ORIGINAL RESEARCH PAPER
Volume - 12 | Issue - 05 | May - 2023 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

# "STUDY OF CLINICAL PROFILE AND OUTCOME OF PATIENTS WITH IMMUNE THROMBOCYTOPENIA."

**Internal Medicine**

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| **Dr. Ram Shinde** | Ex-Post Graduate Resident, Department of Medicine, LTMMC, SION MUMBAI |
| **Dr. Sanket Charpe** | Post Graduate Resident, Department of Medicine, LTMMC, SION, MUMBAI |
| **Dr. Kunal Bawankar*** | Post Graduate Resident, Department of Medicine, LTMMC, SION, MUMBAI *Corresponding Author |
| **Dr. Vrushali Badhan** | Post Graduate Resident, Department of Medicine, LTMMC, SION, MUMBAI |
| **Dr. Pratik Chhajed** | Post Graduate Resident, Department of Medicine, LTMMC, SION, MUMBAI |
| **Dr. Lalana Kalekar** | Associate Professor, Department of Medicine, LTMMC, SION, MUMBAI |
| **Dr. Amruta Digole** | Assistant Professor, Department of Medicine, LTMMC, SION, MUMBAI |

## ABSTRACT

Idiopathic Thrombocytopenic Purpura (ITP) is a relatively uncommon condition that is always diagnosed through exclusion. The demographics of ITP can vary greatly, and there is no clear correlation between platelet count and bleeding manifestations or response to therapy. The aim of this study was to investigate the clinical profile of ITP and analyze the relationship between platelet levels, clinical manifestations, and response to treatment in the in tertiary care centre in Mumbai. To conduct this prospective study, we enrolled 100 patients from haematology OPD and patient were studied for clinical profile and treatment outcome.

## KEYWORDS

Idiopathic Thrombocytopenic Purpura (ITP), Bleeding ,platelet

## INTRODUCTION

The American Society of Haematology defines immune thrombocytopenia purpura (ITP) as isolated thrombocytopenia (platelet count <100,000/microL) with normal white blood cells and normal hemoglobin in the setting of a generalized purpuric rash. ITP without a secondary cause or underlying disorder is known as primary ITP.Secondary ITP is defined as ITP with an underlying cause or disorder, which includes drug-induced or systemic illness-induced (eg. SLE, HIV, CVID, etc).[1]

The etiology of ITP is autoantibody-mediated, usually, immuno globulin G mediated.Patients with ITP develop auto antibodies against platelet membrane proteins, specifically glycoprotein (GP) IIb/IIIa complex, GP Ib/IIa, and GP VI. The antibody-coated platelets are then cleared by tissue macrophages, specifically in the spleen, at an accelerated rate, leading to a shortened half-life of the platelet.[2] These same antibodies also inhibit platelet destruction, leading to thrombocytopenia[2] However, an alternative mechanism has also been proposed involving T-cell mediated cytotoxicity.[3] In this mechanism, cytotoxic T cells attack megakaryocytes in the bone marrow. However, the mechanism is not well understood. Treatment should be restricted to those patients with moderate or severe thrombocytopenia who are bleeding or at risk of bleeding. It should be limited in duration unless demonstrated that symptomatic thrombocytopenia persists. Patients with mild, asymptomatic thrombocytopenia, discovered incidentally on a routine blood count, should not be treated.[8]

The present study was conducted at a tertiary healthcare center to assess the prevalence of primary and secondary ITP, hence to study the laboratory response of ITP to conventional treatment in tertiary care Centre after every 4 months

## AIM AND OBJECTIVES

- To find out prevalence of primary and secondary ITP in tertiary care centre
- To study signs , symptoms and laboratory profile of ITP
- To study bone marrow pattern in primary and secondary ITP
- To study laboratory response of ITP to conventional treatment in tertiary care Centre after every 4 months

### Methodology

This is a prospective observational study conducted over 18 months on 100 patients from Haematology OPD attending the tertiary care hospital. All relevant data including history, examination, laboratory parameter was noted. Laboratory parameters include: CBC, detailed LFT, PT-INR ,DCT-ICT, ANA , USG and Bone marrow studies. Every 4 monthly lab parameters were repeated to study the treatment outcome.

### Inclusion Criteria:

- All patients, age > 18 years, having primary ITP (without trigger)
- All patients, age > 18 years, having secondary ITP ( autoimmune disease, viruses)

### Exclusion Criteria:

- Patients with thrombocytopenia secondary due AFI
- Age <18 year
- Patients with pregnancy associated thrombocytopenia
- Patients with decreased platelet production(BM suppression
- Patient / relatives not willing to participate in the study. myelofibrosis, myelodysplastic syndrome, nutritional deficiency)

### Statistical Analysis

Data entry and data analysis carried out using MS Excel and epi info version 7. Proper statistical analysis is applied with help of Biostatistician using Mann Whiteny U test , paired /unpaired t test or chi square test.

