Journal of Health and Rehabilitation Research 2791-156X JHRR

For contributions to JHRR, contact at email: editor@jhrlmc.com

Original Article

Diagnostic Significance of Hematological Parameters and C-Reactive Protein in Dengue Viral Infection: A Retrospective Cross-Sectional Study

Khushboo Qamar[1], Salman Akhter[2]*, Amina Rahat[3], Khawaja Ejaz Ul Haq[4], Muhammad Bilal Qasim[2], Abdus Salam Khan[5], Bilal Musa[5], Saira Naz[6]

[1]Mphil Scholar, Institute of Basic Medical Sciences, Khyber Medical University Peshawar, Pakistan.
[2]Mphil Scholar, Centre of Biotechnology and Microbiology, University of Peshawar, Pakistan.
[3]Assistant professor, Department of Food and Nutrition, College of Home Economics, University of Peshawar, Pakistan.
[4]Mphil Research Scholar, Centre of Biotechnology and Microbiology, University of Peshawar, Pakistan.
[5]Mphil Scholar, Faculty of Rehabilitation and Allied Health Sciences, Riphah University Islamabad, Pakistan.
[6]Mphil Scholar, Faculty of Medical Microbiology, Abasyn University Peshawar, Pakistan.
Corresponding Author: Salman Akhter, Mphil Scholar; Email: Salmanakhter472@gmail.com

Conflict of Interest: None.

Qamar K., et al. (2024). 4(2): DOI: https://doi.org/10.61919/jhrr.v4i2.782

ABSTRACT

Background: Dengue fever continues to pose significant challenges in public health, particularly within developing countries where it remains endemic. The ability to distinguish dengue infection from other febrile illnesses and assess its severity is crucial. The analysis of hematological parameters and inflammatory biomarkers, particularly C-reactive protein (CRP), offers valuable insights into the disease's progression.

Objective: This study aimed to delineate the severity of dengue fever through detailed evaluation of complete blood count (CBC) and CRP levels, and to establish a correlation between these markers and the clinical severity of the infection.

Methods: In this retrospective cross-sectional study, 135 suspected dengue fever patients from the City University of Science and Information Technology Peshawar were screened using the immune-chromatographic technique (ICT). Among them, 50 individuals (37%) tested positive for dengue. Both CBC and CRP levels were measured, with data analyzed using the statistical package SPSS version 22.0. The study spanned demographic data collection, gender and age distribution assessment, and detailed analysis of hematological parameters alongside CRP to predict disease severity.

Results: Among the confirmed cases, the gender ratio skewed towards males (60%) compared to females (40%), with the most affected age group being 15-25 years (34%). Leukopenia was identified in 58% of patients with a mean WBC count of 2.62 × 10^9/L, neutrophilia in 66% with a mean neutrophil percentage of 80.15%, and lymphopenia in 56% with a mean lymphocyte percentage of 10.28%. Thrombocytopenia was observed in 76% of the cases. Elevated CRP levels were found in 88% of patients, with a mean CRP value of 23.10, indicating a strong predictive correlation with disease severity (p-value= 0.001).

Conclusion: The study reaffirms the role of CBC and CRP levels in the clinical assessment of dengue fever, with both markers being indicative of infection severity. These findings can aid in the early detection and management of dengue fever, potentially guiding decisions regarding the necessity of hospitalization.

Keywords: Dengue Fever, Hematological Parameters, C-Reactive Protein, Complete Blood Count, Thrombocytopenia, Leukopenia, Public Health.

INTRODUCTION

Dengue infection, a mosquito-borne viral disease caused by an arbovirus transmitted via an arthropod vector, remains a significant public health concern globally (1). The genetic structure of the dengue virus (DENV), characterized by a positive-sense single-stranded RNA within an icosahedral core, classifies it under the family Flaviviridae and genus Flavivirus (2, 3). DENV encodes a single polyprotein that undergoes cleavage to form three structural and seven nonstructural proteins, critical for its replication and host interaction (4, 5). Typically presenting with high fever, muscle and joint pain, rash, and gastrointestinal symptoms, dengue can lead

to severe complications like hemorrhagic fever and profound fatigue, symptoms that often subside after a week but may leave lingering effects for weeks (6-8).

The epidemiological profile of dengue in Pakistan has shown significant outbreaks, particularly post-monsoon, with substantial morbidity and mortality rates reported during major outbreaks, such as those in Lahore in 2011 and more recently across 15 districts in Khyber Pakhtunkhwa as per the Integrated Disease Surveillance and Response System (9, 10). These outbreaks underline the urgent need for effective monitoring and control strategies, given the absence of a vaccine or specific antiviral treatments for dengue.

