Observational study on clinicopathological profile of thrombocytopenia cases in a medical college hospital

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Abstract

Introduction: Thrombocytopenia is a commonly encountered condition with varying aetiologies ranging from infective to chronic conditions and malignancies. Knowledge of causes and pattern of disease is helpful in management of cases. **Aims & objectives:** The present study was conducted to assess the causes, clinical profile and findings of laboratory investigations of patients suffering from thrombocytopenia. **Material & Methods:** The present cross-sectional hospital-based study was conducted upon 99 patients suffering from thrombocytopenia. Detailed clinical history, physical examination and reports of laboratory investigations were noted. **Results:** 34.3% patients belonged to the age group of 21-30 years. 57.6% of them were males. Thrombocytopenia was mild (1,00,000-1,50,000) in 24.2% patients, moderate (50,000-1,00,000) in 52.5% and severe (<50,000) in 23.2%. Dengue accounted for 31.3% cases, malaria for 16.2%, enteric fever for 7.1% and septicaemia for 3%. Megaloblastic anaemia was responsible in 24.2% cases. Most common site for bleeding was skin and mucous membrane where bleeding manifested in the form of petechiae, purpura and ecchymosis (18.2%). **Conclusion:** Knowledge of causes and pattern of disease is helpful in management of cases.

Keywords: Observational Study, Platelet Count, Thrombocytopenia

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Introduction

Platelets have important role in formation of blood clot. These cells are non-nucleated and are produced in bone marrow by megakaryocytes. Their size ranges from 2 to 4 μmand contain megakaryocyte- derived messenger RNA (mRNA) which is needed for protein synthesis. These cells are devoid of genomic DNA [1]. Normal platelet count ranges from 150,000-450,000 per μL with mean values of 266,000 and 237,000 per μL in females and males, respectively [2]. About 70 % cells circulate in the blood while 30 % of them remain arrested by the spleen. Its life span ranges from 7-10 days after which these are degraded in the liver or spleen [3].

Decrease in platelet count is termed as thrombocytopenia. Based on severity of decrease, it is subdivided into three groups. Platelet count between 100,000 to 150,000 per μL is classified as mild thrombocytopenia, platelet count between 50,000 to 99,999 per μL as moderate thrombocytopenia and <50,000 per μL as severe thrombocytopenia.

Severe thrombocytopenia has increased risk of bleeding problems. Decrease in platelet count leads to delayed clot formation and prolongation of bleeding time. It can manifest as bleeding in skin and mucous membranes in the form of petechiae, ecchymosis and purpura, epistaxis, gum bleeding, menorrhagia etc [4].

Decrease in platelet count may be caused by decreased production, increased breakdown or trapping of platelets in the spleen. Decreased production of platelets may be due to selective or generalized bone marrow suppression. Viral infections like chickenpox, malignancies like lymphoma, nutritional deficiency of Vit. B12 and folic acid or cytotoxic drugs and toxic chemicals. Increased breakdown is seen in immunological conditions like idiopathic thrombocytopenic purpura, haemolytic uremic syndrome and thrombocytopenia of pregnancy. Increased trapping of platelets in spleen is seen in conditions associated with splenomegaly. Notable conditions are bacterial or parasitic infections, certain malignancies, liver diseases and toxins like vinyl chloride [5].

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Early recognition of degree of thrombocytopenia and its aetiology is helpful in treating the condition in initial stages and preventing the development of complications. More severe and life-threatening bleeding like intracranial haemorrhage can thus be avoided [6].

Aetiology of thrombocytopenia varies from place to place and is dependent upon the locally prevalent infections and environmental exposures. Verma et al found in Varanasi that 14.4% cases were due to sepsis, 12.9% due to malaria and 11.9% due to aplastic anaemia [7] while Paramjit et al observed in Pune that 57.7% cases were due to malaria and only 0.6% were due to aplastic anaemia [8].

Few studies have been conducted regarding causation of thrombocytopenia in this area. Hence, the present study was conducted to explore the common causes of thrombocytopenia in this area.

Aims & objectives

The present study was conducted to assess the clinical profile and findings of laboratory investigations of patients suffering from thrombocytopenia. It also aimed to find the different causes leading to thrombocytopenia.

Material and Methods

Study setting: The present study was hospital-based in nature conducted at the department of Pathology, Mata Gujri Memorial Medical College and Lions Seva Kendra Hospital, Kishanganj. The institute is tertiary level health care facility catering to patients from eastern part of Bihar and adjoining parts of West Bengal. Most of the patients are referred ones from nearby health facilities.

Duration and type of study: The present study was cross-sectional in nature conducted between February 2018 to June 2019. Data collection was done between April 2018 to March 2019.