### Age distribution

In the current study we assessed Age distribution among study subjects. We observed that majority of the study subjects belonged to the age group of 26 to 35 years (41.86%), followed by less than 25 years (23.26%), 36 to 45 years (20.93%). The mean age of the study subjects was $33.79 \pm 11.93$ years.

### Gender distribution

In the current study we assessed Gender distribution among study subjects. We observed that female preponderance was seen in the current study (76.74%), whereas 23.26% subjects were males. The female:male ratio in this study was 3.3:1.

### Diagnosis

In the current study we assessed Diagnosis among study subjects. We observed that Primary ITP was diagnosed among 44.19% study subjects, Among Secondary ITP, SLE was diagnosed among 32.56% study subjects, APLA was diagnosed among 9.3% study subjects, Drug induced was diagnosed among 4.65% study subjects, FSGS with ITP was diagnosed among 2.33% study subjects, HIV with ITP was

diagnosed among 2.33% study subjects, HCV with ITP was diagnosed among 2.33% study subjects, Sjogren's syndrome was diagnosed among 2.33% study subjects.

**Table 1: Diagnosis**

| Types of ITP | | Number of subjects | Percentage |
|---|---|---|---|
| Primary ITP | 19 | | 44.19 |
| Secondary ITP | SLE | 14 | 32.56 |
| | APLA | 4 | 9.30 |
| | Drug induced | 2 | 4.65 |
| | FSGS with ITP | 1 | 2.33 |
| | HCV | 1 | 2.33 |
| | HIV | 1 | 2.33 |
| | Sjogren's syndrome | 1 | 2.33 |
| Total | | 43 | 100 |

**Clinical presentation**

In the current study we assessed Clinical presentation among study subjects. We observed that Fever was reported among 46.51% study subjects, Fatigue was reported among 62.79% study subjects, Petechiae was reported among 86.05% study subjects, Bleeding from mucosal membranes was reported among 55.81% study subjects, Urogenital bleeding was reported among 30.23% study subjects, Increased bleed after small trauma was reported among 9.3% study subjects, Arthralgia was reported among 53.49% study subject, Dry Mouth was reported among 9.3% study subjects, Mouth ulcer was reported among 44.19% study subjects, Breathlessness was reported among 4.65% study subjects, Oliguria was reported among 4.65% study subjects, Oedema was reported among 16.28% study subjects.

**Table 2: Clinical presentation**

| Clinical presentation | Number of subjects | Percentage |
|---|---|---|
| Fever | 20 | 46.51 |
| Fatigue | 27 | 62.79 |
| Petechiae | 37 | 86.05 |
| Bleeding from mucosal membranes | 24 | 55.81 |
| Urogenital bleeding | 13 | 30.23 |
| Increased bleed after small trauma | 4 | 9.30 |
| Arthralgia | 23 | 53.49 |
| Dry Mouth | 4 | 9.30 |
| Mouth ulcer | 19 | 44.19 |
| Breathlessness | 2 | 4.65 |
| Oliguria | 2 | 4.65 |
| Oedema | 7 | 16.28 |

**Laboratory Investigations**

In the current study we assessed LABORATORY INVESTIGATIONS findings among study subjects. The mean levels are as mentioned in the given table:

**Table 3: Laboratory Investigations**

| LABORATORY INVESTIGATIONS | screening | 4 month | 8 month | 12 month |
|---|---|---|---|---|
| Hemoglobin | 9.41 | 10.45 | 10.48 | 12.52 |
| TLC | 7789.77 | 6816.28 | 10846.51 | 6930.23 |
| Platelets | 43439.53 | 129625.58 | 139527.91 | 154488.37 |
| BUN | 10.98 | 11.25 | 11.93 | 11.83 |
| Serum creatinine | 1.07 | 1.10 | 1.03 | 1.09 |
| Sr Na | 136.70 | 136.53 | 139.51 | 138.79 |
| Sr K | 3.92 | 4.03 | 4.26 | 3.81 |
| Total protein | 7.16 | 7.62 | 6.88 | 7.10 |
| Sr Albumin | 3.76 | 3.64 | 3.55 | 3.87 |
| Total bilirubin | 0.65 | 0.61 | 0.56 | 0.55 |
| SGOT | 46.05 | 29.09 | 28.16 | 38.78 |
| SGPT | 38.74 | 26.56 | 33.22 | 43.81 |
| ALP | 94.00 | 80.29 | 75.81 | 83.00 |
| RBS | 135.49 | 124.63 | 115.74 | 109.58 |
| PT | 11.95 | 13.33 | 13.47 | 14.05 |
| INR | 1.23 | 1.33 | 1.30 | 1.36 |
| Calcium | 9.04 | 9.10 | 8.93 | 8.88 |
| Retic count | 1.91 | 0.87 | 0.87 | 0.90 |