In clinical settings, the role of hematological parameters such as white blood cells, red blood cells, and platelets, routinely measured by a complete blood count (CBC), becomes crucial in managing dengue infection (11, 12). Research indicates significant changes in CBC profiles during the infection, particularly from days 3 to 8 of fever, highlighting the presence of leukopenia, thrombocytopenia, and hemoconcentration—key indicators of the disease's progression (13). Additionally, hemoglobin concentration, a vital parameter for oxygen delivery, shows variations linked to the severity of the disease, particularly in cases with plasma leakage (15).

Moreover, the inflammatory response in dengue can be gauged by biomarkers like serum glutamic-pyruvic transaminase, alkaline phosphatase, and notably, C-reactive protein (CRP) (16). CRP levels, which increase significantly in response to inflammation, are instrumental in distinguishing between bacterial and viral infections, and high levels are indicative of severe dengue infection (17-19). The binding of CRP to damaged tissues and pathogens highlights its role in the inflammatory process and its potential as a prognostic marker in clinical settings (20).

Despite the known impact of dengue, significant research gaps exist, particularly in the hematological and biochemical profiling of patients in endemic regions like Pakistan. This study aims to address these gaps by analyzing disease severity through CBC and CRP levels, exploring their potential to serve as predictors for the prognosis of dengue fever. Such research is vital for developing strategies that can enhance early diagnosis, improve patient management, and ultimately curb the global spread of dengue, considering the high global risk of transmission and the crucial role of immunity in disease outcomes.

MATERIAL AND METHODS

This study was conducted as a retrospective cross-sectional and experimental analysis over a period of six months at the Medical Laboratory Technology (MLT) lab of City University of Science and Information Technology (CUSIT), Peshawar, Pakistan. The research aimed to evaluate hematological parameters and C-reactive protein levels in individuals diagnosed with dengue to assess disease severity and potential prognostic indicators.

Participants for the study were recruited from the district of Peshawar, Khyber Pakhtunkhwa (KPK), a region endemic to dengue fever, located approximately 160 km west of Islamabad. According to the 2017 census, Peshawar has a population of 4,269,079. The inclusion criteria specified individuals who tested positive for dengue across both genders. Conversely, the exclusion criteria eliminated those who were asymptomatic for dengue or had other acute infectious diseases such as measles, influenza, and hepatitis.

The sample size comprised 50 confirmed dengue cases, and the collection involved multiple well-established medical facilities within Peshawar, including Lady Reading Hospital, Hayatabad Medical Complex, Khyber Teaching Hospital, and several other private entities such as MMC Hospital and Mercy Teaching Hospital. Blood samples were obtained using sterile syringes, collected into containers such as gel tubes and Ethylene diamine tetra acetic acid (EDTA) tubes to prevent clotting and preserve the blood morphology.

Ethical approval for the study was granted by the Studies Committee of CUSIT, Peshawar, in accordance with ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. All participants received a comprehensive explanation of the study objectives and procedures, and informed consent was obtained prior to sample collection.

Materials and equipment utilized included sterile syringes, tourniquets, gel tubes, EDTA tubes, test tube racks, cotton, alcohol pads, saniplast, pipettes, a centrifuge machine, a hematology analyzer, dengue NS1 antigen strips, normal saline, and a CRP kit. Blood samples were transported to the laboratory under controlled temperature conditions (2-8℃) using carriers equipped with racks and ice packs to ensure the integrity of the samples.

Data analysis was conducted using statistical software to evaluate the relationship between hematological changes and CRP levels as predictors of dengue severity. Statistical significance was assessed through various analytical methods, including t-tests for comparing means and regression analysis to determine correlations between independent and dependent variables. The findings were intended to provide insights into the prognostic value of these markers in the clinical management of dengue.

RESULTS

In the retrospective analysis of 50 dengue-infected patients, a pronounced gender disparity was observed with males constituting 60% and females 40%. All participants tested positive for dengue, showcasing a 100% infection rate within the sampled individuals.

Journal of Health and Rehabilitation Research JHRR

Age distribution skewed towards the younger demographic, with 34% falling within the 15-25 age bracket, closely followed by the 26-35 age group at 32%. Patients aged 36-45 comprised 26%, while the 46-55 age group represented the smallest fraction at 8%. The mean age of participants was 31.76 ± 10.30 years, with males averaging at a slightly younger age of 29.36 ± 10.56 compared to females, who had a mean age of 35.35 ± 8.98 years. Notably, the correlation between age and gender was strongly positive and statistically significant (r = 0.964, p = 0.001).

