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CLINICAL PROFILE AND TREATMENT OUTCOME IN PATIENTS WITH IMMUNE THROMBOCYTOPENIA IN A TERTIARY CARE HOSPITAL IN RAJASTHAN

Internal Medicine

Navin Chhaba Resident, Department of General Medicine, Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan, India

Anchin Kalia* Professor, Department of General Medicine, Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan, India *Corresponding Author

Deepak Gupta Professor, Department of General Medicine, Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan, India

Anil Panwar Professor, Department of General Medicine, Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan, India

Shikha Yadav Resident, Department of General Medicine, Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan, India

ABSTRACT

Background and Aim: Idiopathic Thrombocytopenic purpura is relatively uncommon. It is always diagnosis of exclusion. The demographics of Idiopathic Thrombocytopenic purpura can be very varied. Corelation between platelet count and bleeding manifestations and response to therapy have not been clearly established. The aim of the study was to study the demographics of Idiopathic Thrombocytopenic Purpura in the Rajasthan population and to analyze the possible relationship between platelet levels, clinical manifestations and response to treatment. **Method:** Prospective study was conducted among 100 patients with ITP under the department of General Medicine, Mahatma Gandhi Hospital to study the clinical profile and treatment outcome in patients of ITP in rajasthan. **Results:** Hundred patients were included in the study. Patients with average platelet count of more than 60,000 per cubic millimeter did not have bleeding. 18 percent of patients presented with bleeding manisfestations. The average platelet count in the group was 10,500 per cubic millimeter. Most common bleeding manifestation was bleeding gums followed by cutaneous bleeding. 74 percent had complete response to treatment to first line drugs, 13 percent had complete response to second line drugs and 13 percent had response to third line drugs. Mortality rate was six percent. These patients had average platelet count of less than 10500 cells per cubic milliliter. The results were statistically significant with p value <0.01. **Conclusion:** ITP is a serious condition which, even if infrequently fatal , has a substantial adverse impact on the quality of many patients' daily lives. Identification of common clinical presentation and their relationship to platelet count helps identify patients who are at increased risk for fatal bleeding diathesis

KEYWORDS

Immune Thrombocytopenia, Demographics,Platelet counts.

INTRODUCTION:

The clinical syndrome of bleeding and purpura consistent with the diagnosis of immune thrombocytopenia (ITP) was described by Werlhof long before platelets were identified as a cellular component of blood that plays an essential role in primary hemostasis. Immune thrombocytopenic purpura (ITP) is one of the most common causes of thrombocytopenia. In the American Society of Hematology guidelines, ITP is defined as "isolated thrombocytopenia without clinically apparent underlying conditions or other causes of thrombocytopenia. So it is a condition that is very much a diagnosis of exclusion.

It can be classified based on its causes:
Primary ITP: Primary ITP is an acquired immune thrombocytopenia due to autoimmune mechanisms leading to platelet destruction and underproduction that is not triggered by an overtly associated condition.

Secondary ITP: Secondary ITP is ITP associated with other conditions such as chronic lymphocytic leukemia (CLL), systemic lupus erythematosus (SLE), antiphospholipid syndrome (APS), common variable immunodeficiency (CVID), autoimmune lympho proliferative syndrome (ALPS), selective immunoglobulin (Ig) Deficiency, measles, mumps and rubella (MMR) vaccination, Helicobacter pylori infection, etc.

Drug-induced ITP: Drug-induced immune thrombocytopenia (D-ITP) is thrombocytopenia caused by drug-dependent antiplatelet antibodies that cause platelet destruction. Examples - Heparin, Ibuprofen, Piperacillin, Lorazepam, Abciximab

The time since diagnosis determines whether ITP is classified as newly diagnosed, persistent, or chronic:

- Newly diagnosed – within three months of diagnosis
- Persistent – 3 to 12 months from diagnosis
- Chronic – more than 12 months from diagnosis.

Although it affects any child age group, children between the ages of 2 and 6 are commonly affected. It is a benign disease with a good prognosis and outcome. Most patients with this disorder do not require any therapeutic intervention. A very small number of patients require therapeutic intervention due to profound thrombocytopenia and life-threatening bleeding. Primary ITP is an autoimmune disease characterized by a platelet count <100×109/l in the absence of other secondary causes of thrombocytopenia. In clinical practice, no consensus guidelines for the treatment of this disorder and large differences were found.

Clinical observations and experience indicate a spectrum of manifestations from trivial bruising to catastrophic bleeding. According to some studies, the incidence of fatal bleeding is as high as 10.4%. The literature indicates that older patients appear to have more severe bleeding manifestations.

Symptoms and platelet counts vary among patients. Some patients have no or only mild bleeding symptoms, while others are prone to post-traumatic bruising or spontaneous subcutaneous bleeding such as petechiae or ecchymoses. Mucosal bleeding such as epistaxis, gingival bleeding, blood-filled vesicles in the mouth and menorrhagia occur, but less frequently and fortunately serious or life-threatening bleeding is rare and rarely results in death. However, there is a higher mortality rate among patients with ITP than in the general population.