Study subjects: Study subjects included patients admitted in the hospital and in whom thrombocytopenia was detected in routine blood tests.

Inclusion criteria: Patients above 18 years of age and found to be suffering from thrombocytopenia of any degree were included in the present study.

Exclusion criteria: Those patients who did not give consent for the study, those suffering from thrombocytopenia secondary to liver disease, malignancy, chemotherapy or due to drug-induced were excluded from the study. The patients in whom thrombocytopenia was congenital in nature were also excluded from the study.

Sample size calculation: The study conducted by Patne et al showed that thrombocytopenia was caused due to infections in 63.33% patients [9]. Considering p= 0.6333, q= 0.3667, Z=1.96 for confidence level of 95% and d (absolute precision) = 0.1, sample size was calculated to be 92. Considering non-response rate of 10%, final sample size was 102. Three patients refused to participate in the study and a total of 99 patients were studied.

Sampling methods: Sampling was non-random in nature and the initial 99 patients who fulfilled the selection criteria were included in the present study.

Data collection procedure: Medical Superintendent of the hospital was informed about the purpose and importance of this study and permission was obtained. The patients were selected on the basis of haematological findings from the department of Pathology.

The patients were visited in the wards and consent was taken form them. Detailed socio-demographic and clinical history was obtained. Routine investigations including complete blood count, examination of blood smear, liver function test and renal function test were done.

They were subjected to further investigations like Prothrombin time & INR, activated partial thromboplastin time, bone marrow aspiration, test for HIV infection, Dengue NS1antigen and Dengue IgM, rK -39 test, Lymph node biopsy, and Ultrasound examination if needed.

Data analysis: Data entry was done in Microsoft Excel 2003 and data analysis was done using Statistical Package for Social Sciences (SPSS) v 16.0. Quantitative data were summarized as mean and SD while qualitative data was expressed in terms of frequency and percentage. Appropriate statistical tests were done when needed.

Ethical consideration & permission: Permission was obtained from Institutional Ethics Committee for the study. All the study subjects were informed about the study and consent was taken from them. Those who did not give consent were not included. Confidentiality of records was maintained and data was saved safely.

Results

A total of 99 patients were included in the present study. Age and sex distribution of study subjects as represented in Table-1. It is seen that 34.3% patients belonged to the age group of 21-30 years while 31.3% belonged to the age group of 31-40 years. 57.6% of them were males while females constituted another 42.4%.

Table-1: Socio-demographic profile of study subjects.

Characteristics	Frequency (n=99)	Percentage
Age (in years)		
<20	7	7.1%
21-30	34	34.3%
31-40	31	31.3%
41-50	20	20.2%
51 and above	7	7.1%
Sex		
Male	57	57.6%
Female	42	42.4%

Table-2 shows the severity of thrombocytopenia. It was mild (1,00,000-1,50,000) in 24.2% patients, moderate (50,000-1,00,000) in 52.5% and severe (<50,000) in 23.2%.

Table-2: Severity of thrombocytopenia.

Platelet count (per cmm.)	Frequency (n=99)	Percentage
<50,000	23	23.2%
50,000-1,00,000	52	52.5%
1,00,000-1,50,000	24	24.2%
Total	**99**	**100%**

Table-3 highlighted the aetiology of thrombocytopenia. In more than half (54.9%) of the cases, it was infective in origin. Dengue accounted for 31.3% cases, malaria for 16.2%, enteric fever for 7.1% and septicaemia for 3%. Megaloblastic anaemia was responsible in 24.2% cases, thalassemia in 2%, hypersplenism in 6.1% and chronic liver disease and snake bite each in 2% cases.

Table-3: Aetiology of thrombocytopenia.

Aetiology	Frequency (n=99)	Percentage
Dengue	31	31.3%
Malaria	16	16.2%
Enteric fever	7	7.1%
Septicaemia	3	3%
Megaloblastic anaemia	24	24.2%
Thalassemia	2	2%
Hypersplenism	6	6.1%
Chronic liver disease	2	2%
Snake bite	2	2%
Others	6	6.1%

Table-4 represented the haemorrhagic manifestations in these cases. A total of 39 cases (39.4%) showed bleeding tendency. Most common site for bleeding was skin and mucous membrane where bleeding manifested in the form of petechiae, purpura and ecchymosis (18.2%). Gum bleeding was seen in seven cases (7.1%), vaginal bleeding in four cases (4%) and epistaxis in three (3%). Bleeding manifestations were not seen in 60.6% cases.

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Table-4: Haemorrhagic manifestations.

