ORIGINAL RESEARCH PAPER
Volume - 13 | Issue - 01 | January - 2024 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

CLINICO-HEMATOLOGICAL PROFILE IN FEBRILE THROMBOCYTOPENIA

Pathology

Reshma Anegundi* Department of Pathology, PES Institute of Medical Science and Research,Kuppam-517425, Andhra Pradesh, India. *Corresponding Author

Katella Raja Manoj Khanna Department of Pathology, PES Institute of Medical Science and Research,Kuppam-517425, Andhra Pradesh, India.

Arathi C A Department of Pathology, PES Institute of Medical Science and Research,Kuppam-517425, Andhra Pradesh, India.

ABSTRACT

Background: Febrile thrombocytopenia is one of the common clinical entities in practice. Various infections can cause a low platelet count. Dengue fever is the common cause followed by sepsis, malaria and others. Along with platelet count, other haematological parameters do show some significant changes which help in the diagnosis and prognosis of the disease. Hematocrit and platelet indices especially mean platelet volume and platelet distribution width help in the assessment of the severity in dengue infections.

Aims and Objectives:

1) To study various causes of febrile thrombocytopenia .
2) To analyze the clinical profile and hematological parameters in patients with febrile thrombocytopenia.
3) To analyse hematological parameters in Primary and Secondary dengue patients.

Materials and Methods: A total of 122 febrile thrombocytopenia patients were included in the study. Relevant history and clinical examination data was collected. Complete blood count and peripheral smear were evaluated. Serology test reports were collected from the microbiology department. The hematological parameters, with special reference to platelet indices, were assessed in various causes of Primary and Secondary dengue and non-dengue cases of febrile thrombocytopenic patients. **Results:** Febrile thrombocytopenia was commonly seen in the 2nd decade, with male preponderance. Dengue was the common cause of febrile thrombocytopenia. Thirty-one cases of dengue had bleeding manifestations. There were 11 primary and 60 secondary dengue cases. High hematocrit, atypical lymphocytosis, platelet indices were more significant in secondary dengue. Platelet indices were also significant in dengue with bleeding manifestations. **Conclusion:** Diagnosis of dengue and early management are necessary to avoid complications. Hematological parameters show significant changes in dengue patients and especially in secondary dengue. The simple, cost-effective tests help in the assessment of the disease severity.

KEYWORDS

Febrile thrombocytopenia, dengue, mean platelet volume, hematocrit.

INTRODUCTION:

Platelets are the smallest of the circulating hematologic elements, membrane-bound anucleate fragments of cytoplasm derived from precursor cells in the bone marrow called megakaryocytes. Platelets circulate in the peripheral blood for 7–10 days and the non-viable or aged platelets are removed by the spleen and liver.[1]

Thrombocytopenia is considered when the platelet count is below 150 $x10^9$/ L. Thrombocytopenia in febrile patients can be due to one or more of the following mechanisms- decreased platelet production, direct effect on progenitor cells, hemophagocytosis, antibody-mediated destruction, circulating platelet destruction.[2] Various causes of febrile thrombocytopenia are infections like Dengue, Malaria, Rickettsia, Typhoid, Gram-negative sepsis, EBV, Hepatitis, HIV, CMV, Parvovirus, Mumps and Rubella and malignant conditions like Lymphoma, Leukaemia and other causes are DIC, SLE, HUS, TTP and Aplastic anemia. Febrile thrombocytopenia is usually due to infectious aetiology, dengue being the common cause.[3] Haematological parameters like hematocrit, leucocyte count, atypical lymphocytes, platelet count and Mean Platelet Volume and Platelet Distribution Width help in diagnosis and prognosis, especially in dengue fever and its complications.[2] This study determines the etiology of febrile thrombocytopenia, clinical profile and hematological parameters in patients with febrile thrombocytopenia and haematological parameters in Primary and Secondary dengue patients.

MATERIALS & METHODS

The present study included 122 patients. All patients with febrile thrombocytopenia were included in the study. Neonates with septicemia, febrile patients on medications which induces thrombocytopenia were excluded from the study. The institution ethical committee clearance was obtained.

Patients with thrombocytopenia (inpatient/outpatient) received in Pathology Central Laboratory were reviewed for the history of fever and were evaluated with further clinical data regarding onset and duration of fever. Any associated symptoms like myalgia, joint pains, headache, diarrhea, breathlessness and particularly bleeding manifestations were also evaluated. Examination findings were also recorded from case files and outpatient records.

