



Original Article

Hematologic parameters in thrombocytopenic patients with dengue fever

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ABSTRACT

Background: Dengue fever is an endemic disease in Nepal that has shown increasing incidence each passing year. Dengue has a wide range of clinical presentations and laboratory findings. Thrombocytopenia is a common finding in dengue-infected patients along with other findings like leukopenia, lymphocytosis, raised hematocrit, and elevated liver enzymes. Thrombocytopenia is an indicator of disease severity and can lead to severe bleeding manifestations. This study aims to find the association of thrombocytopenia with other hematologic parameters.

Materials and methods: This retrospective study enrolled 651 dengue patients tested at Patan Academy of Health Sciences who also underwent complete blood count at presentation.

Results: Dengue-infected patients of all age groups with a slight male predominance. Thrombocytopenia was noted in 48.69% of cases. Thrombocytopenia showed a significant association with age ($p=0.009$), total leukocyte count ($p=0.00$), and hemoglobin levels ($p=0.015$).

Conclusions: Thrombocytopenia in dengue patients is frequently encountered. Increasing age, leukopenia, and anemia are factors significantly associated with thrombocytopenia at presentation.

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INTRODUCTION

Dengue is an arthropod-borne infection caused by one of the four serotypes of Dengue virus (DENV), namely DENV-1, DENV-2, DENV-3, and DENV-4. The viral transmission occurs via the bite of infected female *Aedes aegypti* and *Aedes albopictus* mosquitoes. Dengue infection is common in tropical and subtropical climates where vector mosquitoes are abundant. It was first reported in Nepal in 2004 and has since been endemic mainly in the tropical Terai belt of the country.¹ The infection has gradually stretched out to the hilly and mountainous regions of the country with the largest

dengue outbreak in Nepal recorded this year in regards to the number of cases reported nationwide.^{2,3}All four serotypes of the virus have been isolated in Nepal.

Dengue infection may be asymptomatic or can clinically manifest with symptoms ranging from non-specific viral infection to hemorrhagic fever and shock. Platelet counts are notably reduced in infected patients making them susceptible to bleeding. Such thrombocytopenia has been hypothesized to be due to factors like bone marrow depression, infection of megakaryocytes, the release of anti-platelet antibodies destroying platelets, altered vascular permeability, platelet consumption due to disseminated intravascular coagulation, platelet phagocytosis by macrophages.⁴⁻⁶

Alteration of various other hematological parameters are also noted in dengue infection. These include leukopenia, lymphocytosis with atypical lymphocytes on the peripheral blood smear, changes in hematocrit, and alteration in liver enzymes.⁷ This study aimed to evaluate the relationship between thrombocytopenia and other hematological parameters.

MATERIALS AND METHODS

This retrospective study was carried out from January 2022 to August 2022 at the Department of Pathology and Laboratory Medicine of Patan Academy of Health Sciences. The study enrolled all asymptomatic patients during the study period who tested positive for dengue on serology (NS1 antigen, IgM and/or IgG test) and had performed a first contact complete blood count. Dengue-positive cases without complete blood counts were excluded from this study.

Dengue testing was done by rapid solid-phase immunochromatographic test using Dengue Day 1 kit that detects NS1 antigen, IgM, and IgG antibodies. A complete blood count was performed by Sysmex XN-550.

The diagnostic criteria for the hematologic parameters were as follows:⁸

- ◆ Platelet count: 150,000/cu mm to 450,000/cu mm: Normal; < 150,000/cu mm: Thrombocytopenia; > 450,000/cu mm: Thrombocytosis
- ◆ Total leukocyte count (TLC): 4,000-11,000/cu mm: Normal; < 4,000/cu mm: Leukopenia; > 11,000/cu mm: Leukocytosis
- ◆ Hemoglobin (Hb):
 - ✓ In males: 13-18g/dL: Normal; < 13g/dL: Anemia; > 18g/dL: Polycythemia
 - ✓ In females: 11.5-15g/dL: Normal; < 11.5g/dL: Anemia; > 15g/dL: Polycythemia
- ◆ Packed cell volume (PCV): Normal: In males: 40-50%; In females: 36-46%
- ◆ Mean corpuscular volume(MCV): 83-101fL: Normal

- ◆ Mean corpuscular hemoglobin (MCH): 27-32pg: Normal
- ◆ Mean corpuscular hemoglobin concentration (MCHC): 31.5-34.5g/dL: Normal

The data collected was entered into Microsoft excel and analyzed using Statistical Package for the Social Sciences version 20.0. Mean and standard deviation was calculated and Pearson’s correlation was applied for analysis. A p-value of less than 0.05 was considered significant.

