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Clinico-Pathological Profile Of Thrombocytopenia In A Tertiary Care Institute.

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ABSTRACT

Thrombocytopenia is not a disease itself, but a subnormal number of platelets in blood and is one of the most common causes of abnormal bleeding. The patient with thrombocytopenia often presents diagnostic and management challenges. The differential diagnosis is broad because the disorders leading to thrombocytopenia are diverse, with failed production at one extreme and the accelerated destruction at the other. To highlight and diagnose thrombocytopenia and investigate the cause of thrombocytopenia in our tertiary care center. The present study is retrospective, cross-sectional study done on screened 428thrombocytopenia patients which were came to our hematology lab. All patients of proved thrombocytopenia patients were included in the study over a period of 1 years from Sep 2021 to April 2022. Pseudo-thrombocytopenia patients were excluded from the study. All these patients were investigated in a systemic manner, causes of thrombocytopenia were ascertained and data was analyzed. The most common affected age group of thrombocytopenia was 3rd decades and 2nd decades respectively with male predominance. The most common cause of thrombocytopenia is anemia, infection, splenomegaly and alcoholism. Dimorphic anemia, malaria and HIV are the most etiology of anemia and infection respectively. Thrombocytopenia is root cause of abnormal bleeding in many cases. Importance of early and prompt diagnosis of thrombocytopenia is always warranted as treatment differs depending upon the etiology. Thrombocytopenia is multifactorial and a finding that may result from various diseases and clinicopathological approach is important in these cases.

Keywords: Thrombocytopenia, Platelets, Etiology, Multifactorial, Clinicopathological.

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INTRODUCTION

Thrombocytopenia is defined as reduced number of platelets in the circulating blood i.e. less than $150x10^9$/L. Thrombocytopenia is a laboratory finding, not a diagnosis [1]. It is a frequent cause of abnormal bleeding. Pseudothrombocytopenia also must be considered in the differential diagnosis especially in patients who are asymptomatic and it is due to the invitro clumping of platelets after blood collection [2]. The differential diagnosis of thrombocytopenia is enormous but is acquired in most of the patients, due to an autoimmune etiology or underlying disease processes [3]. Most of the patients are diagnosed on routine blood film examination incidentally. Careful examination of the blood film is therefore the best means for narrowing the differential diagnosis [4]. Though suppression of bone marrow and infiltration of marrow by malignancies are important, nonmalignant lesions like infections are equally important as they aid simple treatment and complete recovery. It is crucial to know the correct etiology for appropriate treatment and prognostication [5]. Early recognition and continuous monitoring of patients with thrombocytopenia can avoid bleeding manifestations including fatal intra cranial haemorrhage. Many studies had elucidated on the cause of febrile thrombocytopenia in hospitalized patients and focused on Dengue [6]. Apart from infectious etiology, there are other causes of thrombocytopenia in patients. Hence this study attempted to find the various etiologies of thrombocytopenia in hospitalized patients with a clinicopathological correlation of their presenting features. This present study is focused on the analysis of cases confirmed to have thrombocytopenia based on clinical and relevant laboratory data to arrive at a possibleetiopathogenesis [7,8].

MATERIALS AND METHODS

This prospective study was conducted in Department of Pathology, Swamy Vivekananda Medical College Hospital And Research Institute, Elayampalayam, Tiruchengode, Namakkal District, Tamil Nadu, India from Sep 2021 to April 2022.This study included all inpatient subjects who presented with thrombocytopenia.

Inclusion Criteria

Patients presenting to Swamy Vivekananda Medical College Hospital And Research Institute, Elayampalayam, Tiruchengode, Namakkal District, Tamil Nadu, India who were found to have thrombocytopenia, defined as a platelet count less than $150x10^9$ /L in an automated counter and confirmed by peripheral smear examination.

Exclusion Criteria

Out patients, Patients, whom complete evaluation not possible due to various reasons like inadequate details, discharge etc. Cases of pseudo thrombocytopenia. Peripheral venous blood was obtained from antecubital venipuncture. Blood was transferred in adequate amount into tripotassium EDTA vacutainer for complete blood count, sodium citrate 3.2% for coagulation profile and plain blood for biochemical analysis. The complete blood count was performed using Pentra ES60 automated analyzer (5 part differential) The following parameters were included: Total leukocyte count, differential count, haemoglobin, hematocrit, MCV, MCH, MCHC, red cell mass, red cell distribution width and platelet count. ESR was measured by Westergren‟s method if needed. Peripheral blood smear stained by Leishman stain was examined. Bone marrow aspirate was obtained from posterior superior iliac crest using bone marrow aspiration needle. Smears were stained with Leishman stain. Bonemarrow trephine biopsy was performed, and H&E stained paraffin sections will be examined in cases if needed. Blood with appropriate amount of 3.2% sodium citrate was used for prothrombin time, activated partial thromboplastin time. Clotted blood was used for assessing liver function, renal function test etc. The data was entered in Microsoft excel sheet. Statistical analysis done using SPSS 22.0 (Statistical package for the socialsciences) software.