A complete hemogram was performed for all these cases and serological tests for dengue, malaria, typhoid, hepatitis, chikungunya were performed depending upon the clinical features and examination findings to rule out the causes for febrile thrombocytopenia. Majority of the patients visited the hospital within four to five days of onset of symptoms. In a few patients, the duration was more than 5 to 6 days.

Peripheral venous blood sample was collected in K2 Ethylenediaminetetra-acetic acid (k2 EDTA) vacutainers, and was processed in Beckman Coulter LH 780 Hematology automated five-part analyzer, works on the principle of Volume Conductivity Scatter (VCS) Technology. Red cell indices, total and differential count of leukocytes and platelet indices were recorded. Simultaneously peripheral smear was taken and stained with Leishman Stain. Further the stained smears were examined and studied for red blood cell, white blood cell, platelet morphology and any abnormalities were recorded. Morphological type of anemia if present and presence of hemoparasites were also recorded.

Dengue test (Immunochromatography) results were collected from the Department of Microbiology. NS1 positive, IgM and IgG positive and IgG alone positive cases were included. Malaria (Immuno chromatography) positive cases were documented. However, different species of positive cases were also identified on peripheral smears.

Febrile thrombocytopenia cases with Widal antigen-positive test results were collected. Other test results of Chikungunya, Leptospira, HIV, HBsAg and HCV were also collected wherever relevant in these patients.

Statistical Data

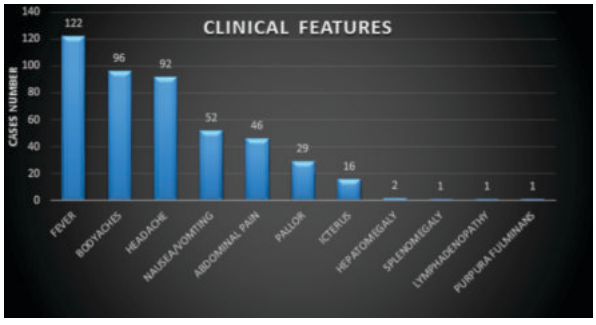
The data was entered into MS Excel 2007 version and further analyzed using SPSS 20. For descriptive analysis, the categorical variables were analyzed using percentages, and the continuous variables were analyzed by calculating the mean ± Standard Deviation.

For inferential analysis, the numerical data were analyzed using "Correlation Test". The categorical data were analyzed using the Chi-square test. Results were correlated, and "p" <0.05 was considered statistically significant.

Normal reference values for all hematologic parameters were referred from Dacie and Lewis Practical Haematology.[4]

RESULTS

The present study included 122 cases of febrile thrombocytopenia. The study population age ranged from 3 to 78 years, with the mean age of 38.09 years. Majority of the patients (27.86%) were in the age group of 21-30years. There were 77 males (63%) and 45 females (37%) with female to male ratio of 1:1.7.The common clinical presentation were body ache and headache, followed by nausea, vomiting and pain abdomen. Few had icterus, one each case had hepatomegaly, splenomegaly and cervical lymphadenopathy. One case of dengue fever had skin lesions , Purpura fulminans.



Graph 1: Clinical features among 122 cases

The bleeding manifestation was reported in 34 cases, out of which, 22 had petechiae, which was the commonest finding (64.7%), followed by hematemesis in 4 (11.7%) patients.

Etiology Of Thrombocytopenia Should Be Added For Next Paragraph Heading

Dengue, malaria and typhoid were the different aetiologies reported in the present study. Dengue (58%) was the commonest cause, followed by malaria(4%) and typhoid(3%).In 35% of the cases aetiology was not established.

Out of 34 patients who presented with bleeding manifestation, 31 cases were positive for dengue and other 3 cases, the aetiology was not identified.

Anemia was seen in 48 (39.3 %) cases. The cause of anemia was not determined in the present study. Pre-existing anaemia or coexisting anaemia was not studied due to the limitations of the study. Morphological categorisation was done and microcytic anaemia constituted 30 cases (24.5%), dimorphic anaemia 15 cases (12%) and macrocytic anaemia 3 cases (2.4%).

The White Blood Cell count ranged from 0.9 - 32.2x10^9/L with a mean value of 7.4x10^9/L. Leukopenia was observed in 43% of cases and leucocytosis in 57% of cases. Further lymphocytosis was observed in 28 cases(22.9%). All 28 cases were dengue positive. Twenty-four (43.6%) cases out of 71 dengue patients had neutrophilia. Lymphopenia (63%) was significantly seen in non-dengue patients. Only 4% of the cases had lymphocytosis in non-dengue patients.