On screening mean platelet count was , while at the end of 12 months the count was 154488.37. The improvement in platelet count was found to be statistically significant. (p-value<0.0001)

**Specific investigations**

In the current study we assessed Specific investigations findings among study subjects. We observed ANA among 53.49% study subjects, Anti ds DNA among 25.58% study subjects, DCT among 16.28% study subjects, RA factor among 2.33% study subjects, ICT among 6.98% study subjects, Anti cardiolopin antibody among 4.65% study subjects, B2GP among 4.65% study subjects, Lupus anticoagulant among 6.98% study subjects. Low C3 level was observed among 20.93%, low C4 level was seen among 6.98% study subjects. 2.33% cases each of HIV and HCV were also reported.

**Urine routine examination**

In the urine routine examination, we observed urine protein among 23.26% subjects, while urine RBCs were observed among 23.26% study subjects.

**IPF value**

In the current study we observed mean IPF value of 15 ± 10.77 (median: 12) among subjects with primary ITP, and 19.95 ± 12.76 (median: 14) in subjects with secondary ITP. Though the mean IPF was comparatively greater in secondary ITP, we could not get statistical significance between the observations.

**Peripheral smear and Bone marrow examination**

In the current study on peripheral smear examination, we observed reduced platelets among all the study subjects. In Bone marrow examination findings among study subjects. We observed Normocellular bone marrow among 46.51% study subjects, Hypocellular bone marrow among 6.98% study subjects, Hypercellular bone marrow among 4.65% study subjects, Megakaryocytes among 11.63% study subjects.

**USG findings**

In the current study we assessed USG findings among study subjects. We observed Normal USG findings among 67.44% study subjects, Hepatomegaly among 2.33% study subjects, altered liver echo texture among 2.33% study subjects, mild ascites among 23.26% study subjects, Hepatosplenomegaly among 2.33% study subjects.

**Clinical comparison between primary and secondary ITP**

In this study we compared the clinical presentation between primary and secondary ITP. We observed that Fatigue (68.42%), Petechiae (78.95%), and Bleeding from mucosal membranes (84.21%) were the commonest presentation in primary ITP, whereas Fever (66.67%), Fatigue (58.33%), Petechiae (91.67%), Arthhralgia (58.33%), Mouth ulcer (62.5%) was the commonest presentation among secondary ITP subjects. Fever and mouth ulcer were significantly associated with secondary ITP (p-value<0.05). And **Bleeding from mucosal membranes was** significantly associated with primary ITP (p-value<0.05)

**Table 4: Clinical comparison between primary and secondary ITP**

| Clinical presentation | Primary ITP | | Secondary ITP | | OR | P-value |
|---|---|---|---|---|---|---|
| | Number of subjects | Percentage | Number of subjects | Percentage | | |
| Fever | 4 | 21.05 | 16 | 66.67 | 7.5 | 0.0027 |
| Fatigue | 13 | 68.42 | 14 | 58.33 | 1.54 | 0.4967 |
| Petechiae | 15 | 78.95 | 22 | 91.67 | 2.93 | 0.23 |
| Bleeding from mucosal membranes | 16 | 84.21 | 8 | 33.33 | 10.66 | 0.00084 |
| Urogenital bleeding | 5 | 26.32 | 8 | 33.33 | 1.4 | 0.618 |
| Increased bleed after small trauma | 4 | 21.05 | 0 | 0.00 | NA | NA |
| Arthralgia | 9 | 47.37 | 14 | 58.33 | 1.5 | 0.47 |
| Dry Mouth | 0 | 0.00 | 4 | 16.67 | NA | NA |
| Mouth ulcer | 3 | 15.79 | 15 | 62.50 | 8.88 | 0.002 |
| Breathlessness | 1 | 5.26 | 1 | 4.17 | 1.27 | >0.05 |
| Oliguria | 1 | 5.26 | 1 | 4.17 | 1.27 | >0.05 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Oedema | 1 | 5.26 | 6 | 25.00 | 6 | 0.081 |
| Alopecia | 0 | 0.00 | 7 | 29.17 | NA | NA |