RESULTS

Maximum number of patients were in the age group 45-64 years followed by 25-44 years constituting about 29% and 27% respectively of the study population. Maximum number of thrombocytopenia cases is of male gender constitutingabout 63% of the study population and female gender is about 37%.About 4 % of the cases had pseudo or spurious thrombocytopenia due to

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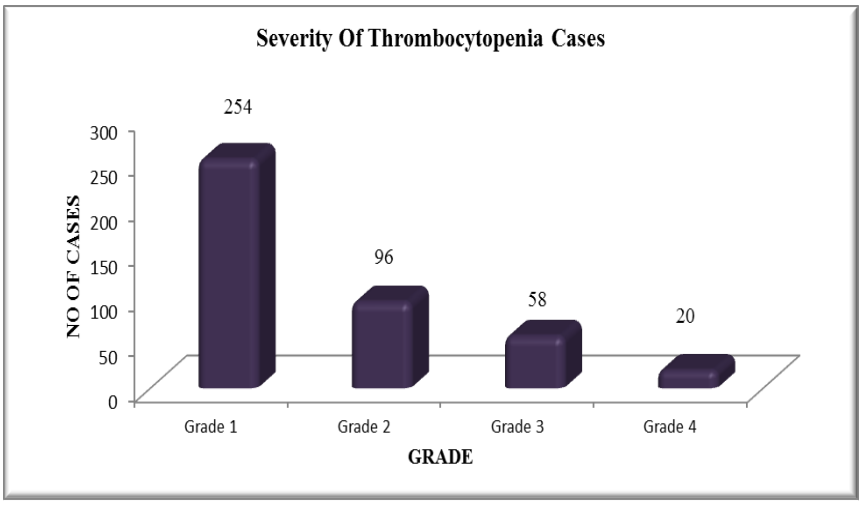
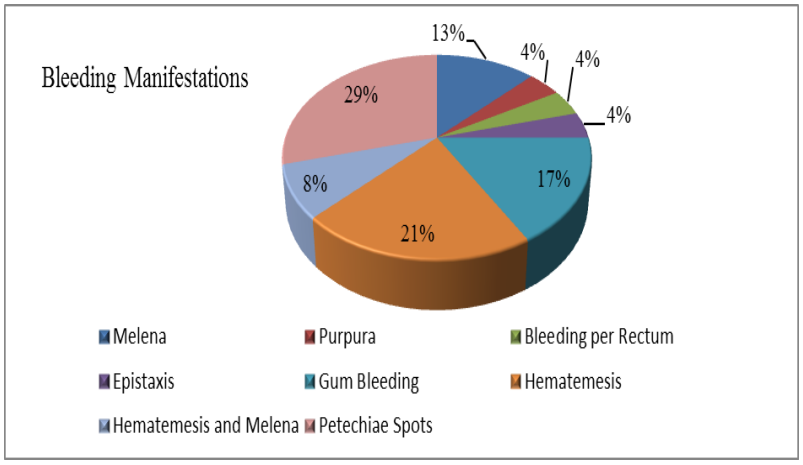
EDTA induced platelet clumping. Out of 428 cases, fever was the most common clinical presentation in 248 cases (57.94%). Chronic kidney disease was the next in frequency with 60 cases 14.02%). Chronic liver disease patients presented with icterus, bleeding manifestations and ascites. Leukaemia cases presented with bleeding manifestations, fever, fatigability and lymphadenopathy. Dengue fever presented with febrile illness, joint pain, body pain, headache, giddiness and bleeding manifestation. Malaria cases presented with fever, chills and rigors. Patients with complaints of fatigability and giddiness came with clinical diagnosis of anaemia. One case of systemic lupus erythematosus had symptom of hematuria. The follow up cases were malignancy cases on post-operative chemotherapy. Enteric fever with fever and abdominal pain. Other cases include post traumatic and post-surgical, pregnancies, patients on long term intake of diuretics and anti-epileptic.

Graph 1: Severity Of Thrombocytopenia Cases



Maximum number of patients had Grade 1 thrombocytopenia and least number had grade 4 thrombocytopenia accounting about 59% and 5% of the study population respectively. The remaining are Grade 2(22%) and grade 3 (14%).

