Section: Pathology

Original Research Article

STUDY OF THROMBOCYTOPENIA IN A TERTIARY CARE HOSPITAL IN EASTERN INDIA

Swagatika Agrawal[1], Anju Prasad[2], K Mohini Rao[1], Pratibha Samant Roy[3]

[1]Professor, Department of Pathology, IMS &SUM II, Bhubaneswar, Odisha, India
[2]Professor, Department of Pharmacology, IMS &SUM II, Bhubaneswar, Odisha, India
[3]Senior consultant, Department of Microbiology, Jagannath Hospital, Bhubaneswar, Odisha, India

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Corresponding Author:
Dr. Anju Prasad,
Email: anjuprasad_2004@yahoo.co.in

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Abstract

Background: Thrombocytopenia is a common clinical problem with various etiologies. This may occur due to decreased platelet production, increased destruction of platelets and differentiation in distribution of platelets. Transient bone marrow suppression and marrow infiltration by malignancies are important causes, certain non-malignant condition such as infections and drugs are equally important as their treatment is simple and complete recovery occurs. Detection of the exact etiology is important for specific treatment and prognostication. **Material method:** In this retrospective study, a total of 113 patients with thrombocytopenia from different departments of hospital were included, graded and evaluated for the cause. **Result** Out of 113 patients 67 patients (59%) were males and 46 patients(41%) were females. The patient's age ranged from 6 months to 75 years. 56 patients (49.6%) presented with Grade 1, 26 patients (23%) presented with Grade 2, 24 patients (21.2%) presented with Grade 3 and 7 patients (6.2%) presented with Grade 4 thrombocytopenia. Infections, anemia and drugs were the main causes of thrombocytopenia, and the less frequent causes of thrombocytopenia were found to be ITP, leukemia, lymphoma, malignancy, chronic liver diseases, hypersplenism and pregnancy . **Conclusion:** The study concludes that thrombocytopenia has many etiologies which can be diagnosed by detailed history and peripheral smear examination supported by bone marrow examination and other relevant investigations.The reasons of thrombocytopenia may differ according to geographic distribution and level of health center. In developing countries, high rate of infections was found to be the chief reason for thrombocytopenia followed by anemia and drugs encountered in a tertiary care hospital.

INTRODUCTION

Thrombocytopenia is defined as reduction in platelet count below the lower limit of 1.5 lakhs/ cu.mm [1]. Normal platelet count ranges from 150–450 x103 / µL. The main function of platelet is control of bleeding in small vessels by the formation of primary platelet plugs and also in secondary haemostasis platelets are essential.[1] Thrombocytopenia can be a life-threatening condition encountered due to various underlying diseases and drug intake and has been associated with spontaneous bleeding into vital organs resulting in significant morbidity and mortality.[2]

Based on the count it is categorized into four grades i.e. grade 1 to grade 4.[3]

Grade 1: 75,000 – 1, 50,000/cu.mm
Grade 2: 50,000 – 75,000/cu.mm
Grade 3: 25,000 – 50,000/cu.mm
Grade 4: <25,000/cu.mm

The aetiology of thrombocytopenia varies widely ranging from marrow suppression to haematological malignancies.[4] Thrombocytopenia may also be caused secondary to infections, drugs etc. Pseudothrombocytopenia is also a cause consist of 1% of sample in haematology departments. EDTA sampling is a major cause of pseudothrombocytopenia. In that condition for correct estimation of platelet count, it should be done from the sample collected in sodium citrate vacutainer. There are three major pathophysiologic mechanisms of thrombocytopenia: decreased production, accelerated destruction and sequestration of platelets.[5] Recently fever with thrombocytopenia is common clinical presentation in tertiary-care hospitals. Severe thrombocytopenia patient presents with spontaneous bleeding (i.e., mucosal, intracranial, gastrointestinal, and genitourinary bleeding), petechiae, bruising and blood loss from organs like brain, heart or kidney. The bone marrow picture may vary depending on the aetiology, from normocellular with non-specific changes to hypercellular with normal to reduced megakaryocytes.

