



ORIGINAL RESEARCH PAPER

Internal Medicine

LEUCOPENIA AS A EARLY PREDICTOR OF THROMBOCYTOPENIA IN DENGUE FEVER PATIENTS: A RETROSPECTIVE OBSERVATIONAL STUDY

KEY WORDS: Dengue fever, leucopenia, thrombocytopenia, predictor, hematological abnormalities

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ABSTRACT

Introduction: The dengue fever is in the form of epidemic in India which occurs usually after rainy season. There is need of adjuvant haematological parameters that can at very initial stage differentiate the dengue fever from other viral fever which are prevalent at the same time. **Aim Of The Study :** This retrospective study was carried out to find association of leukopenia with dengue fever. As screening test for dengue fever are not available in remote areas, so we had tried to access diagnostic power of leukopenia in dengue fever along with thrombocytopenia and its predictive value. **Methods And Materials;** Total 110 dengue fever confirmed by ELISA test for NS1 and/or IgM. Retrieved data were analysed for platelet counts and total leukocyte counts. **Result ;** In Total 110 cases of dengue fever, 55 cases had shown both leukopenia and thrombocytopenia.. The sensitivity of leukopenia alone for diagnosis of dengue fever was only 50.91%, but the specificity was 98.33%. Positive Likelihood Ratio (PLR) of leukopenia to dengue fever was 30.55. Although the sensitivity was decreased to 45.91% if leukopenia with thrombocytopenia was used as diagnostic tool for dengue fever, but specificity was increased up to 99.33% with PLR up to 68.86. The total leukocyte count and platelets were statistically reduced with extreme significance ($P < 0.01$) a multivariate logistic regression analysis revealed that leucopenia was an independent predictor of thrombocytopenia, receiver operator curve has showed that WBC count < 4000 cells had 76.2% sensitivity and 67.1 specificity for predicting thrombocytopenia. **Conclusion;** The leukopenia alone is highly specific for dengue fever, but if combined with thrombocytopenia, specificity is further increased. Leucopenia is a significant predictor of thrombocytopenia in dengue fever patients. Early detection of leucopenia can facilitate timely monitoring and management of thrombocytopenia potentially improving patient outcome.

INTRODUCTION

Dengue fever, a tropical disease caused by the dengue virus, poses a significant public health burden globally, with approximately 390 million infections annually. The disease is characterized by a range of clinical manifestations, from mild febrile illness to severe hemorrhagic fever and shock syndrome.

Hematological abnormalities, particularly leucopenia and thrombocytopenia, are common features of dengue fever and are associated with increased morbidity and mortality.¹

A retrospective, Hospital-based study, which was conducted at a University hospital in southern, enlightened with its Conclusion that leukopenia along with Thrombocytopenia could be used as useful predictive Markers for early diagnosis of dengue fever infection.²

In a study by Lin et al showed that there was significant Leukopenia in 38% of cases of confirmed cases of Dengue fever. After fever onset the leukocytes reached Nadir of 1000-2000/mm³ at 5th to 6th day and Thrombocytes reached nadir 20000-50000/ mm³ at 5th to 7th day. This study suggested that leukopenia in dengue Fever might be caused by virus-induced destruction or Inhibition of myeloid progenitor cells³.

One study by James A et al found that patients with dengue fever Patients had significantly reduced platelets count and Lower leukocytes counts along with neutrophil counts, And a higher frequency of petechiae than other patients Of febrile illness.⁴

Francisca Raimunda F et al studied The laboratory tests, both non-specific [blood count, Platelet count, tourniquet test, prothrombin time (PT), Activated partial thromboplastin time (APTT), liver Function tests and serum albumin concentration] and Specific tests (viral isolation tests and serology for Antibody examination). Most prominent hematological Change, they had observed was leukopenia as well as Sometimes mild leukocytosis at the onset of the

disease, With neutrophilia⁵

MATERIALS AND METHODS

Study Design:

Retrospective observational study

Study site

Patient admitted in the tertiary care hospital Mandya

Study population

110 Patients diagnosed with dengue fever between in the month of July ,August ,September 2024

Inclusion Criteria

1. Confirmed dengue fever diagnosis (NS1 antigen positive or IgM antibody Positive)
2. Age ≥ 18 years

Exclusion Criteria

1. Patients with underlying hematological disorders
2. Patients with chronic liver or kidney disease
3. Patients with HIV/AIDS or immunocompromised status
4. Patients with Other confirmed infections that could causes Leukopenia, such as malaria Or chikungunya.
5. Additionally, patients who were on medications known to affect white blood cell counts were not Included in the study.

Statistics

The Data was analysed by using SPSS 23.0 for windows Software.

RESULTS AND DISCUSSION

Correlation of Leukopenia with Thrombocytopenia:

We had also tried the find out whether there was any correlation between the degrees of thrombocytopenia with the degree of leukopenia. The correlation analysis between degrees of thrombocytopenia with severity of leukopenia was carried out in 110 positive cases.

