

Original Research Article

<https://doi.org/10.20546/ijcmas.2024.1306.016>

## An Analysis of Clinical, Haematological, Biochemical Profile in Dengue IgM Antibody Positive Patients at a Tertiary Care Hospital

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### ABSTRACT

Dengue fever is a seasonal and emerging acute mosquito-borne arboviral illness affecting tropical and subtropical countries. Prevalence of dengue infection increase in monsoon and post monsoon period. These infections may be asymptomatic or may lead to classical dengue fever (DF), or dengue hemorrhagic fever (DHF) with or without shock. Owing to lack of any diagnostic marker and any specific clinical symptoms to identify cases that will have a severe disease outcome, early diagnosis and close monitoring with symptomatic treatment is necessary. Aims and Objectives: To estimate the prevalence of dengue and to co-relate the serological, clinical, haematological and biochemical data for early diagnosis of severity of dengue infection. Materials and Methods: A cross sectional study was conducted over a period of 6 months from April 2023 to June 2023 at ACS Medical College and Hospital, Chennai, a tertiary care center. Serological analysis of 30 dengue IgM antibody positive serum samples by capture ELISA method and correlation between different clinical, serological, hematological and biochemical parameters was done using SPSS software. Results: Out of 30 Dengue IgM positive patients, 26 (86.6%) were males, with mean age group of 15-25 years. 29 (96.6%) patients had fever and 13 (43.3%) had vomiting. 1 patient had co infection with malaria. Thrombocytopenia was observed in 23(76.6%) and leucopenia in 17 (56.6%) patients. 22 (73.3%) patients had elevated transaminases. Conclusion: This study highlights the importance of clinical history, examination and investigations in timely diagnosis. This along with, helps in early treatment and reduces morbidity & mortality rate.

#### Keywords

Dengue fever,  
Dengue  
hemorrhagic fever,  
Dengue shock  
syndrome, Dengue  
virus

#### Article Info

Received:  
25 April 2024  
Accepted:  
29 May 2024  
Available Online:  
10 June 2024

### Introduction

Dengue is a viral infection transmitted to humans through the bite of infected mosquitoes. Dengue virus is a single-stranded positive-sense RNA virus belongs to the Flavivirus genus of the Flaviviridae family (Sharada *et al.*, 2021). The female *Aedes aegypti* and *Aedes albopictus* mosquito during the blood meal transmit the

virus and cause the disease (Rai *et al.*, 2019). The incidence of dengue has grown dramatically around the world in recent decades. The highest number of dengue cases was recorded in 2023, affecting over 80 countries in all regions of WHO (2024). Over the past few years, dengue fever (DF) has become much more common in developing countries like India. This is largely due to unplanned urbanization and population migration from

rural to urban regions, which often lacks basic sanitation services (Trupti Dongre and Pragati Karmarkar, 2015). Incidence of developing DHF-DSS is very high when there is previous infection (Sharma *et al.*, 2018). Dengue is the primary cause of hospital admissions in the majority of Indian states (Sharada *et al.*, 2021).

These infections range from asymptomatic to severe fatal disease that may lead to classical dengue fever (DF), or dengue hemorrhagic fever (DHF) with or without shock (Shah *et al.*, 2019).

The most prevalent type of symptomatic DENV infection frequently manifests as severe headache, fever with bone and joint pain (Rai *et al.*, 2019). A small percentage of dengue patients advance to the disease's severe forms like DHF and DSS which are distinguished by petechiae, hypovolemia, and increased microvascular permeability (Bich Chau *et al.*, 2010).

Secondary infection is often, but not always, linked to the development of a lifelong immunity following infection and the advancement of the illness to more serious levels. Treating dengue infection is still supportive since there are currently no effective antiviral medications available (Bhatt *et al.*, 2013).

Laboratory diagnosis of dengue involves serological testing for the detection of anti-DENV IgM/IgG antibodies or direct detection of virus antigen by Enzyme Linked Immunosorbent Assay (ELISA) and viral nucleic acid by reverse transcription PCR (RT-PCR).

The primary method for diagnosing acute infection is the detection of IgM and IgG anti-dengue virus antibodies and Non Structural 1 (NS1) protein using an in vitro immunochromatographic assay (Karia *et al.*, 2011).

The hallmarks of primary infections are elevated dengue-specific IgM antibodies four to five days after fever onset and elevated IgG antibodies only seven to ten days later. In secondary infections, the level of IgM antibodies is lower than in primary infections, while levels of IgG antibodies rise rapidly, even during the acute phase (Patel *et al.*, 2018).

