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Distinguishing Dengue Fever from Other Feverish Illnesses

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ABSTRACT

Background: Dengue fever is an acute febrile illness, one of the most prevalent viral diseases spread by mosquitoes. Given its similar symptoms, it is challenging to distinguish dengue fever from other febrile infections like malaria, leptospirosis, and typhoid fever. Comparing hematological parameters between patients with dengue and other febrile illnesses can help understand the role of these parameters in distinguishing between the two groups of patients at an early stage, before the availability of more specific tests.

Objectives: The goal is to compare hematological variables to see if they can predict dengue viral infection in patients with febrile illnesses.

Methods: This is a cross-sectional, retrospective, observational study that spans a year. There were 82 patients in total; 41 had positive dengue rapid test results (NS1, IgG, and IgM), and 41 had negative results. These 82 patient's laboratory and demographic data were gathered, and they were then statistically analyzed.

Result: Despite the dengue patients' platelet, PLR, PLT-RBC ratio, absolute lymphocyte count, and absolute monocyte count being significantly higher compared to those of the non-dengue group, their WBC count was significantly lower. In a multiple logistic regression analysis, dengue was found to be positively predicted by PLR (>120).

Conclusion: The findings imply that basic hematological parameters can be useful in identifying dengue from other feverish infections

Keywords: Dengue Fever, Febrile Illnesses, Hematological Variables, Platelet Count, Viral infection, Dengue rapid test.

INTRODUCTION

Febrile illnesses are the most common clinical manifestation seen in hospital settings from developing nations, and it can be brought on by a variety of bacterial, viral, and parasitic conditions, which include scrub typhus, enteric fever, dengue, malaria, and leptospirosis.[1,2] Dengue is an arboviral infection caused by the dengue virus, which is an RNA virus from the family flaviviridae and is spread by the Aedes aegypti mosquito. [1,3] Four serotypes cause the disease, DEN-1 – DEN-4.[4] Dengue fever is among the most serious transmissible diseases.[5] More than 100 countries around the world are affected by the epidemic disease dengue.[4] WHO statistics have indicated that between 50 and 100 million cases of dengue are reported annually.[5]

Dengue can vary from a generalized febrile illness to classic dengue fever, which can go on leading to dengue shock syndrome and dengue hemorrhagic fever.[3] Dengue infections can cause a mild range of symptoms to severe ones.[6] Fever with or without rash is the hallmark of mild dengue fever. In contrast, high fever, intense

headache with eye pain, muscle aches, joint pain, and rash are the signs of more serious infections. Some even experience an acute febrile sickness that includes bleeding, organ damage and shock, which has a high fatality rate.[6,7] The majority of dengue infections cause mild or no symptoms, which resemble other febrile illnesses.[6,8] Due to the lack of specificity in its clinical appearance, dengue cannot be distinguished clinically from other febrile illnesses.[8] Despite this fact, reliance on clinical diagnosis alone is common in dengue-endemic regions.[9] Delays or errors in making a clinical diagnosis might result in improper treatment and even mortality.[7] So early diagnosis, prompt detection of bleeding, and appropriate supportive treatment are important to avoid potentially significant sequelae.[10]

Dengue is diagnosed by using ELISA, RT-PCR, IgM, IgG, and NS1 antigen rapid strip.4 Although they are available, certain diagnostic laboratory tests might not be reliable in the initial phase of illness and certain areas may lack access to these due to a lack of healthcare facilities.3 6 This research is carried out to examine how blood-related measurements can help differentiate between patients with dengue and those with other fever-related illnesses early on, before the availability of more specific tests.