Graph 2: Bleeding Manifestations



Among the study population, about 6% developed bleeding manifestations of which petechiae spots were the commonest accounting about 29% followed by hematemesis which constitutes 21% of all the bleeding manifestations. The remaining are melena (13%), Gum bleeding (17%), purpura(4%),epistaxis (4%), bleeding per rectum(4%), hematemesis and melena (8%)

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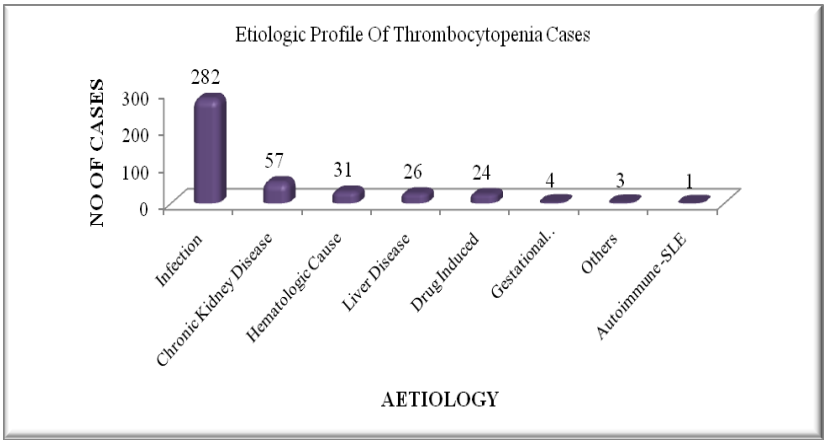
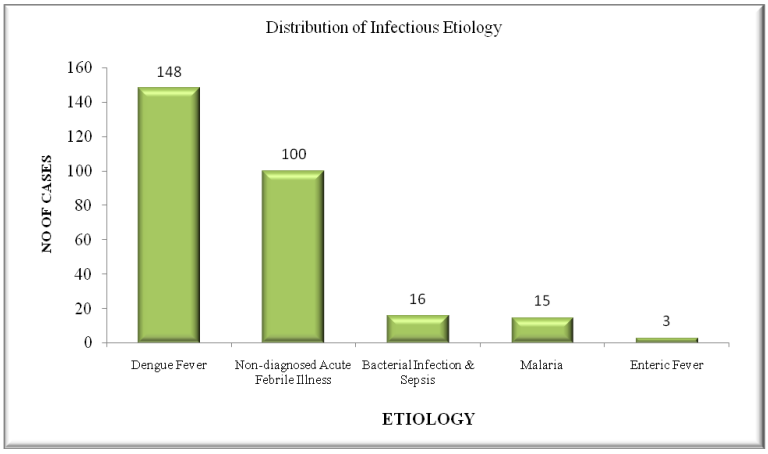
Graph 3: Aetiologic Profile Of Thrombocytopenia Cases



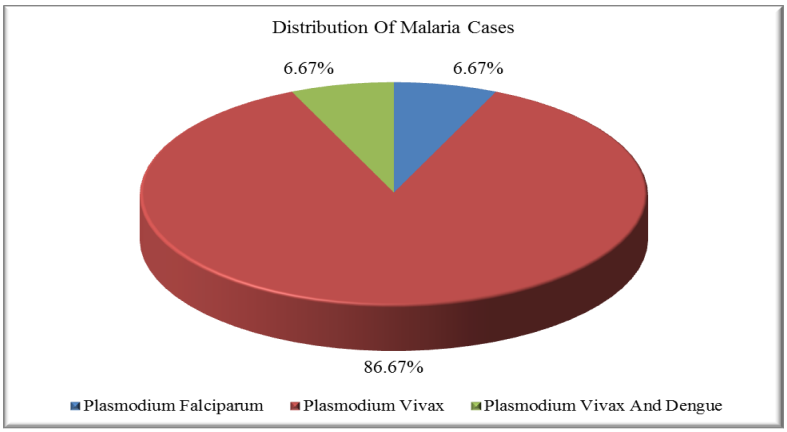
Maximum number of cases of thrombocytopenia is due to infectious aetiology accounting about 65.9% of the study population. The remaining are chronic kidney disease (13.3%), Hematologic cause (7.2%), Drug induced (5.6%), Liver disease (6.1%), Gestational (0.9%), autoimmune-SLE(0.2%) and post traumatic and surgical cases(0.7%).

Graph 4: Distribution Of Infectious Aetiology



Maximum number of the infectious cases were due to dengue viral origin constituting 52.5% of the study population. And the remaining are non-diagnosed acute febrile illness 35.5%, malaria 5.3%, enteric fever 1% and bacterial infection andsepsis 5.7%.

