(International Print/Online Journal)

SJIF IMPACT FACTOR: 5.565
PUBMED-National Library of Medicine ID-101739732

ISSN (Print): 2209-2870
ISSN (Online): 2209-2862

International Journal of Medical Science and Current Research (IJMSCR)
Available online at: www.ijmscr.com
Volume 5, Issue 5 , Page No: 878-883
September-October 2022

IJMSCR

Multiple Shades Of Thrombocytopenia In South Indian Monocentric Study: A Retrospective Study

Dr. B Vinothkumar, Dr. Sunderesh Kamal Chander*, Dr. Yogalakshmi, Dr. Muthuvel E

***Corresponding Author:**
Dr. Sunderesh Kamal Chander

Type of Publication: Original Research Paper
Conflicts of Interest: Nil

Abstract

Aims: To identify the various cause of thrombocytopenia, to grade the thrombocytopenia based on platelet count, to know the distribution of age and sex in the thrombocytopenia

Material And Methods: A retrospective study total of 200 cases reported in Saveetha Medical College, period of three months from October 2021 to December 2021. Blood samples were sent to the department of haematology, for complete blood count, blood samples ran in the automated analyser, and reports showing platelet count less than 150,000 selected and peripheral smear made and reduced platelet count is confirmed

Result: The common cause of thrombocytopenia in the studied cases was dengue and next to that was other acute febrile illnesses. The reduced platelet count is mostly seen in the male sex and the 21- 40 years of age group. Most of the thrombocytopenia cases come under Grade1

Conclusion: Infections, particularly dengue are the most common cause of fever with thrombocytopenia. Next to dengue viral fever, a patient diagnosed with acute febrile illness has a fever with thrombocytopenia.

Keywords: Thrombocytopenia, platelet count, Dengue fever, Covid-19, peripheral blood smear

Introduction

Normal platelet count ranges between 2 * 10^5 and 4 * 10^5/cu mm of blood. The average lifespan of platelets is 7-10 days.

Thrombocytopenia is the reduced platelet count in the peripheral blood below the lower limit of normal. A platelet count of less than 1,50,000 is considered thrombocytopenia. The severity of thrombocytopenia is graded based on the platelet count

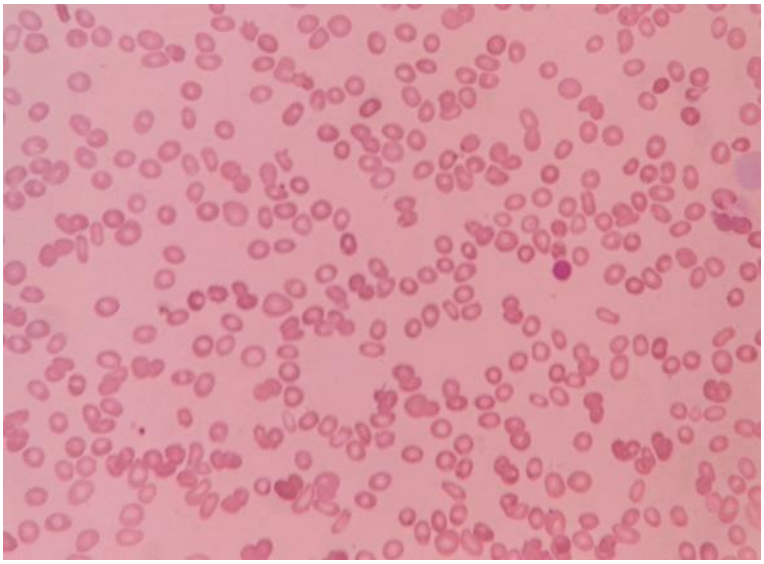
Grade 1 : 100-150 x 10^3 /mL

Grade 2 : 50-100 x 10^3 /mL

Grade 3 : < 50 x 10^3 /mL

Various conditions, the thrombocytopenia are Acute infections, Acute leukaemia, Aplastic and pernicious anaemia, Chickenpox, Smallpox, Splenomegaly, Scarlet fever, Typhoid, Tuberculosis, Purpura, and Gaucher's disease. Thrombocytopenia is associated with abnormal bleeding that includes spontaneous skin purpura, mucosal haemorrhages, and prolonged bleeding after trauma. Spontaneous bleeding was noted when platelet counts are < 20,000, and petechiae/purpura are seen when platelet counts are in the range of 50,000-1,00,000. Four main groups of causes for thrombocytopenia are Reduced platelet production, Increased platelet destruction, Increased destruction of platelet in the spleen (Spleen sequestration), and Dilutional loss.

