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Original Research Article

EVALUATING CLINICAL, LABORATORY, AND IMAGING MARKERS IN DENGUE: ASSOCIATIONS WITH DISEASE SEVERITY AND NS1 ANTIGEN LEVELS

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ABSTRACT

Background: Aim: To study clinical, laboratory and imaging markers of patients of dengue fever and to correlate severity of disease with early presentation (NS1 Antigen positive) and late presentation (IgM Antibody positive).

Materials and Methods: The study was performed on patients with Dengue fever admitted in medicine department of a tertiary care teaching hospital. A total of 200 dengue positive patients were evaluated. The study was conducted during the period between May 2023 to July 2024. This was an observational descriptive study.

Results: In our study of 200 dengue patients, laboratory and imaging evaluation proved pivotal for early diagnosis and risk assessment. NS1 antigen positivity showed a significant positive correlation with radiological findings, particularly ascites, pleural effusion, and gallbladder wall thickening detected by ultrasonography and chest radiography, underscoring its value in identifying plasma leakage. However, NS1 positivity alone did not reliably predict complications such as bleeding, shock, or multi-organ dysfunction.

Conclusion: This study shows dengue severity correlates with early NS1 positivity, warning signs, and imaging abnormalities. Young adults, especially males, were more affected. Combining chest radiography, ultrasonography, and laboratory findings provides a cost-effective strategy for early detection, risk stratification, and improved outcomes, thereby reducing dengue-related morbidity and mortality.

Keywords: NS1 Antigen Levels, Dengue, Imaging Markers, clinical and laboratory.

INTRODUCTION

Dengue fever is the most important arthropod-borne viral infection of humans. Worldwide, an estimated 2.5 billion people are at risk of infection, approximately 975 million of whom live in urban areas of tropical and subtropical countries like Southeast Asia, the Pacific and the Americas.[1] The rural areas are also being increasingly affected in regions of Africa and the eastern Mediterranean. Dengue fever (DF) has become a prominent infectious disease with outbreaks in many parts of the world. DF epidemics have reached almost 120 countries and in many of these countries it has a high incidence.[2]

During recent decades DF has become the second most prevalent mosquito-borne infection after malaria. Cases of DF have reached 50 million, while cases of Dengue haemorrhagic fever (DHF) are touching a staggering several hundred thousand per

year. The most endemic regions include Latin America, Asia, and the Caribbean.

The first outbreak of dengue fever in India was recorded in 1812.[3] In spite of preventive measures taken by the respective governments since then, recurrent outbreaks have occurred, and over the last 10 to 15 years DF has been the major cause of hospitalization and mortality after acute respiratory and diarrheal infections.[4]

This study was done to evaluate the clinical, laboratory and imaging profile to correlate with outcomes and complications of dengue fever.

MATERIALS AND METHODS

The study was performed on patients with Dengue fever admitted in medicine department of a tertiary care teaching Hospital. A total of 200 dengue positive patients were studied. The study was conducted during the period between May 2023 to July 2024. This is an observational descriptive study.

Inclusion Criteria: After clinical evaluation and laboratory investigations, those confirmed patients satisfying the National Vector Borne Disease Control Program (NVBDCP) criteria for Dengue fever, Dengue haemorrhagic fever and Dengue shock syndrome were included in the study. **Criteria for inclusion as Dengue fever in this study (according to NVBDCP GUIDELINES):**

- Fever since 2 to7 days
- Retro orbital pain
- Arthralgia
- Myalgia
- Rash
- Haemorrhagic manifestations

Exclusion Criteria: After clinical evaluation and laboratory investigations, those patients not satisfying the NVBDCP criteria for Dengue fever.

All patients were clinically evaluated with detailed history & examination. All patients were subjected to routine investigations which included complete blood count, peripheral smear, blood urea, serum creatinine, blood sugar, serum bilirubin, serum glutamate pyruvate transaminase and ECG. Besides, all patients were subjected to Dengue NS1 antigen and IgM antibody based on the day of presentation since fever. Baseline chest radiograph and USG of chest & abdomen was carried out for all patients. Based on course of disease, CT scan was carried out for the patients to look for complications.

Outcome variables: The following parameters were assessed.

- Comparison of the severity of the disease when patients presented early (NS1 antigen positive) vs when patients presented late (IgM ELISA positive).
- Clinical features in various stages of dengue infection were noted.
- Imaging features to assess disease severity.

