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Original Article

Pathology Section

Clinicopathological Spectrum of Thrombocytopenia in Sangli District of Western Maharashtra- A Cross-sectional Study

SHEETAL MAHESHKUMAR SALE[1], ISHA BANSAL[2], VAIBHAV PANDURANG MANE[3], DHIRAJKUMAR ARUN MANE[4]

ABSTRACT

Introduction: Thrombocytopenia is now a day's common haematological finding with various aetiologies is the situation where there is low blood platelet count. Aetiology for thrombocytopenia is multi factorial which makes the management challenging.

Aim: To study the clinicopathological spectrum of thrombocytopenia in population of Sangli district, Maharashtra, India.

Materials and Methods: A cross-sectional study was conducted in a tertiary care centre in Sangli district, Maharashtra, India, for a period of two years from July 2019 to June 2021. It included 920 patients with platelet count<1.5 lakh/mm^3 irrespective of their age group. The clinical profile laboratory data and complications of patients with a platelet count of less than 1,50,000/mm^3 were analysed and tabulated. All the collected data was tabulated in MS-Excel and analysed in Statistical Package for the Social Sciences (SPSS) version 20.0 where frequency distribution was used test study variables.

Results: The total sample size was 920 with 546 (59.35%) males and 374 (40.65%) females. Out of 920 patients, majority 392 (42.61%) were diagnosed with infections that lead to thrombocytopenia where dengue was identified as the most common cause having 173 (18.80%) cases followed by other infection and other diseases.

Conclusion: Dengue was observed to be the most common infectious disease causing thrombocytopenia in this study. The present study might help in categorising the level of infection i.e., mild or severe thrombocytopenia. Early signs of bleeding could stop further complications and transformation into high risk towards different morbidities respectively.

Keywords: Anaemia, Dengue, Idiopathic thombocytopenic purpura, Low blood platelet count, Malaria

INTRODUCTION

Platelets are formed by fragmentation of megakaryocytes in the bone marrow and have an average life of 7-10 days, they play a critical role in haemostasis [1]. Thrombocytopenia is defined as platelet count below the normal range for the population (Mean±2SD) [1]. Thrombocytopenia is defined as platelet count <1.5 x10^5/µL and is one of the commonest cause of bleeding [2,3].

The etiology of thrombocytopenia in the Intensive Care Unit (ICU) is multifactorial, sepsis, malignancy, presence of invasive catheters and various medications such as heparin and antibiotics have been found associated with thrombocytopenia. Because of the many confounding factors, establishing the cause of thrombocytopenia in critically ill patients is challenging [4,5].

The management of thrombocytopenia is dependent on the aetiology, and the degree of severity with which it presents [6]. Varied mechanism, underlying thrombocytopenia are decreased production, increased destruction and peripheral pooling of platelets [2,3].

Clinical presentation of thrombocytopenia varies, from being devoid of symptoms to presenting with bleeding episodes. Though it doesn't have an absolute relationship, degree of thrombocytopenia correlates with degree of bleeding manifestation [7]. The present study was conducted with the objective to study the clinicopathological profile of thrombocytopenia.

MATERIALS AND METHODS

The present study is a two year cross-sectional study which was carried out in the Haematology section of Department of Pathology Bharati Vidyapeeth (Deemed to be University) Medical College, Sangli, Maharashtra, India from July 2019 to June 2021, with approval from Institutional Ethical Committee.

Sample size calculation: Sample size was estimated by prevalence formula $n=Z^2pq/L^2$

where, z=standard normal variate at 95% confidence interval (1.96), p=prevalence of thrombocytopenia in general population (14.9-29.3% we took max. I.e. 29.3%)

q=100-p,100-29.3=70.7,

L=allowable error at 97% confidence interval

Total 3% inpatients coming from different departments of our hospital for Complete Blood Count (CBC) and Peripheral smear examination were screened and the cases having platelet count of <1.5 lakhs/mm^3 [6] were included in our study.

Inclusion criteria: The cases which had platelet count of <1.50 lakh/mm^3 irrespective of the age group were included in the study.

Exclusion criteria: Out patients were not included in the study as detailed case sheets were not available to retrieve data.

