ORIGINAL ARTICLE - OPEN ACCESS

International Journal of Medicine and Healthcare Reports DOI: http://dx.doi.org/10.51521/IJMHR.2023.2113

Contents lists available at bostonsciencepublishing.us

International Journal of Medicine and Healthcare Reports

Epidemiology and Clinical Features of Immune Thrombocytopenia Purpura in South-West Nigeria

Patrick Olarenwaju Osho[1], Oluwatosin Idowu Oni[2], Oluwatobiloba Elizabeth Adejumo[3], Medunoye Elihu Iyinolorun[4], Micheal Gbala[5]

[1]*Department of Hematology, University of Medical Sciences Teaching Hospital, Ondo state, Nigeria.*

[2]*Ondo State Pry Health Care Development Agency, Akure Ondo State, Nigeria*

[3]*Department of Medicine, University of Ilorin, Ilorin, Kwara state, Nigeria*

[4]*Department of Family medicine, University of Medical Science Teaching Hospital, Ondo state*

[5]*Department of Obstetrics and Gynecology, University of Medical Science Teaching Hospital, Ondo state*

A R T I C L E I N F O

Article history:
Received 24 April 2023
Revised 18 May 2023
Accepted 22 May 2023
Published 30 May 2023

Keywords: Immune Thrombocytopenia, Purpura, Epidemiology, Prevalence.

A B S T R A C T

Background: Immune thrombocytopenia Purpura is a rare hematological disease especially among indigenous black Africans and black Americans. It is a disease that occurs both in adults and in children.

Aim: This study aims to describe the epidemiology and clinical features of Immune Thrombocytopenia (ITP) in a low income community in Ondo State South West Nigeria.

Materials and Methods: A retrospective study was performed using the case notes of patients with a diagnosis of Immune Thrombocytopenia Purpura from all cases of hematological conditions diagnosed and managed between 2012-2020 at University of medical sciences teaching hospital, Ondo state. The clinical and laboratory findings were extracted from the case records. SPSS-25 was used for statistical calculations.

Results: The hospital incidence rate was 16.52%, with a total of 19 cases of Immune Thrombocytopenia Purpura managed during the period of review. There were 8 males and 11 females with the highest prevalent age range being 15-30 years. Nineteen (100%) patients presented with anaemia, twelve (63.2%) patients presented with fever and 7(36.8%) presented with mucosal bleeds(epistaxis). None of the patients had severe thrombocytopenia, although 11(57.89%) patients had grade 4 thrombocytopenia.

Conclusion: The study showed that ITP has a female predominance and a relatively high prevalence (16.52%) due to the low number of hematological cases. This study has sensitized us on the need to be more suspicious of ITP and facilitate inter departmental collaboration among Specialists. This will enhance the generation of adequate data on the disease especially in a low income community.

Introduction

Immune thrombocytopenia (ITP) is a syndrome in which platelets become coated with auto-antibodies to platelet membrane antigens, resulting in splenic sequestration and phagocytosis by mononuclear macrophages [1]. The resulting shortened life span of platelets in the circulation, together with incomplete compensation by increased platelet production by bone marrow megakaryocytes, results in a decreased number of circulating platelets (< 100 G/L) [1]. It occurs in both adults and children, with a multimodal incidence with the first peak in childhood and second and third peaks in young adults and the elderly. The underlying disease process in childhood ITP and adult ITP may be fundamentally different, as evidenced by the rate of chronic ITP in these patient populations. Although the majority of children have self-limited disease, in adults, ITP is more often a chronic disorder [2,3].

In 2009, an International ITP Working Group (IWG) published recommendations for standardization of definitions and terminology to allow for alignment of research studies and eventually aid in management of patients with ITP. The IWG defined the abbreviation in common use (ITP) to be Immune Thrombocytopenia (neither

* Corresponding author.
P.O. Osho, Department of Hematology, University of medical sciences, Akure, Ondo State, Nigeria.
Tel: +2348034970314; Email: droshopo@unimed.edu.ng or droshopo@gmail.com

Idiopathic nor Purpura) because the pathophysiology is better understood and the majority of both adult and pediatric patients do not present with purpura, even if they have petechiae and bruising [4]. Data regarding the prevalence of ITP is limited due to its rarity. ITP occurs with a global incidence rate of 1.6 to 3.9 per 100,000 patient-years, which increases with age and has a slight female preponderance [5]. A European study using the UK population-based General Practice Research Database (GPRD) gave a crude incident rate of 3.9 per 100,000 patient-years [6]. While a Korean study using the Korean Health Insurance Review and Assessment Service database gave an overall incidence rate of 5.3 per 100,000 person-years [7]. A US study showed that based on the clinical observation that pediatric ITP is less frequently seen in black individuals, the hypothesis that black children have a lower prevalence of pediatric ITP relative to the general population because of differences in disease biology based on race and ethnicity was examined [8], in agreement with the study done at Ile-Ife, south west Nigeria that gave the overall prevalence rate at 0.005% of hospital cases, confirming the rarity of ITP in black population [12].

