IMMUNE THROMBOCYTOPENIC PURPURA (ITP) IN CHILDREN AND ADULTS: INCIDENCE AND BONE MARROW ASPIRATION FINDINGS IN HIWA HOSPITAL, SULAIMANI CITY

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ABSTRACT

Background

Immune thrombocytopenic purpura is an autoimmune disease mainly affecting children.

Objectives

This study aimed to find out the incidence of Immune thrombocytopenic purpura and whether the peripheral platelet destruction affected bone marrow megakaryocytes.

Patients and Methods

This retrospective observational study was performed on 108 confirmed patients admitted to Hiwa Hospital, Sulaimaniyah, Iraq, from January 01, 2018, to December 31, 2021. Socio-demographic features, family history, presentations, and laboratory/ultrasonography findings were recorded.

Results

The incidence of Immune thrombocytopenic purpura in patients aged <18 years, ≥18 years, and >60 years were 5.9, 4.4, and 19.5 per 100,000 persons, respectively. The mean age of patients was 27.7±24.5 years, in which 41.7% were males and 58.3% were females, with the male/female ratio for <18, ≥18, and > 60 of 1.4:1, 0.34:1, and 0.58:1, respectively. Among patients; 17.6% had secondary Immune thrombocytopenic purpura, while the incidence of acute, persistent, and chronic immune thrombocytopenic purpura were 38.9%, 24.1%, and 37%, respectively. Besides, the whole population was at risk of having immune thrombocytopenic purpura; thus, the incidence was 4.96 per 100,000 persons at risk. Additionally, the association of immune thrombocytopenic purpura types was significant with age ($p<0.001$), in which acute immune thrombocytopenic purpura was more in pediatrics, and chronic was more in adults. Furthermore, the association of bone marrow megakaryocytes was significant with peripheral platelets, bone marrow megakaryocytes increased by decreasing peripheral platelets.

Conclusion

Pediatric males and adult females were at more risk of immune thrombocytopenic purpura than others, and the incidence of immune thrombocytopenic purpura increased with aging.

Keywords: *Autoimmune disease; Bone marrow aspiration; Retrospective observational study; Sulaimaniyah.*

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INTRODUCTION

Platelets are discoid-shaped blood corpussels that aggregate to form platelet plugs at the blood vessel's injured site to counteract bleeding in the first phase of hemostasis [1] Besides, platelets also have other functions, such as involvement in the immune system, mediating immune functions, coordinating vascular trafficking, interacting with viruses and bacteria, and participating in wound repair, inflammation, cancer metastasis, and progression [2].

Generally, one-third of the platelets are sequestered in the spleen, and the rest are circulating in the peripheral blood. About 100 x 109/L platelets are released from mature megakaryocytes into the blood circulation each day to maintain the normal range of platelet counts; thus, a constant balance between thrombopoiesis and platelet consumption is maintained [3]. Balanced platelet function and coagulation are crucial for stable blood circulation. If one is not functioning normally, it leads to impaired hemostasis and bleeding complications, including immune thrombocytopenic purpura (ITP)[4].

Immune thrombocytopenic purpura (ITP) is an autoimmune bleeding disorder characterized by decreased platelet counts of <100,000 u/L [5]. The pathogenesis of ITP is not determined, but it is believed to result from the development of an immunoglobulin G autoantibody targeting structural platelet membrane glycoproteins IIb-IIIa that renders platelets vulnerable to being phagocytized by splenic macrophages and liver Kupffer cells [6]. However, other situations, such as thrombopoietin production impairment, childhood contact with some viruses, Helicobacter pylori (H. pylori) infection, and pregnancy, contributed to ITP incidence [7].

Generally, ITP appears as primary (isolated) or secondary in the context of other infections and autoimmune diseases[8]. Also, it might be acute, persistent, or chronic. The first type accounts for the highest incidence (80% of ITP) and is mainly caused by a viral infection that lasts <3 months, while the 2nd type lasts 3-12 months, and the last one might remain for > 1 year [9].

Immune thrombocytopenic purpura appears to be more common in young women, especially during reproductive age and pregnancy, although it affects both genders of all ages. Moreover, its incidence is increasing globally, including in Iraq. Therefore, the current study aimed to find the incidence of ITP for adults and pediatrics in Sulaimaniyah, Northern Iraq, and whether the peripheral platelet destruction affected bone marrow megakaryocytes.

PATIENTS AND METHODS

This retrospective observational study was performed on 108 patients with tentatively diagnosed ITP who were admitted to Hiwa Hematology/Oncology Hospital in Sulaimaniyah, Iraq, from January 01, 2018, to December 31, 2021.