Figure 1: Peripheral blood smear of Thrombocytopenia



Material and Methods

A retrospective study was conducted in saveetha medical college, with a total number of cases of 200, taken in the period of three months from October 2021 to December 2021. The study was carried out in line with research regulations, including the approval of the ethical committee. Blood samples are sent to the department of haematology, for complete blood count, blood samples ran in the automated analyser, and reports showing platelet count less than 150,000/□L(microlitre) are selected and peripheral smear made, and thrombocytopenia is confirmed manually.

Inclusion criteria :

1. Patients with a platelet count less than 150 x 10^3 /□L and confirmed manually after counting in peripheral smear were included.
2. All ages and sex were included in our study.

Exclusion criteria :

Platelet count not less than 150 x 10^3/□L, when manually counted on peripheral smear but show false positive reports in automated analyser report were excluded.

Results :

Out of the total of 200 patients taken for the study, 143 were male and 57 were female patients of thrombocytopenia. As all age group thrombocytopenia patients were included, divided into four groups as the number of cases under (< 20 years of age) were 45, (21-40years of age) were 97, (41-60 years of age) were 40, (>60 years of age) were 18. (Table.1.)

Infections were the most common cause of thrombocytopenia, in this study patients diagnosed with Dengue viral fever (24.50%) came to be the most common cause. Other than that patients diagnosed with an acute febrile illness (22.50%) is the second most common cause. Other common causes were COVID (12%) positive patient with thrombocytopenia, malaria (2%),chronic kidney disease(5.50%), acute appendicitis(1.50%), aplastic anaemia(1%), leukaemia(1.50%), osteomyelitis(1.50%), pregnancy(2.50%), sepsis(7%), typhoid fever(1%), other causes (17.50%).(Table.3.)

Table 1: Age and sex distribution

Sex	No. of cases	Percentage
Male	143	71.5%
Female	57	28.5%
Age groups		
<20	45	22.5%
21-40	97	48.5%
41-60	40	20%
>61	18	9%
Grand Total	**200**	**100.%**

Table 2 : Grading the severity of thrombocytopenia

Grades	No. of cases	PERCENTAGE
GRADE 1	76	38.00%
GRADE 2	69	34.50%
GRADE 3	55	27.50%
Grand Total	200	**100.00%**

Table 3: Spectrum of thrombocytopenia

Causes	No. of cases	Ekta Paramjit, Rajiv Rao, et al.	Lakum DN, Makwana DH, et al.	Percentage
ACUTE APPENDICITIS	3	_	_	1.50%
AFI	45	_	_	22.50%
APLASTIC ANAEMIA	2	0.60%	_	1.00%
CKD	11	_	_	5.50%
COVID	24	_	_	12.00%
DENGUE	49	27.70%	35.40%	24.50%

LEUKEMIA	3	_	_	1.50%
MALARIA	4	57.70%	46.80%	2.00%
OSTEOMYELITIS	3	_	_	1.50%
PREGNANCY	5	_	_	2.50%
SEPSIS	14	4.70%	7.80%	7.00%
TYPHOID FEVER	2	_	4.60%	1.00%
OTHER	35	1.60%	2.80%	17.50%
Grand Total	**200**			**100.00%**

Discussion:

In the present study, we found that infectious cause was the most common cause. Dengue viral fever cases as the common cause of thrombocytopenia, besides that, patients diagnosed with acute febrile illnesses and covid 19 came to be another common cause of thrombocytopenia in our study.