Previously, the pathophysiology of ITP was not understood, but recent studies has been able to shed more light on it. It is now clear that Primary ITP is an acquired immune disorder where the thrombocytopenia results from: (A) pathologic antiplatelet antibodies (an abnormal autoantibody, usually immunoglobulin G (IgG) with specificity for one or more platelet membrane glycoproteins, binds to circulating platelet membranes. Autoantibody-coated platelets induce Fc receptor-mediated phagocytosis by mononuclear macrophages, primarily but not exclusively in the spleen [1]. (B) impaired megakaryocytopoiesis when bone marrow megakaryocytes cannot increase production and cannot maintain a normal number of circulating platelets (C) T-cell–mediated destruction of platelets Some patients who do not have antiplatelet antibodies will have abnormal T cells that result in platelet destruction, whereas in other patients it is T-cell dysregulation that results in autoantibody production [2]. A presumptive diagnosis of ITP can be made if patient history, physical examination, complete blood count, and examination of peripheral blood smears do not suggest other causes of thrombocytopenia [9]. Although some may suggest bone marrow examinations is unnecessary, the recommendations from the IWG is bone marrow examinations in patients >60 years old with newly diagnosed ITP [2]. ITP manifests as a bleeding tendency, easy bruising (purpura), or extravasation of blood from capillaries into skin and mucous membranes (petechiae). Spontaneous remission occurs more frequently in children than in adults, and intracranial bleeding is usually uncommon. Although most cases of acute ITP, particularly in children, are mild and self-limited, intracranial hemorrhage may occur when the platelet count drops below 10×10^9/L ($< 10 \times 10^3$/μL); this occurs in 0.5-1% of children, and half of these cases are fatal [1].

The first line of therapy for ITP is use of corticosteroids ; the most used is prednisone with Approximately, two-thirds of patients achieving a complete or partial response within the first week [10], IVIg therapy which is administered to patients requiring rapid or urgent elevation of platelet count [9] or Anti-D immunoglobulin (anti-D) binds to Rh(D) antigen on erythrocytes, thereby leading to clearance of antibody-coated cells and inhibiting the clearance of opsonized platelets by the reticuloendothelial system; which is effective only in RhD positive individuals [12]. The second line therapy includes splenectomy; the removal of the spleen, also known as the gold standard in the treatment of ITP with a recovery rate of about 60%-70% and Rituximab is a chimeric monoclonal antibody that targets CD20 B-cell surface antigen [9]. Third line therapy includes TPO-RA (romiplostim and eltrombopag). New therapies and recommendations have emerged in the last decade therefore the decision to treat should be based on bleeding severity, bleeding risk, activity level, likely side effects of treatment, and patient preference [9]. This study aims to describe the epidemiology and clinical features of Immune Thrombocytopenia in a low income community; Ondo State.

MATERIALS AND METHODS

Study Area

The research was conducted at the Department of Hematology, University of Medical Sciences Teaching Hospital, Ondo state. The teaching hospital is made up of six former hospitals in Ondo State, namely; Mother and Child Hospital Ondo, Trauma and Surgical Centre Ondo, Kidney Care center Ondo, State specialist hospital Ondo, State Specialist Hospital Akure and the Millennium Eye center, Akure.

Study Design

This was a retrospective study of cases of Immune Thrombocytopenia purpura (ITP) from all cases of hematological conditions diagnosed and managed between 2012-2020 by the Haematologist. Complete Blood Count, Peripheral Blood Film and bone marrow aspirate results were retrieved from the Case notes of the Patients. The database included information on diagnoses and procedures as well as basic demographic information for 115 patients. The overall prevalence of ITP was calculated as the total number of identified ITP cases from the population of hematological patients in the database. Prevalence was calculated and stratified by gender as well as by the following age categories: <15, 15-30, 31-45, >45.