RESULTS

Out of 2314 dengue tests done, 1467 (63.4%) tested positive for dengue. 651 cases had complete laboratory data required for this study. The mean age of the patients was 32.06±16.5 years with a maximum age of 89 years and a minimum of 1 year. Male: Female ratio was 1.2:1 (Figure 1). 197 cases (30.3%) had thrombocytopenia, 317 (48.69%) cases had leukopenia and 84 cases (12.9%) had anemia. The mean values of the hematological parameters are depicted in Table 1.

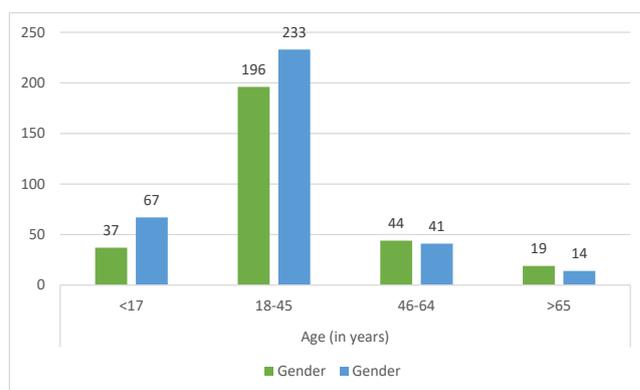


Figure 1: Age and gender-wise distribution of dengue-positive cases

The factors associated with thrombocytopenia were age, total leukocyte count, and hemoglobin levels (Table 2). Older age groups were associated with a higher incidence of thrombocytopenia. Among hematological parameters, leukopenia and anemia were significantly associated with thrombocytopenia among dengue patients (Table 3).

Table 1: Mean of hematological parameters in dengue-positive cases

| Parameters | Mean±SD |
|--------------------------------|----------------|
| Platelet (x10 ⁹ /L) | 171.02 ± 61.27 |
| WBC (x10 ⁹ /L) | 4.531 ± 2.44 |
| Hb (g/dL) | 13.0209 ± 1.74 |
| PCV (%) | 40.2734 ± 4.97 |
| MCV (fL) | 83.54 ± 7.27 |
| MCH (pg) | 27.01 ± 2.59 |
| MCHC (g/dL) | 32.01 ± 1.77 |

Table 2: Distribution of various parameters among dengue positive cases according to platelet count

| Parameters | | Patients with thrombocytopenia (n=256) | Patients with normal platelet count (n= 394) | Patients with thrombocytosis (n=1) | p-value | Likelihood ratio |
|----------------|--------|--|--|------------------------------------|---------|------------------|
| Age (in years) | < 17 | 27 (10.5%) | 77 (19.5%) | - | <0.05 | 14.96 |
| | 17-45 | 175 (68.4%) | 254 (64.5%) | - | | |
| | 45-65 | 39 (15.2%) | 45 (11.4%) | 1 | | |
| | > 65 | 15 (5.9%) | 18 (4.6%) | - | | |
| Gender | Male | 152(59.4%) | 202 (51.3%) | 1 | >0.05 | 5.34 |
| | Female | 104 (40.6%) | 192 (48.7%) | - | | |
| TLC | Low | 173 (67.6%) | 161 (40.9%) | - | <0.001 | 47.51 |
| | Normal | 81 (31.6%) | 222 (56.3%) | 1 | | |
| | High | 2 (0.8%) | 11 (2.8%) | - | | |
| Hemoglobin | Low | 58 (22.7%) | 117 (29.7%) | 1 | <0.05 | 13.63 |
| | Normal | 194 (75.8%) | 277 (70.3%) | - | | |
| | High | 4 (1.6%) | - | - | | |
| PCV | Low | 66 (25.8%) | 105 (26.6%) | 1 | >0.05 | 6.28 |
| | Normal | 181 (70.7%) | 284 (72.1%) | - | | |
| | High | 9 (3.5%) | 5 (1.3%) | - | | |
| MCV | Low | 108 (42.2%) | 192 (48.7%) | 1 | >0.05 | 5.35 |
| | Normal | 147 (57.4%) | 198 (50.3%) | - | | |
| | High | 1 (0.4%) | 4 (1.0%) | - | | |
| MCH | Low | 133 (52.0%) | 235 (59.6%) | 1 | >0.05 | 8.61 |
| | Normal | 122 (47.7%) | 152 (38.6%) | - | | |
| | High | 1 (0.4%) | 7 (1.8%) | - | | |
| MCHC | Low | 69 (27.0%) | 127 (32.2%) | 1 | >0.05 | 8.75 |
| | Normal | 178 (69.5%) | 263 (66.8%) | - | | |
| | High | 9 (3.5%) | 4 (1.0%) | - | | |