The viral parameters, viral load, and NS1 antigen are associated with the severity of the disease; there has been no detailed analysis of viral factors with platelet parameters. In patients with mild or severe cases of dengue infections, thrombocytopenia is common. Studies suggest that reduced platelet count is one of the causes of bleeding in dengue patients. In dengue fever, the platelet count reduces below $150*10^3$ /µL and in many patients, platelet reaches as low as $<40*10^3$/µL during 3rd to7th day of fever[3]. In some severe cases, patients need to be transfused with platelets. In dengue patients, thrombocytopenia develops because of two events: platelet production in the bone marrow is decreased and destruction and clearance of platelets from peripheral blood are increased. Several studies suggest that activation and dysfunction of the platelet are implicated in prothrombotic complications in the Dengue Haemorrhagic Fever and Dengue Shock Syndrome 10,11. Studies report that, the activation of platelet associated with elevated surface P-selectin and apoptosis with increased caspases and phosphatidylserine (PS) expressions in the early days of dengue infection.[4,5,]

Haematological changes in COVID-19-infected patients include reduced lymphocyte and platelet count. Prolonged activated prothrombin thromboplastin time (aPTT), 26% showed increased D-dimer levels, and most showed normal prothrombin time (PT) [7]. SARS-CoV and HCoV-229E have identical antigen characteristics, it was speculated that SARS-CoV-2 and HCoV-229E antigens have some similarities. Human aminopeptidase N (CD13) was a metalloprotease that is present on the cell surfaces of epithelial cells in the intestine, kidneys, and lungs and was a receptor for HCoV-229E. HCoV-229E enters bone marrow cells and platelets via CD13 receptors and induces growth inhibition and apoptosis in the bone marrow, leading to abnormal haematopoiesis and thrombocytopenia [8]. Thrombocytopenia caused by SARS-CoV-2 infection is similar to that of SARS-CoV and HCoV-229E infection. Based on this, it was understood that SARS-CoV-2 similarly inhibits haematopoiesis in the bone marrow via certain receptors causing decreased primary platelet formation and leading to thrombocytopenia. [9]

Thrombocytopenia was a common feature for both plasmodium falciparum and plasmodium vivax malaria. As seen in our study as well, thrombocytopenia was a diagnostic clue to the

presence of malaria. The frequency of thrombocytopenia (i.e., platelet count below $150*10^3$/mm3) in the malaria infection ranges from 24-94% in the literature. In malaria, thrombocytopenia occurs due to the binding of malarial antigens to the surface of platelets that causes antimalarial antibodies to additionally bind to the platelets, leading to immune complexes formation.[2] In our study dengue (24.5%) came to be a common cause, compared with Paramjit (27.7%) and Lakum (35.4%) was the percentage of dengue cases and both these studies show malaria as the common cause, in our study malaria (2%) cases reported. A patient diagnosed with acute febrile illness of unknown aetiology was found to have the second most common thrombocytopenia.

Thrombocytopenia in liver disease was multifactorial. When there was a functional defect of the major platelet receptor GPIIb-IIIa, which plays an important role to mediate both platelet aggregation by linking platelet-platelet through fibrinogen and signalling via receptor-mediated signal transduction [11]. Small peptides containing the Arg-Gly-Asp binding sequence of fibrinogen required for receptor activation and platelet bridging are seen to be accumulating in patients with renal failure. Several mechanisms appear to be playing a role in platelet-mediated bleeding associated with uraemia. First, there appears to be a defect in platelet adhesion, mediated by GPIb-V-IX–vWF interactions, which can be overcome by increasing vWF levels. [12,13] Second, there appears to be a defect in platelet secretion, mediated by increased PGI2 and NO levels in uremic patients and associated with increased platelet cAMP levels. At the same time, platelets from uremic patients contain less ADP, serotonin, and TxA2, emphasizing an acquired storage pool defect caused by uraemia. [14,15] Thrombocytopenia in liver disease not only lead to bleeding risk in patients with liver disease but also complicates therapy[16]. It was caused by splenomegaly and splenic sequestration, relatively reduced production of TPO for the degree of thrombocytopenia, consumption of platelets owing to autoantibodies directed against platelets, or because of bone marrow suppression. [17,18]

Conclusion:

The majority of patients fall under early adulthood with male predominance. Most of the thrombocytopenia cases were because of infectious causes. Among the infectious causes, dengue is the common cause followed by Covid-19 because this study was conducted during a pandemic. Our study findings can be validated in a large sample size and be taken forward for the development of mathematical models with the variables for the prediction of disease dynamics.

Acknowledgement:

I sincerely thank Saveetha Medical College and Hospital, Chennai, for their continued support in the procurement of the research. I also extend heartfelt gratitude to my beloved guide Dr Yogalakshmi E and to my HOD Dr Chitra Srinivasan (Department of Pathology) for the research, experimental design, and ethical approval, critical revision of the manuscript.

