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# LAPAROSCOPIC SPLENECTOMY FOR PATIENTS WITH IMMUNE THROMBOCYTOPENIA

**[1]*Dr. Monier T. Ahmed Altaee, [2]Dr. Hayder Nooruldeen Hayder and [3]Dr. Adil K. Sallom**

[1]Head of Surgery Department /Ibn Sina Training Hospital/Baghdad. Iraq.
[2,3]Baghdad Teaching Hospital, Baghdad. Iraq.

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***Corresponding Author: Dr. Monier T. Ahmed Altaee**

Head of Surgery Department /Ibn Sina Training Hospital/Baghdad. Iraq.

## ABSTRACT

**Background:** Laparoscopic splenectomy (LS) is the one of the most important second-line treatment for patients with Idiopathic thrombocytopenic purpura (ITP) who do not respond to corticosteroids. **Aims:** To identify risk factors associated with persistence thrombocytopenia after LS for ITP patients and to investigate the short complications associated with LS. **Method:** This is a single center prospective study including a total of 40 patients with ITP who undergo LS. Patients were followed up for 30 days after operation. Data regarding the presence of complication (bleeding, hematoma, abscess, atelectasis, pneumonia and others) were recorded. Furthermore, a blood sample was collected from each patient was collected and the platelet count was calculated. The primary end point of the study is the success or failure of LS in treatment of ITP. **Results:** 31 patients (77.5%) had complete response (increase in platelet count >100000 above baseline value), 6 (15%) had response, and 3 (7.5%) had no reaction. 11 (27.5%) encountered complications. No patient had several problems. Abscess and atelectasis were the most prevalent consequences. Two patients (5%), pneumonia, haemorrhage, and hematoma, and one patient (2.5%), had portal site infection. Female gender, comorbidities, and complications substantially predicted non-complete response. **Conclusion:** Refractory ITP patients may safely have laparoscopic splenectomy independent of preoperative PLT. The treatment does not cause blood loss or conversion. Iraqi ITP receiving LS had severe postoperative complications. Female gender, comorbidities, and complications may raise LS failure rates.

**KEYWORDS:** Laparoscopic, splenectomy, patients, immune, thrombocytopenia.

## INTRODUCTION

Immune thrombocytopenia (ITP) has replaced the term 'idiopathic thrombocytopenic purpura'. The name change acknowledges that ITP results from immune system dysregulation rather than being idiopathic (of unknown cause).[1] ITP is diagnosed when platelet counts fall below 100 × 10^9/l, despite the normal threshold being approximately 150 × 10^9/l.[2,3] Annually, ITP affects 1.9-6.4/100,000 children and 1.6-3.9/100,000 adults. Yet, only 30-50% require treatment.[4] Splenectomies occur at a rate of 5% for adult ITP patients, translating to 1-2 splenectomies/year in a million.[5] Primary ITP's exact autoimmune nature remains elusive as it's primarily diagnosed by excluding other conditions.[6] Three central mechanisms contribute to thrombocytopenia: IgG autoantibodies impair platelet production and lead to antibody-mediated platelet phagocytosis.[7] Autoreactive cytotoxic T cells (CD8+) destroy platelets and megakaryocytes.[7,8] The pro-inflammatory environment reduces or impairs T and B regulatory lymphocytes, leading to an uncontrolled proliferation of autoreactive cells.[5] The spleen plays a pivotal role in this disease process by promoting immune imbalance, being the primary site of autoantibody production, and regulating circulating GPIIb/IIIa-reactive T and B cells.[9-12] The spleen also houses long-lived plasma cells not affected by anti-CD20 antibodies.[13] Predicting splenectomy success is challenging. However, younger patients often exhibit better responses.[14,15] while elderly patients may see increased perioperative complications.[16] Factors like the duration of ITP, comorbidities like SLE, and responses to treatments like corticosteroids have been investigated as predictors, but results vary across studies.[17-19] In the 1980s, Indium-labeled autologous platelet scanning showed promise in predicting splenectomy response.[20] The procedure involves

infusing the patient with 111In-labeled platelets and then using scintigraphy to locate platelet clearance sites. A splenic pattern on this scan predicts a higher splenectomy response rate, while hepatic or mixed patterns predict lower rates. However, its adoption remains limited due to technical challenges and availability issues.[20] The present study aimed: to identify risk factors associated with persistence thrombocytopenia after splenectomy for ITP patients, and to investigate the short complications associated with splenectomy and suggesting recommendations to avoid these complications.