AIM:

To study the clinical profile and its relationship to treatment and outcome in patients in Rajasthan.

OBJECTIVES:

1. Study the clinical and laboratory profile of newly diagnosed patients with ITP.
2. To study the response of different treatment modalities after one month.
3. To study the quality of life of patients with immune thrombocytopenia.

MATERIAL AND METHODS:

- Type of Study: A ambespective study
- Place of Study: Mahatma Gandhi Medical College & Hospital, Jaipur
- SELECTION OF CASES: Immune thrombocytopenia outpatients and inpatients attending our institute.

Sample Size:
100 patients with immune thrombocytopenia present to Mahatma Gandhi Hospital.

Inclusion criteria:
a. Patients over 18 years of age.
b. Patients with megakaryocytic thrombocytopenia in absence of any other likely aetiology of thrombocytopenia.
c. Patients with isolated thrombocytopenia without any likely aetiology and response to immunosuppressive therapy.
d. Informed consent

Exclusion criteria:
- Patients aged less than 18 years
- Patients with thrombocytopenia and alikely etiology other then ITP.
- Patients on anticoagulation therapy.

RESULTS

Table 1: Gender distribution among the study subjects

Gender	N	%
Male	39	39
Female	61	61
Total	100	100

Table 2: Age distribution among the study subjects

Age Group (in years)	N	%
18-30	13	13
31-40	22	22
41-50	39	39
51-60	15	15
>60	11	11
Total	100	100

Table 2 shows distribution of subjects according to age and it was found that maximum subjects (39%) were of age group 41-50 years. 22% were in the age group of 31-40 years, 15% were in the age group of 51-60 years, 13% were in the age group of 18-30 years and 11% were above 60 years of age.

Table 3: Clinical profile among the study subjects

Variables	N	%
Petechiae and Purpura	89	89
Ecchymoses	14	14
Oral Bleeds	12	12
Epistaxis	4	4
Intracranial Bleed	1	1
Hematuria	1	1

Table 3 shows clinical profile of study subjects and it was found that 89% had petechiae & purpura,14% had ecchymoses, 12% had oral bleeds, 4% had epistaxis, 1% ahd intracranial bleed, 1% had hematuria.

Table 4: Hematologic characteristics among the study subjects

Variables	Median	Range
Leukocytes (/µL)	8670	3050-35770
Neutrophils (/µL)	6540	1610-26990
Hemoglobin (g/dL)	12.7	5.1-16.4
Platelets (/µL)	10500	2500-62000

Table 4 shows hematologic characteristics among the study subjects and it was found that median value of leukocyte count was 8670 (/µL), range (3050-35770); median value of neutrophils count was 6540 (/µL), range (1610-26990); median value of haemoglobin (g/dL) was 12.7 (g/dL), range (5.1-16.4) & median value of platelet count was 10500 (/µL), range 2500-62000.

Table 5: Response among the study subjects w.r.t. first line Drug

Modalities	Treatment Given To	Complete Response		Partial-No Response	
	N	N	%	N	%
Methyl prednisolone	68	54	54	14	14
Dexamethasone	22	14	14	8	8
Prednisolone	10	6	6	4	4
Total	100	74	74	26	26
Second Line Drug	N	N	%	N	%
Eltrombopag	26	13	13	13	13
Third Line Drug					
MycophenolateMofetil	8	8	8	0	0
Azathioprine	5	5	5	0	0

Table 5 shows response among the study subjects w.r.t. first line drug and it was found that methyl prednisolone shows 54% of complete response & 14% of partial no-response. Dexamethansone shows 14% of complete response & 8 % of partial no-response and prednisolone shows 6% of complete response & 4% of partial no-response.

Response among the study subjects w.r.t. second and third line drug and it was found that eltrombopag shows 13% complete response & 13% partial no-response. Mycophenolatemofetil shows 8% complete response & 0% partial no-response , azathioprine shows 5% complete response & 0% partial no-response.

Table 6: Outcome among the study subjects

Outcome	N	%
Survivor	94	94
Nonsurvivor	6	6

Table 6 shows outcome among the study subjects and it was found that 94% of all subjects survived and 6% of subjects were non-survivor.

DISCUSSION:

Primary immune thrombocytopenia (ITP) is an autoimmune disorder characterized by reduced platelet counts and increased bleeding risk in the absence of other causes associated with thrombocytopenia. ITP may affect patients' lives in many ways, including not only hemorrhagic manifestations, fear of bleeding, and secondary complications that can be associated with therapeutic options, but especially anxiety of the unknown (common in chronic diseases) and reduced energy levels. Severe bleeding is rare in ITP, but more frequent in elderly patients. Paradoxically, patients with ITP are at risk of thromboembolic events. Important symptoms often reported by patients when asked, but which can be easily overlooked, involve the effects of ITP.[48].

