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Original Research Article

Optimizing diagnostic cascades: evaluating the sensitivity of NS1 antigen versus antibody serology in a rapidly evolving dengue outbreak

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ABSTRACT

Background: Dengue fever, caused by DENV-1-4 serotypes, remains a major public health challenge with clinical manifestations ranging from mild febrile illness to severe complications such as Dengue Hemorrhagic Fever (DHF) and Expanded Dengue Syndrome (EDS). During the devastating 2023-2024 outbreak in Bangladesh, rapid and accurate diagnosis became essential for early intervention. This study evaluated the diagnostic performance of NS1 antigen testing compared with IgM/IgG serology and described the clinico-demographic profile of affected patients.
Methods: This prospective observational study was conducted at BIRDEM General Hospital, Dhaka, from June 2023 to February 2024 during the peak dengue epidemic. A total of 292 laboratory-confirmed dengue patients were enrolled. Sociodemographic data, clinical manifestations, and laboratory findings were collected from hospital records following ethical approval. Diagnostic sensitivity of NS1 antigen and antibody serology was compared using SPSS version 26 according to STROBE guidelines.
Results: The mean age of participants was 35.63±15.22 years; 54.8% were male and 83.9% were urban residents. Diabetes mellitus was present in 25.7% of cases. NS1 antigen showed the highest positivity rate (82.3%), whereas IgM and IgG positivity were 13% and 9.2%, respectively. Fever (76%), body ache (63.7%), headache (42.1%), and vomiting (41.1%) were common presenting symptoms. Thrombocytopenia (70.9%) and elevated SGPT (50.3%) were frequent laboratory abnormalities. Neuropsychiatric symptoms such as insomnia and irritability were observed in 7.9% of patients.
Conclusions: NS1 antigen is a superior early diagnostic marker during dengue outbreaks. Early identification of metabolic comorbidities and hepatic involvement may improve timely management and reduce dengue-related morbidity and mortality in resource-limited settings.

Keywords: Bangladesh, Clinical predictors, Dengue fever, NS1 Antigen, Outbreak management, Serology

INTRODUCTION

Dengue fever is currently one of the most important mosquito-borne viral diseases affecting tropical and subtropical countries worldwide. The disease is caused by four distinct serotypes of dengue virus (DENV-1, DENV-2, DENV-3, and DENV-4) belonging to the *Flaviviridae* family. Transmission mainly occurs through the bites of infected female *Aedes aegypti* and *Aedes albopictus* mosquitoes, which commonly breed in stagnant water near densely populated urban areas.[1] Rapid urbanization, climate change, increased population density, and inadequate sanitation have significantly contributed to the expansion of dengue transmission globally.[2,4]

The clinical presentation of dengue infection ranges from asymptomatic illness to severe and life-threatening complications such as Dengue Hemorrhagic Fever (DHF), Dengue Shock Syndrome (DSS), and Expanded Dengue Syndrome (EDS). Patients frequently present with sudden onset of high-grade fever, severe headache, retro-orbital pain, myalgia, arthralgia, vomiting, and rash.[3] in severe cases, dengue may progress to plasma leakage, severe thrombocytopenia, hemorrhage, shock, and multi-organ dysfunction, leading to increased morbidity and mortality if early diagnosis and treatment are delayed.[6,15]

Over the past two decades, dengue incidence has increased dramatically worldwide. It is estimated that approximately 390 million infections occur annually, with nearly 96 million cases manifesting clinically.[3] Asia carries the greatest burden of dengue infection, accounting for almost 70% of global cases.[2] The World Health Organization (WHO) has identified dengue as a major emerging public health threat because of its rapidly expanding geographic distribution and recurrent epidemics.[14] Bangladesh has experienced repeated dengue outbreaks over recent years, with the 2023-2024 epidemic becoming one of the deadliest outbreaks recorded in the country.[1,5]

Previously considered a seasonal urban infection confined mainly to Dhaka city, dengue has now spread widely across different regions of Bangladesh.[13] Environmental changes, irregular rainfall patterns, inadequate vector control programs, and increased human mobility have contributed to sustained viral transmission and recurrent outbreaks.[2,12] Additionally, the coexistence of non-communicable diseases such as diabetes mellitus has complicated disease management, as diabetic patients are more vulnerable to severe dengue manifestations and prolonged hospitalization.[8]

