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Original Research Article

Correlation between Serological and Hematological Markers in Dengue Fever: Insights from a Tertiary Care Hospital

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Abstract:

Background: Dengue is a mosquito-borne viral infection that has become a significant global public health concern, with a wide range of clinical manifestations. It is a leading preventable cause of morbidity and mortality among both children and adults, particularly in tropical and subtropical regions. Early diagnosis is essential for administering appropriate care, which can significantly reduce morbidity. Evaluating both serological and hematological parameters plays a vital role in the diagnosis and prognosis of the disease.

Aims and Objectives: To find out correlation between serological and hematological parameter of dengue.

Methodology: A study was conducted over six months, from September 2023 to February 2024, Total 646 suspected cases of dengue were included in the study and their hematological and serological profiles were recorded. The study was conducted at the Department of Microbiology, C.U. Shah Medical College and Hospital, Surendranagar, Gujarat.

Result: Out of 646 samples, a total of 128 samples were found positive for dengue NS1 antigen, IgM, and IgG antibodies using the Dengue Combo Rapid Test, a qualitative detection method based on rapid chromatographic immunoassay. The most prevalent hematological abnormality observed was thrombocytopenia, affecting 79% of cases, followed by leucopenia in 47% of cases.

Keywords: Dengue Fever,NS1 Antigen, Haemoglobin, Red blood Cell, Total Leukocyte Count, Platelets.

Introduction

Dengue fever is an arthropod-borne viral disease that belongs to the family Flaviviridae and the genus Flavivirus. It is a significant global health concern, particularly prevalent in tropical and subtropical regions. This arboviral disease is primarily transmitted by Aedes mosquitoes, especially Aedes aegypti and Aedes albopictus, which transmit the virus during a blood meal. [1] The virus contains three structural genes that encode the capsid protein (C), membrane protein (M), and envelope protein (E). It also has seven nonstructural (NS) genes that encode the NS1, NS2A, NS2B, NS3, NS4A, NS4B, and NS5 proteins. [2]

The disease manifests in a spectrum of clinical presentations, ranging from mild flu-like symptoms to severe forms such as dengue hemorrhagic fever and dengue shock syndrome. Understanding the immunological and hematological changes in dengue-positive patients is crucial for effective diagnosis, management and prognostication of the disease.[3] When a mosquito bites, the dengue virus infects human monocytes, macrophages, and dendritic cells, initiating a complex immune response. The virus manipulates host immune mechanisms, resulting in increased vascular permeability, thrombocytopenia, and altered hematological parameters. The severity of the disease is influenced by the interaction between viral factors and the host's immune response, with secondary infections often leading to more severe outcomes due to antibody-dependent

enhancement.[5] The diagnosis of dengue fever is based on clinical symptoms, laboratory confirmation, and epidemiological factors. Serological tests, including the detection of dengue virus-specific IgM and IgG antibodies or NS1 antigen, play a key role in early diagnosis.

Management primarily involves supportive care, with an emphasis on fluid management to prevent shock, monitoring for complications and providing symptomatic relief. As there is no specific antiviral treatment for dengue fever, early detection and timely supportive care are crucial for effective management. [6] Serological testing is crucial in diagnosing dengue fever, as it helps determine the stage of infection and the dynamics of the immune response. These tests typically detect dengue virus-specific IgM and IgG antibodies, as well as antigens like the envelope (E) protein and non-structural protein 1 (NS1). IgM antibodies appear early in the infection, indicating a recent or acute infection, while IgG antibodies suggest past exposure or a secondary infection. The presence and timing of these antibodies are key to distinguishing between primary and secondary dengue infections, which directly informs clinical management decisions. [6]

Hematological changes in dengue fever are diverse and play a key role in assessing disease severity. Common findings include leucopenia, thrombocytopenia, and hemoconcentration. Leucopenia typically occurs during the febrile phase and is associated with viral replication. Thrombocytopenia is a defining feature of dengue and can lead to bleeding complications in severe cases. Hemoconcentration occurs as a result of plasma leakage due to increased vascular permeability, a critical factor in the development of dengue hemorrhagic fever and dengue shock syndrome. [1]

Comparing serological and hematological parameters in dengue-positive patients provides important insights into disease progression and severity. For example, patients with secondary dengue infections typically show a faster and stronger antibody response, resulting in earlier detection of IgG antibodies compared to those with primary infections. Additionally, the extent of thrombocytopenia and hemoconcentration is closely linked to disease severity, helping with risk assessment and timely intervention. Understanding the relationship between these markers supports better clinical decision-making, including decisions regarding hospitalization, fluid management, and monitoring for complications. The current study aims to explore and correlate serological and hematological parameters in patients suffering from dengue viral infection. [6]

Materials and Methods

This study was conducted from September 2023 to February 2024 at the Department of Microbiology, C.U. Shah Medical College & Hospital, Surendranagar, Gujarat. The study was approved by the institutional ethics committee of C.U. Shah Medical College & Hospital, Surendranagar, Gujarat.