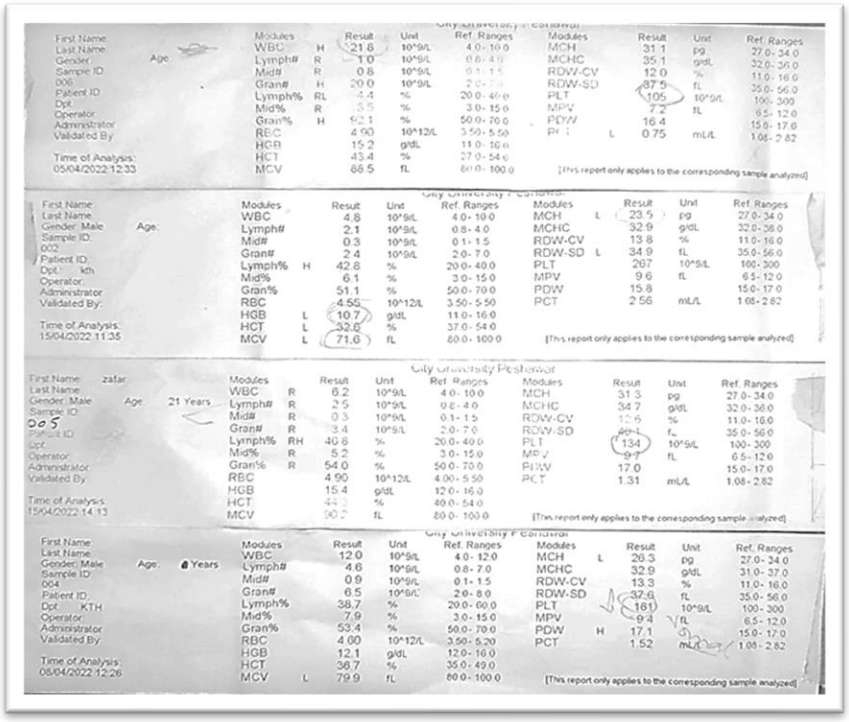

Figure 1 Scan of Respective Lab Values

Hematological assessments further revealed that 58% of the patients experienced leukopenia, with a mean white blood cell (WBC) count of 2.62 × 10^9/L, whereas the remaining 42% had a normal WBC count, averaging 8.48 × 10^9/L. Neutrophil percentages significantly increased to a mean of 80.15% in 66% of patients, indicating neutrophilia, while the rest maintained a normal neutrophil percentage at a mean of 64.70%. Lymphocyte analysis showed a decrease in 56% of the patients, with the mean lymphocyte percentage at 10.28% for those affected, in contrast to a normal mean percentage of 31.86% among the others. The study revealed a significant correlation (r = 0.470, p < 0.001) between lymphocytes and neutrophils counts.

Figure 2 Agglutination on CRP strip indicating CRP positive result

Table 1 Lab Value Characteristics

Sex	Age Years	WBC (x10^9/L)	Lymph%	Gran%	Lymph# (x10^9/L)	Gran# (x10^9/L)	RBC (x10^12/L)	HGB (g/dL)	HCT (%)	MCV (fL)
M		2.8	10%	18%	0.3	0.5	4.53	15.0	42.2	88.5
M		4.8	23.5%	4.4%	1.1	0.2	5.11	15.1	37.6	112
M	21	6.2	25%	3.5%	1.6	0.2	4.90	15.4	44.0	89
M	4	12.0	36%	36.5%	3.7	6.5	4.64	13.1	36.7	79

The study further noted that platelet counts were significantly lower in 76% of patients, indicative of thrombocytopenia, with a mean platelet count of 106.21, as opposed to a mean count of 181.08 in patients with normal platelet levels.

