ORIGINAL PROF-770

# SPLENECTOMY;
## IN IDIOPATHIC THROMBOCYTOPENIA (A RETROSPECTIVE REVIEW)

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**ABSTRACT...** azam103@hotmail.com **Objective:** To assess the role of splenectomy in patients of idiopathic thrombocytopenic purpura. **Design:** It is a retrospective study. **Place and Duration:** This study was conducted at PNS Shifa Karachi, Combined Military Hospital Lahore and Military Hospital Rawalpindi spanning over last 10 years from 1993-2003. **Subjects and methods:** A total of 17 patients were included in the study, which were diagnosed as a case of idiopathic thrombocytopenic purpura after excluding other causes of thrombocytopenia. In all cases steroids were stopped either due to non responsiveness or severe side effects. Splenectomy was done in all 17 patients included in the study, after immunization and maintaining the platelet count with in near normal range by platelet transfusion. Post operative platelet count was monitored and improvement in clinical parameters was recorded. **Results:** All 17 patients showed improvement in platelet count and clinical symptom. Mortality remained zero despite of inclusion of high risk diabetics and hypertensives. **Conclusion**: when steroids become ineffective, splenectomy becomes the definitive therapeutic tool to control the effects of low platelet count.

**Key words:** Idiopathic thrombocytopenic purpura. Splenectomy

## INTRODUCTION

Idiopathic thrombocytopenic purpura is an autoimmune disorder in which 1gG auto-antibody is formed that binds to platelets. Splenic macrophages with Fc receptor bind to antibody-coated platelets and destroy them [1.2.3.4..5] and characteristically spleen is normal in size[3]. It is a diagnosis of exclusion[6].

The estimated incidence is 100 cases per 1 million persons per year, and about half of these cases occur in children[7]. Most of the cases present between 20-50 years age, immune thrombocytopenic purpura in adults is generally chronic, the onset is often insidious. There is 3:1 female preponderance[3.8].

Preliminary screening is done to rule out the causes of secondary forms of the ITP which occur in association with systemic lupus erythematosus, the antiphospholipid syndrome[9] immunodeficiency states (1gA deficiency and common variable hypogamma-globulinemia), lymphoproliferative disorders (chronic lymphocytic leukemia, large granular lymphocytic leukemia, and lymphoma), infections with human immunodeficiency virus and hepatitis C virus, and therapy with drugs such as heparin and guanidine.

It is an auto immune disease affecting the platelets leading to hemorrhage that may constitute a hematological emergency. It should be properly

investigated and treated. Treatment should be directed for underlying conditions as well, as specific measures to raise the platelet count.

The commonest presentation is bruising of the trunks and extremities in association with gum or conjunctival bleeding in males with active disease. In females the presentation includes menorrhagia with other symptoms.

Less commonly haematuria and gastrointestinal haemorrhage may occur. In children there is frequently a history of preceding viral infection, or immunization against diphtheria, pertussis, tetanus, polio, measles or rubella.

Physical examination reveals only few signs, spleen remains infrequently palpable[3]. Most of the symptoms occur with platelet counts of 5-20 x $10^9$/L, in chronic cases it may be 20-25x$10^9$/ L[3.10.]

Bone marrow examination is important not only to exclude leukemia but also to support the diagnosis of ITP. It reveals increased number of megakaryocytes in an acute marrow[3].

Regarding prognosis and management, ITP can be arbitrarily divided into three types:-

1. **Acute ITP** is defined as , when recovery occurs within three months (85%).
2. **Chronic ITP** is defined in those who have not recovered after 06 months (11%).
3. **Intermittent ITP** includes small number of patients who recover but relapse periodically especially with infections (4%).

Acute cases are usually managed by physicians with steroids, high dose immunoglobins, platelet transfusion and very rarely emergency splenectomy is required in intracranial haemorrhage or where bleeding is severe & uncontrolled by above mentioned measures.

Initial treatment is with steroids. Failure to steroid therapy, intolerance to steroids such as psychosis or avascular necrosis of bone; uncontrolled hypertension or diabetes mellitus; active infection, and pregnancy and emergency control of intra cranial bleeding warrants splenectomy as a definitive treatment. High doze intravenous immunoglobulins are expensive. In refractory cases danazole has promising results. Immunosupressive agents also have their role in refractory cases. In severe and refractory cases high dose immune suppression and autologous stem cell transplantation has very good results in symptomatic treatment[3].