Venous blood samples of suspected cases were collected for both hematological and serological tests. For hematological analysis, a complete blood profile was performed using EDTA samples on the UniCelDxH 800 Beckman Coulter Cellular Analysis System. Peripheral blood examination and complete blood counts were conducted for all the samples, and the following hematological parameters were analyzed: hemoglobin (Hb), red blood cell (RBC) count, total leukocyte count (TLC), and platelet count (P/C).

A serum sample was used to detect dengue infection through a qualitative detection method based on the rapid chromatographic immunoassay (Dengue NS1 + IgM/IgG Combo Rapid Dengue Day-1 Test). The sample negative for all serological markers was classified as a dengue-negative case. The mean values of each parameter were calculated using SPSS software, and the Chi-square test was applied to determine the p-value and assess the correlation between hematological and serological parameters.

Result

A total of 646 clinically suspected cases were tested for dengue, of which 128 were found to be positive and 518 were negative. Among the 128 positive cases, the highest number, 46 cases (25.13%), occurred in November, followed by 40 cases (17.17%) in October, and 23 cases (23.46%) in September. Fewer cases were observed in the subsequent months, with 12 cases (17.91%) in December, 4 cases (10.81%) in January, and 3 cases (08.33%) in February (Table No.-1).

Table 1: Month-Wise Distribution of Positive and Negative Samples

Month	Total No. Of Samples	Total No. Of Positive Samples (%)	Total No. Of Negative Samples (%)
Sep-23	98	23 (23.46)	75(76.53)
Oct-23	225	40 (17.17)	185(82.22)
Nov-23	183	46(25.13)	137(74.86)
Dec-23	67	12(17.91)	55(82.08)
Jan-24	37	4(10.81)	33(89.18)
Fab-24	36	3(08.33)	33 (91.66)
TOTAL	**646**	**128** (19.82)	**518** (80.18)

Figure 1 illustrates that, out of the 128 positive cases, 109 (85.15%) were detected during the monsoon and post-monsoon season (September 2023 to November 2023), while only 19 (14.85%) cases were positive during the winter season (December 2023 to February 2024).