Hemoconcentration and thrombocytopenia indicators are the most researched and used haematological criteria for making clinical decisions (Nandwani *et al.*, 2021). The monitoring of the hematocrit concentration should be done in accordance with the number of illness days. It is

important to remember that thrombocytopenia (less than  $100 \times 10^9/L$ ) is linked to a 20% increase in hematocrit from the patient's baseline upon progression to DHF (Azin *et al.*, 2012).

Biochemical variables that are most commonly altered in liver function tests include serum albumin concentrations, gamma-glutamyl transpeptidase and alkaline phosphatase levels, serum aspartate aminotransferase (AST), and serum alanine aminotransferase (ALT) (Azin *et al.*, 2012).

Early diagnosis, close monitoring, and symptomatic treatment are required due to the lack of a diagnostic marker and specific clinical symptoms to identify cases that will have a severe illness outcome (Shah *et al.*, 2019). Monitoring these markers can therefore aid in lowering the morbidity and death associated with dengue (Rai *et al.*, 2019).

This study is aimed to assess the serological and haematological dynamics of patients with dengue fever in order to diagnose early, to increase the sensitivity of the screening by healthcare professionals in the most serious cases and try to identify laboratory markers that may indicate this evolution.

## Materials and Methods

**Study design** – A cross sectional study was conducted over a period of 6 months from April 2023 to June 2023 at ACS Medical College and Hospital, Velappanchavadi, a tertiary care center.

**Ethical consideration and permission** -The study was approved by scientific and ethical committee of the institute.

**Study population** –The population included in this study were all patients who came with symptoms suggestive of Dengue fever.

**Inclusion criteria** –serum samples which were positive for dengue IgM antibody (by capture ELISA method, MICROLISA).

**Exclusion criteria** – serum samples which were negative for dengue IgM antibody (by capture ELISA method, MICROLISA).

**Statistical methods** – using SPSS software.

(1) A data collection form that possessed an extensive list of—(1) **Demographic details**: age, gender, duration of hospital stay, comorbidities, past history of dengue infection; (2) **Clinical history**: presenting signs and

symptoms observed during first examination, duration of illness at admission, vitals examination; and (3) **Hematological parameters:** observed in the first blood sample: hemoglobin level (Hb), total leucocyte count (TLC), hematocrit (Hct), platelet count, mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW-CV); (4) **Biochemical parameters:** transaminase-Aspartate Transaminase (AST) and Alanine Transaminase (ALT) were documented.

The serum samples obtained from suspected dengue infection were initially tested with immunochromatography card tests, a rapid test device for dengue IgM antibody detection.

Consequently, the samples were checked with IgM capture ELISA, MICROLISA method. The positive control and Negative Control from the test kit were put up. The ELISA microtiter plates were read with a Bio-rad ELISA reader. Optical density values were recorded and analyzed, and the results were read according to the manufacturer's instructions.

Hemogram profile was done in Sysmex 7-part Hematology Analyzer.

## Results and Discussion

In the present study, total 30 Dengue positive cases were studied, 26 (86.6%) were males and 4 (13.3%) were females and the male: female ratio was 1.7:1 (Table 2). Majority of cases were in age group of 15 to 25 years (36.6%) (Table 3).

Based on the combination of other infection, 1 (0.3%) had coinfection with malaria and 4 (13.3%) had reinfection (Table 4). Out of 30 patients, 29 (96.6%) had fever, 13 (43.3%) vomiting, 12 (40%) had joint pain with myalgia, 5 (16.6%) had headache, 3 (10%) had rashes as shown in (Table 5).

In this study, 23 (76.6%) had thrombocytopenia, 17 (56.6%) had leucopenia, 8 (26.6%) had lymphocytosis, 5 (25%) had raised ESR, 4 (13.3%) had elevated prothrombin time and 2 (6.6%) had anemia as shown in (Table 6). As per Table 7, 22 (73.3%) patients had elevated liver enzymes and 28 (93.3%) patients had normal bilirubin level. Sodium, potassium and creatinine levels remains unchanged in all patients. Table 8 shows mean values of haematological, biochemical and

serological parameters based on classification of dengue infection according to National Center for Vector Borne Diseases Control. Due to changing climate, urbanization, poor living conditions and inadequate waste management, vector borne diseases like dengue fever are becoming more common.