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The aim of this study is to evaluate the incidence of different etiological causes of thrombocytopenia in a tertiary care hospital. Knowing the exact aetiology is important for specific treatment and prognostication.[6]

MATERIALS AND METHODS

The prospective descriptive study was conducted in the department of Pathology, IMS & SUM II College and Hospital, Bhubaneswar. The study was conducted from January 2024 to April 2024.

The age of the study group ranged from 6 months to 75 years at the time of diagnosis. The age, sex, detailed medical histories, physical examinations and medications were recorded from files. Laboratory findings were recorded using electronic database. Patients whose platelet counts were lower than 1, 50,000/cu.mm were described to have thrombocytopenia and were included in the study. Fully automated haematology analyser was used to determine CBC and was confirmed by peripheral blood film examination. A fresh 4ml sample was withdrawn in an ethylene diamine tetra acetic acid (EDTA) vial and a peripheral smear was prepared with fresh blood. Leishman's stain was poured on the slide and waited for 2 minutes. This allowed the fixation of peripheral blood film in methyl alcohol; a double quantity of buffered water was added dropwise over the slide and mixed for 5 minutes. After washing it in water for 1-2 minutes, the slide was air-dried and then examine in an oil immersion lens.[7]

The peripheral smear examination procedure and staining were carried out by standard methods.

Inclusion criteria

All male and female patients aged 6 months to 75 years with platelet less than or equal to 150 x 103 per µL have been included in this study.

Exclusion criteria

1. Neonates have been excluded from the study.
2. All male and female adults with platelet more than 150x103 per µL have been excluded from the study.

RESULTS

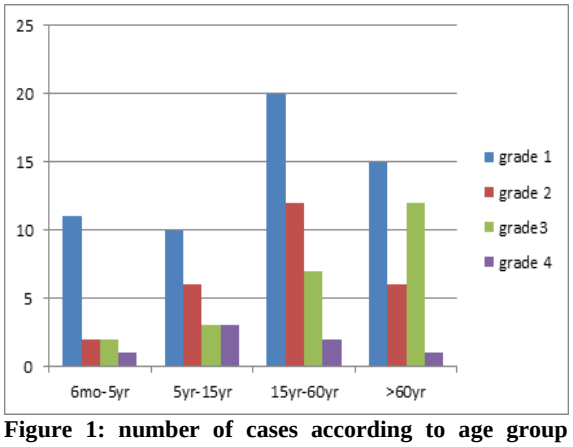

Figure 1: number of cases according to age group distribution and grade of thrombocytopenia

A total of 113 patients who attended the Pathology department 1MS & SUM Campus II Medical College during the study period were included in the study. The age range of the study group was from 6 month to 75 years. Most of the cases (36.3%) belonged to age group of 15-60 years. Among the 113 patients, 56 patients (49.6%) presented with Grade 1, 26 patients (23%) presented with Grade 2, 24 patients (21.2%) presented with Grade 3 and 7 patients (6.2%) presented with Grade 4 patients.

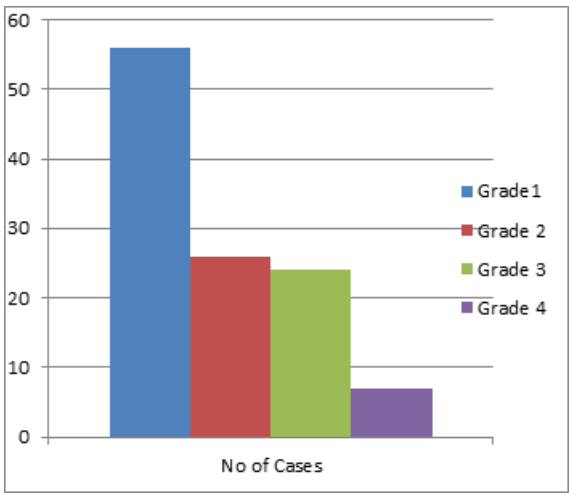

Figure 2: Number of cases according to grade of thrombocytopenia

Out of the 113 cases, 67 patients (59%) were male and 46 patients (41%) were female.

