Splenectomy in sickle cell haemoglobinopathies

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ABSTRACT

Background: Sickle cell disease is one of the common haemoglobinopathies in the world. Among its various clinical presentations, splenic complications are associated with high morbidity and substantial mortality, the only effective preventive strategy for which is prophylactic splenectomy. The aim of the present study was to observe the safety and effectiveness of splenectomy to prevent frequent requirement of hospitalizations, blood transfusions and splenic complications in patients of sickle cell disease.

Methods: The study was carried out in 72 patients of SCD with splenomegaly who underwent splenectomy for some indication in the surgery department of VSSIMSAR, Burla during the period from October 2016 to September 2018. Their preoperative baseline hematological parameters and frequency of transfusion requirement was compared with postoperative status.

Results: Of these 72 SCD patients, 49 (68.7%) patients had repeated requirement of blood transfusion and hypersplenism, 22 (30.5%) patients had history of one or more episodes of splenic sequestration crises, one patient had splenic abscess. After splenectomy the mean increase in haemoglobin level, TLC and TPC was respectively 2.83±0.9 gm%, 1.7±0.8 lac/cm3 and 2726±1618/cm3. Operative mortality was 0%. None of the patients required any blood transfusion and no major postoperative complications during 6 months follow up period.

Conclusions: The morbidity of the patients of SCD in terms of repeated hospitalizations, blood transfusion, living with a huge spleen, accompanying symptoms and its complications can be effectively minimized by the elective splenectomy. With good preoperative preparation and post-operative management, splenectomy in SCD patients is a safe procedure with minimal risk of post-operative complications.

Keywords: Sickle cell disease, Hypersplenism, Splenectomy

INTRODUCTION

Sickle cell disease is one of the common haemoglobinopathies in the world.1 It is an inherited structural abnormality of haemoglobin, a most common monogenic disorder with autosomal recessive inheritance globally.2,3 Based on 1981 census figures of population in India, it was estimated that there were 24,34,170 carriers and 1,31,375 sickle cell homozygotes among the tribes in India.4,5 The spleen plays a central role in the pathology of sickle cell disease which undergoes gradual fibrosis due to microvascular occlusion.6,7 During this, there may occur episodes of acute splenic sequestration crisis, hypersplenism, massive splenic infarction and splenic abscess which are associated with an increased morbidity and substantial mortality too.8 The Asian haplotype of HbS mutation recognized in India is in many ways different from the African counterpart. It is associated with high level of HbF which has been suggested to be one of the causes of persistent splenic enlargement in India.2,4,9 This makes the patients vulnerable to suffer life threatening splenic complications, one of the effective preventive strategies of which, is elective splenectomy. This study was carried out to observe the post-operative
The demographic characters of these 72 patients are represented below in Table 1. The mean age of presentation was 12.9±6.3 years with 50% of the patients presenting in the second decade and 16.6% in their third decade also.

### Table 1: Demographic characters.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Number of patients</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤10</td>
<td>24</td>
<td>33.3</td>
</tr>
<tr>
<td>11-20</td>
<td>35</td>
<td>48.6</td>
</tr>
<tr>
<td>21-30</td>
<td>12</td>
<td>16.6</td>
</tr>
<tr>
<td>≥30</td>
<td>01</td>
<td>1.3</td>
</tr>
</tbody>
</table>

49 (68.05%) patients had repeated requirement of blood transfusion and hypersplenism as the indication for splenectomy, 22 (31.9%) patients had history of one or more episodes of splenic sequestration crises, one patient had splenic abscess.

The average preoperative haemoglobin level was 6.56±0.9 gm%, the total WBC count was around 7176±2245/mm$^3$. total platelet count was 213±0.57 lac/mm$^3$. Mean rate of blood transfusion preoperatively was 9.2 per year. The average spleen size of the patients was 17.5±1.46 cmm as measured by ultrasonography.

### Figure 1: Pre and post-operative haemoglobin.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Pre-splenectomy Mean±SD</th>
<th>Post-splenectomy Mean±SD</th>
<th>Mean change±SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin (gm%)</td>
<td>6.56±0.9</td>
<td>9.44±0.5</td>
<td>2.83±0.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>TLC (per cmm)</td>
<td>7176±2245</td>
<td>9293±928</td>
<td>2726±1618</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>TPC (per cmm)</td>
<td>2.13±0.57</td>
<td>3.6±0.5</td>
<td>1.7±0.8</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
The spleen undergoes progressive fibrosis at variable rates in different patients of African origin. But the Asian haplotype of HbS mutation is quite different from the African type. The Asian haplotype, though causes a milder illness, is associated with high level of foetal haemoglobin which has been shown to be one of the causes of persistent splenomegaly.\(^4,5\) The greater frequency and later peak incidence of splenomegaly in association with hypersplenism has been documented in Indian homozygous sickle cell disease patients.\(^2,5\) The late persistent splenomegaly adds to the morbidity of the patients by predisposing them to the complications as above. Splenic enlargement does not imply normal function, and the enlarged spleen may act only as a reservoir for blood with markedly deranged reticuloendothelial system function.\(^6\)