## METHOD

A single-center prospective study was conducted at the Department of Surgery/Baghdad Medical City between 1st January to 31st December 2021. The research secured approval from the Arab Council of Medical Specialization.

### Participants

- **Total Number:** 40 ITP patients set to undergo Laparoscopic Splenectomy (LS).

### Inclusion Criteria

- All ITP patients of both genders preparing for LS.
- Age should be 18 years or older.

### Exclusion Criteria

- Those who had previous laparoscopic or open surgery.
- Pregnant women.

### Ethical Measures

- Obtained written consent from all participants after explaining the study's objective.
- Assured the confidentiality of participants' data, which would be used solely for research.

**Surgical Technique:** LS was performed using a standard three-trocar technique. Notable steps included avoiding splenic tissue spillage, searching and removing any accessory spleens, and placing a drainage tube in the left upper quadrant as a post-op bleeding or pancreatic fistula indicator.

**Follow-Up:** Patients were tracked for 30 days post-surgery. They were asked to visit the center weekly. Information collected included:

- Demographic details.
- Duration of disease.
- Treatment protocols.
- Complications like bleeding, hematoma, abscess, atelectasis, pneumonia, etc.
- Blood samples to assess platelet counts.

**Endpoints:** The study's primary goal was to evaluate the success or failure of LS in treating ITP based on three criteria

- **Complete Response:** Normal platelet count (>100,000/mL) 30 days post-surgery, no medication, and no spontaneous bleeding.
- **Response:** Increase in platelet count between >30,000/mL and <100,000/mL 30 days post-surgery, at least doubling the baseline count, discontinuation of medication, and no spontaneous bleeding.
- **Non-response:** Platelet counts failing to rise above 30,000/mL or an initial increase but drop to values <30,000/mL within 30 days after the procedure. Needing ongoing or restarted medication like steroids to maintain standard platelet counts, or spontaneous bleeding within 30 days post-surgery.

**Statistical Analyses:** Utilized SPSS (version 25) for all statistical assessments. Continuous variables were presented as mean and standard deviation or median and range, based on distribution. The relationship of different factors with the response rate was determined using Fisher's exact test and t-test as applicable. A p-value < 0.05 indicated significance.

## RESULTS

The mean age of the patients was 31.18±13.77 years (range 3-67 years). Stratifying the age into categories revealed that the age group 16-30 years was the most common accounting for 45% of the patients, followed by age group >45 years (37.5%) and then 31-45 years (35%). The age group 3-15 years was the least common accounting for 7.5% of the patients (Fig 1).

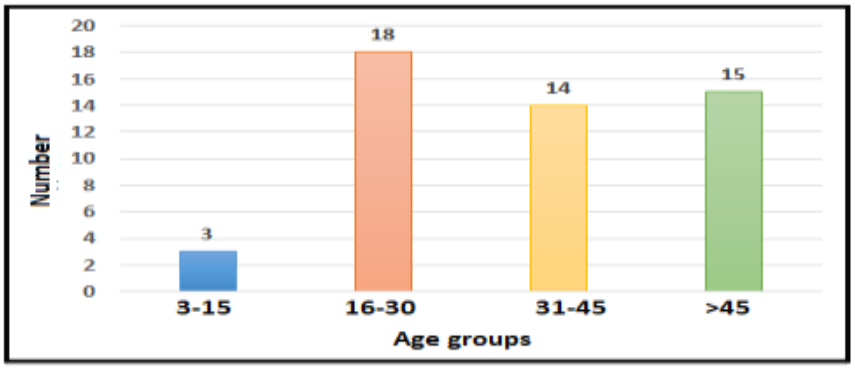


**Figure 1: Age distribution of the patients.**

Sixteen patients (40%) were males, and 24 patients (60%) were females. Thus the male: female ratio was 0.67:1 (Figure 3-2).