Statistical Analysis: The data obtained was coded and entered into Microsoft Excel Worksheet. The categorical data was expressed as rates, ratios and proportions and comparison was done using chi-square test. The continuous data was expressed as mean ± standard deviation (SD). The diagnostic accuracy of NS1 antigen testing, in predicting dengue infection was determined by sensitivity, specificity, positive predictive value and negative predictive value. Kappa agreement was used to correlate the agreements. A probability value ('p' value) of less than or equal to 0.05 was considered as statistically significant.

RESULTS

In this study most of the patients (58%) were aged less than 30 years followed by 30 to 40 years (16%), 41 to 50 years (12%) and 51 to 60 years (19%). The mean age of the study population was 33.29 ± 13.14 years. 68% of patients were males and 32% of females. The male to female ratio was 2.12:1.

According to NVBDCP guidelines, all patients (100%) satisfied the clinical case definition of dengue fever. 7.5% patients fulfilled the diagnostic criteria for Dengue haemorrhagic fever while 4% patients were found to be suffering from Dengue shock syndrome. Out of the 200 patients in the study, 5% also had co-infection with malarial parasite. Patients were graded into three categories of hospitalization based on duration of onset of symptoms. 17% patients got hospitalized within 2 days of symptom onset while 19% got hospitalized after 7 days of symptom onset. Majority of the patients (64%) were hospitalized within 2-7 days of symptom onset.

Symptoms were recorded for all 200 patients. All patients presented with fever (100%). Headache and myalgia was reported by 82% and 75% of patients respectively. Less common symptoms include bleeding manifestations, arthralgia and rashes which were present in 24%, 32% and 37% of the patients respectively. [Table 1]

Table 1: Symptoms Wise Distribution

Symptoms	Number of Patients
Fever	200 (100%)
Headache	164 (82.0%)
Myalgia	150 (75.0%)
Rash	74 (37.0%)
Arthralgia	64 (32.0%)
Bleeding manifestation	51(25.5%)
Retro orbital pain	8 (4.0%)

On clinical evaluation at presentation, all patients had tachycardia (100%). Narrow pulse pressure was recorded in 59 % of the patients. 46% of patients had hepatosplenomegaly on examination. 16 % patients had clinically demonstrable haemorrhagic manifestations in the form of petechiae, purpura or ecchymosis. Other subset of recorded signs included tachypnoea, postural hypotension, cold clammy extremities and increased capillary refill time. Out of 51 patients (25.5%) who presented with symptoms of bleeding manifestations, 35.4% had petechiae. Life threatening bleeding was present in three patients, out of which one patient had hematemesis and two patients suffered from intracranial bleed. [Table 2]

Table 2: Bleeding Manifestation Distribution

Bleeding manifestation	Number of patients
Petechiae	17 (33.3%)
Epistaxis	9 (17.6%)
Purpura	6 (11.7%)
Bleeding per rectum	5 (9.8%)
Bleeding per vagina	4 (7.8%)
Hematuria	3 (5.8%)
Bleeding per vagina	4 (7.8%)
Life threatening bleed	3 (5.8%)

All patients were monitored for various complications which can develop during the course of disease. Most common complications being ascites, pleural effusion, hepatitis and acute kidney injury which were present in 34%, 38%, 27% and 19.5 % of patients respectively. A small subset of patients also developed life threatening complications as mentioned in table 3. [Table 3]

Table 3: Distribution of various complications

Complication	Number of patients
Pleural effusion	76 (38%)
Ascites	68 (34%)
Hepatitis	54 (27%)
Acute kidney injury	39 (19.5%)
Proteinuria	39 (19.5%)
Circulatory collapse	8 (4%)
ARDS	7 (3.5%)
Intracranial bleed	2 (1%)
ADEM	1 (0.5%)
Myocarditis	1 (0.5%)

Various laboratory tests were done to assess the disease progression & complications. On evaluation of hemogram, 14.5 % patients had haemoglobin less than 10 gm/dl while thrombocytopenia was present in 88% of the patients with leukopenia being present in 55% of the patients. Out of 176 patients with thrombocytopenia, 56 patients had severe thrombocytopenia with platelets count being <50,000/mm³. On LFT evaluation, high bilirubin levels were recorded in 27% of the patients with 38% patients having elevated SGPT. Coagulation profile (PT, INR, aPTT) was altered in 6% of the patients. Various laboratory investigations carried out are as mentioned in table 4. [Table 4]