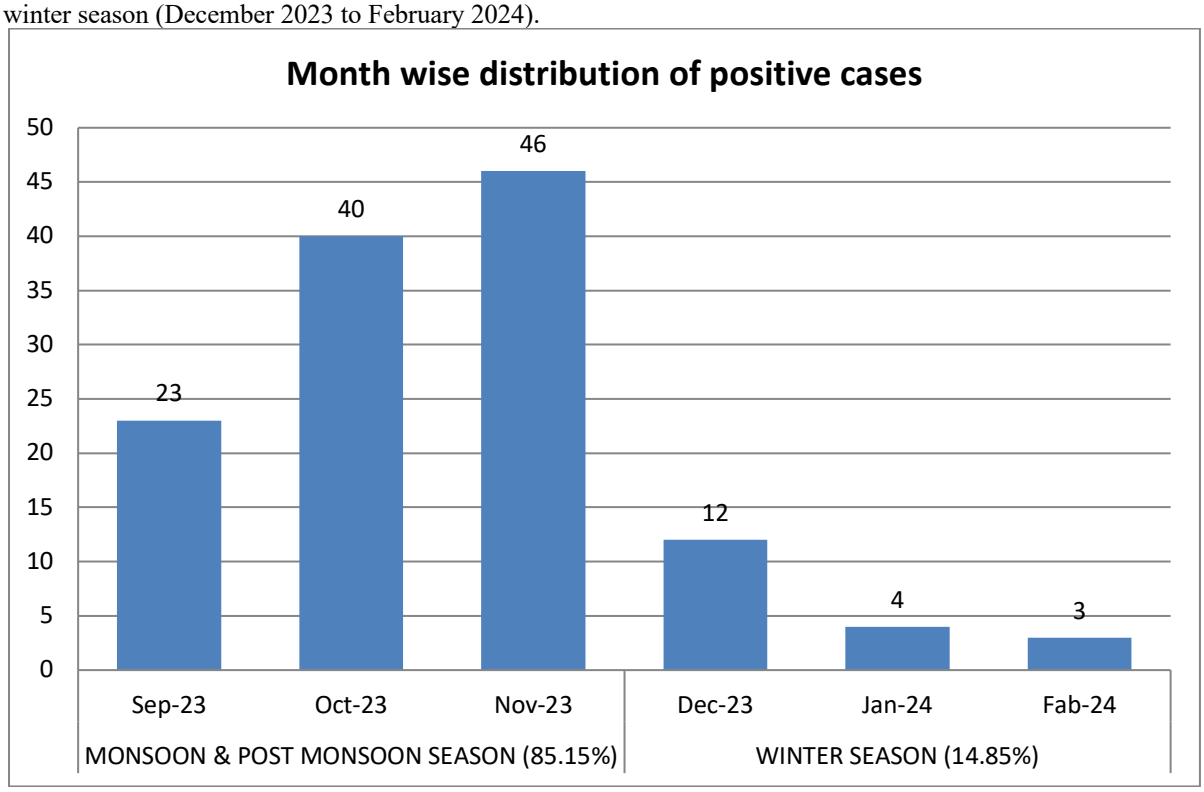

Figure 1: Month wise distribution of positive cases

The data shows that among 128 dengue-positive patients, 78 were male and 50 female. In males, the highest number of cases (49, or 62.82%) were in the 16-30 years age group, followed by 21 cases (26.92%) in the up-to-15 year's group. Fewer cases were seen in the 31-45 years (5 cases) and above 60 years (3 cases) groups. Similar pattern was found in female patients also. Dengue was less common in older age groups, particularly those above 45 (Table No. 2).

Table 2: Demographic Data Distribution According To Age and Gender

Gender	Total N=128	Age Group	No. Of Dengue Positive Cases
Male	78	Upto 15	21
		16-30	49
		31-45	5
		46-60	Nil
		Above 60	3
Female	50	Upto 15	11
		16-30	25
		31-45	8
		46-60	2
		Above 60	4

Based on the serological markers, the majority of patients tested positive for NS1 antigen (116 cases, or 90.62%), followed by NS1 and IgM (6 cases, or 4.68%), IgG (3 cases, or 2.34%), IgM (2 cases, or 1.56%), and both IgG and IgM (1 case, or 0.78%) (Table No. 3).

Table 3: Distribution According To Serological Marker

Serological Marker	No. Of Dengue Positive Cases (%)
NS1	116 (90.62)
NS1&IgM	6(4.68)
IgG	3(2.34)
IgM	2(1.56)
IgG & IgM	1(0.78)

However, a significant fall was not noted in the leukocyte count (mean value: 4438/cu mm), but a decrease in platelet count (mean value: 103,601/Cu mm) was observed.

Table No.4 shows the relationship between various hematological parameters (i.e. Hemoglobin (Hb), Red Blood Cells (RBC), Total Leukocyte Count (TLC), Platelet Count (PLT)) and serological parameters (i.e. NS1 antigen, IgM, IgG) in dengue-positive patients. The table includes the mean values of each parameter, standard deviation (SD), and the p-value for statistical significance for different combinations of serological markers. TLC (Total Leukocyte Count) shows significant variations between different serological groups, particularly with NS1, NS1 + IgM, and IgM, IgM + IgG groups, indicating possible immune responses or bacterial co-infections.

RBC and Hemoglobin levels show little to no significant differences across the serological groups. Platelet counts (PLT) did not show statistically significant differences between groups except for minor variations, which may be influenced by factors like bleeding or immune response.

Table 4: Correlation Between serological and hematological marker

Sr. No.	Name of Hematological parameter	Name of Serological parameter	No.	Mean	SD	P Value
1	HB	NS1	116	12.8	2.06	0.659
		NS1 + IgM	6	13.1	3.46	0.801
		IgG	3	12.9	1.53	0.941
		IgM	2	13.5	3.11	0.766
		IgM + IgG	1	14.1	-	1.000
2	RBC	NS1	116	4.5	0.66	0.140
		NS1 + IgM	6	4.5	0.95	0.706
		IgG	3	5.2	0.86	0.071
		IgM	2	5.02	0.91	0.517
		IgM + IgG	1	4.7	-	**0.006**
3	TLC	NS1	116	4369	2134.28	**0.005**
		NS1 + IgM	6	4761	2636.46	**0.024**
		IgG	3	4133	928.74	**0.000**
		IgM	2	8250	6019.16	**0.043**
		IgM + IgG	1	3800	-	**0.000**
4	PLT	NS1	116	103586	72669.159	0.073
		NS1 + IgM	6	63000	24083.1	0.472
		IgG	3	108000	129577.1	0.134
		IgM	2	213000	97076.1	0.405
		IgM + IgG	1	114000	-	0.996

***<0.05 is significant, HB- Hemoglobin, RBC-Red blood Cell, TLC-Total Leukocyte Count, PLT- Platelets.**

Discussion

Dengue epidemics are commonly associated with the rainy season. A study conducted in Assam, Lucknow (India), and Pakistan found that dengue transmission occurs throughout the year, with a peak during the monsoon and post-monsoon season