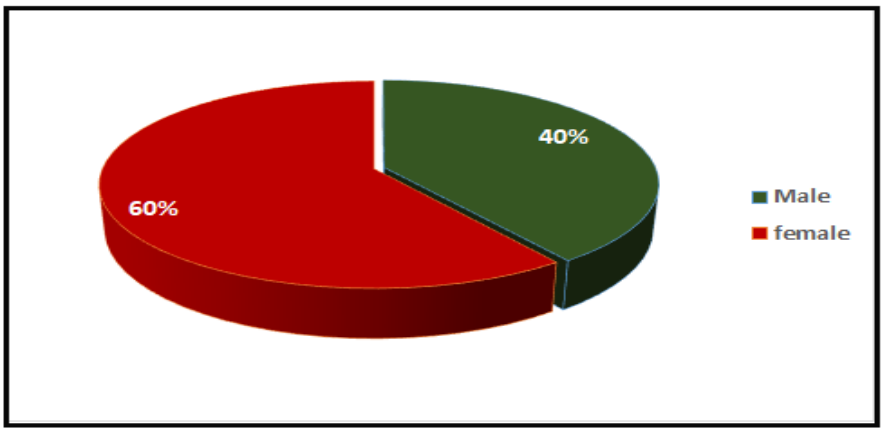


**Figure 2: Gender distribution of the patients.**

**Perioperative Characteristics of the Patients**

The mean preoperative PLT count was 83.18±13.77 $\times10^9$/L (range= 12-206 $\times^{109}$/L). the majority of patients (72.5%) had PLT less than 100 $\times10^9$/L. Each of Diabetes mellitus and hypertension was reported in 2 patients (5%). Most patients do require intraoperative platelet transfusion. In this regard, 50% of patients needed one pint, while 22.5% and 7.5% of them needed two and three pints, respectively. Only one patient had blood loss during operation. However, blood transfusion was performed for 6 patients (15%). In 2 patients (5%) the operation was converted into open surgery (Table 1).

**Table 1: Perioperative characteristics of the patients.**

| Variables | Frequency | Percentage |
|---|---|---|
| **Platelet count×$10^9$/L** | | |
| <100 | 29 | 72.5 |
| ≥100 | 11 | 27.5 |
| **Past Medical History** | | |
| No comorbidity | 38 | 95 |
| DM | 2 | 5 |
| HTN | 2 | 5 |
| **Platelet transfusion** | | |
| No need | 8 | 20 |
| One pint | 20 | 50 |
| Two pints | 9 | 22.5 |
| Three pints | 3 | 7.5 |
| **Operative blood loss** | | |
| No | 39 | 97.5 |
| Yes | 1 | 2.5 |
| **Operative blood transfusion** | | |
| No | 34 | 85 |
| Yes | 6 | 15 |
| **Conversion for open surgery** | | |
| No | 38 | 95 |
| Yes | 2 | 5 |

**Postoperative complications**

After one month follow up, six types of complications were encountered, the most common of which was abscess (7.5%) and atelectasis (7.5%). Infection of portal site was reported in two patients (5%), while each of pneumonia, bleeding and hematoma was reported in one patient (2.5%) as shown in table 3-3. Collectively, 11 patients (27.5%) had some type of complication. None of the patient's experience more than on complications.

**Table 2: postoperative complications.**

| Variables | Frequency | Percentage |
|---|---|---|
| Abscess | 3 | 7.5 |
| Atelectasis | 3 | 7.5 |
| Infection | 2 | 5 |
| Pneumonia | 1 | 2.5 |
| Bleeding | 1 | 2.5 |
| Hematoma | 1 | 2.5 |

**Response Rate**

After one month follow up, the mean platelet count was 435.89±303.82×$10^9$/L (range 10-1725×$10^9$/L). Complete response (increase in platelet count >100000 over baseline value) occurred in 31 patients (77.5%), response (increase in platelet count >30000 to <100000 over baseline value) in 6 patients (15%) and no response (increase in platelet count < 300000 over baseline value) in 3 patients (7.5%) as shown in figure 3.

