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Original Research Article

Evaluation of Thrombocytopenia in a Tertiary Care Centre

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Abstract: Thrombocytopenia is a common clinical problem with many etiological causes. This may result due to decreased platelet production, increased destruction of platelets and differentiation in distribution of platelets. Although 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 is the rule. Detection of the exact etiology is important for specific treatment and prognostication. In this retrospective study, a total of 120 patients with thrombocytopenia from different departments of hospital were included, graded and evaluated for etiology. 66 patients(55%) were female and 54 patients(45%) were male. The patients' age ranged from 6 months to 80 years. 35 cases(29%) showed Grade 1 thrombocytopenia, 17 cases(14%) Grade 2, 24 cases(20%) Grade 3 and 44 cases(37%) had counts less than 25000/cu.mm, i.e Grade 4 thrombocytopenia. Infections, leukemia, and immune thrombocytopenia represented majority of the cases, and the less frequent causes of thrombocytopenia were found to be drugs, chronic liver disease, multiple myeloma and others. The study concludes that thrombocytopenia has a wide spectrum of causes 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 main reason for thrombocytopenia followed by malignant diseases encountered in a tertiary care hospital.
Keywords: Thrombocytopenia, Bone marrow suppression, Bone marrow infiltration, Non-malignant conditions

INTRODUCTION

Thrombocytopenia can be a life-threatening condition encountered due to various underlying diseases and has been associated with spontaneous bleeding into vital organs resulting in significant morbidity and mortality [1].

Thrombocytopenia is defined as reduction in platelet count below the lower limit of 1.5 lakhs/cu.mm [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 etiology of thrombocytopenia varies widely ranging from transient marrow suppression to hematological malignancies [4]. Thrombocytopenia may also be caused secondary to infections, drugs etc. There are three major pathophysiologic mechanisms of thrombocytopenia: decreased production, accelerated destruction and sequestration of platelets [5].

The bone marrow picture may vary depending on the etiology, from normocellular with non-specific changes to hypercellular. According to etiology, degree and duration of impairment clinically can lead to bleeding manifestations ranging from petechial rash to blood loss from organs like brain, heart or kidney. Knowing the exact etiology is important for specific treatment and prognostication [6].

The aim of this study is to evaluate the incidence of different etiological causes of thrombocytopenia and study the bone marrow changes in them in our tertiary care hospital.

MATERIALS AND METHODS

The present study was conducted at the Department of Pathology, Calcutta National Medical College & Hospital during a period from January, 2015 to June, 2015.A total of 120 patients for whom bone

marrow aspiration was advised were included. The age of the study group ranged from 6 months to 80 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.

Platelet count was performed by automated SYSMEX KX 21 cell counter and value was correlated by direct peripheraland EDTA-blood smear examination. Values lower than <10,000/cu.mm was checked by Neubaur's platelet counting chamber. Pseudothrombocytopenia was excluded by direct peripheral smear examination.

The bone marrow examination procedure and staining were carried out by standard methods. Bone marrow trephine biopsy was done and examined in selected cases.

Bone marrow findings, clinical features and other investigations are correlated to establish the cause of thrombocytopenia.

Statistical Package for Social Sciences version 15.0 for Windows was used as software for statistical analysis of research data.

RESULTS

A total of 120 patients who attended the Pathology Department in Calcutta National Medical College during the study period were included in the study. Out of the 120 cases, 54 patients(45%) were male and 66 patients (55%) were female.

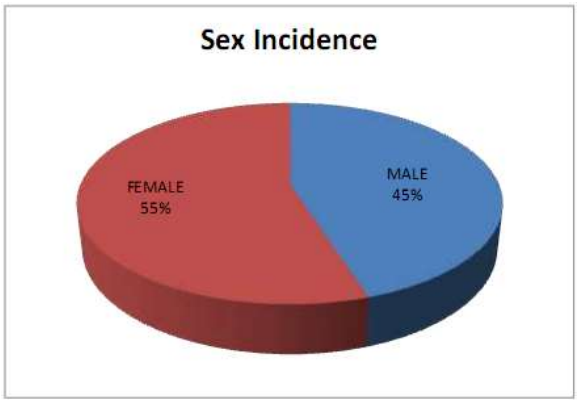

Fig. 1: Male and female ratio in the study

The age of the study group ranged from 6 months to 80 years. Most number of cases(34%) belonged to 11 – 20 years age group.