Atypical lymphocytes (AL) >10% were considered atypical lymphocytosis and assessed on peripheral smear examination. Atypical lymphocytes were seen in 59 out of 71 dengue cases. The percentage of atypical lymphocyte varied from 08% to 16% with a mean of 12%. Atypical lymphocytes in dengue patients with bleeding manifestations was observed in 35.4%. The percentage of atypical lymphocytes was higher in secondary dengue (55%) than in primary dengue (36%).

The platelet count in 122 patients ranged from 6 x10^9/L to 122 x10^9/L, with a mean platelet count of 79.35 x10^9/L, only seven patients had counts less than 15 x10^9/L. The lowest value recorded was 6 x10^9/L.

Thrombocytopenia was graded into the mild, moderate and severe degree.

Majority of the patients had moderate thrombocytopenia (48.36%). Severe thrombocytopenia was seen in 29 cases (23.77%) and mild in 27.87% of cases.

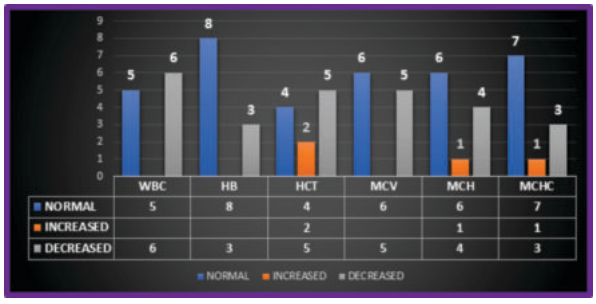
Out of 71 dengue cases, there were 35 cases of moderate thrombocytopenia, 28 with severe thrombocytopenia and 8 cases with mild thrombocytopenia.

Thirty-four patients of 122 cases, had bleeding manifestations, and 31 were positive for dengue. The mean platelet count in these cases was 39.24 x10^9/L. Among 31, only 7 had a severe degree of thrombocytopenia, 19 had moderate, and 5 cases had a mild degree of thrombocytopenia.

Dengue cases were categorised into primary and secondary dengue based on the rapid test. The cases positive for NS1, IgM and negative for IgG were categorised as primary dengue. The cases positive for IgM and IgG, or positive for only IgG were categorised as secondary dengue. The tests were conducted within 2 to 5 days of onset of fever.

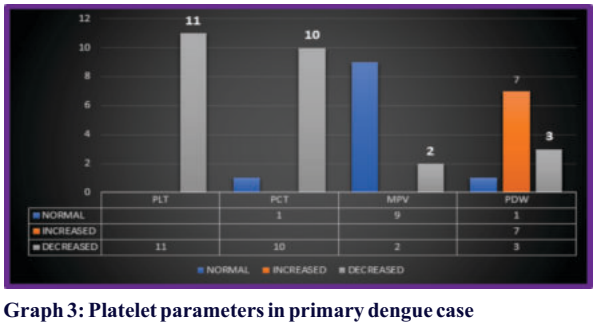
Table 1: Case distribution of primary and secondary dengue based on a rapid test.

NS1	IgG	IgM	Number of cases	
+	-	+	11	Primary infection
-	+	+	11	Secondary infection
-	+	-	49	Secondary infection



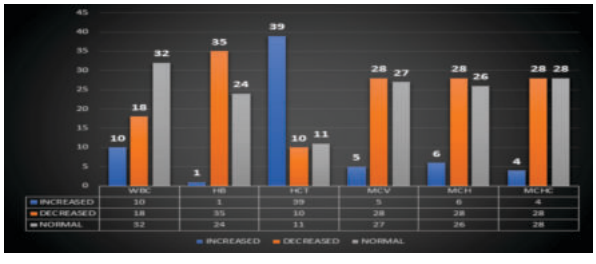
Graph 2: WBC and RBC parameters in primary dengue cases

HCT was increased in 2 of 11 cases. Leukopenia was observed in 6 of 11, and there were 3 cases of anaemia.