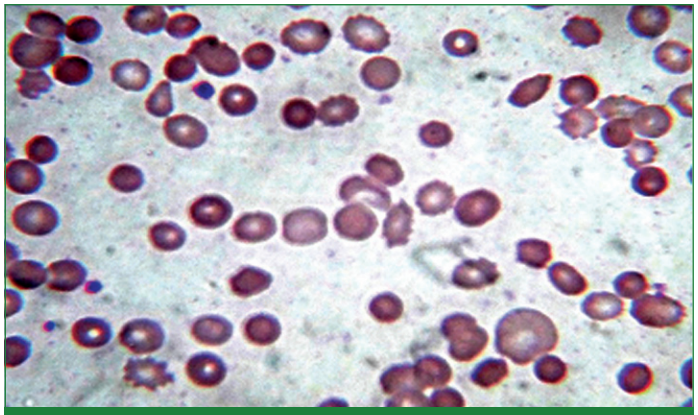
Study Procedure

Haemoglobin (Hb), total count and differential count, platelet count were done on five part automated analyser and platelet count was counterchecked on peripheral blood smear.

Principle of automated analyser- It works on the principle of aperture impedance technology. Blood cells being poor conductors of electricity are suspended in electrically conductive electrolyte solution which is then made to flow from an outlet chamber in an inner chamber through a 100 um diameter orifice. When cell passes through orifice during the counting process the cell imparts resistance to the electrical conductivity between the electrodes

which is recorded electronically as a voltage pulse, the height of pulses being proportional to the volume of cells passing through the orifice. Number of such voltage pulses recorded correspond to the counting of cells.

Peripheral smears made from venous blood collected in CBC bulb anti coagulated in Ethylenediaminetetraacetic Acid (EDTA) after being stained by Leishman stain were examined under high power and oil immersion for Red Blood Cell (RBC) morphology, Differential White Blood Cells (WBC) count, parasite if any and platelet count by counting ten consecutive fields in the representative area, taking the mean and multiplying it by 10,000 or 15,000 depending upon the width of the eye piece and count was given in per mm^3. The CBC bulb was checked for presence of blood clot. The smears were studied for presence of platelet aggregates and platelet satellitium to rule out pseudo thrombocytopenia [Table/Fig-1]. If found present, the samples of the respective patients were repeated using citrate bulb and were screened again. In case they were found normal, they were excluded from the study. Investigations like reticulocyte count, Erythrocyte Sedimentation Rate (ESR) and bone marrow aspiration were done wherever necessary.



[Table/Fig-1]: Peripheral smear showing thrombocytopenia.

Data of complete medical history and examination were retrieved from the case files. Haematology and other laboratory test results were associated with clinical findings to decide the aetiology of thrombocytopenia and relation of degree of thrombocytopenia with severity of clinical manifestations and degree of thrombocytopenia with aetiology.

STATISTICAL ANALYSIS

All the collected data was tabulated in MS-Excel and analysed in SPSS version 20.0 where frequency distribution was used to test study variables.

RESULTS

Total number of cases of thrombocytopenia which formed the study group during the period of two years from July 2019 to June 2021 was 920. This comprised 3%, out of 30,000 of the total requisitions received from the inpatients admitted in the hospital by the haematology section of the Department of Pathology.

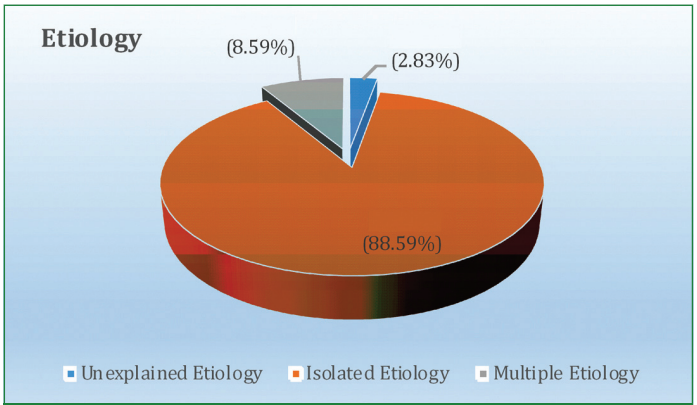
The commonest age group for thrombocytopenia in this study was between 15-34 years followed by 35-54 years and 55-74 years accounting for 328 (35.65%), 258 (28.04%) and 159 (17.28%) cases respectively. Out of 920 cases 546 (59.35%) were males and 374 (40.65%) were females. A definite male preponderance was seen in overall picture as well as in almost all age groups. The overall male to female ratio was 1.45:1 [Table/Fig-2].

In this study out of 920 cases, 815 (88.59%) had isolated etiology, 79 (8.59%) had more than one etiology and 26 (2.83%) had unexplained etiology [Table/Fig-3].