DISCUSSION

Among the 651 cases of dengue included in this study, all age groups were affected and most cases were among 18 to 45 years of age similar to other studies.^{6,9,10} 84% were adults above 18 years of age and 54.1% were males (54.1%). These values are similar to other studies conducted in Nepal¹⁰, India¹¹, and Srilanka¹² showing 51.3%, 59.41%, and 66.2% male preponderance. This might be due to more outdoor exposure among males as compared to females. The prevalence of thrombocytopenia was 30.3% at presentation. Studies from western Nepal showed 22.5% thrombocytopenic patients similar to our study¹⁰ while other studies from Nepal,⁹ India¹³, and Brazil⁶ found 47.6%, 50.9%, and 40.3% prevalence. The discrepancy may be due to the smaller sample size (n=347 and 387 respectively) in these studies. Also, platelet counts fluctuate over time during the infection with the lowest count just prior to the reduction of fever i.e. around 3 to 6 days after the onset of illness.⁶ This study has evaluated the laboratory parameters at the time of presentation (i.e. first contact complete blood count), hence the platelet count may yet to decline in many cases leading to a low prevalence of thrombocytopenia. Studies

done on admitted patients showed a prevalence as high as 97%.¹⁴ Also, earlier presentation to the hospital may be one of the reasons for the lesser occurrence of thrombocytopenia at first contact.

48.69% had leukopenia in the current study. This value was similar to studies from Nepal¹⁰ (55.3%) and India¹³ (57.5%). Mean hemoglobin and hematocrit was 13.02g/dL and 40.27% similar to a study by Priyanka et al.¹¹ Plasma leakage in dengue results in higher hemoglobin and hematocrit levels. Hematocrit was elevated in 2.15% of cases in the current study whereas the values were 32.07% and 23.33% in studies by Murmu et al¹³ and Yousuf Md et al.¹⁵ The disparity may be due to the higher prevalence of anemia in Nepal and earlier presentation of patients as hematocrit level varies during the illness. Mean MCV, MCH, and MCHC values were similar to that in a study by Kotepui et al.¹⁶ which were higher values than non-infected patients.

Thrombocytopenia showed a significant correlation with age, total leukocyte count, and hemoglobin level in this study. Increasing age was identified as another risk factor for thrombocytopenia in the current study. Castilho et al.⁶ concluded that patients more than 65 years were three times

more likely to develop thrombocytopenia. The presence of co-morbidities, medications and low immune function are contributory factors for higher incidence with increasing age. Males showed more incidence of thrombocytopenia, similar to the study by Castilho et al.⁶ however, the value was not statistically significant in our study.

Leukopenia also showed a significant association with thrombocytopenia similar to other studies.^{6,17} Dengue virus suppressing the bone marrow is attributed to the reduction in white blood cell counts in these patients.¹⁷ Hemoconcentration and increased hematocrit are common findings in dengue and correlate with the severity of dengue. Hemoglobin levels were significantly associated with thrombocytopenia in this study. Castilho et al.⁶ also noted significantly higher hemoglobin in thrombocytopenic patients. 64% of patients with increased hematocrit had thrombocytopenia similar to the study by Joshi et al.¹⁸ However, the association of hematocrit with thrombocytopenia was not significant, similar to the finding by Castilho et al.⁶

Among the red blood cell indices, none of the three indices were significantly associated with thrombocytopenia in our study whereas Castilho et al.⁶ noted the association of high MCH with thrombocytopenia. MCH values were identified as the most sensitive parameter in differentiating dengue and malaria by Kotepui et al.¹⁶ The mean values of MCH were similar in this study and Kotepui's¹⁶ study, however, not significantly associated with thrombocytopenia.

CONCLUSIONS

Dengue outbreaks are intensifying in Nepal with every passing year with numerous complications arising from the infection. Dengue infection is known to cause thrombocytopenia in most cases and this study aimed to find other associated hematological parameters. Increasing age, leukopenia, and high hemoglobin levels were significantly associated with an increased risk of thrombocytopenia. Hematocrit, although an indicator of clinical severity, did not correlate significantly with thrombocytopenia in this study.