The Ethical Committee of the Kurdistan Higher Council of Medical Specialties (KHCMS) approved the study proposal (No. 201, 24/01/2021), and a formal acceptance letter was obtained from Hiwa Hematology/ Oncology Hospital before starting the study. We were also aware of the confidentiality of the patient's data.

Patients with low platelet count who were tentatively diagnosed with ITP were included in this study without age or gender restrictions. Patients with deficiencies due to dilution in pregnancy, underlying bone marrow failure, bleeding tendencies due to coagulation factor deficiencies, or other hematological disorders were excluded from this study.

Socio-demographic features, such as age and gender, and family history of ITP were recorded. Clinical presentations of ITP, including ecchymosis, epistaxis, gum bleeding, menorrhagia, and hematuria, were also reported. Regarding the distributions of the secondary ITP, the patient's history of H. pylori, systematic lupus erythematosus (SLE), antiphospholipid syndrome, and chronic lymphocytic leukemia were checked. Also, laboratory findings, including hemoglobin (Hb) level, white blood cell (WBC) count, reticulocyte count, platelet (PLT) count, prothrombin time (PT), partial thromboplastin time (PTT), bone marrow aspirate, and screening for hepatitis B virus (HBV), hepatitis C virus (HCV), cytomegalovirus (CMV), and human immunodeficiency virus (HIV), with spleen size assessment by ultrasonography (US) were recorded. Additionally, bone marrow aspiration was also reported to determine the correlation between peripheral platelet count and megakaryocyte. Then, based on the American Society of Hematology 2019 guidelines for ITP, the ITP types were categorized into acute (<3 months), persistent (3-12 months), and chronic (>12 months)[9].

The statistical package for Social Science (IBM SPSS, Chicago, USA, version 26.0) was used to analyze the data using descriptive and inferential statistics. Also,

the Pearson Chi-Square test was used to determine the significance of the association between independent and dependent variable pairs. A p-value of ≤0.05 was considered a statistically significant association.

RESULTS

During our data collection, 1112 blood disorder cases were coded with ITP at Hiwa Hospital, from January 01, 2018, to December 31, 2021, in Sulaimaniyah Governorate residences. Among them, we only selected 108 cases typically diagnosed with ITP, while other cases were diagnosed with different hematological diseases and some of them were normal.

According to the official website of the Kurdistan Region Statistics Office (KRSO), the population of Sulaimaniyah Governorate at the beginning, i.e., in 2018, was 2175523, including 769176 children <18 years old, and 1406347 adults of 18 years and older, including 97367 adults of >60 years old [10]. In our study, the incidence was 4.96 per 100,000 persons at risk for ITP. Based on the age groups, the incidence of ITP in patients aged <18 years (46 people, 42.6%) was 5.9, adults of 18 years and older (62 people, 57.4%) was 4.4, and >60 years (19 people; 17.6%) was 19.5 per 100,000 persons at risk. Based on the year, in 2018, the number of ITP cases was 27, and in 2019 was 30. On the other hand, in 2020, case numbers decreased sharply (22), but cases rose again in 2021 to 29 (Table 1).

In the current study, the age of patients ranged from 1 to 76 years, with a mean of 27.7±24.5. Most patients (42.6%) were <18 years old, while the least patients (17.6%) were >60 years old. Regarding the gender distribution, 45 (41.7%) were males, and 63 (58.3%) were females, with a male-to-female ratio of 0.7:1. Besides, the male-to-female ratios of <18, 18-60, and > 60 were 1.4:1, 0.34:1, and 0.58:1, respectively. Also, no patient (0.0%) was reported to have a family history of ITP. Therefore, the female gender was more predominant (29.6%), aged 18-60 (Table 2). Additionally, most patients (59.3%) presented with ecchymosis, followed by epistaxis (11.1%), menorrhagia (10.2%), gum bleeding (9.3%), and hematuria (2.7%) (Table 3). Furthermore, all patients had normal Hb, WBC, PT, PTT, reticulocyte count, and viral tests; however, platelet count was low in all the patients (Table 4). Regarding the distributions of the causes of secondary ITP, H. pylori was reported to be more frequently associated with secondary ITP in adults (7.4%), while season flu (7.4%) was more frequently associated with pediatric age. However, SLE (3.7%), antiphospholipid syndrome (1.9%), and Chronic lymphocytic leukemia (0.9%) secondary to ITP were also found in patients aged ≥18 years (Table 5). Regarding the classification of ITP among patients, 42 (38.9%) patients had acute, 26 (24.1%) had persistent, and 40 (37%) had chronic ITP. The association of ITP types was statistically significant with the age groups (p<0.001). The acute type was more in pediatrics, and a predilection toward chronicity was present in adults (Table 6). Furthermore, bone marrow aspiration was performed for 63 (58.4%) patients who did not respond to the 1st line of treatment. Among them, 11 (10.2%) patients were <18 years and 52 (48.1%) were ≥18 years. Increased bone marrow megakaryocytes were significantly (p=0.004) associated with decreased peripheral platelet counts, as seen in Table (7). Moreover, all the patients (100%) were presented with normal-sized spleen upon ultrasonography.