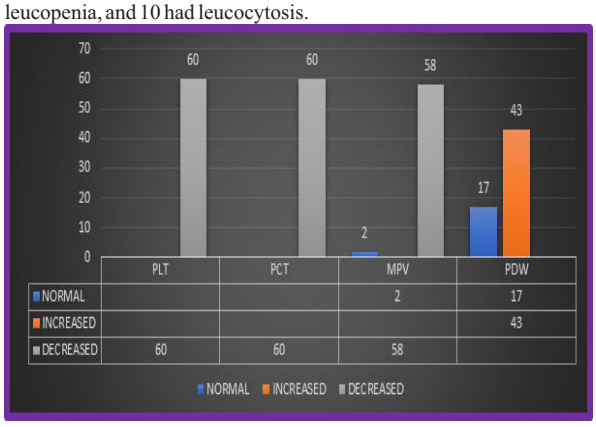
Graph 3: Platelet parameters in primary dengue case

In primary dengue (11) cases, 10 cases showed a decrease in PCT and increased PDW in 7 cases which was a significant finding.



Graph 4: WBC and RBC parameters in secondary dengue cases

Out of 60 (88.73%) secondary dengue cases, 35(58%) cases had anemia, and 39(65%) cases had increased hematocrit. However, the cause for anemia in these 35 cases was not established due to the limitations of the study. There was no significance in other RBC parameters observed in secondary dengue cases.Eighteen had leucopenia, and 10 had leucocytosis.



Graph 5: Platelet parameters in secondary dengue cases

Out of 60 secondary dengue positive cases, all (100%) cases showed decreased PCT, 58(96%) cases showed a decrease in MPV and 43(71.6%) cases showed increased PDW which was a significant finding.

Table 2: Significance Of Platelet Parameters In Primary And Secondary Dengue Cases

	PCT	MPV	PDW
Primary dengue(11)	P=0.3928	P=0.2047	P=0.1296
Secondary dengue(60)	P=0.0328	P=0.0571	P=0.0486

All 31 cases of dengue with bleeding manifestations were of secondary dengue. Hematocrit was raised in more than 50% of secondary dengue cases. Atypical lymphocyte were also significant in secondary dengue, and also platelet parameters were significant in secondary dengue.

Table 3: Case distribution among risk assessment factors in primary and secondary dengue.

	Primary dengue-11 (no of cases)	Secondary dengue-60 (no of cases)
Bleeding manifestations	4	31
Raised haematocrit	2	39
Atypical lymphocytosis	4	33
Moderate and severe thrombocytopenia	10	53
Decreased MPV	2	58
Decreased PCT	10	60
Increased PDW	7	43

The mean MPV, PDW and PCT were calculated in dengue cases with bleeding and without bleeding manifestations.

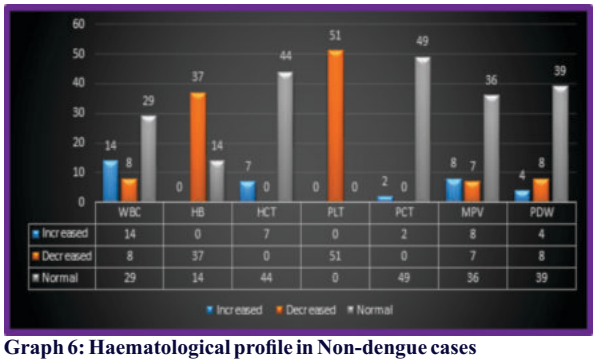
MPV, PCT and PDW were significant in dengue patients with bleeding. MPV (p=0.97) was not significant in dengue patients without bleeding, whereas PDW was significant (0.0052) in these patients. MPV and PDW were independent significant risk assessment factors in dengue patients with bleeding.

Table 4: Significance Of Platelet Parameters In Dengue Patients With Bleeding And Without Bleeding Manifestations

Dengue patients	PCT	MPV	PDW
Patients with bleeding	P=0.054	P=0.050	P=0.0024
Patients without bleeding	P=0.468	P=0.978	P=0.0052

A 6-year male child with dengue fever presented with cervical lymphadenopathy. Fine needle aspiration (FNA) was done. Cytology smears showed atypical lymphocytes and lymphoplasmacytic cells, suggesting a viral etiology(Fig 1).

There were 51 non-dengue cases in the present study. Thirty-seven of 51 non-dengue cases had anemia. However, the cause of anemia was not established. No other significant findings were observed. Hematocrit was normal in the majority of the cases, compared to increased hematocrit in dengue positive cases.