The total number of cases which presented with bleeding was 74/920 (8.04%). The maximum number of cases of thrombocytopenia which had bleeding had platelet count of <20,000 and were 15/47 i.e.

Age group (in years)	Gender		Total	Percentage
	Male	Female		
<15	61	39	100	10.87
15-34	212	116	328	35.65
35-54	146	112	258	28.04
55-74	86	73	159	17.28
≥75	41	34	75	8.15
Total	546 (59.35%)	374 (40.65%)	920	100

[Table/Fig-2]: Age wise and sex wise distribution of cases studied for thrombocytopenia.



[Table/Fig-3]: The pie chart showing distribution of cases according to aetiology of thrombocytopenia.

(31.91%). The [Table/Fig-4] indicates the risk of bleeding increases as platelet count decreases.

While discussing about clinical profile of thrombocytopenia it was found that infection was the major sign and symptoms of thrombocytopenia in 398 (42.61%) cases followed by anaemia in 279 (30.33%) cases, and other type of causes for thrombocytopenia respectively [Table/Fig-5].

Platelet count (lakh/cmm)	Total no. of cases	Cases with bleeding	Percentage of bleeding
1 to 1.5	295	17	5.76
0.5 to 1	362	13	3.59
0.2 to 0.5	216	29	13.43
<0.2	47	15	31.91

[Table/Fig-4]: Distribution of platelet count of cases presenting with Thrombocytopenia.

Sign and symptoms	Frequency	Percentage
All infections	392	42.61
Anaemia	279	30.33
Miscellaneous (jaundice, fever, body ache, ascites, breathlessness, and post vaccination etc.)	53	5.76
Use of Myelo-suppressants	42	4.57
Alcoholism	36	3.91
Obstetric causes (P.I.H, Abruption)	35	3.80
Snake bite	31	3.37
Haematological malignancies	29	3.15
Traumatic brain injury	11	1.20
Moderate splenomegaly	5	0.54
ITP (Idiopathic Thrombocytopenic purpura)	3	0.33
DIC (Disseminated Intravascular Coagulation)	4	0.43

[Table/Fig-5]: Distribution of causes leading to thrombocytopenia.
PIH: Pregnancy induced hypertension

Also, aetiology of diagnosis among cases with thrombocytopenia is shown in [Table/Fig-6]. Out of 920 patients 392 were identified with infection as the cause of thrombocytopenia. It was observed that 173 (18.80%) were diagnosed with dengue. Malaria was diagnosed

as the second most cause in 10.76% cases, followed by 4.57% cases of septicaemia, 4.46% cases of viral fever, 3.15% cases of bacterial infection, 0.87% other infections [Table/Fig-6].

Infection	Frequency	Percentage
Dengue	173	18.80
Malaria	99	10.76
Septicaemia	42	4.57
Viral fever (including coronavirus)	41	4.46
Bacterial infection	29	3.15
Viral Hepatitis	4	0.43
HIV	3	0.33
Leptospira	1	0.11
Total	392	42.61

[Table/Fig-6]: Distribution of cases of Infection leading to thrombocytopenia.
HIV: Human Immunodeficiency Virus

DISCUSSION

Platelets were observed for the first time in 1860 by Zimmerman et al. They have important role in primary and secondary haemostasis. Thrombocytopenia is a common haematological finding in todays times with various aetiologies where there is low blood platelet count. The present cross-sectional study included 920 patients suffering from thrombocytopenia. Male to female ratio of 1.45:1 was observed. Similar findings were observed by Kumar A et.al., [8] Also, Verma S et al., [9] observed male preponderance with 62.6% sufferers being male. Similar findings were observed by Shah et al (male-54%) [10], Vimal et al., (59.2%) [11], Mittra et al., (70.3%) [12].

Majority of the patients (35.65%) belonged to the age group of 15-34 years. Similarly, Verma et al., observed that 40.8% were of the patients belonged to the age group 26-50 [9]. Also similarly in study conducted by Shah HR et al., it was found that thrombocytopenia in the age group 21-30 years was about 30% [10].