Journal of Health and Rehabilitation Research 2791-156X JHRR

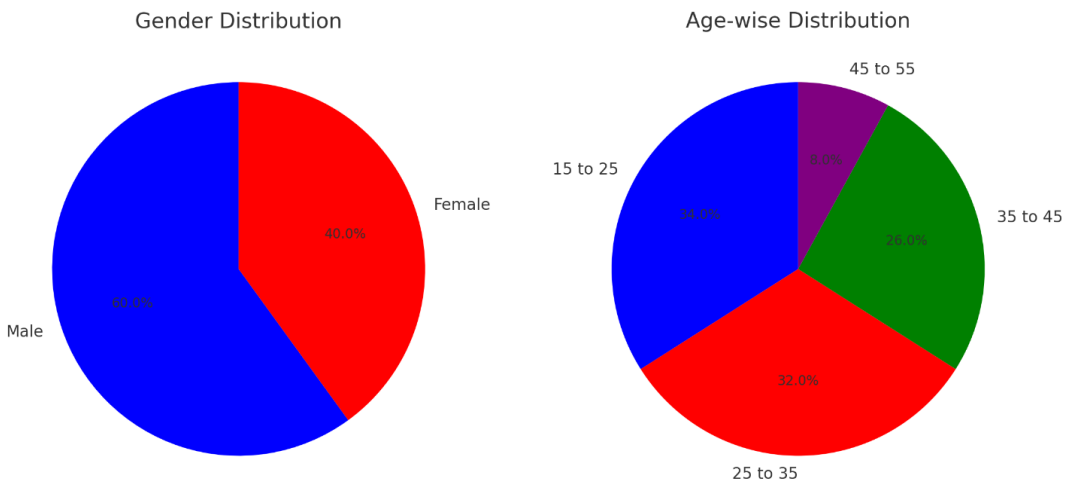

Figure 3 Age and Gender Distribution

Concerning inflammatory markers, CRP levels were elevated in 88% of the patients, underscoring its potential as a biomarker for disease severity. The mean CRP level across the cohort was 23.10, with a standard deviation of 13.67. Statistical analysis confirmed a significant positive correlation between WBC count and CRP levels ($r = 0.401$, $p = 0.004$).

The data underscores the hematological impact of the dengue virus and emphasizes the potential of CRP as a marker for assessing the severity of the infection. The significant alterations in WBC, neutrophil, lymphocyte, and platelet counts demonstrate the virus's systemic effect, with the young adult population appearing most susceptible. The robust statistical association between these hematological parameters and CRP levels provides a foundation for future research into targeted treatments and diagnostics.

DISCUSSION

In the wake of the surging dengue virus outbreaks, particularly in developing countries, there has been a growing concern regarding its impact on public health. This virus has primarily affected tropical regions, prompting a reevaluation of diagnostic criteria and prognostic indicators. The study at hand was orchestrated to dissect the implications of dengue infection through the lens of complete blood count (CBC) parameters and C-reactive protein (CRP) levels, leveraging these markers as potential predictors for the infection's severity.

A cohort of 135 individuals suspected of dengue infection was initially considered, from which 37% were ultimately diagnosed with the disease. Notably, the male subset represented a larger proportion of the infected group, accounting for 60% compared to the 40% prevalence observed in females. This gender-based disparity aligns with previous regional research by Shahid M, Amin I, Afzal S, Fatima Z, Zahid S. et al., who documented a similar male predominance in KPK and Punjab (21), though it diverges from findings by Suleman M, Faryal R, Alam MM, Khurshid A, Sharif S, et al., who reported a higher infection rate among females in KPK (22). The predilection for males in this study could be attributed to increased exposure from outdoor activities, a hypothesis that warrants further investigation.

Age distribution within the infected population indicated a concentration of cases among younger age groups, especially notable within the 15-25 year cohort. The findings from Gadhwal AK, Ankit BS, Chahar C, Tantia P, et al., which reported higher infection rates among older individuals in Singapore (23), serve to underscore the demographic variations in disease prevalence that might be attributed to differing social behaviors or immune status across age groups.

Hematological parameter evaluation revealed a significant incidence of leukopenia in the patient population. The mean WBC count in leukopenic individuals was markedly reduced, paralleling findings from Chaloemwong, J., Tantiworawit, A., Rattanathammethee, T., Hantrakool, et al. (59). Neutrophil percentage was notably elevated among individuals with neutrophilia, which was consistent with the results reported by Patel, K., Patel, D., & Das, V. K. et al. (25). Furthermore, lymphocyte percentages decreased significantly in more than half of the patients, with overall mean values resonating with those reported by Patel, K., Patel, D., & Das, V. K. et al., and corroborated by findings from Jayadas, T. T. P., Kumanan, T., Arasaratnam, V et al. (60, 61).