LIMITATIONS

This study enrolled dengue patients who had complete blood count at presentation. The variable timing of presentation has contributed to variations in the hematological parameters of the patients. Also, the unavailability of hematological findings in more than half of the patients was a shortcoming of this study.

REFERENCES

1. Pandey BD, Rai SK, Morita K, et al. First case of Dengue virus infection in Nepal. *Nepal Med Coll J* 2004; 6: 157–159. [Website](#)

2. Adhikari N, Subedi D. The alarming outbreaks of dengue in Nepal. *Trop Med Health* 2020; 48: 1–3. [Crossref](#)
3. World Health Organization (10 October 2022). Disease Outbreak News; Dengue fever - Nepal. URL: [Website](#)
4. de Azeredo EL, Monteiro RQ, De-Oliveira Pinto LM. Thrombocytopenia in dengue: Interrelationship between virus and the imbalance between coagulation and fibrinolysis and inflammatory mediators. *Mediators Inflamm*; 2015. [Crossref](#)
5. Chao CH, Wu WC, Lai YC, et al. Dengue virus nonstructural protein 1 activates platelets via Toll-like receptor 4, leading to thrombocytopenia and hemorrhage. *PLoS Pathog*; 15. [Crossref](#)
6. Castilho BM, Silva MT, Freitas ARR, et al. Factors associated with thrombocytopenia in patients with dengue fever: a retrospective cohort study. *BMJ Open* 2020; 10: e035120. [Crossref](#)
7. Azin FRFG, Gonçalves RP, Pitombeira MH da S, et al. Dengue: Profile of hematological and biochemical dynamics. *Rev Bras Hematol Hemoter* 2012; 34: 36–41. [Crossref](#)
8. Bates I, Lewis SM. Reference ranges and normal values. In: Bain BJ, Bates I, Laffan MA, et al. (11th ed) *Dacie and Lewis Practical Haematology*. Elsevier Churchill Livingstone, 2016.
9. Jaiswal NK, Chaudhary S, Chaudhary N. Clinico-laboratory observations and outcome of dengue infection in a tertiary care hospital of western Nepal: An observational cross-sectional study. *Journal of Universal College of Medical Sciences* 2017; 5: 3–7. [Crossref](#)
10. Dhungana D, Banstola B, Banjara M. Clinical and haematological profile of dengue among adult patients at a tertiary care hospital in Pokhara. [Crossref](#)
11. Priyanka P, Dinesh US. Differentiating between Dengue Fever from Other Febrile Illnesses Using Haematological Parameters. *National Journal of Laboratory Medicine* 2018; 7: 6–10. [Crossref](#)
12. Bodinayake CK, Nagahawatte ADS, Devasiri V, et al. Outcomes among children and adults at risk of severe dengue in Sri Lanka: Opportunity for outpatient case management in countries with high disease burden. *PLoS Negl Trop Dis* 2021; 15. [Crossref](#)
13. Murmu M, Singh LK, Kamble SS, et al. Clinico-laboratory profile of dengue patients in a tertiary hospital of Eastern India. *Int J Res Med Sci* 2018; 6: 1600. [Crossref](#)
14. Kadavar SS, Lokapur V, Nadig D, et al. Hematological parameters in dengue fever: A study in tertiary care hospital. *Indian Journal of Pathology and Oncology* 2020; 7: 218–222. [Crossref](#)
15. Yousuf Khan M, Venkateshwarlu C, Sandeep N, et al. A Study of Clinical and Laboratory Profile of Dengue Fever in a Tertiary Care Hospital, Nizamabad, Telangana State, India. *International Journal of Contemporary Medical Research* 2016; 3: 2383–2387. [Website](#)
16. Kotepui M, Phunphuech B, Phiwklam N, et al. Differentiating between dengue fever and malaria using hematological parameters in endemic areas of Thailand. *Infect Dis Poverty* 2017; [Crossref](#)
17. Kalayanarooj S, Vaughn DW, Nimmannitya S, et al. Early Clinical and Laboratory Indicators of Acute Dengue Illness. *J Infect Dis* 1997; 176: 313–321. [Crossref](#)
18. Joshi AA, Divyashree BN, Gayathri BR. Hematocrit Spectrum in Dengue: A Prospective Study. *Int J Sci Study* 2018. [Crossref](#)