Graph 5: Distribution Of Malaria Cases



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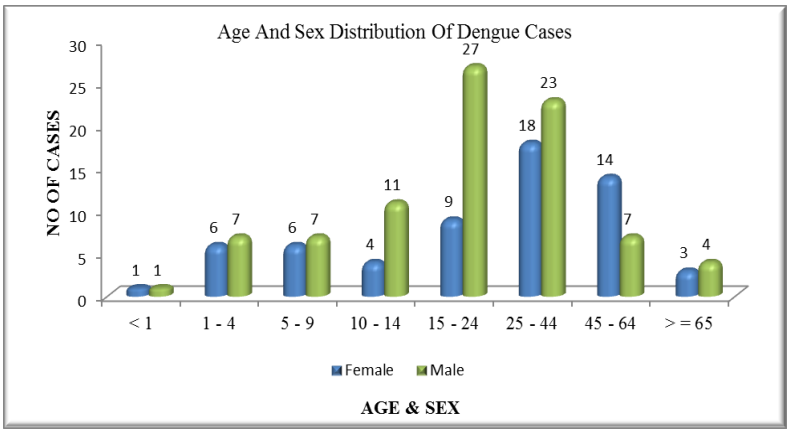
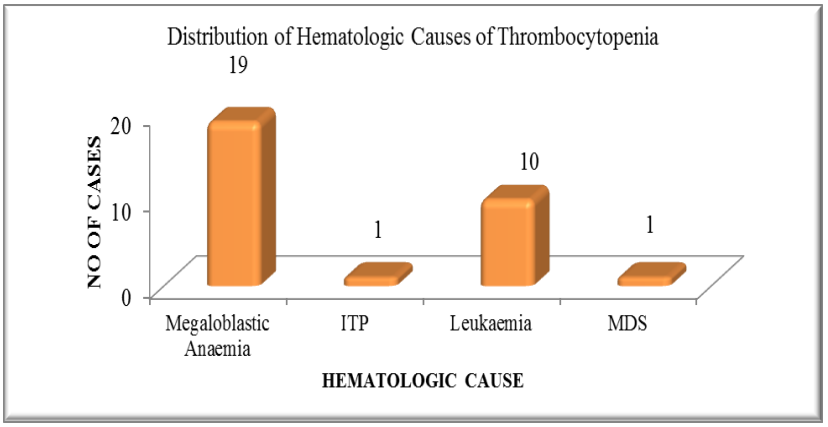
Among the malarial cases, 93.3% of the cases were due to species Plasmodium vivax (One P.vivax case had dengue co-infection). Plasmodium falciparum -6.67%

Graph 6: Age And Sex Distribution Of Dengue Cases



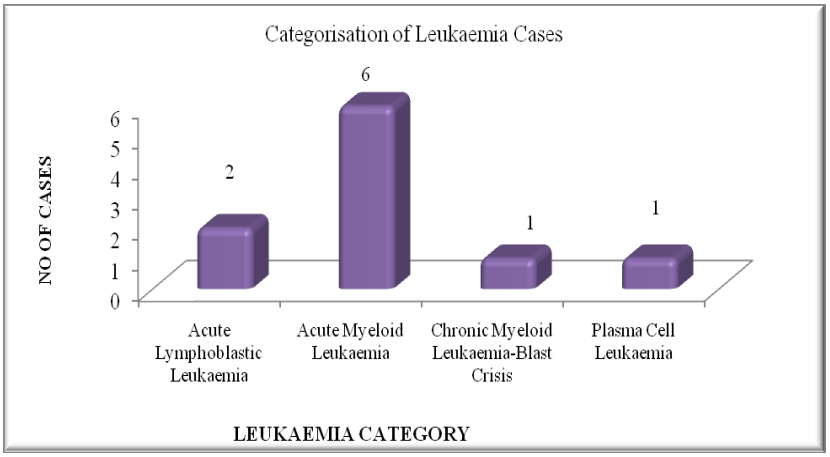
Dengue infection is found to be common in male patients in the age group 25-44 years followed by 15-14 years.

Graph 7: Distribution Of Hematologic Causes OfThrombocytopenia



About 61.3% of the hematologic cause of thrombocytopenia were megaloblastic anaemia followed by leukaemia 32.3%, Immune mediated thrombocytopenia 3.2% and myelodysplastic syndrome 3.2%.