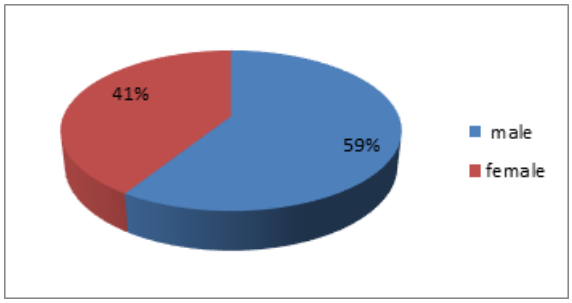

Figure 3: Sex incidence

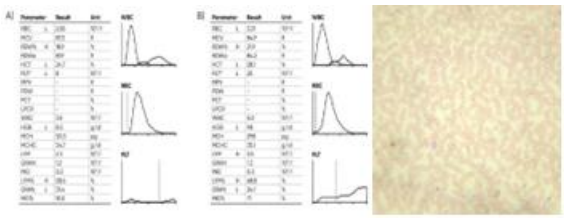

Figure 4: A, B, C- Samples with low PLT count (A) & (B), confirmed by microscopic examination(C)

The commonest presenting symptoms were fever in 76 cases (67.3%), bleeding manifestations in 28 cases (24.8%) and 9 cases (7.9%) were other symptoms were jaundice, hepatosplenomegaly and lymphadenopathy.

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Causes of thrombocytopenia

The most common cause for thrombocytopenia in this study was infection seen in 50 cases (44.3%) followed by anemia in 18 cases (16%) and post medication in 18 cases (16%). Other causes were leukaemia in 5 cases (4.4%), ITP in 2 cases (1.7%) , hypersplenism in 3 cases (2.8%), aplastic anemia in 3 cases (2.7%), malignancy in 9 cases (7.9%), lymphoma in 2 cases (1.7%) , chronic liver disease in 2 cases (1.6%), and pregnancy in 1 case (0.9%).

[Figure 3] shows auto analyser results with histogram and microscopic examination of peripheral smear.

Table 1: age wise distribution of no of patients falling into grading criteria

Age group	Grade 1 (75000 - 1.5lakh)	Grade2(50000-75000)	Grade 3(25000-50000)	Grade 4(<25000)
6month-5yr	11	02	02	01
5yr -15yr	10	06	03	03
15yr-60yr	20	12	07	02
>60yrs	15	06	12	01

Causes of thrombocytopenia

Table 2: frequency of cases

	No of cases (n-113)	Percentage (100%)
Viral infection	43	38.1%
bacterial infection	07	6.2%
Anemia	18	16%
ITP	02	1.7%
Leukaemia	05	4.4%
Lymphoma	02	1.7%
Drugs	18	16 %
Malignancy	9	7.9%
Hypersplenism with haemolytic anemia	3	2.8%
Chronic liver disease	02	1.6%
Aplastic anemia	03	2.7%
Pregnancy	01	0.9%

DISCUSSION

Thrombocytopenia is a life-threatening condition if severe. Therefore, detecting the cause and treatment of this condition is most important. To investigate the cause of thrombocytopenia, medical history, physical examination and basic laboratory tests is mandatory and preliminary steps. Thrombocytopenia can be caused by medical conditions (such as problems with your bone marrow suppression, anemia, liver disease, infections, immune conditions and blood clotting disorders) cancers (such as leukaemia, lymphoma or myeloma) some medicines, including heparin.