Bleeding site	Frequency	Percentage
Skin and mucous membrane	18	18.2%
Gum	7	7.1%
Per vagina	4	4%
Epistaxis	3	3%
Hematemesis	1	1%
Haematuria	1	1%
Others	3	3%
Multiple sites	2	2%
No manifest bleeding	60	60.6%

Table-5 signified the findings of peripheral smear examination. Anaemia was present in 46.5% cases, leucopenia in 7.1% and pancytopenia in 15.2%. Selective thrombocytopenia was seen in 31.3% cases.

Table-5: Peripheral smear examination.

Peripheral smear	Frequency	Percentage
Anaemia	46	46.5%
Leucopenia	7	7.1%
Pancytopenia	15	15.2%
Thrombocytopenia	31	31.3%
Total	**99**	**100%**

Figure-1 represented the findings of physical examination. Splenomegaly was seen in 16.2% cases, hepatomegaly in 17.2% and hepatosplenomegaly in 10.1%.
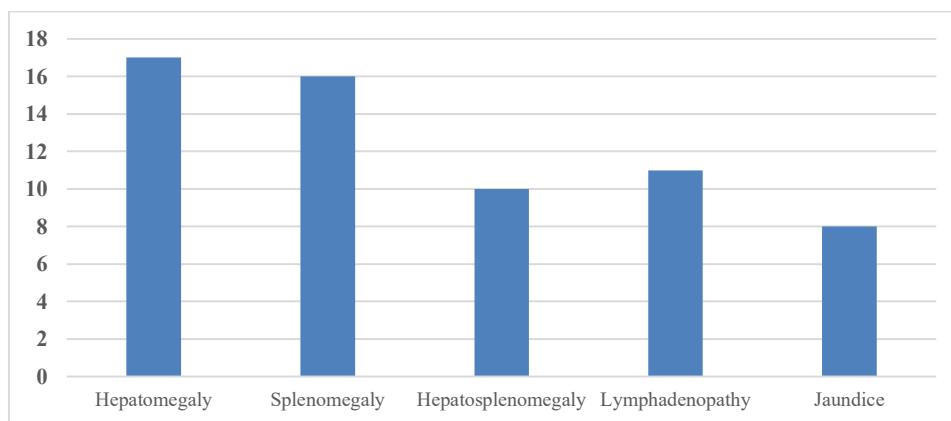
Figure 1: Findings of physical examination

Discussion

The present cross-sectional study included 99 patients suffering from thrombocytopenia. Male: female ratio of 1.36:1 was observed. Verma et al also found male preponderance with 62.6% patients 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], Paramjit et al (68%) [8] and Patne et al (60%) [9]. Majority of the patients (65.6%) belonged to the age group of 21-40 years. Verma et al observed that 40.8% were of the patients belonged to the age group 26-50 [7]. Shah et al found highest incidence of thrombocytopenia in the age group 21-30 years (30%) [10]. Paramjit et al also found that 52.3% cases were in the age group 20-39 years [8]. However, Vimal et al had slightly different observation who reported that most of the cases belonged to the age group 41-60 years (37.4%), followed by 21-40 years (33.4%) which was observed in southern part of India [11]. Moderate thrombocytopenia was seen in about half of the patients (52.5%) while the condition was severe in 23.2%.

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Verma et al reported that mild thrombocytopenia was present in 41.2%, moderate in 34.9% and severe in 23.9% [7]. Vimal et al reported that majority of the patients (54.2%) presented with a platelet count between 50,000-1,00,000 and 25.8% presented with a platelet count between 1,00,000 to 1,50,000 similar to the findings of the present study [11]. However, Mittra et al found that mild thrombocytopenia was present in 22.2%, moderate in 33.3% and severe in 44.4% [12].

In more than half (54.9%) of the cases, it was infective in origin. Dengue accounted for 31.3% cases, malaria for 16.2%, enteric fever for 7.1% and septicaemia for 3%. Megaloblastic anaemia was responsible in 24.2% cases, thalassemia in 2%, hypersplenism in 6.1% and chronic liver disease and snake bite each in 2% cases.

Verma et al explored causes of thrombocytopenia in detail and reported that common causes of thrombocytopenia in their setting were sepsis in 14.4%, CLD in 12.9%, malaria in 12.2%, aplastic anemia in 11.9% and viral illness in 9.9%. Patients, whose platelet counts returned to normal within 6 weeks follow-up, were classified as acute and whose not, classified as chronic.

Causes of acute thrombocytopenia include megaloblastic anemia, sepsis, malaria, typhoid fever, dengue and other viral illness. Out of which most common cause was sepsis (28.6%) followed by malaria (24.4%). Causes of persistent (chronic) thrombo-cytopenia were aplastic anemia, myelodysplastic syndrome (MDS), hypersplenism, hematological malignancies and chronic liver disease.