**Comparison of investigations findings among primary and secondary ITP**

In the current study we observed that mean ESR (p-value: 0.0082), ANA positivity (p-value: 0.00001), and presence of normocellular bone marrow (p-value : 0.0122) was significantly higher in secondary ITP subjects as compared to primary ITP subjects. The mean platelet count at screening in primary ITP was comparatively lesser (**37573.68**), as compared to secondary ITP (**48083.33**). However the findings are not statistically significant. (P-value: 0.132)

**Table 5: Comparison of investigations findings among primary and secondary ITP**

| Clinical comparison between primary and secondary ITP | | Primary ITP | | Secondary ITP | | P -value |
|---|---|---|---|---|---|---|
| | | N | % | N | % | |
| Mean age | | 37.68 years | | 30.70 years | | 0.027 |
| Gender | Male | 6 | 31.58 | 4 | 16.67 | 0.25 |
| | Females | 13 | 68.42 | 20 | 83.33 | |
| Hematological investigations | Mean hemoglobin on screening | 9.62 | | 9.25 | | 0.31 |
| | Mean IPF | 19.94 | | 15.002 | | 0.087 |
| | Mean platelet count at screening | 37573.68 | | 48083.33 | | 0.132 |
| | Mean ESR | 21.78 | | 34.16 | | 0.0082 |
| | ANA positivity | 3 | 15.79 | 20 | 83.33 | 0.00001 |
| | ds-DNA positivity | 0 | 0.00 | 11 | 45.83 | NA |
| XRAY finding | Consolidation | 3 | 15.79 | 1 | 4.17 | 0.19 |
| | Effusion | 0 | 0.00 | 5 | 20.83 | NA |
| USG findings | Ascites | 1 | 5.26 | 10 | 41.67 | 0.0065 |
| | Other findings | 0 | 0.00 | 3 | 12.50 | NA |
| Bone marrow examination | Megakaryocytes increased | 2 | 10.53 | 3 | 12.50 | >0.05 |
| | Normocellular | 2 | 10.53 | 11 | 45.83 | 0.0122 |
| | HYPOCELLURE/DILUTE | 2 | 10.53 | 1 | 4.17 | >0.05 |
| | HYPERCELLULAR | 0 | 0.00 | 2 | 8.33 | NA |
| | NOT AVAILABLE | 2 | 10.53 | 7 | 29.17 | NA |

**Outcome**

We observed that complete response was seen among 70% study subjects, Some Response was seen among 25% study subjects, No response was seen among 5% study subjects. We compared the observations between primary and secondary ITP. We observed increased total response among subjects with secondary ITP as compared to primary ITP, however the statistical significance could not be observed. (The chi-square statistic is 3.7841. The p-value is .051743. Not significant at p <0 .05).

**Table 6 : Outcome**

| Outcome | Primary ITP | | Secondary ITP | |
|---|---|---|---|---|
| | Number of subjects | Percentage | Number of subjects | Percentage |
| No response | 4 | 21.05 | 0 | 0.00 |
| Some Response | 2 | 10.53 | 2 | 8.33 |
| Total response | 13 | 68.42 | 22 | 91.67 |
| Total | 19 | 100.00 | 24 | 100.00 |
| Significance | The chi-square statistic is 3.7841. The p-value is .051743. Not significant at p < .05. | | | |

**Overall treatment**

In the current study majority of the study subjects were managed with Tab Prednisolone (51.16%), followed by Tab Prednisolone + Azathioprine (27.91%), Prednisolone + MMF (11.63%), Drug was stopped among drug induced ITP (4.65). HAART was given among 2.33%, and DAA therapy was administered among 2.33% study subjects.

**Drug response**

In the current study we assessed Drug response among study subjects. We observed that among primary ITP cases, majority received Tab Prednisolone + Azathioprine (26.32%), 73.68% received prednisolone.

Among SLE cases, majority received **Tab Prednisolone + Azathioprine** (50%), among drug induced ITP, respective drugs were stopped, among HIV subjects HAART was administered, cases with HCV, DAA therapy was administered. Among other types of ITP such as APLA, Evans, Sjogrens syndrome, prednisolone was administered. The subjects with primary ITP achieved complete response among 52.63% cases with prednisolone only, while 15.78% required Prednisolone + Azathioprine. Whereas in secondary ITP, in order to achieve complete response Prednisolone + Azathioprine (27.16%), Prednisolone + MMF (20.83%), and prednisolone (25%) regimens were administered.