The male to female ratio in our study is 1: 0.69 similar to the finding of Patel Akruti et al and Verma Deepsikha et al.[8-10] Studies in the general population and in different geographical isolates showed no difference in platelet count in men and women until the age of 15, but subsequently women constantly had more platelets than men, with a slow, progressive, parallel decline with aging in both sexes. Maximum cases of thrombocytopenia belonged to 15 to 60 years. This is in accordance to the finding of Das AK et al.[9] Adolescents and young adults (AYAS) are recognized as a specific age group with different thrombocytopenic symptoms, disease course, treatment goals, side effects are different from children and adults. AYAS are of particular interest in oncology and transition medicine.[11-18]

In our study in Pathology Department, we got most common cause for thrombocytopenia is viral infection which constituted 38.1% of the cases. Similar finding was seen in study conducted by Das AK et al.[9] Infections are the main causes of thrombocytopenia, observed most frequently after viral infections. The mechanism of thrombocytopenia in viral infection is immune-mediated platelet destruction with or without megakaryocyte damage. Megakaryocytes containing inclusion bodies are seen in varicella, cytomegalovirus, infectious mononucleosis, chicken pox, dengue, hepatitis and other parvovirus infection. Thrombocytopenia in dengue may arise either from decreased production of cells from the bone marrow or from increased peripheral destruction of platelets and clearance from peripheral blood. A high mean platelet volume (MPV) indicates enhanced platelet destruction in patients. MPV is usually either high or normal in dengue patients; therefore, excessive platelet destruction could be the main reason for thrombocytopenia in dengue patients.[19-21]

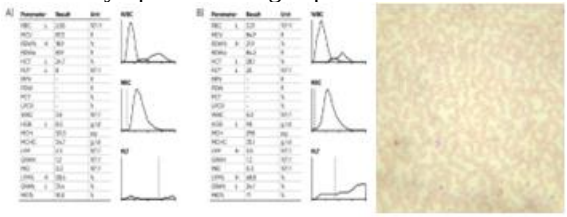

Figure 5: A, B, C- Samples with low PLT count (A) & (B), confirmed by microscopic examination(C).

Mild thrombocytopenia presents in gestational period; moderate-severe thrombocytopenia can occur in preeclampsia and HELLP (haemolysis, elevated

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liver enzymes, low platelet count) syndrome. In our study pregnancy was responsible for 0.9% cases of thrombocytopenia.

Anemia and drugs were the second major cause with a frequency of 16%, comparable to study conducted by Mehmet Ali et al,[11] showed leukaemia represented the most of the cases with thrombocytopenia.

In 2.5% of instances in our study, thrombocytopenia as a result of iron deficiency anemia [IDA] was discovered. Relative thrombocytosis is mainly caused by iron deficiency anemia. Nevertheless, recent research has suggested that thrombocytopenia may also be caused by iron deficient anemia.[19,20] The association between IDA and platelet is complex; iron deficiency is usually associated with either normal platelet counts or thrombocytosis. In rare conditions, IDA can be associated with thrombocytopenia, and there if IDA corrected the thrombocytopenia correct concurrently.[21,22] Rarely, with the correction of IDA, some patients develop transient neutropenia.[23]

1.8% of the patients in our series developed megaloblastic anemia. The primary cause of pancytopenia is megaloblastic anemia. For this reason, there are extremely few cases of megaloblastic anemia with isolated thrombocytopenia. Due to a vitamin B12 and folic acid deficit, ineffective thrombopoiesis in the bone marrow results in hypoproduction of platelets in megaloblastic anemia.

When leukaemia or lymphoma enters the rapid and blastic phases of the disease, thrombocytopenia may occur as a result of cytotoxic therapy. Megakaryopoiesis suppression may result from leukemic cell invasion of the marrow. 85% of the leukaemia patients in this series had acute leukaemia. Therefore, if a patient has severe bleeding and thrombocytopenia, the doctor should consider leukaemia and do the appropriate evaluations for an early diagnosis. Immune thrombocytopenia was diagnosed by the excluding of other causes of thrombocytopenia and by increased number of megakaryocytes in the bone marrow.[24,25] The pathogenesis of ITP has been attributed to platelet antibody production and resultant Platelet destruction: results in an increase in megakaryocyte mass with more number of immature megakaryocytes.