Dengue is a common disease that affects nearly 31 states and union territories in India, mostly in urban areas and towns. Kerala, Tamil Nadu, Karnataka, Orissa, Delhi, Maharashtra, and Gujarat have reported the highest number of instances. From India, all four dengue serotypes have been isolated (Shah *et al.*, 2019).

Out of 30 positive patients, only 4 (13.3%) females have been reported. The lower infection rates in females of Asian community could also be due to the fact that many of them remain at home and are less exposed to this vector borne infection.

Also, the immune response in females is more competent than in males, resulting in greater production of cytokines, thus providing protection. Rai *et al.*, (2019) 1 (0.14%), Patel *et al.*, (2018) 1 (37%), Shah *et al.*, (2019) 1 (17.3%) also found the similar findings (Rai *et al.*, 2019; Patel *et al.*, 2018; Shah *et al.*, 2019).

In this study, we found that the mean age group affected was 21-30 years. This was consistent with the other studies on dengue in India like Sharada *et al.*, (2021) 1 (83%). Out of 30 patients 1 had co infection of Malaria. Malaria is common with dengue because the mode of transmission is same (Karia *et al.*, 2011).

Fever was observed on admission in 96.6% DENV positive patients. This finding is important clinically as sometimes dengue patients may be ignored when there is no fever on admission (Chandana Wijesinghe *et al.*, 2022; Banerjee *et al.*, 2011).

Bleeding tendencies were significantly higher among DENV positive patients. Notably, 27.7% of DENV-2 positive patients had bleeding tendencies.

These findings are in agreement with studies done in different geographical regions (Chandana Wijesinghe *et al.*, 2022). DF is nicknamed "breakbone fever" and it was therefore not surprising that the 12 (40%) patients as per Table 5 had muscle, bone, and joint pains similar to the findings of Eric S. Halsey *et al.*, (2012) 1 study (74.5%).

**Table.1** Dengue case classification and level of severity according to WHO guidelines

<b>GROUP A - Dengue without warning sign (mild dengue)</b>	<b>GROUP B -Dengue with warning sign (moderate dengue)</b>	<b>GROUP C - Severe dengue</b>
<ul style="list-style-type: none"> <li>• Fever</li> <li>• Normal platelet count</li> <li>• Without complication</li> <li>• No evidence of capillary leakage</li> </ul>	<ul style="list-style-type: none"> <li>• Fever</li> <li>• Abdominal pain</li> <li>• Bleeding manifestation</li> <li>• Giddiness/headache</li> <li>• Increase in hematocrit/ decrease in platelet value</li> </ul>	<ul style="list-style-type: none"> <li>• Shock</li> <li>• Bleeding</li> <li>• Organ involvement (dysselectrolytemia, acidosis)</li> </ul>

**Table.2** Distribution of cases according to gender

<b>Gender</b>	<b>Cases (n=30)</b>	<b>Cases (%)</b>
<b>Males</b>	26	86.6
<b>females</b>	4	13.3

**Table.3** Distribution of cases according to age.

<b>Age in Years</b>	<b>Cases (n=30)</b>	<b>Cases (%)</b>
<b>0-10 years</b>	7	23.3
<b>11-20 years</b>	9	30
<b>21-30 years</b>	11	36.6
<b>31- 40 years</b>	3	10
<b>&gt;41 years</b>	nil	Nil

**Table.4** Distribution of cases with co infection and re infection

<b>n=30</b>	<b>Cases (n)</b>	<b>Cases (%)</b>
<b>Co infection</b>	1	0.3%
<b>Re infection</b>	4	13.3%

**Table.5** Distribution of cases according to symptoms

<b>Symptoms</b>	<b>Cases (n)</b>	<b>Cases(%)</b>
<b>fever</b>	29	96.6
<b>Vomiting</b>	13	43.3
<b>Joint pain with myalgia</b>	12	40
<b>Abdomen pain</b>	2	6.6
<b>Rashes</b>	3	10
<b>Headache</b>	5	16.6
<b>Subconjunctival haemorrhage</b>	2	6.6

**Table.6** Distribution of various haematological parameters

Tests	Normal n	Abnormal n
Haemoglobin	28 (93.3%)	2 (6.6%)
Total count	13 (43.3%)	17 (56.6%)
Differential count	22 (73.3%)	8 (26.6%)
Platelet	7 (23.3%)	23 (76.6%)
Prothrombin time	26 (86.6%)	4 (13.3%)
ESR	15 (75%)	5 (25%)