Inclusion criteria

- Patients diagnosed with ITP by clinical diagnostic manifestations of ITP
- Patients diagnosed by a hematologist

Exclusion criteria

- Patients with other causes of thrombocytopenia
- All data were entered into Statistical Package for Social Sciences (SPSS software version 25). Descriptive statistics was computed to determine frequency and percentage.

RESULTS

Out of the total 115 cases with hematological conditions, there was a total of 19 (16.52%) patients reported to have ITP. A total of Eight (42.1%) were males and Eleven (57.9%) were females with a ratio of 1:1.4. There was no significant association of gender with prevalence of ITP (P=0.381). The highest prevalence was observed with the age group of 15-30 years (36.8%) followed by 31-45 years (31.6%) then >45years, (21.1%) and the least being <15years, (10.5%). There was no significant association between age group and the prevalence of ITP (P=0.515). All the ITP patients presented with anaemia while 12 out of the 19 patients presented with fever and 7 presented with mucosal bleeds (epistaxis) while the other forms of presentation are shown in table 1. There were no significant differences between the mean PCV and platelet count of male and female patients; 27.87±8.932 versus 26.27±7.760 (P= 0.392) and 21.75±4.892 versus 23.82±9.474 (P=0/329) respectively as shown in Table 3. Platelet counts of $<25 \times 10^9$/ L was found in 11(57.89%) of the patients. Also 8 (42.11%) patients had PCV of <25. The site for aspiration was in the anterior ilium in 12 (63.2%) of the patients and the posterior ilium in 7(36.8%) of the patients. All the patients presented with low PCV. Only one case had both Megaloblastic anaemia occurring together with ITP. The overall prevalence rate was 16.52% of the hospital cases between 2012-2020.

Patients ID	Clinical Presentation of patients with ITP n=19						
	Severe anaemia	Fever	Splenomegaly	High PCV	Mucosal bleeds	Gum Bleeding	Bilateral paresthesia
1	+	-	-	-	-	-	-
2	+	-	-	-	+	-	+
3	+	+	-	-	-	-	-
4	+	+	-	-	+	-	-
5	+	-	-	-	+	-	-
6	+	+	-	-	-	-	-
7	+	+	-	-	-	-	-
8	+	+	-	-	+	-	-
9	+	-	-	-	-	-	-
10	+	+	-	-	-	-	-
11	+	+	-	-	-	-	-
12	+	-	-	-	-	-	-
13	+	+	-	-	-	-	-
14	+	+	-	-	+	-	-
15	+	+	-	-	-	-	-
16	+	-	-	-	+	-	-
17	+	+	-	-	-	-	-
18	+	+	-	-	+	-	-
19	+	-	-	-	-	-	-
Total(%)	**19(100%)**	**12(63.2%)**	**0(0%)**	**0(0%)**	**7(36.8%)**	**0(0%)**	**1(5.3%)**

+: Indicates presence while, -: Indicates absence

Table 1: Clinical Presentation of patients with ITP at University of Medical Science Teaching Hospital, Ondo from 2012-2020.

Prevalence of ITP			
Age group(yrs.)	Male N(%)	Female N(%)	Total N(%)
<15	1(5.3%)	1(5.3%)	2(10.5%)
15-30	6(31.6%)	1(5.3%)	7(36.8%)
31-45	0(0%)	6(31.6%)	6(31.6%)
>45	1(5.3%)	3(15.8%)	4(21.1%)
Total	8(42.1%)	11(57.9%)	19(100%)

Table 2: Distribution of confirmed ITP cases in relation to age and group N=19.

Variable	Sex		P
	Male	Female	
Mean PCV± SD	27.87±8.935	26.27±7.760	0.392
Platelet×10^9/L ±SD	21.75±4.892	23.82±9.474	0.329

Table 3: Comparison between PCV and Platelet counts of male and female ITP cases.

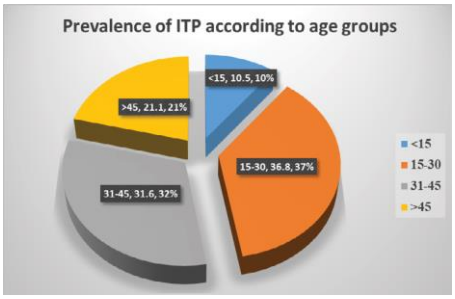

Figure 1: A pie chart showing the prevalence of ITP according to age groups.