MATERIALS & METHODS

A retrospective cross-sectional analytical observational study was conducted on 82 patients. After approval by the IEC, the patients were divided into two study groups based on the results of the dengue rapid test (NS1, IgG, IgM). One group was called the "dengue group', comprising 41 patients who tested positive for dengue virus infection. The other group was called the "non-dengue group', comprising the remaining 41 patients who tested negative for dengue virus infection. The non-dengue group consisted of leptospirosis, typhoid, malaria, and viral fever patients who tested negative for dengue virus infection. The study was conducted over 1 year in a tertiary care hospital. Adult patients (over 18 years of age) presenting with fever at a tertiary care hospital, clinically suspected of dengue infection, and tested for dengue virus infection using "Dengue Rapid (NS1, IgG, IgM)" tests will be included in the study. Cases in which routine hematologic tests (blood counts) were not performed or were unavailable will be excluded from the study. Demographic and lab data were collected from hospital records, including age, sex, UHID, and blood test request date. Key hematological parameters such as total WBC count, platelet count, PCV (HCT), differential leukocyte counts, and RBC count were obtained from an automated analyzer. Additionally, the Neutrophil-lymphocyte ratio (NLR), Platelet-lymphocyte ratio (PLR), Monocyte-lymphocyte ratio (MLR), Platelet-to-RBC ratios, Absolute Neutrophil Count (ANC), Absolute Lymphocyte Count (ALC), Absolute Monocyte Count (AMC), and Absolute Eosinophil Count (AEC) were calculated.

STATISTICAL ANALYSIS

The continuous data's normality was evaluated using the Kolmogorov-Smirnov test. The T-test was used to analyze the normally distributed data (P-value > 0.05), and the mean and standard deviation were tabulated. On the other hand, the Mann-Whitney U Test was used to compare the non-normally distributed data, and the results were tabulated with the median and range. Either the chi-squared test or Fisher's exact test was used to analyze categorical variables. To determine the laboratory traits linked to dengue positivity, a univariate analysis was conducted on both laboratory-positive and laboratory-negative dengue cases. To determine whether any of these haematological parameters could independently or in combination predict positivity for dengue viral infection in patients presenting with febrile illnesses, variables that were considered statistically significant in the univariate analysis were

included in the multivariate analysis using a logistic regression model. A P-value below 0.05 is considered statistically significant.

RESULT

A total of 82 patients were included, of whom 41 had positive dengue viral fever, and the rest, who were admitted with fever, were classified in the non-dengue group.

Table 1: Comparison of age and hematological parameters by t-Test

Variables	Groups	Mean	SD	P- Value
Age	Dengue	41.5122	17.03984	0.459
	Non dengue	38.9268	14.30278	
RBC	Dengue	4.6244	1.09786	0.459
	Non dengue	4.5185	0.77798	
PCV	Dengue	38.3976	8.06748	0.184
	Non dengue	36.3073	5.87709	
Neutrophil	Dengue	67.8829	15.27959	0.184
	Non dengue	68.0049	15.43932	
Monocyte	Dengue	9.9317	4.56522	0.182
	Non dengue	8.6561	3.99481	

The dengue group and non-dengue group had a mean age of 41.51 and 38.92, respectively [Table 1].