The commonest presenting symptoms were fever in 72 cases(60%), bleeding manifestations in 30 cases(25%) and other symptoms were jaundice, hepatosplenomegaly and lymphadenopathy.

Among the 120 cases, 35 patients(29%) had Grade 1, 17 patients(14%) had Grade 2, 24 patients(20%) had Grade 3 and 44 patients(37%) had Grade 4 thrombocytopenia.

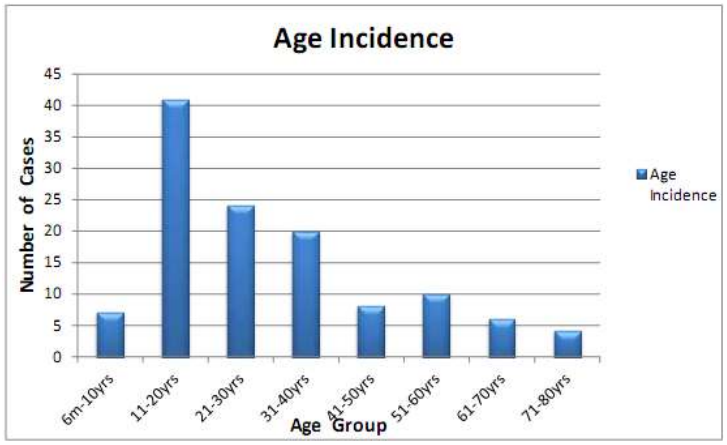

Fig. 2: Number of cases according to age group distribution

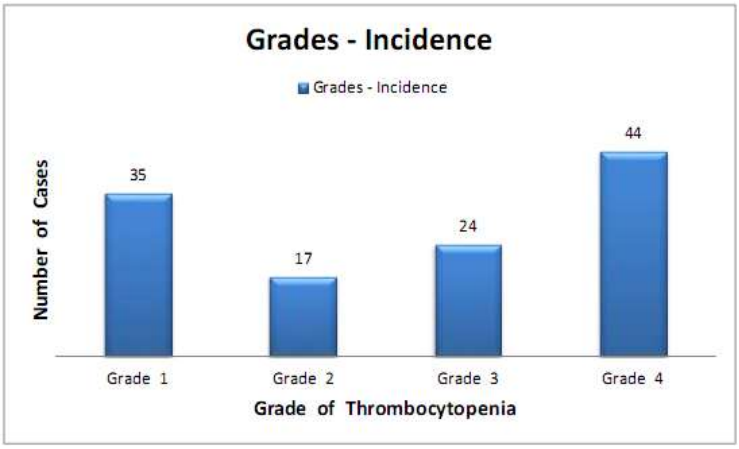

Fig. 3: Grades of thrombocytopenia based on platelet count

The most common cause for thrombocytopenia in this study was infection seen in 35 cases(29.2%).Other causes were leukemia in 24 cases(20%), ITP in 14 cases(12%) followed by chronic liver disease in 12 cases(10%), post-medication in 10 cases(8%), gestational in 5 cases(4%), multiple myeloma in 3 cases(2.5%), hypersplenismin 3 cases(2.5%), iron deficiency anemia in 3 cases(2.5%) (3) .There was a single case each of myelofibrosis, myelodysplastic syndrome, aplastic anemia, autoimmune hemolytic anemia and 4% cases remained undetermined.

Table 1: Frequency of condition

Condition	No. of cases n = 120	Percentage n = 100%
Infection	35	29.2
Leukemia+ lymphoma +metastasis of solid tumor	24	20.0
ITP	14	12.0
Chronic liver disease	12	10.0
Post-medication	10	8.0
Gestational	05	4.0
Multiple myeloma	03	2.5
Hypersplenism	03	2.5
Iron deficiency anemia	03	2.5
Megaloblastic anemia	02	1.8
Myelofibrosis	01	0.8
Myelodysplastic syndrome	01	0.8
Aplastic anemia	01	0.8
Autoimmune hemolytic anemia	01	0.8
Undetermined	05	4.0

DISCUSSION

In severe thrombocytopenia, life-threatening bleeding may be occur, so detecting the cause of thrombocytopenia and its treatment may be lifesaving. To investigate the cause of thrombocytopenia, medical history, physical examination and basic laboratory tests should be the preliminary steps.