Graph 6: Haematological profile in Non-dengue cases

The other causes of febrile thrombocytopenia identified were malaria and typhoid. In the present study, out of 122 patients, 5 cases were positive for malaria serology and peripheral smear examination. Two cases were Plasmodium falciparum, and the other three were positive for P.vivax.

The lowest haemoglobin percentage was in plasmodium falciparum (7.2gm %) and the lowest platelet count 40 x10^9/L was reported in each case of plasmodium vivax and plasmodium falciparum. No bleeding manifestations were seen in any of the cases.

Among four cases of typhoid fever no significant changes were seen except lymphopenia, and 2 cases had increased PDW. And lowest haemoglobin noted in our study was 3.5 gm%, and the lowest platelets 45 x10^9/L in one case.

Aetiology was not established in 42 cases of febrile thrombocytopenia.

Twenty-eight cases had anemia with lowest haemoglobin value of 3.6 gm%. Leucocytosis was seen in 11 cases and leukopenia in 6 cases with the lowest value of 1.3x10^9/l. Majority of the (21) cases had a mild degree of thrombocytopenia in 18 cases with the lowest platelet value being 28x10^9/L.

Figure 1 depicts the cytology smear of cervical lymphadenopathy showing atypical lymphocytes in a single case.

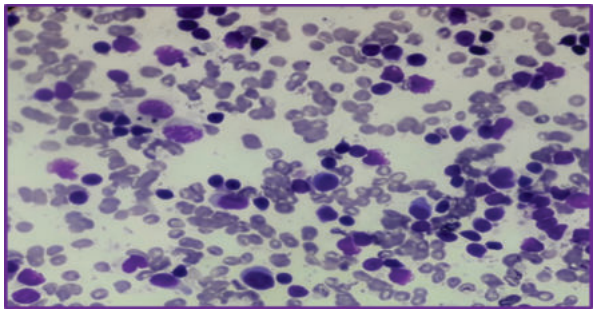


Fig 1: Cytology smears showing atypical lymphocytes, plasma cells. MGG (40X)

DISCUSSION

Febrile thrombocytopenia is a distinct entity and is commonly seen in tropical infectious diseases. Many infections like malaria, dengue fever, enteric fever, leptospirosis and other viral infections can result in thrombocytopenia. It is a therapeutic challenge to the clinicians because of varied aetiology and unpredictable outcome and their complications.[5]

Thrombocytopenia is a manifestation of varied infectious and non-infectious aetiologies. Some infectious diseases like sepsis, dengue or malaria can result in mortality of patients. The mortality in these cases is not directly associated with the degree of thrombocytopenia but is associated with multiorgan dysfunction.[6]

Dengue fever is a major public health problem in tropical and subtropical countries. In India, dengue is endemic in 29 states and notifiable disease in 14 states.[7] Hence, establishing the cause of thrombocytopenia in patients with fever can be helpful in the timely management of patients.

Serological tests and haematological parameters help in the diagnosis and risk assessment in infections, especially dengue.

The male to female (1.7:1) ratio was comparable with other studies done by Lakshmi Prasanna Gutti et al.[8] , Smitha Subhas Chandra Kadadavar et al.[9] , Katiyar et al.[10] , Raghunandan Meena et al. [11] and D K Sunitha et al. [12] in which males were predominantly affected.

The maximum number of cases, 63 (27%) were in the age group of 21 to 30 years is the present study. A similar study done by Katiyar et al.[10] and Raghunandan Meena et al. [11] reported 10-20 years being the most common age group .

Bodyache and headache were the commonest clinical symptoms in the present study. In a study done by Ramesan K et al.[13] nausea and vomiting were the commonest symptoms and also observed 33.1% of hepatomegaly and 8.2% of splenomegaly . Hepatomegaly was observed in 1.6% and splenomegaly in 0.8% in the present study. Five patients were diagnosed with hepatitis as a complication of dengue infection, 3 of them presented with jaundice. A single case of dengue patient presented with purpura fulminans. Acute infections manifest with almost similar clinical symptoms, and hence, awareness of clinical presentations and complications is essential for further investigation and for better management.

In the present study, 34 (27.8%) patients presented with bleeding manifestation. Petechiae (22 cases) was the commonest bleeding manifestation observed, compared to similar studies done by Amita A Gandhi et al., [14](33%), Katiyar et al.,[10](31%), Gondali et al. [15] (14%) who also reported similar findings.

Dengue infection was the common (58.1%) cause of febrile thrombocytopenia in our study . A similar observation was also made by Gudi Srinivas et al.,[16]who reported dengue as the primary cause of thrombocytopenia (69%).