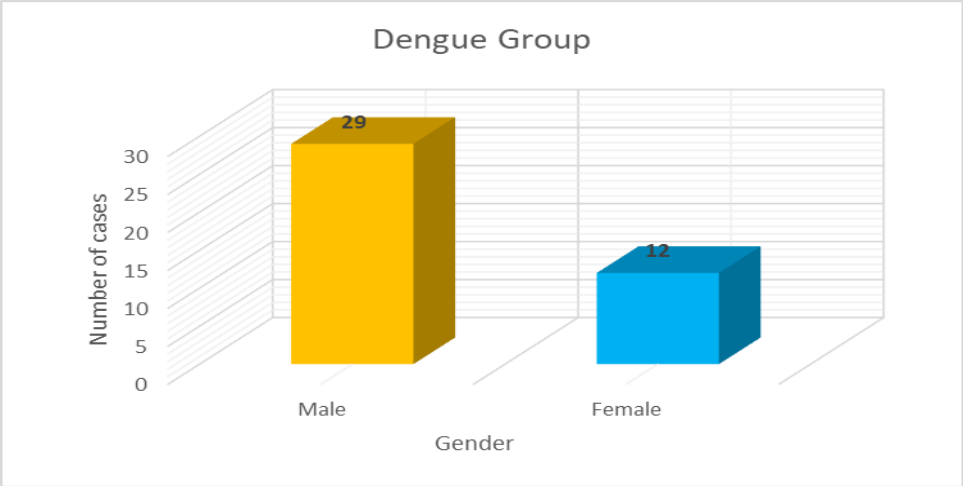

Figure 1: Distribution of gender among dengue group

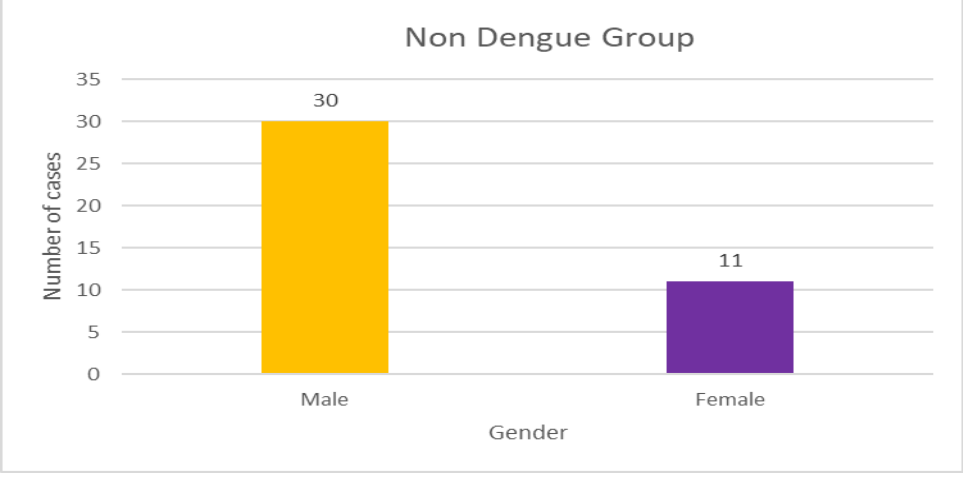

Figure 2: Distribution of gender among a non-dengue group

In both cases, males are affected more than the females (Dengue: -29 males and 12 females, non-dengue: -30 males and 11 females), but there is no significant difference (*P* value 0.806) [Figures 1 and 2].

Table 2: Comparison of hematological parameters by Mann-Whitney U Test

Variables	Dengue Median (IQR)	Non-dengue Median (IQR)	P- Value
WBC (×10^3)	5.3750 (8.3100-12.0850)	5.5600 (3.8100-9.2700)	0.028
Platelet (×10^3)	250 (146-305)	118 (59-200)	0.000
Lymphocyte	18.40 (11.65-23.35)	17.70 (10.90-28.75)	0.817
Eosinophil	0.50 (0.15-2.50)	0.50 (0.05-2.30)	0.634
Basophil	0.30 (0.20-0.50)	0.30 (0.20-0.40)	0.412
NLR	3.8967 (2.6900-6.7808)	3.9378 (2.0354-7.0011)	0.878
MLR	0.4891 (0.3408-0.7861)	0.4461 (0.2771-0.8021)	0.401
PLR	140.66 (116.09-222.17)	117.77 (53.8-167.92)	0.038
PLT- RBC Ratio	0.519 (0.0313-0.660)	0.0223 (0.0146-0.0465)	0.000
Abs. Neutrophil Count	5189.88 (3203.75-9680.20)	3960.00 (2171.67-7574.59)	0.100
Abs. Lymphocyte Count	1340.96 (908.89-2312.52)	953.75 (712.45-1599.09)	0.024
Abs. Monocyte Count	798.30 (472.36-1103.14)	500.25 (286.93-799.56)	0.006
Abs. Eosinophil Count	48.07 (9.81-188.13)	30.32 (4.66-91.54)	0.303

The platelet count, Platelet-lymphocyte ratio (PLR), PLT-RBC ratio, absolute lymphocyte count, and absolute monocyte count were significantly higher in the dengue group compared to the non-dengue group ($P < 0.05$), while the WBC count was significantly lower in the dengue group ($P < 0.05$). Other parameters such as RBC, PCV, neutrophil count, monocyte count, lymphocyte count, eosinophil count, basophil count, NLR, MLR, absolute neutrophil count, and absolute eosinophil count showed no significant differences between the groups ($P > 0.05$) [Table 2].