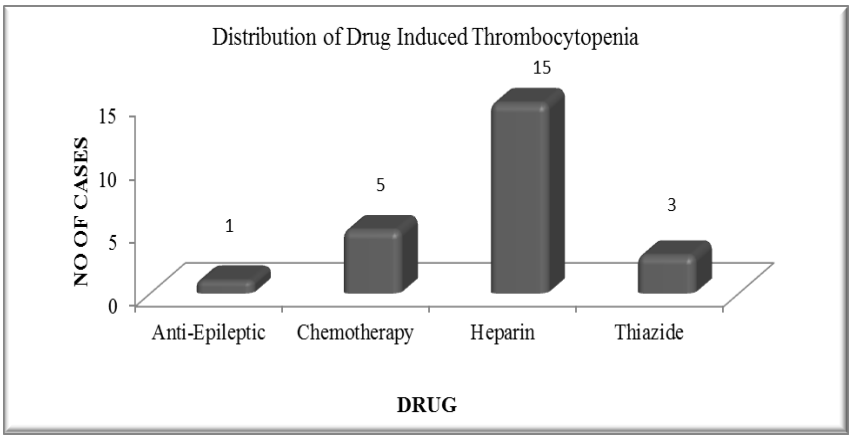
Graph 7: Categorisation Of Leukaemia Cases



ISSN: 0975-8585

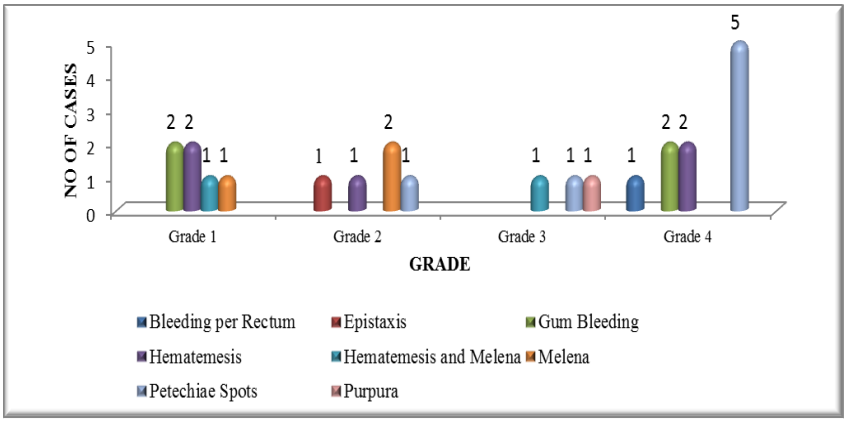
Among the hematologic malignancies, acute myeloid leukaemia accounts 60% of the study population followed by acute lymphoblastic leukaemia 20%, Plasma cell leukaemia and chronic myeloid leukaemia-Blast crisis 10%.

Graph 8: Distribution Of Drug Induced Thrombocytopenia



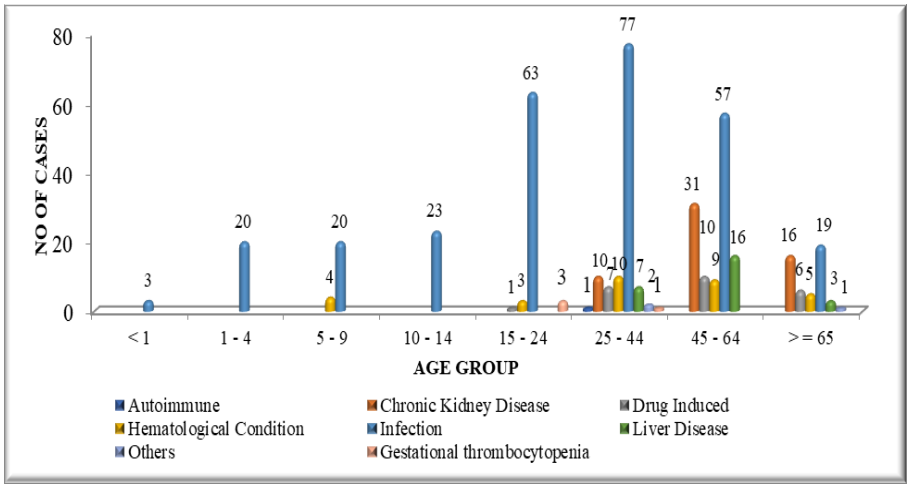
Among drug induced thrombocytopenia cases 62.5% is due to heparin, 20.8% chemotherapy, 12.5% thiazides and 5.2% antiepileptic.