The chronic group has modified causes of treatment at different levels. They continue to have thrombocytopenia once the steroids are weaned off (this is the group of patient referred to Surgeon). In this group of patients there is no justification to keep the platelet counts up with long term steroids because the complications of such therapy far exceeds the benefits.

## MATERIAL & METHODS

**Patients:** A review of 17 patients of ITP was carried out. All patients were diagnosed as idiopathic thrombocytopenic purpura after exclusion of other causes of thrombocytopenia see Table I.

**Inclusion Criteria:** All thrombocytopenic patients irrespective of age and sex were included

- Who have no secondary cause of thrombocytopenia like cirrhosis, drugs and pregnancy.
- Who were non responsive to steroid treatment or have severe side effects due to steroid.
- Patients who got relapse after initial glucocorticoid treatment.
- Patients who were diagnosed as ITP of more than 06 weeks duration and continue to have platelet count less than 10,000/cmm with or without bleeding.
- Transient response to therapy and platelet count is less than 30,000 /cmm.
- Patients in second trimester or girls approaching menarche who failed to steroid therapy and intravenous immunoglobulins

and platelet count less than 10,000/cmm or bleeding problem with platelet count less than 30,000/cmm.

**Steroid responders** were those who met the following criteria and were excluded from the study:

- Increase in the platelet count of at least 30000 per cubic millimeter.
- A platelet count of more than 50000 per cubic millimeter by day 10 after the initiation of treatment.
- Cessation of bleeding on taking steroids.

**Steroid non responders** which were defined as:

- An increase in the platelet count of less than 30,000 per cubic millimeter.
- Platelet count of more than 50,000 per cubic millimeter or less by day 10. Seven of the patients were having severe side effects due to steroids.
- Steroid intolerance was defined as patients developing gastric ulcer and bone pains, psychosis, diabetes mellitus, uncontrolled hypertension and pregnancy.

## PROCEDURE

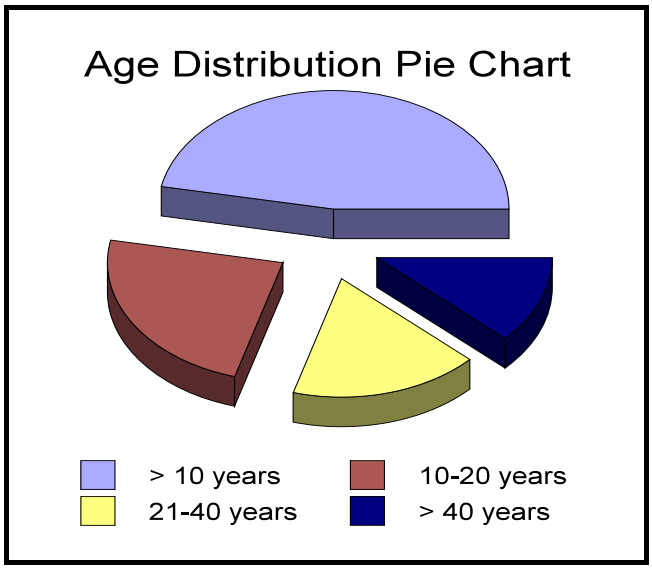
All patients underwent splenectomy with prior vaccination against Strept. Pneumoniae, Haemophilus Influenza and Neisseria meningitides 02 weeks prior to the procedure. Pre, peri and post operative antibiotic cover with broad spectrum antibiotics was provided to cater for infection. Midline laparotomy incision was made in all 17 cases to avoid post operative haematoma in the incision.

A pre operative platelet count of about 25 – 35 x $10^9$/L was assured by platelet transfusions. Rest of the platelet transfusion were done after splenic artery legation. The overall platelet count during operation & immediate preoperative period was maintained at 50,000/μL. Steroids were tapered off in all cases with consultation of physicians.

Follow up: All the 17 patients were followed up by regular platelet count and clinical examination regarding bruisability, spontaneous bleeding from gums, in joints and purpuric spots. Females were especially looked after for their menstrual flow. All patients were instructed to contact immediately in case of any sign of infection even mild sore throat to OPSI. All patients revealed remarkable improvement in platelet count which was maintained even 5 years after the splenectomy. The overall progress was excellent. There was no mortality related to procedure.

## RESULTS

17 patients were included in the study. 41% were less than 20 years age, and 59% were above 20 years age. Median age 24, mean age 23.73 and Mode was found to be 30. (Table II). Female preponderance was noted in the ratio of 10:7 (Table III).