Dengue cases were categorised into primary and secondary based on IgM and IgG antibodies and NS1 antigen based on rapid test. There were 11 primary and 60 secondary dengue cases. Kevin John et al.[7] reported 76.2% of secondary dengue and Khalid Hamid Changal et al.[17] reported 66.7% of secondary dengue in their study. The early diagnosis of secondary dengue is crucial as it is a risk factor for the development of severe dengue.[17]

Haemoglobin values ranged from 3.4 gm% to 18 gm%, with a mean of 10.97 gm %. There were 48 cases (39.3%) of anaemia, compared to a higher incidence reported by Lakshmi Prasanna Gutti et al.,[8] Garachew Ferede et al.,[18] Gomathi Chenna Reddy et al.[19] and Ramesan et al. [13]

In dengue mean haemoglobin observed was 11.8 gm % with P-value 0.0034, which is statistically significant. Mean haemoglobin in malaria cases was 11.7 with P-value =0.3324.Typhoid cases had a mean haemoglobin level of 8 gm/dl with P value=0.1220.

Haemoglobin is one of the most common parameters affected by infections, especially like malaria and dengue. However, the cause of anemia in present study was not identified due to the limitations of the study. The pre-existing anemia or the coexisting anemia due to the underlining aetiology was not ruled out in any of the cases.

Overall there were 45% of cases with increased haematocrit in the present study. There were 58 (81.6%) cases of increased haematocrit in dengue cases in the present study compared to the lower incidence reported by Lakshmi Prasanna Gutti et al., [8]Ramesan et al, [13] Gomathi Chenna Reddy et al. [19]and Garachew Ferede et al.[18]

The increase in hematocrit was due to hemoconcentration because of increased intravascular plasma permeability which is the main pathogenesis in dengue. [18]

However, the haematocrit was measured once only during the assessment in the study. The serial measurement of haematocrit on different days would probably give an idea about the true rise in haematocrit. Haematocrit can still be used as a risk assessment factor because it is an indicator of plasma leakage. However, in our study haematocrit was statistically significant with a p-value of =0.0017. haematocrit was increased in 65% of cases of secondary dengue.

Of the 122 cases, White blood cells also showed variations. Leukopenia was observed in 43% cases which was correlated with the studies done by Lakshmi Prasanna Gutti et al. [8] (73%) and Smita Surendhra Masumathi et al (15.6%).[20]

Leucocytosis was observed in 57% of cases. Studies done by D K Sunitha et al.[12]reported leucocytosis in 8% of cases.

In the present study, 59 out of 71 dengue cases (83%) showed atypical lymphocytosis.

There were 40% of the cases with atypical lymphocytosis in secondary dengue. There were 29% of atypical lymphocytosis in dengue with bleeding manifestations. Choong Shi Hui et al. [21] reported atypical lymphocytosis in 4.07% of dengue patients with bleeding.

The atypical lymphocytes are antibody immune reaction for the dengue virus, because of which there is an increase in anti-dengue IgG antibodies during secondary dengue infection. Atypical lymphocytosis can be considered as a useful parameter to differentiate dengue infection from other viral infections.[22]

Majority of the patients in the present study presented with moderate thrombocytopenia (48.36%) which was correlated with the studies done by Hariprasad S et al.[5] 55%), Raghunandan et al.[11] (70%), Gondali et al.[15] (78%) . We also reported 35% of moderate thrombocytopenia in dengue patients.

Many mechanisms have been explained for thrombocytopenia in dengue patients like bone marrow suppression by the virus, immune platelet destruction, and peripheral consumption of platelets. [23] However, the degree of thrombocytopenia did not correlate with bleeding manifestations.

Platelet indices were evaluated in dengue with and without bleeding and in primary and secondary dengue cases. The mean MPV of < 9 fl indicates suppression of the bone marrow, which may be by the virus as one of the pathogenesis of thrombocytopenia in dengue patients. High MPV indicates increased marrow activity, and hence MPV can be a marker of bone marrow activity.[23]

In our study, the mean MPV was 6.9 fl in a moderate degree of thrombocytopenia cases and 5.2 fl in a severe degree of thrombocytopenia. A low MPV can also suggest the risk of bleeding. Hence correlation of platelet count and MPV with bleeding and severity of the disease can be a predictor of disease outcome.[24]

However, there was an increase PDW in 50 out of 71 dengue cases, but the mean PDW in a moderate and severe degree of thrombocytopenia was not significantly raised.

