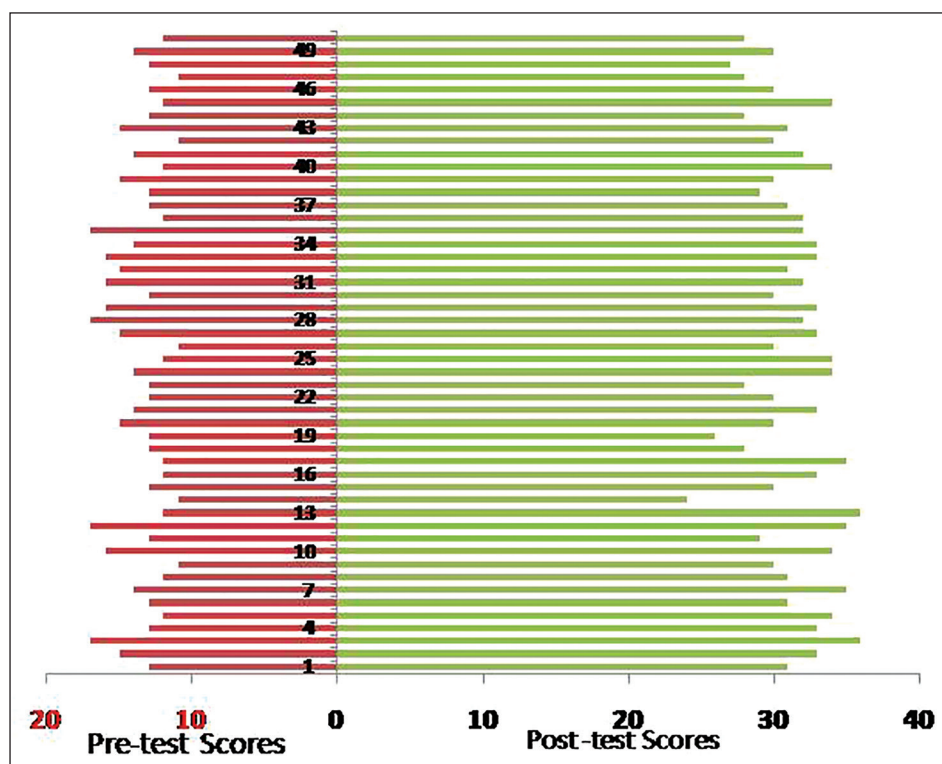
All children posted for splenectomy underwent assessment as per the standardized protocol [Table 1] at the time of hospitalization for splenectomy (pretest) and 2-years following splenectomy (posttest) for comparison of the composite QOL index. The pre- and post-test values of composite QOL Index of these children were plotted graphically [Graph 1], and the results of the same were analyzed using paired *t*-test.

The children are on regular follow-up. They visit the thalassemia unit once a month for the 1st year following splenectomy and 2-3 monthly thereafter. Parents are informed about the immune-compromised status of these children and are instructed about healthcare precautions to be taken. School authorities are informed accordingly. Follow-up assessment aims to assess their health and well-being, documents benefits of splenectomy and a search is made to pick-up infections occurring because of hyposplenism. Our longest follow up is to 5 years (mean follow-up of 2½ years) postsplenectomy. Parents are counseled about genetic transmission of the thalassemia trait, and antenatal counseling is also provided in the subsequent pregnancy whenever applicable.

Table 1: Thalassemia protocol/scale

Item number	Item description	Scoring details	Just before splenectomy (pretest)	2 years following splenectomy (posttest)
1	General perception of health	Poor-1 Fair-2 Good-3 Excellent-4		
2	Capacity to play	Not at all-1 Up to 10 min-2 Up to 1/2 h-3 >1/2 h-4		
3	Dyspnoea	Breathlessness at rest-1 Breathlessness on mild exertion-2 Breathlessness on severe exertion-3 No breathlessness-4		
4	Hemoglobin drop before transfusion	9 g-4 8 g-3 7 g-2 6 g-1		
5	Number of hospitalizations for blood transfusions per year (school absentees per year)	>20 times-1 15-20 times-2 10-15 times-3 <10 times-4		
6	Sleep pattern	Undisturbed-4 Mild disturbance (arousals <2 times)-3 Moderate disturbance (arousals 3-5 times)-2 Severe disturbance (arousals >5 times)-1		
7	Height percentile (for age)	>50-4 35-50-3 20-35-2 <20-1		
8	Weight percentile (for age)	>50-4 35-50-3 20-35-2 <20-1		
9	Bodily pain	None-4 Mild-3 Moderate-2 Severe-1		
10	Feeling	Cheerful-4 Happy-3 Tired-2 Nervous-1		
	Composite QOL Index (Grand Total)			