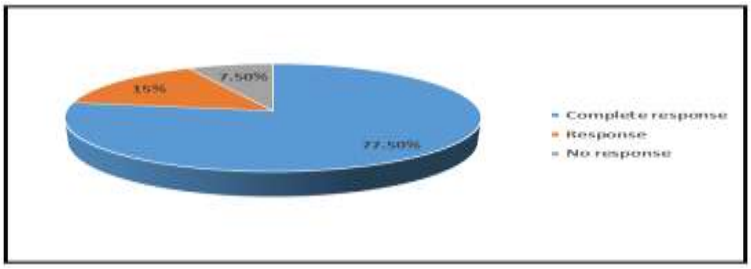


**Figure 3: Response rate.**

**Association of demographic and clinical characteristics with the response**

Due to small numbers of response and non-response case, and for statistical purpose, the two groups were merged in one emerged in one group (no or partial response). Out of nine included factors, three showed a significant association with response rate. The vast majority (88.89%) of no or partial response cases were females compared with 51.61% in complete response group with a significant difference. Similarly, none complete response group had past medical history versus 22.22% of no or partial response group who had diabetes or hypertension, with highly significant difference. Finally, 44.44% of patients with no or partial response developed postoperative complications compared with only 9.68% among complete response group who developed such complication with a significant difference (Table 4).

**Table 3: Association of demographic and clinical characteristics with the response.**

| Variables | Complete response (n=31) | No or partial response (n=9) | p-value |
|---|---|---|---|
| **Age, years** | 29.52±12.6 | 36.16±16.79 | 0.160 |
| **Gender** | | | |
| Male | 15(48.39%) | 1(11.11%) | **0.044** |
| Female | 16(51.61%) | 8(88.89%) | |
| **Initial Platelet count×$10^9$/L** | | | |
| <100 | 23(74.19%) | 6(66.67%) | 0.656 |
| ≥100 | 8(22.81%) | 3(33.33%) | |
| **Past Medical History** | | | |
| No comorbidity | 31(100%) | 7(77.78%) | **0.007** |
| Yes | 0(0%) | 2(22.22%) | |
| **Platelet transfusion** | | | |
| No need | 6(19.35%) | 2(22.22%) | |
| One pint | 15(48.39%%) | 5(55.56%) | 0.808 |
| Two pints | 8(25.81%) | 1(11.11%) | |
| Three pints | 2(6.45%) | 1(11.11%) | |
| **Operative blood loss** | | | |
| No | 30(96.77%) | 9(100%) | 0.558 |
| Yes | 1(3.23%) | 0(0%) | |
| **Operative blood transfusion** | | | |
| No | 28(90.32%) | 6(66.67%) | 0.080 |
| Yes | 3(9.68%) | 3(33.33%) | |
| **Conversion for open surgery** | | | |
| No | 29(93.55%) | 9(100%) | |
| Yes | 2(6.45%) | 0(0%) | 0.434 |
| **Complication** | | | |
| No | 28(90.32%) | 5(55.56%) | **0.016** |
| Yes | 3(9.68%) | 4(44.44%) | |

## DISCUSSION

The current study primarily investigated ITP patients, observing that most non-responsive to first-line therapy were young females. This aligns with global findings. Heink-Polle et al.[21] in a comprehensive meta-analysis confirmed that young age and female gender, along with the presence of antinuclear antibodies, were predominant factors predicting steroid resistance and chronic ITP progression. Similarly, Shojaiefard et al.[22] reported a higher prevalence of refractory ITP among females under 40. In our research, 80% of participants required preoperative platelet transfusion. Yet, surgical complications were rare, with only one instance (2.5%) of intraoperative bleeding. Zychowicz et al. [23] highlighted the importance of platelet levels in dictating intraoperative transfusion requirements. However, our findings of low complication rates can be attributed to the majority of our patients possessing a platelet count over 50,000/mm^3 and no prevailing comorbidities.