The PDW is a volume variability of platelet size and a measure of anisocytosis or platelets size. It is a direct measure of platelet size variability during platelet activation.[24]

The PCT is an index of the biomass of platelets in peripheral blood.[25] Platelet indices were statistically significant in all secondary cases.

The diagnosis of dengue and considering the primary and secondary infections is important for monitoring and identifying the disease's risk of severe form.

Bleeding manifestations, haematocrit, atypical lymphocytes and platelet indices were significant in secondary dengue. However, no such comparable studies of platelet indices in secondary dengue were available.

There were 5 cases of hepatitis complications in dengue in the present study. Sriram Pothapregada et al. [26] reported hepatitis in 11.4% of dengue fever cases, out of which two children developed fulminant hepatic failure, and Kevin John John et al.[7] reported a high incidence (65.8%) of hepatitis at the time of presentation. The hepatitis is usually due to active viral replication, direct cytopathic injury, host immune response.[26]

Only 2 cases had renal complications in our study. Dengue fever can cause acute kidney injury. Dengue causes plasma leakage, shock, reduced renal perfusion and acute tubular necrosis.[18]

Thrombocytopenia is commonly seen in plasmodium falciparum, plasmodium Vivax and mixed infections. Clinical bleeding is not a common feature in malaria .[27] Amit A Gandhi et al.[14] reported more plasmodium falciparum malaria in his study who had severe thrombocytopenia.

Thrombocytopenia with anaemia is a clue for malaria diagnosis in patients with fever and associated clinical features. In complicated malaria, low platelet is due to Disseminated Intravascular Coagulation along with platelet endothelial activation and multifactorial aetiology like few postulated mechanisms are, macrophage activation leading to platelet destruction, high cytokines, immunological destruction due to antiplatelet IgG, oxidative stress, shortened half-life in peripheral blood, sequestration in non-splenic areas and partly due to thrombocytopenia due to clumpings of platelets. The lowest haemoglobin in malaria cases noted in our study was 7.2 gm%. However, the pre-existing anemia was not ruled out.

Among 4 cases of typhoid, the lowest haemoglobin noted in our study was 3.5 gm%, and the lowest platelet count was $45x10^9$/l in one case. Thrombocytopenia can be due to platelet activation when antibody level rises. Bacteria or toxins may activate platelets. It can cause qualitative and quantitative platelet abnormality.[6]

Aetiology was not established in 42 cases of febrile thrombocytopenia, 28 cases had anemia with lowest haemoglobin value of 3.6 gm%. Leucocytosis was seen in 11 cases and leukopenia in 6 cases with the lowest value of 1.3 $x10^9$/L. Twenty one cases cases had a mild degree of thrombocytopenia followed by a moderate degree of thrombocytopenia in 18 cases with the lowest platelet value being 28 $x10^9$/L.

CONCLUSION

In India and worldwide, dengue is still a significant public health problem. Soon, it may become a vaccine-preventable disease. However, until then, diagnosing and treating dengue with or without various complications is still a challenge to clinicians. Risk assessment factors do help in the management of the disease.