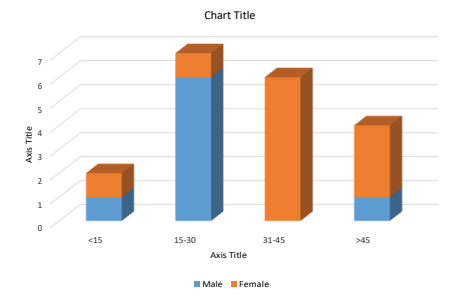

Figure 2: A chart showing the prevalence of ITP according to age groups and gender.

DISCUSSION

ITP is a rare disease worldwide, and even rarer among the black Africans and African Americans. This study shows that only Nineteen (16.52%) of 120 patients with hematological history at the University of medical sciences teaching hospital, Ondo state had ITP over an 8-year period or 2.4 *cases per annum,* this prevalence rate seems higher than earlier studies by Salawu *et al* (0.005% of hospital cases.) [12] and Hassan *et al* (0.002%) [13]. ITP is asymptomatic in some patients; however, when present, bleeding is the most common symptom and can be mild as in petechiae, purpura and epistaxis, or severe and even life threatening in cases of intracranial hemorrhage, and massive gastrointestinal or urinary tract bleeding.

The highest prevalence age category of ITP was 15-30 years which is in accordance with a study by Salawu *et al* [12] which shows that the median age was 21 years. However, this contrasts with a study by Hassan *et al* [13] which showed that the highest prevalent age group was <18 years. This study showed no correlation of increase in age with either an increase or decrease in prevalence which contrasts with a UK based study that showed that ITP prevalence increased with increasing age [14]. Similar to previous studies, this study also indicates the predominance of females in ITP cases over males and most especially among the prevalent age group. However, the reason for the gender disparity is yet to be accounted for.

Major site of BMA aspiration was at the anterior ilium with few done at the posterior ilium despite the fact that higher yield is gotten from the posterior ilium than the anterior ilium. This was in contrast to a study by Pierini *et al*, which a higher concentration and yield of colony-founding connective-tissue progenitors were greater when aspirate was obtained from the posterior compared with the anterior iliac crest [15]. Fever was the most common form of presentation followed by mucosal bleeds (epistaxis) while gum bleeding was not present. These presentations are in contrast to purpura usually common in Caucasian patients due to the nature of their skin tone. Although, Salawu *et al* identified gingival bleeding as the most common presentation, while Hassan *et al* identifies epistaxis as the most common form of presentation. This may be explainable, due to the fact that our patients are black.

Skinned and thus identifying early pinpoint petechial hemorrhages may be difficult. Nineteen (100%) patients presented with anaemia, this may be due bleeding that previously occurred before coming to the hospital and 11(57.89%) patients had grade 4 thrombocytopenia (platelet count of $<25 \times 10^9$/L), but none had very severe thrombocytopenia or platelet count of $<10 \times 10^9$/L. Only one (5.3%) patient in the study had bilateral paresthesia and one case had a concurring megaloblastic anaemia along with ITP. Complications resulting from BMA aspiration such as hemorrhage at site of aspiration were not encountered in our study and bone marrow examination was successfully carried out without any serious bleeding. Similar observations were made in a study by Shosh *et al* [16].

LIMITATION

The prevalence rate (16.52%) seems high but is actually due to the fact that the sample population is quite low as compared to that of other studies due to lack of inadequate data. The low number of hematological cases may also be due to the fact that some of the haematology cases are managed by Physicians in other Departments such as internal Medicine, Family Medicine/General practice and Paediatrics.

CONCLUSION

Immune Thrombocytopenic Purpura (ITP) is a relatively uncommon disease more so in our region, largely due to lack of adequate data. For most patients with ITP and/or the patient's caregivers, effective management of the disease requires an understanding of the natural history of ITP, which often comes via counseling from healthcare providers and most of the time there is lack of adequately skilled personnel that can contribute to the diagnosis and management of ITP. Also late presentation as seen in this study where all cases of ITP already had severe anaemia before being brought to the hospital or referred as majority of the patients have financial constraint to carry out necessary tests. This may be due to the out-of- pocket payment system predominant in the country. Another factor causing low sample population may be poor referral to hematologists due to misdiagnoses of the condition by the patient's physician.

RECOMMENDATIONS

Hospital ground rounds should be resuscitated because they provide an opportunity for physicians to come together and discuss complex cases like ITP, share knowledge and expertise, and improve patient outcomes. Early diagnosis should be carried out on patients with hematological malignancies so as to rule out other causes of thrombocytopenia and aid in treatment and management of the patients. Government should provide insurance policies that would help patients with the cost of treatment so as to prevent catastrophic health spending which is a major bane to seeking early medical attention. Well trained specialist should be readily on ground and physicians should be enlightened on early referral of ITP patients to hematologists for diagnoses and treatment. More studies should be conducted on ITP across facilities in Ondo state.