Postoperatively, 27.5% encountered complications. Although Zychowicz et al.[23] suggested no correlation between platelet count and complication rate, our relatively higher complication percentage might be due to inadequate hygiene practices post-discharge. Notably, infections were traced back to pathogenic microorganisms, highlighting potential hygiene issues.

Our data indicated a 77.5% complete response rate to the Laparoscopic Splenectomy, with non-response at 7.5%. When juxtaposed with global figures, our rate aligns. A multicenter study reported an 86% response rate[24] Systematic reviews have cited success rates, emphasizing an approximate 28% five-year failure rate for the procedure.[25] Various elements, including age and comorbidities, can sway the response rate. Our higher response rate might owe to the youthful sample and the negligible presence of comorbidities. Moreover, gender, complications, and comorbidities were notably associated with a non-complete response in our study. While some research, like that of Kojour et al.[14] aligns with our findings, emphasizing older age as a potential non-response predictor, our study didn't find preoperative platelet count significant in predicting complete response, unlike others.[26] This could stem from our sample's generally high platelet count. Interestingly, our data suggests a connection between female gender and non-complete response, which may be hormonally driven, as supported by Stachowiak et al.[27]

## CONCLUSION

Laparoscopic splenectomy is a safe and feasible surgical approach in patients with refractory ITP regardless of the preoperative PLT. The procedure is not associated with increased blood loss or high conversion rate. There is a relatively high rate of postoperative complications in Iraqi ITP undergoing LS. Each of female gender, presence of comorbidity and/or complication may increase the failure rate of LS.

## REFERENCES


1. Rodeghiero F, Stasi R, Gernsheimer T, et al. Standardization of terminology, definitions and outcome criteria in immune thrombocytopenic purpura (ITP) of adults and children: report from an international working group. Blood, 2009; 113: 2386-2393.
2. Frederiksen H, Lund Maegbaek M, Nørgaard M: Twenty-year mortality of adult patients with primary immune thrombocytopenia: a Danish population-based cohort study. Br J Haematol, 2014; 166: 260-267.
3. Matzdorff A, Meyer O, Ostermann H, et al. Immune Thrombocytopenia – Current Diagnostics and Therapy: Recommendations of a Joint Working Group of DGHO, ÖGHO, SGH, GPOH, and DGTI. Oncol Res Treat, 2018; 41(Supl 15): 1-3.
4. Moulis G, Palmaro A, Montastruc JL, et al. Epidemiology of incident immune thrombocytopenia: a nationwide population-based study in France. Blood, 2014; 124: 3308–3315.
5. Rodeghiero F. A critical appraisal of the evidence for the role of splenectomy in adults and children with ITP. Br J Haematol, 2018; 181(2): 183-195.
6. Neunert C, Lim W, Crowther M, et al. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. Blood, 2011; 117: 4190–4207.
7. Zufferey A, Kapur R, Semple JW. Pathogenesis and therapeutic mechanisms in Immune Thrombocytopenia (ITP). J Clin Med, 2017; 6: 16.
8. Grozovsky R, Begonja AJ, Liu K, et al. The Ashwell-Morell receptor regulates hepatic thrombopoietin production via JAK2-STAT3 signaling. Nature Medicine, 2915; 21: 47–54.
9. Kuwana M, Okazaki Y, Kaburaki J, et al. Spleen is a primary site for activation of platelet-reactive T and B cells in patients with immune thrombocytopenic purpura. J Immunol, 2002; 168: 3675–3682.
10. Martinez-Gamboa L, Mei H, Loddenkemper C, et al. Role of the spleen in peripheral memory B-cell homeostasis in patients with autoimmune thrombocytopenia purpura. Clin Immunol, 2009; 130: 199–212.
11. Olsson B, Ridell B, Jernas M, et al. Increased number of B-cells in the red pulp of the spleen in ITP. Ann Hematol, 2012; 91: 271–277.
12. Daridon C, Loddenkemper C, Spieckermann S, et al. Splenic proliferative lymphoid nodules distinct from germinal centers are sites of autoantigen stimulation in immune thrombocytopenia. Blood, 2012; 120: 5021–5031
13. Mahevas M, Patin P, Huetz F, et al. B cell depletion in immune thrombocytopenia reveals splenic long-lived plasma cells. J Clin Inves, 2013; 123: 432–442.
14. Kojouri K, Vesely SK, Terrell DR, George JN. Splenectomy for adult patients with idiopathic thrombocytopenic purpura: a systematic review to assess long-term platelet count responses, prediction