Table 4: Laboratory Investigations

Laboratory investigations	Parameters	Number of patients
Serum sodium	<135 mEq/L	132 (66.0%)
Albumin	<5.5 g/dL	111 (55.5%)
Serum potassium	>5.5 mEq/L	93 (46.5%)
SGPT	>55 IU/dL	76 (38%)
Creatinine	>1.5 mg/dL	69 (34.5%)
Platelets	< 50,000/mm3	56 (28 %)
Bilirubin	>1.2 mg/dl	54 (27%)
Urine routine	Albuminuria	39 (19.5%)
ABGA	Metabolic acidosis	15 (7.5%)
Coagulation profile	Prolonged	12 (6.0%)

Table 5: Chest Radiograph Findings

Findings	Number of patients
Normal Radiograph	106 (53%)
Pleural Effusion (unilateral & bilateral)	76 (38%)
Pulmonary Infiltrates / Edema	18 (9%)

Out of 200 patients subjected to chest radiography, pleural effusion was recorded in 76 patients with bilateral effusion being recorded in 52 patients. All 56 patients with severe thrombocytopenia <50,000/mm³ were found to have pleural effusion ($p < 0.05$). All 200 patients who underwent chest

radiography were also scanned on chest ultrasonography with 50 % of the patients detected to have pleural effusion. These patients included 12 % patients who were found to have normal chest radiograph, highlighting the importance of USG being sensitive to detect small quantity of pleural effusions which were not visualized on chest radiograph.

Table 6: USG Findings

Findings	Number of patients
Normal chest scan	100 (50 %)
Pleural effusion	100 (50 %)
Gall bladder wall thickening	94 (47 %)
Ascites	68 (34 %)
Normal abdomen scan	58 (29 %)
Hepatomegaly	42 (21 %)
Features of polyserositis	40 (20 %)
Pericholecystic fluid	22 (11 %)
Splenomegaly	16 (08 %)

Abdominal ultrasonography was also performed on all 200 patients which revealed Gall bladder wall thickening as a most common isolated finding in 47 % patients (Fig 1). Ascites was found in 34 % of patients with 20 % of patients showing massive ascites. All these 20 % patients with massive ascites had severe thrombocytopenia & were also found to have features of polyserositis in the form of pleural effusion, GB wall thickening and hepatomegaly ($p < 0.05$).

Computed tomography scans were also performed in 10 % of the cases which presented with life threatening manifestations or developed life threatening manifestations like severe breathlessness, altered sensorium & haematuria during the course of disease. Out of 20 patients who underwent CT scans, 08 patients were scanned for chest, 04 were scanned for head & 08 were scanned for both chest & abdomen. Four patients were diagnosed with pulmonary edema (Fig 2), two patients each with ARDS & Intracranial bleed.

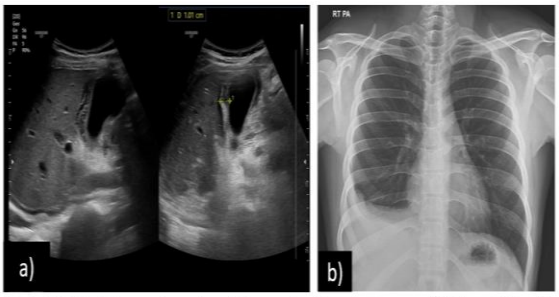

Fig 1: a) USG abdomen of a patient of dengue showing edematous and thickened GB wall suggestive of serositis b) Chest radiograph of the same patient showing right sided pleural effusion consistent with the serositis

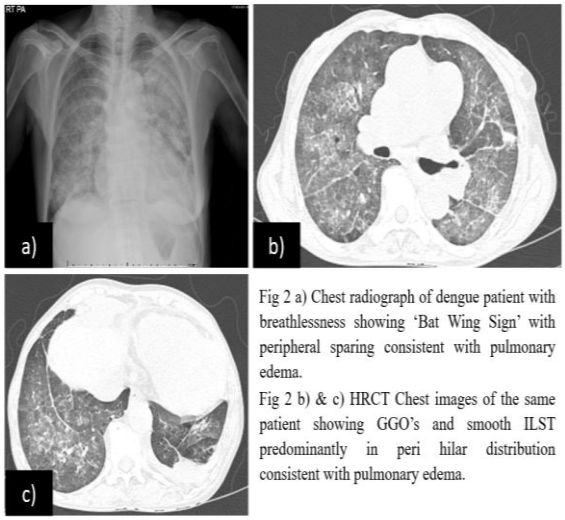

Fig 2 a) Chest radiograph of dengue patient with breathlessness showing 'Bat Wing Sign' with peripheral sparing consistent with pulmonary edema.