The study also reported significant thrombocytopenia, a common abnormality in dengue patients, echoing the research by Anwar, F., Ahmad, S., Haroon, M., Haq, I. U. et al., from the Mardan district, and findings from Nandwani, S., Bhakhri, B. K., Singh, N., Rai, R.et al., who documented reduced platelet counts in a pediatric cohort (26, 27). The implications of these hematological changes are profound, as they not only signal the infection's progression but also assist clinicians in stratifying patients based on the severity of their symptoms.

CRP, an acute phase reactant synthesized by the liver, serves as a beacon of infection or inflammation, with concentrations escalating in severe viral infections or bacterial comorbidities. This study's CRP findings are corroborated by the research from Manipal, India,

Journal of Health and Rehabilitation Research 2791-156X JHRR

where severe dengue patients exhibited markedly elevated median CRP levels, a trend also noted by Chen, R., & Vasilakis, N. et al. (29). The high CRP levels observed in the majority of this study's patients underscore its utility as a reliable diagnostic aid in ascertaining the severity of dengue fever.

Reflecting on the study's strengths, the use of CBC and CRP offered an insightful glimpse into the severity of dengue infections, providing clinicians with valuable tools for early detection and potential hospitalization needs, particularly in elderly patients. However, the study is not without limitations. The gender distribution discrepancy warrants a more extensive analysis to discern the underlying causes. Furthermore, the sample size, although adequate for preliminary analysis, could be expanded in future research to enhance the generalizability of the findings.

CONCLUSION

In conclusion, the insights gleaned from this study illuminate the pathophysiological underpinnings of dengue fever and solidify the role of CBC and CRP in the clinical assessment of this disease. Recommendations stemming from these findings advocate for the integration of these parameters in routine diagnostics to bolster the efficacy of clinical management strategies for dengue. Additionally, public health initiatives focusing on reducing male exposure to dengue vectors and reinforcing preventive measures across all age groups could mitigate the incidence of this debilitating disease.

REFERENCES

1. Patel K, Patel D, Das VK. Hematological Parameters and Its Utility in Dengue Fever: A Prospective Study. Int J Sci Res. 2016;5(4):1077-9.
2. Durrani MR, Iqbal MD, Munir N, Jamal A. Dengue Hemorrhagic Fever-Epidemic in Karachi: Pakistan (2006-2016) Experience at a Tertiary Care Centre. Pak J Surg. 2017;33(1):53-58.
3. Khan J, Ghaffar A, Khan SA. The Changing Epidemiological Pattern of Dengue in Swat, Khyber Pakhtunkhwa. PLoS One. 2018;13(4):e0195706.
4. Waseem T, Latif H, Shabbir B. An Unusual Cause of Acute Abdominal Pain in Dengue Fever. Am J Emerg Med. 2014;32(7):819-e3.
5. Khan J, Khan I, Ghaffar A, Khalid B. Epidemiological Trends and Risk Factors Associated with Dengue Disease in Pakistan (1980–2014): A Systematic Literature Search and Analysis. BMC Public Health. 2018;18(1):1-13.
6. Shams N, Amjad S, Yousaf N, Ahmed W, Seetlani NK, Farhat S. Dengue Knowledge in Indoor Dengue Patients from Low Socioeconomic Class; Aetiology, Symptoms, Mode of Transmission and Prevention. J Ayub Med Coll Abbottabad. 2018;30(1):40-44.
7. Duarte JL, Diaz-Quijano FA, Batista AC, Giatti LL. Climatic Variables Associated with Dengue Incidence in a City of the Western Brazilian Amazon Region. Rev Soc Bras Med Trop. 2019;52.
8. Azin FRFG, Gonçalves RP, Pitombeira MHDS, Lima DM, Castelo Branco I. Dengue: Profile of Hematological and Biochemical Dynamics. Rev Bras Hematol Hemoter. 2012;34:36-41.
9. Chen CC, Lee IK, Liu JW, Huang SY, Wang L. Utility of C-Reactive Protein Levels for Early Prediction of Dengue Severity in Adults. Biomed Res Int. 2015;2015.
10. Rao AA, Raaju RU, Gosavi S, Menon S. Dengue Fever: Prognostic Insights From a Complete Blood Count. Cureus. 2020;12(11).
11. Vuong NL, Le Duyen HT, Lam PK, Tam DTH, Chau NVV, Van Kinh N, Yacoub S. C-Reactive Protein as a Potential Biomarker for Disease Progression in Dengue: A Multi-Country Observational Study. BMC Med. 2020;18(1):1-13.
12. Mukherjee S, Saha B, Tripathi A. Clinical Significance of Differential Serum-Signatures for Early Prediction of Severe Dengue Among Eastern Indian Patients. Clin Exp Immunol. 2022.
13. Chaloemwong J, Tantiworawit A, Rattanathammethee T, Hantrakool S, Chai-Adisaksopha C, Rattarittamrong E, Norasetthada L. Useful Clinical Features and Hematological Parameters for the Diagnosis of Dengue Infection in Patients with Acute Febrile Illness: A Retrospective Study. BMC Hematol. 2018;18(1):1-10.
14. Mallhi TH, Khan AH, Adnan AS, Sarriff A, Khan YH, Jummaat F. Clinico-Laboratory Spectrum of Dengue Viral Infection and Risk Factors Associated with Dengue Hemorrhagic Fever: A Retrospective Study. BMC Infect Dis. 2015;15(1):1-12.
15. Ho TS, Wang SM, Lin YS, Liu CC. Clinical and Laboratory Predictive Markers for Acute Dengue Infection. J Biomed Sci. 2013;20(1):1-8.
16. Jameel T, Mehmood K, Mujtaba G, Choudhry N, Afzal N, Paul RF. Changing Haematological Parameters in Dengue Viral Infections. J Ayub Med Coll Abbottabad. 2012;24(1):3-6.
17. Gawoski JM, Ooi WW. Dengue Fever Mimicking Plasma Cell Leukemia. Arch Pathol Lab Med. 2003;127(8):1026-1027.