## DISCUSSION

ITP is usually diagnosed after precluding other potential causes of thrombocytopenia. A diagnosis is performed in patients with a low platelet count (<100 $x10^9$/L) with no evidence or history of an underlying condition, which can lead to thrombocytopenia, including a physical examination, evaluation of blood counts and visual examination of blood smears.

**Demographic characteristics**

In our study subjects belonged to the age group of 26 to 35 years (41.86%), followed by less than 25 years (23.26%), 36 to 45 years (20.93%). The mean age of the study subjects was 33.79 ± 11.93 years . And female preponderance was seen in the current study (76.74%), whereas 23.26% subjects were males. The female: male ratio in this study was 3.3:1.

**Diagnosis**

Primary ITP was diagnosed among 44.19% study subjects, Among Secondary ITP, SLE was diagnosed among 32.56% study subjects, and APLA was diagnosed among 9.3% study subjects.

**Clinical presentation**

Fever was reported among 46.51% study subjects, Fatigue(62.79%) Petechiae -86.05% ,mucosal bleeding -55.81% , Urogenital bleeding-30.23% subjects, Increased bleed after small trauma -9.3% , Arthralgia -53.49% study subject, Dry Mouth -9.3% ,Mouth ulcer - 44.19% , Breathlessness - 4.65% , Oliguria- 4.65%, Edema 16.28% .

**Forsthye and colleagues**[65] reported a severe bleeding episode that required rescue medication (intravenous immunoglobulin, corticosteroid injections or platelet transfusions) in 10, 2% of adult ITP patients within 6 months after starting therapy with thrombopoietin receptor agonists (TRO- RA). **In a retrospective evaluation** of the McMaster ITP registry, Arnold et al. found that 56% of ITP patients experience clinically significant bleeding at some point during their disease course and 2.2% had ICH.[66]

**Cohen et al**[83] identified 49 cases of fatal hemorrhage in 1718 patients from pooled ITP case series. **Cortelazzo et al**[84] **o**bserved an overall incidence of hemorrhagic events of 3.2% per patient-year in patients with ITP. Hemorrhagic events at similar platelet counts occurred in 10.4% of patients > 60 years, compared to 0.4 percent in patients under age 40. A previous history of hemorrhage also predicted bleeding (relative risk 27.5). **Michel et al** compared the incidence of bleeding and other outcomes in 55 ITP patients older than 70 years (mean age 77.8 ± 6.1 years) with those of a younger cohort (mean age 40.3 ± 14.9 years). The median platelet count at diagnosis did not differ between the two groups, though bleeding symptoms were more frequent in the older (82%) versus the younger (62%).

**Clinical comparison between primary and secondary ITP**

We observed that Fatigue (68.42%), Petechiae (78.95%), and Bleeding from mucosal membranes (84.21%) were the commonest presentation in primary ITP, whereas Fever (66.67%), Fatigue (58.33%), Petechiae (91.67%), Arthralgia (58.33%), Mouth ulcer (62.5%) was the commonest presentation among secondary ITP subjects. Fever and mouth ulcer were significantly associated with secondary ITP (p-value<0.05). And Bleeding from mucosal membranes was significantly associated with primary ITP (p-value<0.05).

**Sadia Sultan et al** in their study also reported similar findings. They

found increased incidence of bleeding from mucosal membranes significantly more in primary ITP cases, as compared to secondary ITP.[149]

**Management and drug response**

The subjects with primary ITP achieved complete response among 52.63% cases with prednisolone only, while 15.78% required Prednisolone + Azathioprine. Whereas in secondary ITP, in order to achieve complete response Prednisolone + Azathioprine (27.16%), Prednisolone + MMF (20.83%), and prednisolone (25%) regimens were administered.

## CONCLUSION

ITP has a significant negative impact on the daily life of patients, even if it is not necessarily fatal. Petechiae ,fatigue and mucosal bleed are common and persistent symptom associated with ITP, and there is no consistent response to medications. Unfortunately, clinical practice lags behind the available information on the diagnosis and treatment of ITP. The wide variety of diagnostic methods for ITP leads to unnecessary tests, which can increase costs and lead to the neglect of some recommended studies. To address these issues, more research is needed about the use and effectiveness of different treatments in the general population, and local guidelines need to be developed to facilitate research and improve patient care.

**Conflict Of Interest**

The Authors have no conflicts of interest that are directly relevant to the content of this clinic-pathological case

**Financial Resources**

There are no financial resources to fund this study.

**Informed Consent**

Informed Consent was obtained from the patient.

**Author's Contribution**

All the authors contributed equally to the case report.

**Data And Materials Availability**

All data associated with this study done at tertiary care centre hospital are present in the paper

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