In 29.2% of 120 patients referred to Pathology Department with thrombocytopenia the reason was infection and it was the most frequent reason of thrombocytopenia. Leukemia were at the second major cause with a frequency of 12%, comparable to study conducted by Mehmet Ali *et al* showed leukemia represented the most of the cases with thrombocytopenia.

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. While two-thirds of patients with bacteraemia may have

mild or moderate thrombocytopenia, one-third of patients may develop severe thrombocytopenia (<50.000/cu.mm) [7]. At our series, 25% of infection cases had sepsis. The incidence of thrombocytopenia should be considered for the patients in intensive care unit with sepsis. Krishnan et al had a study about patients with thrombocytopenia in ICU and they reported that those with thrombocytopenia had higher mortality than those without thrombocytopenia [8]. Other causes of infection causing thrombocytopenia are malaria, kala-azar, and leptospirosis. Dealing effectively with the infection may reduce the incidence of patients presenting with thrombocytopenia.

Thrombocytopenia at leukemia or lymphoma can develop as a result of cytotoxic therapy or when the disease progresses to the accelerated and blastic phases. Marrow infiltration by leukemic cell can causes suppression of megakaryopoiesis. At this series, acute leukemia accounted for 85% of patient with leukemia. So, in a patient with severe thrombocytopenia and bleeding, the physician should think of leukemia and make necessary evaluation for early diagnosis.

Immune thrombocytopenia was diagnosed by the exclusion of other causes of thrombocytopenia and by increased number of megakaryocytes in the bone marrow [9]. 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.

Splenomegaly, immune thrombocytopenia and inadequate thrombopoietin production are the causes of thrombocytopenia in chronic liver disease [10]. At our series, 10% of patients had thrombocytopenia due to chronic liver disease comparable to Hermos *et al* 13.4% chronic liver disease patient had severe thrombocytopenia [11].

At drug-induced thrombocytopenia, severe thrombocytopenia can occure immediately after the first administration of antithrombotic agents that block fibrinogen binding to platelet GP IIb-IIIa, such as abciximab, tirofiban, eptifibate [12, 13]. At our series, the frequency of drug-induced thrombocytopenia was found as 8%. In our patients, the most common causative drug for thrombocytopenia was heparin and others are Amiodarone, Captopril, Linezolid, Rifampin, Valproate etc. Among the drug-related thrombocytopenia, heparin-induced thrombocytopenia (HIT) deserves particular attention [14, 15].

Mechanisms of gestational thrombocytopenia are not clear. The differential diagnosis between primary ITP and gestational thrombocytopenia is important [16, 17]. Pregnancy rate at our series, cases was found as 4%. Patients with gestational thrombocytopenia typically had platelet counts above 70,000/cmm i.e. Grade 1. It occurs at the 3rd trimester of pregnancy and resolves spontaneously after child birth.

Thrombocytopenia due to Iron deficiency anaemia was found in 2.5% cases at our series. Iron deficiency anaemia is usually the cause of relative thrombocytosis. However some studies reported that Iron deficiencyanaemia may also causes thrombocytopenia [18, 19].

At our series, 1.8% of patients had megaloblasticanaemia. Megaloblasticanaemia is the one most important cause of pancytopenia [20]. For this reason, megaloblasticanaemia with isolated thrombocytopenia is found in very less number of patients.

CONCLUSION

The clinico-hematological and etiological analysis of 120 cases with thrombocytopenia in our tertiary care hospital revealed infections are common etiology of thrombocytopenia in developing countries due to lower socioeconomic status. Malignant diseases are common cause of thrombocytopenia in tertiary health center due to more number of referral cases and also in developed countries where elderly population is higher. So, the leading cause of thrombocytopenia in our study is preventable and treatable. Thus, improving the socioeconomic status and preventing infection will decrease the incidence of thrombocytopenia. The causes of thrombocytopenia are quite variable. For clarifying this issue, both in developing and developed countries, more studies involving higher number of patients should be performed.

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