Table 3: Multivariable logistic regression analysis of dengue cases by different parameters

Independent variables	Odds ratio	p-value	95% CI for R	
			Lower	Upper
PCV >40%	2.379	0.095	.860	6.582
Platelet <100000	2.243	0.197	.658	7.645
PLR > 120	3.158	0.015	1.253	7.957

Using independent variables, multiple logistic regression analysis was performed to predict dengue cases by various factors. In this study, multivariate analysis shows, the platelet-lymphocyte ratio >120 (p-value 0.015) as a predictor with positive associations to confirm dengue, while the platelet count < 100000 (*P*-value 0.197) and PCV >40% (p-value 0.095) show negative associations [Table 3].

DISCUSSION

Differentiating dengue fever from other febrile illnesses that share similar characteristics is quite challenging. A total of 82 patients participated in this study; 41 tested positive for the 'Dengue Rapid (NS1, IgG, IgM)' test, while 41 tested negative for the same test. The current investigation reveals a significant difference in the hematological parameters between dengue and non-dengue cases. However, there is no noticeable difference in the demographic information of the two groups. The study

does indicate that patients with dengue fever tend to be older than those without dengue, but this difference is not statistically significant (P-value > 0.05). Research by Huang SY et al.[18] found that dengue patients are generally older than non-dengue patients, while a study by Priyanka P et at [3] and Vidya MS et al [13] indicated younger patients with dengue but identified no significant difference.

Our study noted a male predominance in both dengue and non-dengue cases, consistent with findings from Nandasena CK et al.[4] and Juliansen A et al.[6] We observed a lower white blood cell (WBC) count in dengue patients, which aligns with Nandasena CK et al.[4] and Laoprasopwattana K et.,[10] studies that suggest the dengue virus may induce bone marrow suppression. Interestingly, we found a higher platelet count in the dengue group compared to other febrile illnesses, despite most studies, Priyanka P et al [3], Tiwari K et al [15,] and Conroy AL et al [19,] indicating thrombocytopenia in dengue. Research by Chaloemwong J et al.[11] showed that thrombocytopenia was not present on the first day in dengue patients, while some non-dengue patients did have reduced counts. The higher platelet counts in our findings could be due to data collected in the early stages of the illness.

Additionally, the dengue group displayed significantly higher levels of the platelet-lymphocyte ratio (PLR) and other parameters compared to the non-dengue group. While Kotepui M et al. [12] found lower absolute monocyte counts in dengue patients, our study did not reveal significant differences in several other blood parameters. A PLR greater than 120 may help distinguish dengue from non-dengue fevers, with a PLR odds ratio of 3.158. Conroy AL et al. [19] identified leukopenia and thrombocytopenia as valuable indicators, supported by findings from Juliansen A et al. [6] Priyanka P et al. [3,] and Kadadavar SS et al. [17]

CONCLUSION

The study comparing dengue fever to other febrile conditions, we found several significant factors: low total leukocyte count, high absolute lymphocyte and monocyte counts, and elevated platelet-to-lymphocyte ratio (PLR), platelet-to-red blood cell (PLT-RBC) ratio, and platelet count. We concluded that thrombocytopenia is not a reliable early diagnostic marker, but the PLR may help predict dengue viral fever, suggesting that basic hematological parameters could effectively distinguish dengue from other febrile diseases.

Declaration by Authors

Ethical Approval: Approved

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