Graph 9: Correlation Of Severity Of ThrombocytopeniaWith Bleeding Manifestations



Bleeding manifestations are common among Grade 4 thrombocytopenia cases

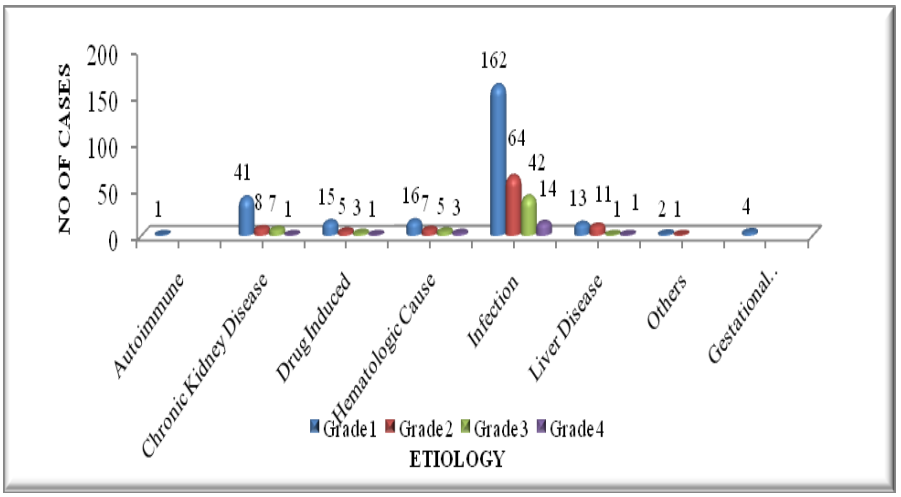
Graph 10: Correlation Of Age With Aetiology



ISSN: 0975-8585

Infectious aetiology is more common among the age group 25-44 years and chronic kidney disease among 45-64 years.

Graph 11: Correlation Of Severity Of ThrombocytopeniaAnd Aetiology



Grade 1 thrombocytopenia is higher in all aetiologies

Figure 1: ITP-Bone Marrow Biopsy Showing Hypercellular Marrow With Megakaryocytic Hyperplasia (Mature And Immature Megakaryocytes)

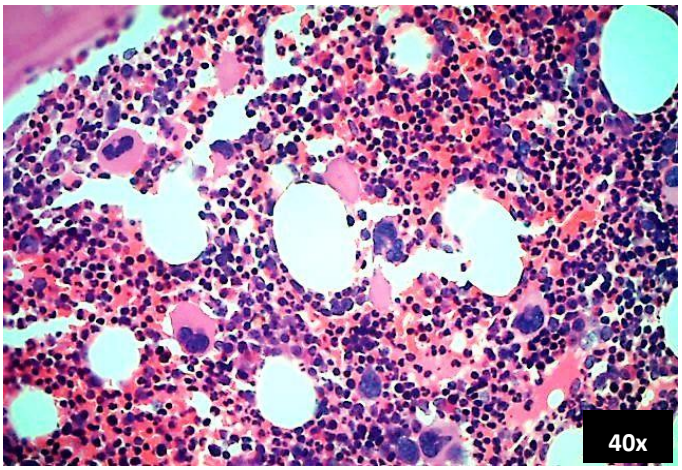
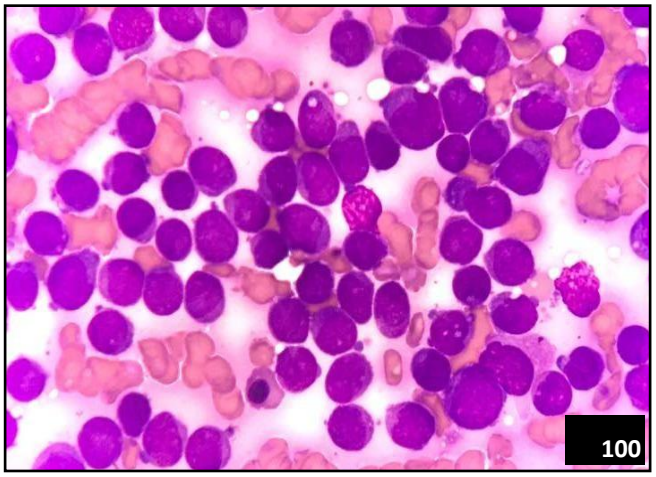
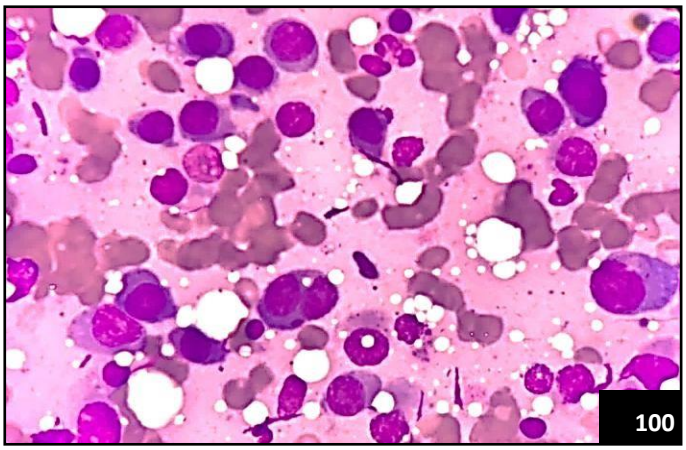