Table 1. Number of patients with ITP from January 2018 to December 2021.

Year	Age (Year) (No., %)			Total (No., %)
	<18	18-60	>60	
2018	17.0 (63)	8.0 (29.6)	2.0 (7.4)	27.0 (100)
2019	10.0 (33.3)	15.0 (50)	5.0 (16.7)	30.0 (100)
2020	12.0 (54.6)	7.0 (31.8)	3.0 (13.6)	22.0 (100)
2021	7.0 (24.1)	13.0 (44.8)	9.0 (31.1)	29.0 (100)
Total	**46.0 (42.6)**	**43.0 (39.8)**	**19 (17.6)**	**108 (100)**

Table 2. The age and gender distribution among enrolled ITP patients.

Gender	Patient's Age Range (Year, %)			Total (No., %)
	<18	18-60	>60	
Male	27 (25)	11 (10.2)	7 (6.5)	45 (41.7)
Female	19 (17.6)	32 (29.6)	12 (11.1)	63 (58.3)
Total	**46 (42.6)**	**43 (39.8)**	**19 (17.6)**	**108 (100)**

Table 3. Clinical presentations of the ITP in patients.

Clinical presentation	Age (Year, %)		Total (%)
	<18	≥18	
No bleeding	0 (0.0)	8 (7.4)	8 (7.4)
Ecchymosis	33 (30.5)	31 (28.7)	64 (59.3)
Epistaxis	7 (6.5)	5 (4.6)	12 (11.1)
Gum bleeding	4 (3.7)	6 (5.6)	10 (9.3)
Menorrhagia	2 (1.9)	9 (8.3)	11 (10.2)
Hematuria	0 (0.0)	3 (2.8)	3 (2.7)
Total	**46 (42.6)**	**62 (57.4)**	**108 (100)**

Table 4. Laboratory findings of the patients with ITP.

Laboratory test	Frequency	
Hb (g/dL)	Mean±SD	12.8±1.5 (9.8 to 15.8)
Platelet (109/L) *	Mean±SD <18 Year	28.2±18.9 (13.5 to 38.2)
	Mean±SD 18- 60 Year	46.5±19.7 (30 to 60)
	Mean±SD >60 Year	45.9±16.1 (35 to 55)
Reticulocyte count	Mean±SD	1.7±0.8 (0.9 to 2.5)
WBC (109/L)	Mean±SD	6.9±1.4 (4.5 to 10.8)
PT (second)	Mean±SD	12.1±0.9 (11.2 to 13.1)
PTT (second)	Mean±SD	28.3±1.3 (25.3 to 34.7)
Viral (HCV, HBV, HIV, CMV)	Negative (%)	108 (100)

Hb: Hemoglobin; PT: Prothrombin time; PTT: Partial thromboplastin time; SD: Standard deviation; WBC: White blood cell, HBV: Hepatitis B virus, HCV: Hepatitis C virus, CMV: Cytomegalovirus, HIV: Human immunodeficiency virus. * Significant at P<0.001

Table 5. Causes of secondary ITP among patients.

Secondary ITP	Age (Year, %)		Total (%)
	<18	≥18	
H. pylori	2.0 (1.9)	8.0 (7.4)	10.0 (9.3)
Systemic lupus erythematosus	0.0 (0.0)	4.0 (3.7)	4.0 (3.7)
Anti-phospholipid syndrome	0.0 (0.0)	2.0 (1.9)	2.0 (1.9)
Chronic lymphocytic leukemia	0.0 (0.0)	1.0 (0.9)	1.0 (0.9)
After influenza viral infection (season flu)	8.0 (7.4)	0.0 (0.0)	8.0 (7.4)
Total	**10.0 (9.3)**	**17.0 (15.7)**	**25.0 (23.25)**

Table 6. The association of patients' age groups with the types of ITP.