Journal of Health and Rehabilitation Research 2791-156X JHRR

18. Vickers I, Harvey K, Nelson K, Brown M, Bullock-DuCasse M, Lindo J. Evaluation of OneStep Dengue NS1 RapiDip™ InstaTest and OneStep Dengue Fever IgG/IgM RapiCard™ InstaTest During the Course of a Dengue Type 1 Epidemic. Diagn Microbiol Infect Dis. 2017;89(4):271-275.

19. Haq I, Zahir F, urRehaman A, Ullah N, Khan J, Qamar N, Khan Y. Evaluation of Change in Hematological Parameters and Epidemiological Identification of Dengue Virus Infection at District Peshawar, Khyber Pakhtunkhwa, Pakistan. Int J Mosquito Res. 2021;8(1, Part A):11-18.

20. Gadhwal AK, Ankit BS, Chahar C, Tantia P, Sirohi P, Agrawal RP. Effect of Carica Papaya Leaf Extract Capsule on Platelet Count in Patients of Dengue Fever with Thrombocytopenia. J Assoc Physicians India. 2016;64(6):22-26.

21. ABDULLAH SA, Salman M, Din M, Khan K, Ahmad M, Khan FH, Arif M. Dengue Outbreaks in Khyber Pakhtunkhwa (KPK), Pakistan in 2017: An Integrated Disease Surveillance and Response System (IDSRS)-Based Report. Pol J Microbiol. 2019;68(1):115.

22. Chaloemwong J, Tantiworawit A, Rattanathammethee T, Hantrakool S, Chai-Adisaksopha C, Rattarittamrong E, Norasetthada L. Useful Clinical Features and Hematological Parameters for the Diagnosis of Dengue Infection in Patients with Acute Febrile Illness: A Retrospective Study. BMC Hematol. 2018;18(1):1-10.

23. Jayadas TTP, Kumanan T, Arasaratnam V, Gajapathy K, Surendran SN. The Clinical Profile, Hematological Parameters and Liver Transaminases of Dengue NS1 Ag Positive Patients Admitted to Jaffna Teaching Hospital, Sri Lanka. BMC Res Notes. 2019;12(1):1-5.

24. Anwar F, Ahmad S, Haroon M, Haq IU, Khan HU, Khan J, Shah IA. Dengue Virus Epidemics: A Recent Report of 2017 from District Mardan, Khyber Pakhtunkhwa Province, Pakistan. Int J Mosquito Res. 2019;6(1):46-49.

25. Nandwani S, Bhakhri BK, Singh N, Rai R, Singh DK. Early Hematological Parameters as Predictors for Outcomes in Children with Dengue in Northern India: A Retrospective Analysis. Rev Soc Bras Med Trop. 2021;54.

26. Rao R, Nayak S, Pandey AK, Kamath SU. Diagnostic Performance of C-Reactive Protein Level and Its Role as a Potential Biomarker of Severe Dengue in Adults. Asian Pac J Trop Med. 2020;13(8):358.

27. Chen R, Vasilakis N. Dengue—Quo Tu Et Quo Vadis?. Viruses. 2011;3(9):1562-1608.