Figure 2: AML: Bone marrow aspirate is hypercellular with infiltration of myeloblasts



ISSN: 0975-8585

Figure 3: Plasma cell leukaemia-Bone marrow aspirate showing neoplastic plasma cellswith moderate to marked degree of pleomorphism and binucleation.



DISCUSSION

The age and severity of thrombocytopenia and associated findings in this study are similar to that of other studies. The most common cause of newly diagnosed thrombocytopenia in this study is of infectious etiology and Dengue was the most common cause [9]. Various mechanisms have been hypothesized to explain the mechanism of thrombocytopenia in Dengue infections. Bone marrow suppression during the acute phase of the illness can occur because of affected progenitor cells and infected stromal cells and dysregulated bone marrow production [10]. Thrombocytopenia can also occur because of platelet sequestration, activation of the complement system and consumptive coagulopathy. Autoantibodies against blood-coagulation-related molecules and endothelial cells have been described and antiplatelet antibodies have been implicated in platelet lysis [11]. Mild to moderate thrombocytopenia is a common finding in all forms of malaria, but severe thrombocytopenia is very common in falciparum malaria. In our study, we encountered 8 cases of malaria, out of which 1 case of falciparum malaria had platelet count of 40,000 and rest 7 cases of vivax malaria had counts between 50,000 to 1,00,000. None of them had bleeding manifestations [12]. Different mechanism contributes to thrombocytopenia in malaria including direct lysis of platelets by plasmodium by both immunological and non-immunological mechanisms, oxidative stress mediated destruction [13]. of the platelets. Thrombocytopenia in malaria is well tolerated because of platelet activation and enhanced agreeability [14]. and bleeding manifestations are rare in acute episodes of malaria because of the hyperactive platelets enhancing the hemostatic responses. Bicytopenia and subclinical disseminated intravascular coagulation is a very common finding in enteric fever which is contributed by bone marrow suppression and hemophagocytosis .Pancytopenia and isolated thrombocytopenia in enteric fever is rare [15]. This is because hematological findings in enteric fever may not follow a prototype pattern in presentation in tropical regions. But a differential diagnosis of enteric fever should also be kept in mind when evaluating a patient of fever with isolated thrombocytopenia [16]. Thrombocytopenia is an early finding in septicemia and can give a clue to the treating physician in clinically suspected cases and has prognostic significance during the management. It can result from activation of the platelets which bind to the endothelium and get sequestered Immunologically mediated destruction of platelets can also occur by nonspecific antibodies and hemophagocytosis [17]. Thrombocytopenia in liver disease occurs because of portal hypertension and splenic sequestration. The liver being the site of thrombopoietin, reduction of functional liver cell mass in chronic liver diseases, leads to suppressed thrombopoiesis and subsequent peripheral thrombocytopenia [18]. Mild thrombocytopenia is frequently encountered in chronic kidney disease possibly because of reduced thrombopoietic activity. Platelet dysfunction and impaired platelet-vessel wall interaction may also add on and can result in complex hemostatic disorders in patients with end stage renal disease [19]. Thrombocytopenia in malignancies is contributed by diverse factors like systemic chemotherapy, involvement of marrow by tumour, microangiopathic disorders and secondary immune thrombocytopenia [20]. Apart from above conditions thrombocytopenia can occur as a combined or isolated finding in many hematological conditions like megaloblastic anemia, aplastic anemia and hypersplenism. Iron deficiency anemia is commonly associated with reactive thrombocytosis, but thrombocytopenia can occur in severe cases [21]. The miscellaneous causes of thrombocytopenia were infections like HIV, connective tissue disorders and drug induced [22].

CONCLUSION

Thrombocytopenia with or without bleeding manifestations is a common problem encountered in routine clinical practice. The treatment decision, treatment response and prognostication would depend on aetiopathogenesis of thrombocytopenia. Pathologists should highlight this point to help the clinician manage the patients in an appropriate and beneficial manner. Supportive parameters like good peripheral smear examination, coagulation profile, bone marrow evaluation and certain biochemical parameters with the clinical profile helps in narrowing the aetiology and increasing treatment benefits. The point that all thrombocytopenia are not immune mediated should be remembered and attempts should be made to rule out other possible aetiologies. Causes of thrombocytopenia vary with geographic variation. Study in our tertiary care hospital revealed infections are common cause of thrombocytopenia due to lower socio-economic status in developing countries. The leading cause of thrombocytopenia in our study is both curable and preventable. Preventing the infection can decrease the incidence of thrombocytopenia.