QOL = Quality of life



Graph 1: Graph (Box and Wilson Plot) showing comparison of quality of life index scores pre- and post-operatively

RESULTS

Between January 2010 and December 2012, out of 360 cases registered at our center, 55 cases with hypersplenism and increased PRBC transfusion requirement underwent complete open splenectomy. Five patients above 16 years were excluded from the study. Of the remaining 50 cases, there were 35 males and 15 females, between 5 and 16 years. Mean age of the study population was 9 years. Two children were HIV positive. Open splenectomy was performed in all 50 children via transverse left upper quadrant incision. One child with cholelithiasis underwent concomitant cholecystectomy. None of the children had injuries to neighboring organs such as stomach, pancreas, colon or the diaphragm. None of them required re-explorations for bleeding from delayed/secondary hemorrhage. No patient had tube drain related complications. None of them had burst abdomen/major surgical site wound infection. None of the patients developed deep vein thrombosis or portal vein thrombosis. There were no major perioperative complications. Two late deaths occurred during the study period. Eight children developed long bone fractures, following trivial trauma, but they all healed well without deformities. One child developed complications from cerebrovascular thrombosis and received Warfarin. The common infections noted in children following splenectomy were upper respiratory tract infections, pulmonary tuberculosis, minor skin abscesses and dental caries. Urinary tract infections were common among girls. Blood cultures were sent in children who had prolonged fever postoperatively. Of 20 children, cultures in 10 children had grown *Klebsiella*.

At a mean follow-up of 3 years, all children continue to reap the benefits of splenectomy. Their transfusion requirement remains low as compared to the preoperative value of 200-350 cc/kg/year. Frequency of Hb drop has decreased, and the Hb levels are maintained at a higher range >8 gm%. Transfusion requirement has decreased, and interval has increased from 10 days to 20-30 days. There is average rise of 17.8 in the QOL Index from the preoperative level of 13.5 at a follow-up of 2-years, indicating improvement in health status following splenectomy. The variance (of QOL index) is 2.98 preoperatively and 6.87 postoperatively. The “P value” obtained on analysis of composite QOL indices using paired *t*-test is >0.001 that is statistically significant.

DISCUSSION

β -thalassemias are a group of hereditary blood disorders characterized by anomalies in the synthesis of the beta chains of Hb, resulting in variable phenotypes ranging from severe anemia to clinically asymptomatic individuals.^[3] The worldwide annual incidence of symptomatic individuals is estimated to be 1/1,00,000 population.^[3] Though categorized as a hematological disorder, it causes multisystem involvement damaging the heart, liver, bones, kidneys and many endocrine glands; leading to significant morbidity in these children.^[3-6] Our study mainly focuses on the objective assessment of the impact of splenectomy on QOL of these children with symptomatic hypersplenism.

Various authors like Machado *et al.*, al-Salem *et al.*, al Hawsawi *et al.* have previously published series with splenectomy in thalassemia

patients and the benefits of splenectomy have been found to be unequivocal by one and all.^[2,7-9] Various series by Targarona *et al.*, Wolff *et al.* have detected decreased PRBC transfusion requirement and less drop in Hb following splenectomy.^[10,11] However, none of the previously published studies have taken into account and objectively assessed the impact of splenectomy on overall QOL of children with β -thalassemia. Our's is the first ever study of this kind.

Poddubnyi *et al.* have used the standard short-form-36 (SF-36) scale in children with benign hematological disorders including thalassemia. They found improvement in almost all parameters of life quality after laparoscopic splenectomy.^[12] However, we found the application of the SF-36 scale, which is a general indicator of health status commonly used in adults to be tedious, time-consuming and impractical in children as young as 5-16 years. Ware and Sherbourne, the inventors of the SF-36 scale themselves have utilized this scale in patients above 14 years of age.^[13] Based on the concept of SF-36 scale, we employed our own modifications and have formulated a standardized protocol/scale [Table 1] for assessment of QOL of children with β -thalassemia having symptomatic hypersplenism. It records the rise in QOL and objectively documents the improvement in overall QOL of these children following splenectomy.