Clinically easy bruise ability was found in 58%. Haemarthrosis was found in 12% and all were males. Pateachea in 58%, menorrhagia was the main symptom in 67% of the females, and bleeding gums was found in 47% and 50% of the children were

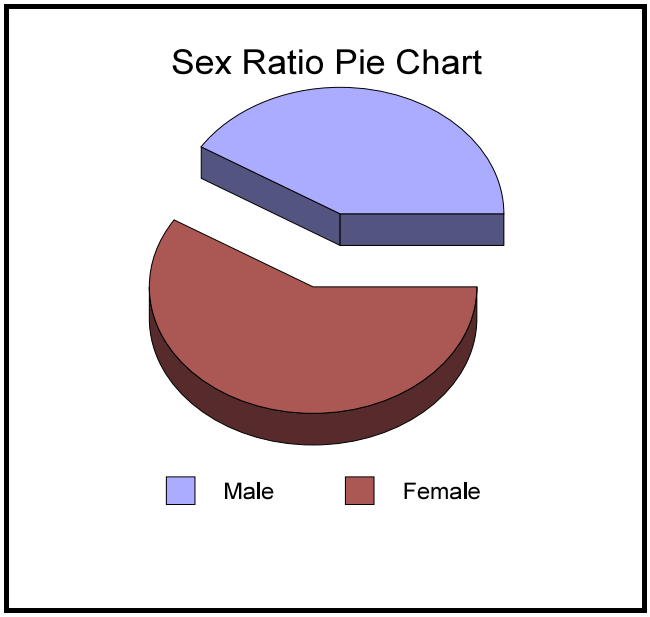
affected.

| Table- I Differential Diagnosis of ITP | |
|---|---|
| **Sr. No.** | |
| 1. | **Falsely Low Platelet Count**<br>In Vitro platelet clumping<br>Giant Platelets |
| 2. | **Common Causes of Thrombocytopenia**<br>Drug Induced<br>Quinidine, heparine, quinine, sulphonamide drugs<br>Pregnancy<br>Viral infections like Rubella, infectious mono nucleosis, AIDS.<br>Hypersplenism due to chronic liver diseases |
| 3. | **Other causes Mistaken for ITP**<br>Mylodysplasia<br>Congenital Thrombocytopenia<br>Chronic DIC |
| 4. | **ITP associated with other diseases**<br>SLE<br>Lymphoproliferative diseases. |

| Table- II Age Distribution (n= 17) | | |
|---|---|---|
| **Sr. No** | **Age in years** | **No. of patients** |
| 1 | Under 10 years | 8 |
| 2 | 10 - 20 years | 4 |
| 3 | 21 - 40 years | 3 |
| 4 | More than 40 years | 2 |

| Table-III Sex Ratio | | |
|---|---|---|
| **Sr. No** | **Sex** | **Number of Patients** |
| 1 | Male | 7 |
| 2 | Female | 10 |

The mean platelet count before treatment was 11,820 per cubic millimeter (range, 3000 to 40,000 per cubic millimeter and after splenectomy it raised to more than 220 x $10^9$/L at an average.




| Table- IV Mode of Presentation | | |
|---|---|---|
| **Sr.No** | **Symptoms/Signs** | **%age** |
| 1 | Easy Bruisability | 58 |
| 2 | Haemarthrosis | 12 |
| 3 | Pataechea | 57 |
| 4 | Bleeding gums | 47 |
| 5 | Menorrhagia | 41 (All female) |
| 6 | Intra cranial Hemorrhage | Nil |
| 7 | Splenomegaly | Nil |

All the patient have been treated by physicians with steroids and immuno-suppressants for variable period ranging from 6-months to 10 years. Treatment record was not available. The platelet count was found to be 3000-40000/cmm at the time of operation. Three diabetic and two hypertensive were among the patients who underwent splenectomy. In no case OPSI was reported. And post operative wound haematoma was found in one patient. There was no operative mortality in the studied group.

| Table V Post Operative Out come | | |
|---|---|---|
| **Sr. No** | **Parameters** | **Results** |
| 1 | Platelet count | > 220000/c.m. |
| 2 | OPSI | Nil |
| 3 | Mortality | Nil |
| 4 | Morbidity | |
| | a. Post op. wound haematoma. | 01 |
| | b. Wound infection | Nil |

## DISCUSSION

Treatment plan of the patient with ITP must consider the age, severity of illness and anticipated natural course of the disease [3]. Splenectomy is considered an alternative if after one to two years has relapsed after diagnosis and thrombocytopenia persists. There are no absolute indications of splenectomy and each case has to be considered on its own merit[11].