Age group (Year)	ITP type (No., %)			Total (No, %)	p-value
	Acute	Persistent	Chronic		
<18	29 (26.9)	11 (10.2)	6 (5.6)	46 (42.6)	**<0.001***
≥18	13 (12)	15 (13.9)	34 (31.5)	62 (57.4)	
Total	42 (38.9)	26 (24.1)	40 (37)	108 (100)	

*** Significant difference**

Table 7. Association of peripheral platelet count and the bone marrow megakaryocytes.

Platelet group (×109/L)	Bone marrow megakaryocyte (No., %)			Not indicated (No., %)	p-value
	Increased	Normal	Total		
<30	18 (16.7)	11 (10.2)	29 (26.9)	25 (23.1)	
30-49	6.0 (5.6)	5.0 (4.6)	11 (10.2)	11 (10.2)	
50-100	7.0 (6.5)	16 (14.8)	23 (21.3)	9.0 (8.3)	**0.004***
Total	**28 (25.9)**	**32 (29.6)**	**63 (58.4)**	**45 (41.6)**	

*** Significant difference**

DISCUSSION

In the current study, we collected all the patients with ITP without age or gender restrictions in Sulaimaniyah Governorate for four consecutive years, and we found 108 patients who fulfilled the inclusion criteria. Therefore, we calculated the incidence of ITP, which was 4.96 per 100,000 persons at risk per year. This outcome was lower than that found by Lee (5.3 per 100,000 people)11 and by Weycker (6.1 per 100,000 people in the USA).12 However, our record was higher than that reported in the France study done by Moulis et al. 13, which was 2.9 per 100,000 people.13 Generally, the incidence ranges from 1.6 to 3.9 per 100,000 people, which increases with age.14 The differences between incidences in the various studies might be due to the different diagnostic criteria.15 Some studies calculated the incidence for pediatric patients and others for adult patients.

In this study, the patient's ages with ITP ranged from 1 to 76 years; the majority (46 people, 42.6%) were <18 years old. This finding was more than the results found by Marieke et al.16 who reported that 22.4% of their study sample was aged <18 years. The incidence of ITP increases with aging, possibly due to the higher incidence or increased risk of bleeding as a presenting complaint. Regarding the male-to-female ratio in the current study (0.7:1), the finding is comparable to other studies that selected mixed pediatrics and adult patients and found that adult females were more frequently afflicted with ITP.16,17 In contrast, another study conducted in France found males to be affected more by ITP.13

In this study, no patients (0.0%) had a family history of ITP. Similar results were found in another study,18 while another study mentioned that 20% of patients had a family history of ITP1.

The presented features of patients with ITP were due to hemostasis defects, and in the current study, we nearly found some clinical presentations, including ecchymosis, followed by epistaxis, then menorrhagia, gum bleeding, and hematuria. Similar outcomes were found in a retrospective cohort study.19 However, a retrospective study in Iran mentioned petechiae, purpura, and ecchymosis with rarely observed severe bleeding.20 Whereas bruising, epistaxis, and gum bleeding as the commonest clinical presentations in adults and children were found in a study conducted in Pakistan; they also reported more severe bleeding in acute cases with increased menstrual bleeding in females.21

We found that 38.9% of ITP cases were acute, 24.1% were persistent, and 37% were chronic, with a significant association between ITP types and the age groups in which a predilection toward chronicity was present in adults; however, acute ITP was more frequent in pediatrics. Considerably, 64 (19%) acute ITP, 50 (15%) persistent, and 226 (66%) chronic were found in seven European countries from 2009 to 2012.22

Furthermore, the association between the bone marrow megakaryocytes and peripheral platelet counts was statistically significant. The frequency of megakaryocytes in bone marrow increased when the frequency of peripheral platelets decreased. Similar outcomes were also found in another study conducted in China.23

Moreover, the findings of this study supported the theories of ITP pathogenesis, in which 9.3% and 3.7% of the ITP patients had H. pylori/seasonal flu and SLE, respectively. In this respect, H. pylori was found in ITP patients, and clinical H. pylori eradication was suggested to treat ITP.7 However, other studies conducted in Jordan24 and Denmark25 stated that ITP was significantly more common in patients with lymphomas, hematological malignancies, and solid cancers, while arterial and venous thromboembolism

were found in patients with ITP in a study conducted in the USA.26

Conclusions

The incidence of ITP in Sulaimaniyah Governorate was near to the recorded data of other countries, and the incidence increased with aging. Acute ITP was more frequent at younger ages; however, chronic ITP was more frequent in adults. The number of bone marrow megakaryocytes increased with the decrease in peripheral platelet counts.

Conflicts of Interest

The authors had nothing to disclose.

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