Fig 2 b) & c) HRCT Chest images of the same patient showing GGO's and smooth ILST predominantly in peri hilar distribution consistent with pulmonary edema.

NS1 antigen test & IgM antibody test was carried out for all 200 patients with 114 (57%) patients being positive for NS1 Antigen. 80 patients out of these 114 patients were investigated 2-3 days after the onset of symptoms. Out of 200 patients, 43% (86 patients) tested positive for IgM Antibody out of which 60 patients tested positive after 5th day of onset of symptoms (Table 8). A statistically significant correlation was found between disease severity and NS1 Antigen. Patients with positive NS1 antigen were more found to have Gallbladder wall thickening ($p < 0.01$), pleural effusion and ascites ($p < 0.05$)

Table 7: Day wise distribution of serological tests

Day from onset of symptom	Number of patients positive for NS1 Ag	Number of patients positive for IgM Ab
1	20	0
2	34	0
3	43	0
4	10	1
5	4	32
6	3	16
7	0	30
>7	0	7

Out of 200 patients, 85.5% patients were managed conservatively while 8% required transfusion of blood product (platelet rich concentrate / whole blood/packed cells). 2% patients also required inotropic support while 0.5% needed haemodialysis. 3.5% of the patients needed non-invasive ventilatory support in the form of BiPAP while 0.5% had to be mechanically intubated.

While 199 patients recovered completely with the treatment, one death was recorded in the patient who was hospitalized for a longer duration due to multiple complications of dengue shock syndrome in the form of ARDS with intracranial bleed, acute kidney injury, pancytopenia and hypotension. While statistically significant correlation was found between NS1 antigen & ultrasound findings, no statistically significant correlation could be established between severity of disease & the serological markers of NS1 antigen or IgM antibody positivity.

DISCUSSION

Dengue fever continues to pose a major global public health challenge, particularly in endemic regions such as South and Southeast Asia. The evaluation of clinical, laboratory, and imaging markers is vital not only in predicting the severity of illness but also in guiding early treatment thereby reducing morbidity and mortality. Our study conducted on 200 patients with confirmed dengue infection, provides insights into the associations of demographic characteristics, symptom and sign distribution, NS1 antigen positivity, and imaging findings with disease severity and outcomes.

In our study, the mean age was 33.9 years. This observation parallels findings from other Indian and Southeast Asian studies,[5,6,7] done by Khan, Kisat et al & Ukey, Bondade et al where the disease burden is disproportionately higher among the productive age group. The vulnerability of this population can be attributed to increased outdoor exposure and higher likelihood of mosquito contact.

The gender distribution revealed 2.1:1 in favour of male predominance. This finding was comparable to other studies which include Amker, Arima et al,[8,9] Several sociocultural factors such as increased outdoor activity among men, thereby increasing Aedes aegypti exposure. Therefore, our findings reinforce the need for public health messaging and preventive measures directed at young and middle-aged adults, who contribute the most socioeconomically.

The most common presenting symptoms in our study were fever & headache, followed by myalgia, rash, arthralgia and bleeding manifestations which were comparable to other studies,[10,11,12] conducted by Kumar, Rao et al, Daniel, Rajamohanan et al & Hasan, Riaz et al. These findings are consistent with the classical description of dengue fever. Bleeding manifestations, ranging from mucosal bleeding to petechiae, were observed in a subset of patients. Their occurrence correlated with thrombocytopenia and higher severity grades, in agreement with the WHO classification of dengue. In our study, 24% patients presented with bleeding manifestations which was comparable to the studies conducted by Bashir, Mohammad et al & Fujimoto, Koifuan et al.[18,19]

Rash was noted in nearly one-third of the patients. These symptom and sign distributions highlight the heterogeneous clinical presentation of dengue, emphasizing the importance of maintaining a high index of suspicion, particularly during seasonal epidemics. 64 % of the patients were hospitalized between 2-7 days from onset of symptoms which was comparable to other studies conducted by Gibson, Reinaldo et al & Woon, Hor et al.[13,14] This can be attributed to widespread availability of NS1 antigen testing. Our data also showed that patients who were hospitalized earlier in the course of illness had lower incidence of severe dengue, fewer complications, and better overall survival.