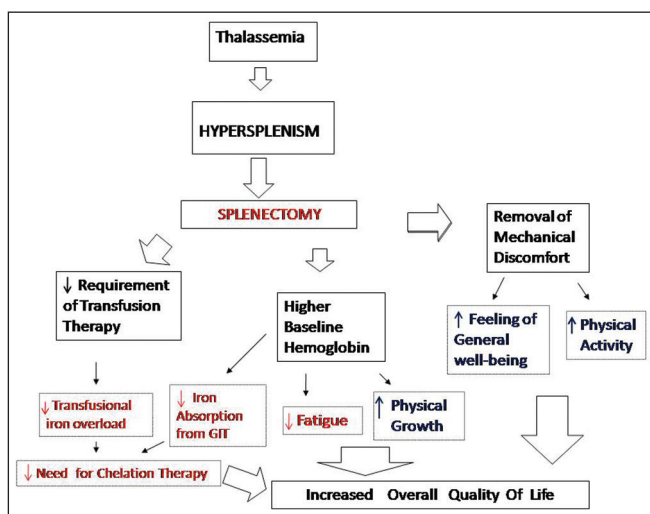
The mechanisms by which splenectomy imparts its benefits can be postulated as follows (Schematic Representation 1). By means of operative removal of large bulk of tissue eating away the blood cells, it decreases the requirement of PRBC transfusion therapy. Similarly, by reducing the number of PRBC transfusions per month, it prevents problems associated with transfusional iron overload, which is a major concern in patients with thalassemia. In addition, by maintaining higher baseline Hb value and preventing frequent Hb drops, it decreases iron absorption from the gut (chronic anemia produces an increase in iron absorption from the gastro-intestinal tract); thereby decreasing the need for chelation therapy, which in itself is associated with long-term sequelae.^[5] Removal of mechanical discomfort from the massively enlarged spleen gives a feeling of general well-being and helps in increased physical activity in these children. Furthermore,

the less Hb drop leads to less fatigue, increased physical growth and improves the overall QOL of these children.^[5]

Portal vein thrombosis is a recognized complication after splenectomy in β -thalassemia major due to the chronic hypercoagulable state that exists in childhood thalassemia.^[14] Various authors like Al-Hawsawi *et al.* have reported portal venous thrombosis in children undergoing splenectomy especially within the 1st month following splenectomy.^[14,15] We did not have any incidence of portal venous thrombosis. However, we had one child with cerebrovascular thromboembolic complication as has been described by DeBaun *et al.*^[5] He responded well to Warfarin. The postsplenectomy infectious complications noted were upper respiratory tract infections, pulmonary tuberculosis, minor skin abscesses, dental caries and urinary tract infections among girls, similar to the studies. However, we do not have detailed microbiological data of these infectious complications. Wolff *et al.*^[11] have reported mortality. Two deaths attributable to septicemia occurred in our study beyond 2 years following splenectomy, one being a seropositive child.

The objective assessment of QOL focuses on what the individual can do and is important in defining the degree of health.^[16] In our study, the composite QOL index rose from the preoperative level of 13.5 to 31.3, 2 years postoperatively. There were many hurdles in objectively calculating the QOL index, e.g., growth assessment of the children 2 years postsplenectomy might be partly influenced by the pubertal growth spurt since at least one-third of our children were above 10 years at the time of postoperative assessment and since we do not have pre and postoperative hormonal data for comparison of the same. However, growth assessment is definitely one of the major determinants of the overall QOL. Morsy *et al.* have studied echocardiographic changes in splenectomized and nonsplenectomized individuals.^[17] They have described left ventricular diastolic dysfunction in splenectomized individuals having reserved left ventricular systolic dysfunction preoperatively. Also, they (splenectomized individuals) are at a higher risk of developing pulmonary hypertension.^[17,18] We had two-dimensional ECHO done on all children preoperatively. Many of them had ejection fraction between 50% and 60%. Two-dimensional ECHO done on follow-up has shown stabilization of cardiac function in few of our children. However, because of technical problems, we could not get two-dimensional ECHO in all children postoperatively. In spite of above limitations simplicity, sensitivity, objectivity, good internal consistency and minimal inter-rater variability are major advantages of this particular standardized protocol/scale devised by us. In addition, it is less time-consuming, requiring <10-15 min to complete the entire assessment. Majority of our children are on regular follow-up, and we plan to present an extended comparative study of composite QOL index on long-term follow-up in near in future.

Furthermore, this is the largest study from the Indian subcontinent treating thalassemia children. Though regular PRBC transfusions and chelation therapy along with splenectomy improve life expectancy and QOL, there is life-long risk of postsplenectomy infections and so far, there is no definite cure for these children. There is ample scope to utilize new strategies for specific therapy like bone marrow



Schematic Representation 1

transplantation, peripheral blood stem cell transplantation, specific gene therapy^[6] and fetal Hb augmentation^[19] in these children to ease their life in future.

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