Statement of Ethics:

This study was approved by the Ethics Committee of Saveetha Medical and Hospital. As this study was a retrospective study, there was no patient privacy data such as patient name, ID number, telephone, and address involved. Only demographic information and laboratory testing data of patients were collected and analysed in this study.

Reference

1. Essentials of Clinical Pathology by Shirish M Kawthalkar, 2nd edition.
2. Skudowitz RB, Katz J, Lurie A, Levin J, Metz J. Mechanisms of thrombocytopenia in malignant tertian malaria. Br Med J 1973;2:515-8.
3. Wang WK, Chao DY, Kao CL, Wu HC, Liu YC, Li CM, et al. High levels of plasma dengue viral load during defervescence in patients with dengue hemorrhagic fever: implications for pathogenesis. Virology 2003;305(Jan (2)):330–8.
4. Thomas L, Verlaeten O, Cabié A, Kaidomar S, Moravie V, Martial J, et al. Influence of the dengue serotype, previous dengue infection, and plasma viral load on clinical presentation and outcome during a dengue-2 and dengue-4 coepidemic. Am J Trop Med Hyg 2008;78(Jun (6)):990–8.
5. Parveen N, Islam A, Tazeen A, Hisamuddin M, Abdullah M, Naqvi IH, et al. Circulation of single serotype of Dengue Virus (DENV-3) in New Delhi, India during 2016: a change in the epidemiological trend. J Infect Public Health 2019;12(Jan(1)):49–56.

6. Ojha A, Nandi D, Batra H, Singhal R, Annarapu GK, Bhattacharyya S, et al. Plateletactivation determines the severity of thrombocytopenia in dengue infection. Sci Rep 2017;7(Jan (1)):41697.
7. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, Qiu Y, Wang J,Liu Y, Wei Y, Xia J, Yu T, Zhang X, Zhang L (2020) Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 395(10223):507–513. https://doi.org/10.1016/s0140 6736(20)30211-7
8. Yeager CL, Ashmun RA, Williams RK, Cardellichio CB, Shapiro LH, Look AT, Holmes KV (1992) Human aminopeptidase N is a receptor for human coronavirus 229E. Nature 357(6377):420–422. https://doi.org/10.1038/357420a0
9. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS,Manson JJ, Hlh Across Speciality Collaboration, U. K (2020) COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet. https://doi.org/10.1016/S0140-6736(20)30628-0
10. Gallup JL, Sachs JD. The economic burden of malaria. Am J Trop Med Hyg 2001;64(Suppl):85-96.
11. Zwaginga JJ, Ijsseldijk MJ, Beeser-Visser N, de Groot PG, Vos J, Sixma JJ. High von Willebrand factor concentration compensates a relative adhesion defect in uremic blood. Blood. 1990;75(7):1498-1508.
12. Mannucci PM, Remuzzi G, Pusineri F, et al. Deamino-8-D-arginine vasopressin shortens the bleeding time in uremia. N Engl J Med. 1983; 308(1):8-12.
13. Noris M, Remuzzi G. Uremic bleeding: closing the circle after 30 years of controversies? Blood. 1999;94(8):2569-2574.
14. Eknoyan G, Brown CH III. Biochemical abnormalities of platelets in renal failure. Evidence for decreased platelet serotonin, adenosine diphosphate and Mg-dependent adenosine triphosphatase. Am J Nephrol. 1981;1(1):17-23.
15. Schafer AI, Levine S, Handin RI. Regulation of platelet arachidonic acid oxygenation by cyclic AMP. Blood. 1980;56(5):853-858.
16. Giannini EG, Peck-Radosavljevic M. Platelet dysfunction: status of thrombopoietin in thrombocytopenia associated with chronic liver failure. Semin Thromb Hemost. 2015;41(5):455-461.
17. Aster RH. Pooling of platelets in the spleen: role in the pathogenesis of "hypersplenic" thrombocytopenia. J Clin Invest. 1966;45(5):645-657.
18. Pereira J, Accatino L, Alfaro J, Brahm J, Hidalgo P, Mezzano D. Platelet autoantibodies in patients with chronic liver disease. Am J Hematol.1995;50(3):173-178.