The complications associated with dengue are a direct consequence of viral virulence, host immune response, and the capillary leak syndrome. In our study of 200 patients, the dominant complications observed during the critical phase were ascites & pleural effusion. These complications reflect the importance of highlighting the pathophysiology of capillary leak resulting in third-space collections manifesting as ascites and pleural effusion. Our observations were comparable with findings of Acharya, Rodrigo et al.[15]

Other subset of complications were pertaining to end organ damage in the form of hepatitis, and acute kidney injury. Hepatitis can be explained by direct viral hepatotropism and immune-mediated cytotoxicity. Patients with liver involvement were more likely to have concurrent ascites and gallbladder wall edema, reflecting systemic vascular leak. The pathogenesis of dengue-related AKI can be explained by multiple factors which include hypovolemia/renal hypoperfusion from plasma loss, rhabdomyolysis, direct viral or immune-mediated renal injury, and sepsis/secondary infections. A recent meta-analysis estimated a pooled AKI prevalence around the single digits (approximately 6–11% across studies), while cohort studies in hospitalized or severe dengue populations report higher rates (often >10%) as mentioned in study done by Bushi al.[16]

In our study, the most consistent laboratory abnormalities were disturbances in the hemogram — chiefly thrombocytopenia accompanied by leukopenia and variable haemoconcentration — together with deranged liver function tests. Thrombocytopenia is the single most commonly reported hematologic alteration in dengue and was a pervasive finding in our series. Mechanisms include decreased platelet production (bone-marrow suppression), immune-mediated platelet destruction, and platelet activation/consumption during systemic inflammation. Leukopenia (particularly neutropenia)

was also commonly observed, consistent with marrow suppression seen in acute dengue. These findings were comparable to the Malathesa, Ashwini et al study.[17]

In our study of 200 laboratory-confirmed dengue patients, imaging—principally abdominal/chest ultrasonography and chest radiography—played a central role in detecting plasma leakage, guiding risk stratification, and informing early management decisions. Ascites, pleural effusion and gallbladder wall thickening were the principal imaging abnormalities identified, and their presence correlated clinically with warning signs, NS1 positivity and need for closer monitoring.

Importantly, the presence of pleural effusion on chest radiography was strongly correlated with NS1 positivity and higher disease severity. Patients with bilateral effusions or larger collections were more likely to require hospitalization, fluid management, and supportive interventions. Gallbladder wall thickening, often described as a hallmark ultrasonographic finding in dengue, was strongly predictive of disease severity, correlating with abdominal pain and elevated liver enzymes.[20]

Another important finding in our study was role of NS1 antigen testing. The imaging findings of ascites, pleural effusion and gallbladder wall thickening showed a clear positive correlation with these radiological markers. This observation can be explained by the fact that NS1 positivity reflects a higher antigen burden during the early febrile phase, which in turn is associated with the endothelial perturbation that produces sonographic third-spacing.[21] Despite this concordance between NS1 and radiological findings, NS1 positivity in our cohort did not independently predict clinical complications.

To summarize, our study provides a systematic integration of clinical, laboratory, and imaging parameters in a sizable cohort of 200 patients, providing a holistic view of disease stratification. Few clinically relevant points include timely NS1 antigen testing which is a valuable early diagnostic and prognostic tool, especially in the first week of illness. Consistency of Imaging findings (pleural effusion, gallbladder wall thickening, ascites) complement laboratory markers and should be routinely considered in patients with warning signs. Young adults remain the most vulnerable group, emphasizing targeted preventive measures. Early risk stratification using combined markers allows timely fluid management, prevention of shock, and improved outcomes.

While our study provided meaningful insights, it is not without limitations. Being a single-centre study, generalizability to other populations may be limited. Serial measurements of NS1 antigen titers were not performed, which could have provided additional data on dynamic correlations with severity. Additionally, not all patients underwent advanced imaging or serological follow-up due to resource constraints. Future multicentric studies with larger samples and serial monitoring are warranted.

CONCLUSION

This study demonstrates that dengue severity is closely linked with early NS1 antigen positivity, clinical warning signs, and characteristic imaging abnormalities. Age and gender patterns highlight the disease burden in young adults, with males slightly more affected. The integration of chest radiography and ultrasonography with laboratory and clinical findings offers a practical, low-cost strategy for early identification of severe cases. Early recognition and stratification based on these parameters can substantially improve patient outcomes and reduce dengue-related mortality.

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