The most common cause of thrombocytopenia in this present study was observed as dengue i.e. 18.8%. The most common cause of newly diagnosed thrombocytopenia in this study was of infectious etiology. Dengue is infectious disease caused by dengue virus and causes acute febrile illness to severe dengue hemorrhagic shock. The major cause of thrombocytopenia in dengue fever is combination of weakened thrombopoiesis with platelets segregation according to Azeredo EL de et al., and Srichaikul T et al., [13,14] activation of the associated system according to Krishnamurti C et al., [15] and auto antibodies against blood coagulation related molecules and antiplatelet antibodies mediated platelet lysis by Lin FC et al., and Lei HY et al., [16,17,18]. The second most cause of thrombocytopenia was malaria 10.76%. As per Srivastava et al. Thrombocytopenia is the most common finding in falciparum and vivax malaria. Immune mediated lysis, sequestration in the spleen and dyspoietic process in the marrow with diminished platelet production have been postulated. Malarial parasite can induce abnormalities in platelet structure and function [19]. The motive of thrombocytopenia in malaria is direct lysis of platelets through plasmodium by Fajardo et al., [20]. The incidence rate observed in this study was 3%. Also, other cases of infection included septicemia 4.57%, bacterial infection 3.15%, Viral fever which also included coronavirus infection 4.46% and other infections 1%.

In present study late onset thrombocytopenia of short duration was the presentation by the patients affected by novel coronavirus disease and epistaxis and purpura were most common symptoms. The results were in concordance with other study by Mocan et al., [21] where severe thrombocytopenia as a Manifestation of COVID-19 Infection was observed. The mechanism of thrombocytopenia in corona virus infection postulated are destruction of platelets by immune system, inhibition of platelet synthesis by direct infection of bone marrow by virus and also by platelet aggregation in lungs resulting in platelet consumption and micro thrombi formation (Mechanism of thrombocytopenia in COVID-19 patients by Xu P et al., [22].

In this present study one case of post vaccination thrombocytopenia was documented, patient presented with deep vein thrombosis. The present study shows that the maximum number of cases of thrombocytopenia which had bleeding had platelet count of <20,000 and were 15/47 i.e. (31.91%). Also this study indicates the risk of bleeding increases as platelet count decreases.

Bleeding time isn't extended till the platelet count is less than 100,000/µL; for platelet counts above 20,000/µL, medical manifestations are mild, frequently limited to clean bruising. At much less than 10,000/µL, the hazard of spontaneous mucocutaneous bleeding (epistaxis, gingival bleed, menorrhagia, petechiae, and ecchymoses) and life-threatening, spontaneous intracranial hemorrhage, or gastrointestinal bleeding will increase rapidly by Sekhon SS et al., [23].

There is scarcity of availability of literature on thrombocytopenia in a clinicopathological setup. Especially in developing nations such as India, in the course of monsoons there's an increase in incidences of thrombocytopenia, periodically, which may prove fatal due to bleeding episodes. The underlying cause of such instances have been found to be infectious in origin. There is a pressing need to study and categorize the etiological factors of thrombocytopenia in order to take precautionary measures.

Limitation(s)

There are some limitations in study. Firstly, the study was done in tertiary care hospital, thus, referral bias was unavoidable. It was a single centre study and multicentric studies need to be conducted for the generalizability of results. Follow-up of cases after treatment was not done in these patients.

CONCLUSION(S)

The preventable causes of thrombocytopenia like infections and anaemia are present in high percentage. Hence most of cases of thrombocytopenia have a favourable prognosis. Early detection of infections like dengue, leptospira, viral hepatitis and malaria using serological tests may help in preventing complications. While evaluating a case of thrombocytopenia for aetiology, contribution of multiple factors leading to thrombocytopenia should be kept in mind. Anti-neoplastic therapy cycles are known to cause thrombocytopenia hence should be used with regular follow-up and supervision. Cases of haematological malignancies and obstetric causes should be observed for thrombocytopenia. Cases with severe thrombocytopenia should be treated on urgent basis to prevent disastrous effects.

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PARTICULARS OF CONTRIBUTORS:
1. Associate Professor, Department of Pathology, Bharati Vidyapeeth (Deemed to be University) Medical College and Hospital, Sangli, Maharashtra, India.
2. Assistant Professor, Department of Pathology, Bharati Vidyapeeth (Deemed to be University) Medical College and Hospital, Sangli, Maharashtra, India.
3. Professor and Head, Department of Pathology, Bharati Vidyapeeth (Deemed to be University) Medical College and Hospital, Sangli, Maharashtra, India.
4. Statistician, Department of Directorate of Research, Krishna Institute of Medical Sciences (Deemed to be University), Karad, Maharashtra, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Sheetal Maheshkumar Sale,
12471, Sri Krishna Bunglow, Mali Plot, South Shivajinagar,
Sangli, Maharashtra-416416, Sangli, Maharashtra, India.
E-mail: drshitalsale@yahoo.com

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