The correlation coefficient was +0.34. Which was considered

as significant at the level of $p < 0.01$. So it was concluded that there was high correlation between severities of thrombocytopenia with the degree of leukopenia.

Studies on severe neutropenia and Leukopenia in dengue fever were scarce, and its clinical significance is still uncertain. 1912 RTPCR confirmed adult dengue fever patients were admitted to the CDC, Singapore between 2005 and 2008. It had been found that severe neutropenia, defined as absolute neutrophilic count (ANC) $\leq 5000/\text{cumm}$, was found in 11.8% on first day.

ANC nadir occurred on illness day 5. But severe neutropenia was not predictive of more severe disease and not associated with secondary bacterial infections, prolonged hospital stay, prolonged fever, or fatal outcome⁶.

56 (26.6%) patients out of 216 dengue fever IgM positive cases showed leukopenia and 161 (77.1%) patients showed neutropenia in retrospective study done at AKU university in Karanchi.⁷

Majority of patients were discharged without any adverse reaction. It was concluded that haematological parameter were also important clue and should be tested, when a patient came with sign and symptoms of dengue fever.

The role of immunological factors in the pathogenesis of Dengue fever Hemorrhagic Fever (DHF), particularly Dengue fever Shock Syndrome (DSS) was also studied. The complement activity, circulating immune complex (IC), histamine level, platelets and leucocytes were determined in the blood of 30 patients and 43 healthy persons. Besides other parameters, the leukocyte count was significantly reduced ($P < 0.001$). Furthermore, a marked correlation was found between the changes of the above parameters and the clinical stages of the disease.⁸

In the DENV-1 study among the clinically apparent dengue fever patients the mean leukocyte count was $3000/\text{cumm} \pm \text{SD } 780/\text{cumm}$. Although minimum leukocyte counts $P = 0.28$ and the duration of leukopenia ($P = 0.55$) did not reveal significant correlation⁴. Leukopenia was frequently found and may be accompanied by varying degrees of thrombocytopenia.

zong-Shiann et al suggested that leukopenia along with thrombocytopenia was useful for early diagnosis of dengue fever infection. The most notable laboratory findings in confirmed dengue fever case were included leukopenia ($2966 \pm 1896/\text{cumm}$), thrombocytopenia ($102 \pm 45 \times 103/\text{cumm}$). The positive predictive value (PPV) was high for combination of leukopenia with thrombocytopenia.⁷

In the study conducted by Francisca Raimunda F et al leukopenia was the most prominent hematological change, sometimes with counts of less than $2000/\text{cumm}$, as shown in our study in which there were 51% cases were of leukopenia with 15 patients having leukocytes less than $2000/\text{cumm}$ ³.

In present study leukopenia as single parameter had shown high specificity (98.33%) and low PLR. [Table 2] The specificity along with PLR was more increased if the leukopenia was combined with thrombocytopenia. [Table 4]

The t-test showed that the reduction in both total leukocyte count and platelets were statistically extremely significantly ($P < 0.001$) in dengue fever patients as compared to normal age and gender matched healthy control. [Table 5]

The correlation analysis of degree of thrombocytopenia with severity of leukopenia showed the correlation coefficient as +0.34, which is considered as significant at the level of $p < 0.01$ suggesting a high correlation between them.

Table 1: Details of total 110 cases with leukocyte count and platelets counts

	Number & %	Leukocyte count per cumm	Number & %	Platelets count per cumm	Number & %
Dengue fever positive	110 (43%)	<4000	56 (51%)	<1.5 lac	93 (89%)

Table 2: Evaluation of leukopenia alone as diagnostic test

Statistic	Value
Sensitivity	50.91%
Specificity	98.33%
Positive Likelihood Ratio	30.55
Negative Likelihood	0.50

Table 3: Combined parameters study

Platelets + TLC	Dengue fever positive cases
<1.5 + <4000	51
<1.5 + >4000	43
>1.5 + <4000	7
>1.5 + >4000	9
Total	110

Table 4: Evaluation of leukopenia combined with thrombocytopenia as diagnostic test

Statistic	Value
Sensitivity	45.91%
Specificity	99.33%
Positive Likelihood Ratio	68.86
Negative Likelihood	0.54

Table 5: Comparative study of total leukocyte count in dengue fever patients

	Patient (Mean +/- SD)	Control Mean +/- SD	P value
No of cases	220	300	<0.001
TLC (cells/cumm)	5383 +/- 3116	8308.0 +/- 2639	
Platelet	0.8427 +/- 0.51	1.98 +/- 0.45	

CONCLUSION

There is significant reduction in leukocyte count as well as platelets count in dengue fever patients and high correlation between severities of thrombocytopenia with the degree of leukopenia. We have concluded our study that the duo of leukopenia and thrombocytopenia can be used as good negative predictor for dengue fever. Leukopenia is a significant predictor of thrombocytopenia in dengue fever patients.

Early detection of leukopenia can facilitate timely monitoring and management of thrombocytopenia, potentially improving patient outcomes.

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