of response, and surgical complications. Blood, 2004; 104(9): 2623-2634.
15. Park YH, Yi HG, Kim CS, et al. Clinical Outcome and Predictive Factors in the Response to Splenectomy in Elderly Patients with Primary Immune Thrombocytopenia: A Multicenter Retrospective Study. Acta Haematol, 2016; 135(3): 162-171.
16. Mahevas M, Michel M, Godeau B. How we manage immune thrombocytopenia in the elderly. Br J Haematol, 2016; 173(6): 844-856.
17. Kim M, Park KM, Shin WY, Choe YM, Lee KY, Ahn SI. Platelet count evolution as a predictor of outcome after splenectomy for immune thrombocytopenic purpura. Int J Hematol, 2017; 105(4): 433-439.
18. Law C, Marcaccio M, Tam P, Heddle N, Kelton JG. High-dose intravenous immune globulin and the response to splenectomy in patients with idiopathic thrombocytopenic purpura. N Engl J Med, 1997; 336(21): 1494-1498.
19. Salib M, Clayden R, Clare R, et al. Difficulties in establishing the diagnosis of immune thrombocytopenia: An agreement study. Am J Hematol, 2016; 91(8): E327-329.
20. Sarpatwari A, Provan D, Erqou S, Sobnack R, David Tai FW, Newland AC. Autologous 111 In-labelled platelet sequestration studies in patients with primary immune thrombocytopenia (ITP) prior to splenectomy: a report from the United Kingdom ITP Registry. Br J Haematol, 2010; 151(5): 477-487.
21. Heitink-Pollé KM, Nijsten J, Boonacker CW, et al. Clinical and laboratory predictors of chronic immune thrombocytopenia in children: a systematic review and meta-analysis. Blood, 2014 Nov 20; 124(22): 3295-307.
22. Shojaiefard A, Mousavi SA, Faghihi SH, Abdollahzade S. Prediction of response to splenectomy in patients with idiopathic thrombocytopenic purpura. World J Surg, 2008 Mar; 32(3): 488-93
23. Zychowicz A, Radkowiak D, Lasek A, et al. Laparoscopic splenectomy for immune thrombocytopenia in patients with a very low platelet count. Wideochir Inne Tech Maloinwazyjne, 2018; 13(2): 157-163.
24. Vianelli N, Galli M, de Vivo A, et al. Efficacy and safety of splenectomy in immune thrombocytopenic purpura: long-term results of 402 cases. Haematologica, 2005; 90(1): 72-77.
25. Mikhael J, Northridge K, Lindquist K, et al. Shortterm and long-term failure of laparoscopic splenectomy in adult immune thrombocytopenic purpura patients: a systematic review, Am. J. Hematol, 2009; 84: 743e748.
26. Duperier T, Brody F, Felsher J, et al. Predictive factors for successful laparoscopic splenectomy in patients with immune thrombocytopenic purpura. Arch Surg, 2004; 139: 61–6.
27. Stachowiak, G.; Pertyński, T.; Pertyńska-Marczewska, M. Effect of transdermal hormone therapy on platelet haemostasis in menopausal women. Ann. Agric Environ. Med, 2015; 22: 167–171.