Acute splenic sequestration is characterized by a tender, rapidly enlarging spleen due to the trapping of sickled erythrocytes and other blood constituents. This may lead to shock due to loss of effective circulating volume and fall in the haemoglobin concentration at least 2 g/dl from baseline, usually with evidence of reticulocytosis and often moderate to severe thrombocytopenia.\(^7,8\) The condition is potentially fatal and requires prompt resuscitation and transfusions. However, recurrence carries a 20% mortality rate and can occur in 50% of those who survive.\(^7\) The natural history and prognosis of this fatal complication in our country is yet to be studied. As a means to prevent future acute splenic sequestration crisis, elective splenectomy has been indicated in children older than 2 or 3 years of age after the first episode of the crisis.\(^10,11\)

Hypersplenism is defined as a clinical syndrome characterised by splenic enlargement, any combination of anaemia, leukopenia or thrombocytopenia, compensatory bone marrow hyperplasia and improvement after splenectomy. The patients become transfusion dependent to maintain haemoglobin level. Chronic hypersplenism may occur as early as 1 year but is most common between 5 and 10 years and is unusual after 15 years.\(^12\) But in our study hypersplenism was found to persist

Mean requirement of blood transfusion in the 6 months post-operative period was 0.264 with 25\(^{th}\) quartile being 0 and 75\(^{th}\) quartile 0 (Figure 3). Only three patients required hospitalization for upper respiratory tract infection in the 6 months follow up period, which were managed with standard antibiotics and discharged in stable conditions. One patient suffered two episodes of painful crisis on 20\(^{th}\) and 45\(^{th}\) post-operative day and was managed with analgesics and blood transfusion.

**DISCUSSION**

The splenic complications lie behind the major part of the pathological events in the early life of sickle cell disease patients which are acute sequestration, hypersplenism, splenic infarction leading to functional asplenia, splenic abscess. Acute splenic sequestration crisis is known to be the most common cause of early deaths in these patients.\(^3\) The spleen undergoes progressive fibrosis at variable rates in different patients of African origin. But the Asian haplotype of HbS mutation is quite different from the African type. The Asian haplotype, though causes a milder illness, is associated with high level of foetal haemoglobin which has been shown to be one of the causes of persistent splenomegaly.\(^4,5\) The greater frequency and later peak incidence of splenomegaly in association with hypersplenism has been documented in Indian homozygous sickle cell disease patients.\(^2,5\) The late persistent splenomegaly adds to the morbidity of the patients by predisposing them to the complications as above. Splenic enlargement does not imply normal function, and the enlarged spleen may act only as a reservoir for blood with markedly deranged reticuloendothelial system function.\(^6\)

All of the patients underwent complete splenectomy by open method. Operative mortality was 0%. Average duration of post-operative stay in the hospital was 7 days. 10 patients had fever and 8 patients had surgical site infections during this period and were managed conservatively. During the 6 months follow up period, average (mean of the values observed at 1 month, 3 months and 6 months post-operatively) post-operative haemoglobin was 9.44±0.5 gm% (Figure 1), TLC 9293±928/cmm, TPC 3.6±0.5 lac/cmm (Figure 2). The average rise in postoperative haemoglobin was 2.83±0.9 gm%, TLC raised by 2726±1618/cmm, TPC raised by 1.7±0.8/cmm (Table 2). Wilcoxon signed rank test was used for comparison between pre and post-operative data (p<0.0001).

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beyond 15 years in 8 out of 72 (11%) patients of which one patient presented at 30 years of age.

Though chronic transfusion remains another option in dealing with these complications, the post transfusion reduction of the load of sickled cells lessens the possibility of splenic atrophy and retains the risk of subsequent sequestration attacks. Chronic repeated transfusion of blood or blood products carries its own risks of alloimmunisation, blood borne infections, transfusion reactions, iron overload etc. The requirement of frequent admissions for transfusion is an added stress on the part of the patient and their parents and also a burden on the healthcare system in view of the low availability of matched blood. In view of this, elective splenectomy appears a more rational treatment option. But this is often avoided in the hope that the spleen will face the natural fate of autoinfarction in sickle cell disease patients and the patients need not be offered a major surgical intervention and be deprived of the immunological role of spleen in combating different infections. As stated above the spontaneous splenic atrophy has been less frequent in Indian variety of the disease. The study of splenic function by colloid scan by Pearson and colleagues demonstrated that in children with SS disease, after each episode of sickle cell crisis, pitted red cell count increases indicating the gradual loss of splenic function with every attack. So the return of normal immunological function of the spleen after episodes of crisis is unlikely. With good pre and post-operative care splenectomy appears to be a safe, effective and better option in the management of patients of sickle cell haemoglobinopathies with splenic complications in this region. The risk of post-splenectomy sepsis found out in past studies is approximately 2% but increases substantially if splenectomy is performed before 4 years of age. None of the patients included in our study developed overwhelming post-splenectomy sepsis in the six months post-operative follow up period. However, long term follow up studies are needed to know the late complications and the post-splenectomy quality of life of the patients.

Splenectomy quality of life has been shown by previous studies that with modern anaesthetic and surgical techniques, elective splenectomy appears to be a safe and fairly minor procedure and the arguments against splenectomy in the patients of SCD with splenic complications like acute splenic sequestration crisis and hypersplenism are less convincing.

CONCLUSION

Although splenectomy has not been proven to increase survival, it significantly reduces the morbidity of the patients of SCD by reducing frequency of hospitalization for transfusion, giving relief from a huge spleen and its accompanying symptoms and preventing the dreaded complications of future acute splenic sequestration crisis. With good preoperative preparation and post-operative management, splenectomy in SCD patients is quite a safe procedure with minimal risk of post-operative major complications.

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REFERENCES