There is no means of predicting an individual patient's response to splenectomy [10]. Results of numerous studies indicate that approximately two thirds of patients have a response, generally within days [12]. Patients with platelet counts below 50,000 per cubic millimeter may require corticosteroids, intravenous immune globulin, or anti-D immune globulin before surgery [3].

However, splenectomy can often be performed, if necessary, without additional therapy, even in patients with low platelet counts[8]. In experienced hands, laparoscopic splenectomy is another novelty with short-term and long-term benefits and complications. The use of laparoscopic surgery also speeds recovery and shortens hospitalization. Splenic radiation has been used as short-term treatment in patients who are too frail to undergo surgery.[13]

Acute cases are usually managed by physicians with steroids, high dose immunoglobins[14]; platelet transfusion and very rarely emergency splenectomy is required where bleeding is severe & uncontrolled by above mentioned measures.

The chronic group includes the patient having modified causes of treatment at different levels [15,16.] They continue to have thrombocytopenia once the steroids are weaned off (this is the group of patients referred to Surg).

In this group there is no justification to keep the platelet counts up with long term steroids because the complications of such therapy far exceed the benefits.

## ROLE OF SPLENECTOMY

Behaviour of ITP is different in children and adults[3]. In children disease regresses spontaneously in 75% after one attack which is ushered by viral illness. Steroids are first choice in treatment. Splenectomy is reserved for those children who have relapsed and girls approaching menarche [17.18.] In adults the disease runs a protracted course so use of steroid should be considered in first place followed by splenectomy in treatment failure, in relapses, in steroid side effects and in emergency case where intra cranial bleeding is life threatening. Though in acute phase of ITP splenectomy is contraindicated, still its role is established in massive uncontrollable bleed[18]. These are no absolute indications of splenectomy and each case has to be considered on its own merit as the main object is to keep the patient symptom free. Low platelet count is compatible in those who have to live in relatively trauma free environment, mostly indoor. Those with outdoor activities more aggressive treatment including the splenectomy is to be considered[17].

There are two schools of thought in this regards and "Pros and cons" of operations must be discussed with the patient and family before splenectomy because:-

### IN FAVOR OF SPLENECTOMY

It is very effective in elevating the platelets count to normal levels in at least 90% of cases. In others the counts are above levels necessary to prevent bleeding. In our experience splenectomy has never failed to normalize platelet counts. The effect is very rapid – within a day in my experience and some claim as soon as the splenic artery is clamped.

It gives a good quality of life. Although the morbidity and mortality from intracranial hamorrhage from chronic ITP is low but patients with chronic ITP do not lead normal lives – their activities are restricted and contact sports are prohibited. Moreover they are subject to psychological stress of the long illness.

Splenectomy gives freedom from worry about intra cranial hemorrhage (ICH), unexpected surgery, accidents and menorrhagia in adolescence. Although the risk of ICH is extremely low but it is not absent. Moreover the patients are prone to bleeding when platelet counts drop after an inter-current infection. One is never sure when to undergo major surgery following accidents, so splenectomy as a prophylactic measure do have an edge.

### AGAINST SPLENECTOMY

The greatest disadvantage of splenectomy is the very real but small danger of over whelming post splenectomy infection (OPSI) usually due to pneumococcus or meningococcus or Haemophilus influenza. Its incidence is generally in the range of 1-0.5 percent and mortality is 50-90%. A high index of suspicion is important to make an early diagnosis usually based on fever and positive culture. The duration of symptoms from onset to shock from adrenal hemorrhage can occasionally be very short.

The low incidence of OPSI can be further reduced by the use of polyvalent pnemococcal, Vaccine before splenectomy and prophylactic administration of monthly benzathine penicillin 1.2 mega units for at least 02 years post splenectomy.

## CONCLUSION

Splenectomy almost always relieves bleeding symptoms. It ensures good quality of life, abates the psychological stress of chronic illness and signals at freedom from worry about ICH, unexpected surgery, accidents and menorrhagia in adolescence girls. The low but significant risk of OPSI has to be carefully considered & managed well before and after the operations.

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