Most common cause was chronic liver disease (25.3%) followed by aplastic anemia (23.3%) [7]. Shah et al reported that the most common cause of thrombocytopenia was malaria (31%) followed by Megaloblastic anemia (26%) and dengue fever (18%) [10].

The etiological diagnosis of patients in South India was reported by Vimal et al as Dengue (21.67%), Malaria (6.7%), Enteric fever (5.9%), Septicemia (5%), Chronic liver disease (16.7%), Chronic kidney disease (3.4%), Diabetes (7.7%), Malignancy (1.67%), Coronary artery disease (3.4%), Pregnancy (5%) Hematological disorders (18.4%) and miscellaneous (5%) [11].

Paramjit et al observed in Pune that Infectious etiology was the most important cause, with malaria (57.7%) being the principal reason. Other common causes included dengue (27.7%), liver disease (7.7%), and sepsis (4.7%) [8].

It is evident from the above discussion that common causes of thrombocytopenia are related to locally prevalent infections and disease patterns. In areas with Malaria and Dengue, these constitute important causes. In other areas, other infections and chronic conditions are mainly responsible.

A total of 39 cases (39.4%) showed bleeding tendency. Most common site for bleeding was skin and mucous membrane where bleeding manifested in the form of petechiae, purpura and ecchymosis (.2%). Gum bleeding was seen in seven cases (17.9%), vaginal bleeding in four cases (4%) and epistaxis in three (3%). Bleeding manifestations were not seen in 60.6% cases. Verma et al also found that skin manifestations in the form of petechiae, ecchymosis were most common bleeding manifestation and was seen in13% patients. Gum oozing and epistaxis was present in 8.6% of cases.

Patients complaining of acute onset blurred vision were examined with direct ophthalmoscope to look for fundal bleed which was present in 5.6%. Active gastrointestinal bleed and vaginal bleed was present in 7% and 2.4% cases and required urgent platelet transfusion [7].

Shah et al also had similar observation who commented that most common bleeding manifestation was in skin and mucous membrane (33%) followed by gum bleeding (25%) and bleeding per vagina (19%). The major clinical bleeding in the form of intracranial hemorrhage was detected in only one patient (3%). ITP (42%) and dengue fever (33%) were common etiologies associated with skin and mucous membrane bleeding. In patients with gum bleeding, dengue fever (33%) and Megaloblastic anemia (33%) were common causes, while in patients with per vaginal bleeding, ITP (58%) was the common etiology [10].

Anaemia was present in 46.5% cases, leucopenia in 7.1% and pancytopenia in 15.2%. Selective thrombocytopenia was seen in 31.3% cases. Verma et al reported that isolated thrombocytopenia, thrombo-cytopenia with anemia, thrombocytopenia with leucopenia and pancytopenia was present in 29.1%, 37.1%, 31.2% and 2.5% patients respectively.

Macrocytic anemia was present in megaloblastic anemia and in all other cases, it was mainly normocytic normochromic type. Anemia is an important accompaniment of thrombocytopenia. In all the patients with pallor and having high risk of thrombocytopenia, platelet count must be done to rule out this condition [7]. Splenomegaly was seen in 16.2% cases, hepatomegaly in 17.2% and hepatosplenomegaly in

10.1%. Shah et al have concluded that splenomegaly was found in 1/4th of patients with thrombocytopenia.

While splenomegaly as a part of Hypersplenism itself causes thrombocytopenia, many diseases like malaria, enteric fever etc. are associated with Splenomegaly. Most common cause of splenomegaly was malaria (56%) followed by cirrhosis of liver (24%) [10].

Vimal et al was of opinion that 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 [11].

Conclusion

It might be concluded from the present study that thrombocytopenia was more common in males and in the age group of 21-30 years. Bleeding was seen in 39.4% cases mainly in skin and mucous membranes. About half of the patients had moderate to severe thrombocytopenia. About half of the cases had thrombocytopenia due to infective reasons. Early identification and timely treatment can help in proper management of cases.

What the study adds to the existing knowledge?

Literature regarding pattern and aetiology of thrombocytopenia are limited in number. Majority of the cases are infective in origin. As thrombocytopenia is a commonly encountered condition with probability of severe consequences, the present study gives insight to common causes of thrombocytopenia in this area as well as the profile of cases in terms of severity and clinical findings. This will help in ensuring timely interventions for preventable conditions and reduction in morbidity and mortality.

Author's contribution

- **Dr. Ajay Kumar:** Designed the study and collected data.
- **Dr. Avinash Priyadarshi:** Design of study protocol and ensured proper methodology for scientific soundness.
- **Dr. Sanjay Kumar:** Guided the research work as the senior-most member of the team.
- **Dr. Prabhat Kumar Lal:** Data analysis and review of literature.

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