Thrombocytopenia is the most common haematological abnormality encountered in patients with chronic liver disease (CLD) occurring in 64%–84% of patients with cirrhosis or fibrosis. Thrombocytopenia in chronic liver illness is caused by splenomegaly, immunological thrombocytopenia, and inadequate thrombopoietin production. 1.6% of patients in our series had thrombocytopenia as a result of chronic liver illness. Thrombocytopenia has been attributed to hypersplenism, namely, the increased pooling of platelets in a spleen enlarged by congestive splenomegaly secondary to portal hypertension.[24]

The most common symptom is fever with combined cause viral and bacterial infection. This finding is comparable with.[9] The other symptoms are petechiae, purpura, nose bleeds, heavy menstrual bleeding, gum bleeding which may show as blood on your toothbrush and swollen-looking gums, blood in stool, blood in the pee (urine), hematemesis or having blood in your vomit, is a symptom of upper gastrointestinal haemorrhage.

Common viral causes of thrombocytopenia are dengue, hepatitis B & C, influenza, SARS Covid, herpes, cytomegalovirus, HIV, hepatitis C, Ebstein-Barr virus, parvovirus, mumps, varicella, rubella.[12] The most common cause of thrombocytopenia in our study is dengue. Nakao et al,[13] had similar finding.

Common bacterial causes of thrombocytopenia are Leptospirosis, brucellosis, scrub typhus. Malaria, babesiosis intracellular parasite infections are associated with thrombocytopenia with haemolytic anaemia.[14] In 6.2% cases bacterial infection was the cause of thrombocytopenia in our study.

The cause of anaemia associated with thrombocytopenia are nutritional, aplastic and haemolytic anaemia. Nutritional anaemia is the most common cause. Among nutritional anaemia iron deficiency, Vitamin B 12 and folic acid deficiency are most common.[14]

Drug induced immune thrombocytopenia is caused by heparin, quinine, sulfonamides, ampicillin, vancomycin, piperacillin, acetaminophen, ibuprofen, naproxen, cimetidine, glycoprotein IIb/IIIa inhibitors,[15,16] other over the counter remedies, supplements, foods like african bean, sesame seeds, walnuts and beverages (herbal teas and cranberry juice), drug-induced non-immune thrombocytopenia is caused by drugs like valproic acid, daptomycin, linezolid. Drugs caused thrombocytopenia (DIT) can be a consequence of decreased platelet production (bone marrow suppression) or accelerated platelet destruction (especially immune-mediated destruction). In our study drugs implicated in the causation of thrombocytopenia were Heparin, valproic acid, linezolid and rifampicin.

CONCLUSION

Our study shows males are more affected. In case of viral infections dengue/dengue-like fever is the most common diagnosis made in adult patients who are newly detected to have thrombocytopenia at admission. Bacterial infection with septicemia and DIC is common causes in hospitalised patients. 2nd most common causes are anemia and drugs. Patients with thrombocytopenia tend to have bleeding manifestations. Dengue was the most common aetiology in patients with bleeding secondary to thrombocytopenia.

Iron deficiency anemia and megaloblastic anemia are commonest type of anemia with thrombocytopenia. Pregnancy associated thrombocytopenia is a physiological cause. Drugs like heparin, valproic

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acid, linezolid and rifampicin caused thrombocytopenia.

The clinico-hematological and etiological evaluation of patients with thrombocytopenia in our tertiary care centre found out infections are the most common cause of thrombocytopenia in growing nations because of low socioeconomic status. In contrast to other higher referral centres which handle more referral cases where malignancy is the most common cause of thrombocytopenia, in our study malignancy is less common cause. Thus, enhancing the socioeconomic status and prevention of infections will lower the prevalence of thrombocytopenia. The reasons of thrombocytopenia are variable. To have a better understanding of the various aetiologies of thrombocytopenia and its treatment more extensive research into the subject is required.

Declaration of patient consent

The authors certify that they have got received all suitable affected person consent forms. In the form, the affected person has given his consent for his pictures and different scientific records to be pronounced with inside the journal. The affected person knows that call and initials will now no longer be posted and due efforts can be made to hide identity, however anonymity can't be guaranteed.

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