Hence the present study was conducted among patients of immune thrombocytopenia attending OPD and admitted in IPD at Mahatma Gandhi Medical College & Hospital, Jaipur from March 2020 to July 2022 to assess the clinical profile and it's co-relation with treatment and outcome in patients of immune thrombocytopenia of Rajasthan.

Gender

In the current study it was found that 61% of subjects were female and 39% of subjects were male.

Srinivasan D et al (2015) reported that 22 were men(36.7%) and 38(63.3%) were women. Cuervo D M et al (2019) in their study revealed that 67.3% were female and the median age was 48 years old, the majority being younger than 60 years old. The results were similar to our study showing the occurrence of this disease more in females as compared to females.

Age

Present study showed that maximum subjects (39%) were of age group 41-50 years. 22% were in the age group of 31-40 years, 15% were in the age group of 51-60 years, 13% were in the age group of 18-30 years and 11% were above 60 years of age.

Patne SV et al (2017) shows that maximum number of cases were seen in 21-30 years of age group (32.5%) followed by 31-40 years (25.8%) and results were similar to our study showing the disease is more common in younger age group as compared to elder ones.

Clinical Profile

Clinical profile of study subjects shows that 89% had petechiae & purpura,14% had ecchymoses, 12% had oral bleeds, 4% had epistaxis, 1% had intracranial bleed, 1% had hematuria in the present research.

Petechiae (64%) and bruising of unknown origin (65%) were among

the most frequent patient-reported signs and symptoms at diagnosis in a study done by Cooper et al (2021). Similar findings were observed in our study where petechiae was the most common symptom found.

Patne SV et al (2017) in their study found that various signs with thrombocytopenia, most common sign was splenomegaly (16.66%) followed by hepatomegaly (13.33%), hepatosplenomegaly (7.5%), jaundice (11.66%) and reactive lympadenopathy (6.66 %).

Hematologic Characteristics

Hematologic characteristics shows that median value of leukocyte count was 8670 (/µL), range (3050-35770); median value of neutrophils count was 6540 (/µL), range (1610-26990); median value of haemoglobin (g/dL) was 12.7 (g/dL), range (5.1-16.4) & median value of platelet count was 10500 (/µL), range 2500-62000 in the current research.

Cuervo DM et al (2019) in their study found that , the median platelet count at presentation was 11000/µL with an interval between 0 and 79000/µL, median leukocyte count was 9090(/µL), median neutrophil count was 6650(/µL), average haemoglobin was 13.6 g/dL. The values were almost similar to our study showing the values between the specific range of parameters.

Management & Responses To Treatment

In the present study it was found that among first line drugs methylprednisolone (68%) was mostly used . In second line of drugs eltrambopag (26%) was used and in third line of drugs mycophenolatemofetil (8%) was used for management of subjects.

Response w.r.t. first line drug showed that methyl prednisolone shows 54% of complete response & 14% of partial no-response. Dexamethansone shows 14% of complete response & 8 % of partial no-response and prednisolone shows 6% of complete response & 4% of partial no-response. Response w.r.t. second and third line drug showed that eltrombopag shows 13% complete response & 13% partial no-response. Mycophenolatemofetil shows 8% complete response & 0% partial no-response , azathioprine shows 5% complete response & 0% partial no-response.

Methyl prednisolone alone was given in 52 patients (86.6 percent) as first line of treatment. 37(61.7) patients showed complete response. 11 patients (18.33 percent) showed incomplete response. 12(20 percent) patients had no response. 21 patients (35 percent) received second line treatment. Of this 12 (57.1 percent) showed complete response, 7(33.3 percent) showed partial response and two patients (9.6 percent) showed no response in a study done by Srinivasan D et al (2015).

Of the total population, 54 patients received first-line treatment with steroids, dexamethasone (61%), methylprednisolone (20.5%), and prednisolone (18.5%) in a study done Curveo et al (2019).

By comparing the results of our study with the past literature it was found that corticosteroids, typically prednisone, are the backbone of the initial treatment.

Outcome

In the present study it was found that that 94% of all subjects survived and 6% of subjects were non-survivor.

Several studies show that mortality is less than 1%, though published reports of mortality in immune thrombocytopenia were limited (Blanchette V et al , 2010). Mortality rate was 5% in a study done by Srinivasan D et al (2015). Baloch et al (2017) showed a mortality rate of 11%. The mortality was high in this current study because the sample size was very small.

CONCLUSION:

ITP is a serious condition which, even if infrequently fatal , has a substantial adverse impact on the quality of many patients' daily lives. Fatigue was a frequently reported, persistent and severe symptom associated with ITP, which at best did not appear to consistently respond to platelet-increasing. Clinical practice in the real world is lagging behind the information available for the approach to the diagnosis and treatment of ITP. There is a wide variety of approaches to the diagnosis of ITP, which increases costs due to unnecessary tests and other occasions that the recommended studies are not performed. More information is needed in the population in terms of the use and efficacy of different therapies. Local guidelines need to be developed to address these concerns and, in this way, continue research in the population.

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