**Table.7** Distribution of liver function tests parameters.

Test	Normal n	Elevated n
Total bilirubin	28 (93.3%)	2 (6.6%)
SGOT	8 (26.6%)	22 (73.3%)
SGPT	9 (30%)	21 (70%)
Urea	29 (99.7%)	1 (0.3%)
Creatinine	30(100%)	
Sodium	30(100%)	
Potassium	30(100%)	

**Table.8** Classification of dengue infection according to National Center for Vector Borne Diseases Control

Cases	n	Haematology (mean)			Biochemical (mean)		Serology		
		Hb	TC	PLT	SGOT	SGPT	NS1 Ag	IgM	ELISA
WS -	28	14	3000	1 lakh	119	77	75%	5%	100%
WS +	1	15	3000	82,000	1	0	+	-	+
SD	1	12	3000	10,000	70	42	NA	NA	+

(WS – warning sign, SD – severe dengue)

Comparing peripheral blood parameters (hemogram) to the normal reference range showed a large range of variance from normal to decrease or increase. The classical hematological derangements described in dengue infection are thrombocytopenia, leucopenia, and hemoconcentration (Nandwani *et al.*, 2021). Thrombocytopenia is caused by depressive viruses that decrease bone marrow in addition to the direct and antibody-mediated death of platelets and megakaryocytes. Dengue fever is known to cause leukopenia, which is caused by the virus directly suppressing the bone marrow (Patel *et al.*, 2018). These results were likewise reported by most of the patients; however, a considerable percentage also showed anemia and leukocytosis.

In the present study thrombocytopenia was observed in 23 (76.6%) and leucopenia in 17 (56.6%) as observed in (Patel *et al.*, 2018) 1 (86.5%).

There is a wide range of hepatic dysfunction associated with dengue, from asymptomatic increase of transaminases to fatal fulminant hepatic failure (Anusha Mruthyunjaya Swamy *et al.*, 2021). In our study, 73.3% of patients had elevated transaminases. SGOT was elevated in 73.3% of the patients and SGPT in 70% of the patients, which was similar to the findings of various other studies (Ding *et al.*, 2016; Anusha Mruthyunjaya Swamy *et al.*, 2021). Dengue fever as a disease is self-limiting. Morbidity and mortality are caused by dengue haemorrhagic fever. Since there is no antiviral



medication available, supportive therapy, fluid and electrolyte supplementation, and other treatment methods are available. Therefore, rather than waiting for the condition to worsen, an early and rapid diagnosis together with a full clinical, haematological, biochemical profile is useful in providing the patient with early supportive treatment. The only method to stop the disease's spread is through vector control as there are currently no vaccines for it.

Rapid urbanization in developing countries increases prevalence of dengue. Effective implementation of vector control measures through efforts toward vector breeding source reduction help in reduction of the dengue prevalence in community. Laboratory changes associated with dengue fever begins to appear on day three, peak on day five, and return to normal by day eleven. The current study's findings have emphasized the significance of the clinical assessment, as well as the haematological and biochemical profiles, in early assessment of severity in dengue patients.

This would minimize the risk of major DF complications leading to morbidity and mortality would be reduced.

### Limitations

This study has some limitations. First, our utilization of a clinic based passive surveillance system, compared with hospital-based surveillance, most likely sampled patients with less severe disease.

The important limitations of this study were the relatively short study duration of six months and that we did not correlate the parameters with day of illness.

### Acknowledgements

I would like to acknowledge the immense support given by my Assistant Professor DrA. Asha and, Dr B. Ananthi my guide and HOD for providing inputs of their knowledge and guiding me in the study. Besides I would like to thank my family who were supportive in this project.

### Author's Contributions

All authors listed have made a substantial, direct and intellectual contribution to the work and approved for publications.

### Funding

None.

### Data Availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

### Declarations

**Ethical Approval** Not applicable.

**Consent to Participate** Not applicable.

**Consent to Publish** Not applicable.

**Conflict of Interest** The authors declare no competing interests.

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### How to cite this article:

Rajalakshmi, K., A. Asha and Ananthi, B. 2024. An Analysis of Clinical, Haematological, Biochemical Profile in Dengue IGM Antibody Positive Patients at A Tertiary Care Hospital. *Int.J.Curr.Microbiol.App.Sci.* 13(6): 148-154. doi: <https://doi.org/10.20546/ijcmas.2024.1306.016>