REFERENCES

[1] Bhalara SK, Shah S, Goswami H, Gonsai RN. Clinical and etiological profile ofthrombocytopenia in adults: A tertiary care hospital based cross sectional study. Int Jr Med Sci 2018;66:33–6.

[2] Achalkar GV. Jemds.com 2017;6(37):3003–6.

[3] Shrestha A, Karki S. Evaluation of EDTA induced pseudothrombocytopenia and the effect of alternative anticoagulants. 2014;4:626–9.

[4] V. Gazzaniga LO. The discovery of platelets and their function. Vesalius 2001;VII(1):22–6.

[5] Paramjit E, Rao R, Sudhamani S, Roplekar P, Shaffi Z, Roy S. Spectrum of thrombocytopenia : A clinicopathological study with review of the literature. 2016;2016–9.

[6] Azeredo EL De, Monteiro RQ, Pinto LM. Thrombocytopenia in Dengue: Interrelationship between Virus and the Imbalance between Coagulation and Fibrinolysis and Inflammatory Mediators Thrombocytopenia in Dengue: Interrelationship between Virus and the Imbalance between Coagulation andFibrinoly. 2015;(August).

[7] Tejinder Singh.atlas and text of hematology. 3rd Edition Avichal PublishingCompany; 2010.

[8] John Greer, John forester, et.al. Wintrobe's Clinical Hematology. 12th Edition.Philadelphia: Lippincott William & Wilkins;2009: vol.2.

[9] Stasi R. How to approach thrombocytopenia 2012;191–7.

[10] Adewoyin AS, Nwogoh B. Peripheral blood film - a review. Ann Ibadan Postgrad Med 2014;12(2):71–9.

[11] Al-Hosni ZS, Al-Khabori M, Al-Mamari S, Al-Qasabi J, Davis H, Al-Lawati H, et al. Reproducibility of manual platelet estimation following automated low platelet counts. Oman Med J 2016;31(6):409–13.

[12] Gomes Oliveira RA, Takadachi MM, Nonoyama K, de Oliveira Barretto OC. Is automated platelet counting still a problem in thrombocytopenic blood? Sao Paulo Med J 2003;121(1):19–23.

[13] Sudalaimuthu M, Ganapathy S, Rajendran K, Arunachalam S. A novel method to estimate platelet counts from peripheral smears: A study comparing a new method of platelet estimation with existing methods. Ann Pathol Lab Med 2017;4(1).

[14] Pešová M, Staňo Kozubík K, Pál K, Šmída M, Baloun J, Radová L, et al.Inherited thrombocytopenias. Transfuze a Hematol Dnes 2018;24(1):14–26.

[15] Bennett CM. Drug-induced Thrombocytopenia. Transfus Med Hemost 2009;21(4):487–90.

[16] Rajashekar RB, Mahadevappa A, Patel S. Evaluation of Thrombocytopenia in Megaloblastic Anemia by Platelet Indices and Megakaryocytes- Comparison with Hypoproduction and Hyperdestruction 2017;6(1):18–22.

[17] Gomber S, Kela K, Dhingra N. Clinico-Hematological Profile of MegaloblasticAnemia. 1998;

[18] Morris V, Spraker H, HOward S, Ware R, Reiss U. Severe Thrombocytopenia with Iron Deficiency Anemia. Pediatr Hematol Oncol 2010;27(5):413–9.

[19] Bhasin TS, Sharma S, Manjari M, Mannan R, Kansal V, Chandey M, et al.Changes in megakaryocytes in cases of thrombocytopenia: Bone marrowaspiration and biopsy analysis. J Clin Diagnostic Res 2013;7(3):473–9.

[20] 20.Stéphan F, Thiolière B, Verdy E, Tulliez M. Role of hemophagocytic histiocytosis in the etiology of thrombocytopenia in patients with sepsis syndrome or septic shock. Clin Infect Dis Off Publ Infect Dis Soc Am 1997;25(5):1159–64.

[21] François B, Trimoreau F, Vignon P, Fixe P, Praloran V, Gastinne H. Thrombocytopenia in the

sepsis syndrome: role of hemophagocytosis and macrophage colony-stimulating factor. Am J Med 1997;103(2):114–20.

[22] Hariprasad S, Sukhani N. Evaluation of clinical profile of febrile thrombocytopenia: an institutional based study 2017;4(6):1502–5.