Financial support and sponsorship

Nil

CONFLICTS OF INTEREST

There are no conflicts of interest

References

1. Craig M Kessler, Hira Latif, Julia M Cunningham. Immune Thromboctyopenia (ITP). MedScape. 2021. Available on https://emedicine.medscape.com/article/202158-overview
2. Lambert MP, Gernsheimer TB. Clinical updates in adult immune thrombocytopenia. Blood, The Journal of the American Society of Hematology. 2017 ;129(21):2829-35.
3. Schulze H, Gaedicke G. Immune thrombocytopenia in children and adults: what's the same, what's different? Haematologica. 2011; 96(12):1739-1741.
4. Rodeghiero F, Stasi R, Gernsheimer T, Michel M, Provan D, Arnold DM, Bussel JB, Cines DB, Chong BH, Cooper N, Godeau B. Standardization of terminology, definitions and outcome criteria in immune thrombocytopenic purpura of adults and children: report from an international working group. Blood, The Journal of the American Society of Hematology. 2009 ;113(11):2386-93.
5. Kohli R, Chaturvedi S. Epidemiology and Clinical Manifestations of Immune Thrombocytopenia. *Hamostaseologie*. 2019;39(3):238-249. doi:10.1055/s-0039-1683416
6. MariekeSchoonen, W., Kucera, G., Coalson, J., Li, L., Rutstein, M., Mowat, F., Fryzek, J. and Kaye, J.A. Epidemiology of immune thrombocytopenic purpura in the General Practice Research Database. British Journal of Haematology.2009; 145: 235-244. https://doi.org/10.1111/j.1365-2141.2009.07615.x
7. Lee JY, Lee JH, Lee H, Kang B, Kim JW, Kim SH, Lee JO, Kim JW, Kim YJ, Lee KW, Kim JH. Epidemiology and management of primary immune thrombocytopenia: a nationwide population-based study in Korea. Thrombosis Research. 2017 Jul 1;155:86-91.
8. Kim TO, Grimes AB, Kirk SE, Gilbert MM, Reed HD, Staggers KA, Walker LA, Arulselvan A, Cohen AS, Lambert MP, Despotovic JM. Racial variation in ITP prevalence and chronic disease phenotype suggests biological differences. Blood. 2020 Jul 30;136(5):640-643. doi: 10.1182/blood.2020004888. PMID: 32559763; PMCID: PMC8212348.
9. Nomura S. Advances in Diagnosis and Treatments for Immune Thrombocytopenia. Clinical Medicine Insights: Blood Disorders. 2016;9. doi:10.4137/CMBD.S39643.
10. Schoonen W.M., Kucera G., CoalsonJ.et al. Epidemiology of immune thrombocytopenic purpura in the general practice research database. *Br J Haematol.* 2009; 145: 235–244
11. Cooper N. Intravenous immunoglobulin and anti-RhD therapy in the management of immune thrombocytopenia. *HematolOncolClin North Am.* 2009; 23: 1317–1327
12. Salawu L, Durosinmi MA. Immune thrombocytopaenicpurpura: 11-year experience in Ile-Ife, Nigeria. *Afr J Med Med Sci*. 2001;30(1-2):99-103.
13. Hassan A, Adebayo A, Musa AU, Suleiman AM, Ibrahim IN, Kusfa IU, et al. Clinical feature and management of immune thrombocytopenic purpura in a tertiary hospital in Northwest Nigeria. Niger Med J 2017;58:68-71
14. Bennett D, Hodgson ME, Shukla A, Logie JW. Prevalence of diagnosed adult immune thrombocytopenia in the United Kingdom. *AdvTher*. 2011;28(12):1096-1104. doi:10.1007/s12325-011-0084-3

15. Pierini M, Di Bella C, Dozza B, Frisoni T, Martella E, Belloti C, Remondini D, Lucarelli E, Giannini S, Donati D. The posterior iliac crest outperforms the anterior iliac crest when obtaining mesenchymal stem cells from the bonemarrow. J Bone Joint Surg Am. 2013 Jun 19; 95 (12): 1101-7.

16. Shorsh J.R, Nawsherwan S.M, Hogar I.M.S> Evaluation of the role of bone marrow evaluation in diagnosis of hematological diseases in Hematocology centers in Iraqi Journal of Hematology,2016;5(1):98-113