REFERENCES

1) Williams JL.The Platelets. In:MacKenzie SB. Clinical Laboratory Hematology.3rd ed. Edinburgh:Pearson;2016.
2) Guclu E, Durmaz Y, Karabay O. Effect of severe sepsis on platelet count and their indices. Afr Health Sci.2013;13:333-8.
3) Vishnuram P, Natarajan K, Karuppusamy N, Karthikeyan S, Kiruthika J, Muruganathan A. Evaluation of Febrile Thrombocytopenia Cases in a South Indian Tertiary Care Hospital. J Assoc Physicians India. 2018 May;66(5):61-4.
4) Bain BJ, Bates I, Laffan MA, Lewis SM. Dacie and Lewis Practical Hematology. 12th ed: Elsevier ;2017.
5) Hariprasad S, Sukhani N. Evaluation of clinical profile of febrile thrombocytopenia:An institutional-based study. Int J Adv Med. 2017;4:1502-5.
6) Kumar P, Chandra k. A Clinical study of febrile Thrombocytopenia: A Hospital-Based Retrospective Study.Indian J Clin Prac.2014;24: 952-7.
7) Kevin John, Karthik Gunasekaran, John Davis Prasad et al. Predictors of major bleeding and mortality in dengue infection: A retrospective observational study in a tertiary care centre in South India. Hindwai. 2019; 1-6.
8) Gutti P L, Vegesna S, Pundarikaksha V et al. A study of clinical and lab profile of fever with thrombocytopenia. Int J of Con Med Res; 2017: 4 (5) 1057-61.
9) Kadadavar S S, Lokapur V, Nadig D, Prabhu M H, Masur D. Hematological parameters in dengue fever: A study in tertiary care hospital. Indian J Pathol Oncol 2020;7(2):218-22.
10) Katiyar V, Khare R. Systemic evaluation of febrile thrombocytopenia. Int J of Adv In Med. 2018; 5: 91-5.
11) Meena R, Kumar Meena N. Clinical profile of fever with thrombocytopenia in tertiary hospital Jhalawar medical collage. JMSCR, 2016;4:14535-39.
12) Suneetha DK, Inbanthan J, Sahana E, Shashank MS. Common aetiology of acute fever with thrombocytopenia in a tertiary care hospital, Mysuru. Int J Sci Res Publ.2016;4:61-4.
13) Ramesen K, Kumar MKA, Villioyot B et al. clinical profile of dengue fever in a tertiary care centre in north Kerela. Int J Res Med Sci 2017; 5:4297-301.
14) Gandhi A A, Akholkar J P. Clinical and laboratory evaluation of patients with febrile thrombocytopenia. NJMR. 2015;5: (1) 43-6.
15) Gondhali MP, Vethekar M, Bhangale D, Chaudhary K, Chaudhary M.Patrike G et al. Clinical assessment of fever with thrombocytopenia -A prospective study. Int J Med Res Health Sci. 2016;5(1):258-77.
16) Srinivas Gudi, Rajeswara Yarram. Study of clinical and laboratory profile in patients of fever with thrombocytopenia and its outcome during hospital-a study at RI; MS, A tertiary care hospital at Ongole. J. Evaluation Med Dent. Sci. 2018;7:3092-95.
17) Changal, K H, Raina H AB, Raina A et al. "Differentiating secondary from primary dengue using IgG to IgM ratio in early dengue: an observational hospital-based clinico-serological study from North India." BMC infectious diseases vol. 16,(1) 715-28.
18) Getachew Ferde, Moges Tiruneh, Ebba Abate et al. A study of clinical, haematological and biochemical profiles of patients with dengue viral infections in northwest Ethopia: Implications for patient management. BMC Inf Dis. 2018; 18 (6): 1-6.
19) Gomati Chenna Reddy, Nagendra K. Clinical and diagnostic features of dengue hemorrhagic fever in children. Int J Contemp Ped. 2018; 5 (3): 791-97.
20) Masamatti S S, Vijay C, Bhat A. Laboratory and etiological profile of febrile thrombocytopenia cases- A cross-sectional study. Nat J of Lab Med 2016; (5): 44-8.
21) Chaloemwong J, Tantiworawit A, Rattanathammethee T et al. Useful clinical features and haematological parameters for the diagnosis of dengue infection in patients with acute febrile illness: 2018 18(20): 1-10.
22) Clarice CSH, Abeysuriya V, de Mel S, Uvindu Thilakawardana B, de Mel P, de Mel C, et al. (2019) Atypical lymphocyte count correlates with the severity of dengue infection. 2019; 14; (5), 1-11.
23) Wayez A, Zafar L, Aijaz M, Afroz N. Study of platelet indices in dengue fever with thrombocytopenia and the correlation of immature platelet fraction (IPF) platelet recovery. Arch Hematol Case Rep Rev 2020: 5(1): 01-5.
24) Mukker P, Kiran S. Platelet indices evaluation in patients with dengue fever; Int J Res Med Sci. 2018 Jun;6(6):2054-59.
25) Shradha K, Sasidharanapalli S, G. Arun Kumar et al.Utility of platelet parameters in serologically proven dengue cases with thrombocytopenia. Ind J Hemato Blood Transf. 2018; 34 (4): 703-06.
26) Sriram P, Banupriya K, Mahalakshmi T. Clinical profile of atypical manifestations of dengue fever. Int J Ped. 2016; 83 (6): 493-99.
27) Raikar S R, Kamdar P K, Dabhi A S. Clinical and laboratory evaluation of patients with fever with thrombocytopenia. Ind J of Clin Practice, 2013; 4: 360-3.