(Dutta P et al. [16] Khan et al.[17]; Tripathi et al.(18)). Similarly, in the current study, the majority of cases (85.15%) were reported during the monsoon and post-monsoon seasons (September to November), while 14.85% occurred in the winter season (December to February)[16]. In our study, a slight male predominance was observed, with 60.9% of patients being male and 39.1% female. Similar findings were reported by Patel PM et al.[10] and Rai et al.(1) where a higher number of male patients were noted. Hypothetically, some studies suggest that the increased risk of dengue exposure in males could be attributed to occupational and recreational activities that lead to greater exposure to mosquito bites. While dengue fever affects all age groups in India, younger age groups are more commonly infected. This observation is supported by our study, where the highest number of cases was found in the 16-30 years age group. Similar results were reported by Dinkar et al.[19] and Naik NS et al.[20].

In the current study, leucopenia was observed in 47.6% of cases, which is similar to the findings of Jameel et al.[17] at 56%, Patel PM et al.(10) at 44%, and Rai et al.(1) at 37% [1, 16, 17]. However, other studies, such as those by Arshad et al.[18] and Rashmi et al.(19), reported leucopenia in a larger proportion of patients, ranging from 49% to 60% [18, 19]. Leucopenia is typically caused by bone marrow suppression during the acute phase of the infection. A small subset of patients (1.5%) showed leucocytosis, which may be attributed to a secondary bacterial infection or the presence of hemorrhagic shock.[1]Thrombocytopenia is a common finding in dengue patients, and in the present study, it was observed in 79% of cases. Similar results were reported by Rai et al.[1] at 62.6% and Patel PM et al.[10] at 58.4%.

The mean platelet count in this study was also reduced to 120 × 10^3/μL. This decrease in platelet count may be attributed to several factors, including direct bone marrow suppression by the virus, anti-dengue antibody-mediated platelet destruction, peripheral consumption of platelets, and isolated viral replication within platelets. Additionally, the release of high levels of platelet-activating factor may promote platelet consumption and increase the adhesiveness of vascular endothelial cells, further contributing to thrombocytopenia. A significant reduction in platelet count was observed as the disease progressed, particularly in secondary dengue infections, highlighting the importance of regularly monitoring platelet levels during the course of illness to prevent bleeding complications.[1]Out of the 646 cases tested for the NS1 antigen, 116 cases (90.62%) were positive exclusively for NS1 antigen, 4.68% were positive for both NS1 and IgM antibodies, and 1.56% were positive only for IgM antibodies.

In comparison, studies by Rai et al.[1] and Mehta et al.[11] reported that 72.3% and 64.4% of cases, respectively, were positive only for NS1 antigen, while 9% and 35.6% of cases were positive solely for IgM antibodies. (Table 5)

Table 5: Correlation of serological marker with other studies.

Sr. No.	Serological marker	Present study Surendranagar (%)	Mehta et al. [11] Jamnagar (%)	Rai et al. [1] Dehradhun (%)
1	NS1	90.62	64.5	72.3
2	NS1 & IgM	4.68	-	11.9
3	IgG	2.34	-	-
4	IgM	1.56	35.5	9
5	IgG & IgM	0.78	-	2

The NS1 antigen is now available for early diagnosis of dengue infection, detectable from day 1 of fever in both primary and secondary infections. When NS1 is positive, repeat testing is unnecessary, as it serves as a highly specific marker for dengue.

This underscores the importance of including NS1 testing in diagnostic panels, as a significant number of cases could be missed without it. [11]

Dengue-specific IgM/IgG antibodies have long been used for diagnosis, but they may not be detectable before the third day of fever in secondary dengue infections. IgG is less reliable due to its persistence from both clinical and subclinical infections, making it harder to interpret results.

In endemic areas, IgM is a better marker for acute and secondary dengue cases, while rising IgG titers in paired serology help confirm infections. However, repeat testing for confirmation is often not feasible in routine practice. NS1 antigen testing within the first four days of illness eliminates the need for repeat testing. [11]

In conclusion, the current study found that dengue cases were significantly higher during the monsoon and post-monsoon season compared to the winter season. The majority of patients tested positive exclusively for the NS1 antigen using the Dengue NS1 + IgM/IgG Combo Rapid Test.

A higher number of dengue-positive cases were observed in male patients than in female patients, with most cases occurring in the 16–30 years age group. Platelets count and Total leukocyte count was the only hematological parameter that reported consistently low in all the dengue positive cases.

The study clearly reveals that disease is seasonal in nature and poses significant morbidity. The robust strategy needs to be implemented to prevent the cases of dengue during and after the monsoon season.

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