Timely laboratory confirmation remains essential for appropriate patient management during outbreaks. Among available diagnostic methods, detection of dengue NS1 antigen is considered highly effective during the early febrile phase of infection, whereas IgM and IgG antibodies generally become detectable later in the disease course.[6,8] Early identification through NS1 antigen testing enables clinicians to recognize high-risk patients promptly and initiate supportive treatment before progression to severe disease. Despite increasing dengue prevalence in Bangladesh, limited studies have compared the diagnostic performance of NS1 antigen and antibody-based serological tests during large-scale outbreaks.

Therefore, this study aimed to evaluate the diagnostic sensitivity of NS1 antigen compared with Dengue IgM and IgG serology among laboratory-confirmed dengue patients admitted to BIRDEM General Hospital during the 2023-2024 outbreak. The study also assessed the clinico-demographic characteristics, laboratory findings, and disease outcomes associated with dengue infection in a tertiary care hospital setting.

METHODS

This prospective observational study was conducted at BIRDEM General Hospital, Dhaka, Bangladesh, from June 2023 to February 2024 during the peak dengue outbreak period. A total of 292 laboratory-confirmed dengue patients admitted to the hospital were enrolled consecutively.

Patients of both sexes aged ≥18 years with confirmed dengue infection by NS1 antigen and/or IgM/IgG serology were included in the study. Patients with incomplete clinical records, coexisting severe chronic illnesses, or alternative confirmed infectious diseases were excluded.

Detailed sociodemographic information, clinical presentations, comorbidities, laboratory parameters, and outcome variables were collected from hospital records using a structured data collection form. Diagnostic evaluation included Dengue NS1 antigen, Dengue IgM, and Dengue IgG testing. Additional laboratory investigations included platelet count, C-reactive protein (CRP), serum glutamic pyruvic transaminase (SGPT), and HbA1c levels where indicated.

Patients were monitored for disease progression, complications, duration of hospital stay, and clinical outcomes. Glycemic status was categorized based on HbA1c levels, where HbA1c >6.5% was considered uncontrolled glycemia.Ethical approval for the study was obtained from the Institutional Review Board of BIRDEM General Hospital. Patient confidentiality was strictly maintained throughout the study.

All data were analyzed using Statistical Package for the Social Sciences (SPSS) version 26. Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequency and percentage. Chi-square test was used to determine associations between categorical variables, and p-values <0.05 were considered statistically significant.

RESULTS

Demographic and clinical characteristics

A total of 292 patients were enrolled during the dengue epidemic. The cohort's mean age was 35.63±15.22 years, with a notable male predominance (54.8%). A significant majority of the participants resided in urban areas (83.9%) and maintained an active lifestyle (63.4%). Regarding metabolic health, 68.5% of the patients had a normal Body Mass Index (BMI), while 25.7% (n=75) were known to have diabetes mellitus (DM).

Clinical presentation was primarily characterized by high-grade fever (>102° F), reported in 76% of cases, typically lasting between 2 and 5 days. The most prevalent constitutional symptoms accompanying the febrile phase were body ache (63.7%), headache (42.1%), and vomiting

(41.1%). While hemodynamic status remained stable for most, 5.1% of patients presented with systolic hypotension (<90 mm Hg).

Table 1: Baseline clinico-demographic characteristics of the study population (n=292).

Variable	Statistics
Age (years), Mean±SD	35.63±15.22
Gender (male), n (%)	160 (54.8)
Residence (urban), n (%)	245 (83.9)
Lifestyle (active), n (%)	185 (63.4)
Diabetes mellitus, n (%)	75 (25.7)
Fever grade (high), n (%)	222 (76.0)

Laboratory and diagnostic profiles

The Diagnostic Sensitivity Analysis (Bar Diagram) at figure 1 illustrates the significant disparity in the sensitivity of diagnostic markers. The NS1 antigen emerged as the primary sentinel marker with a positivity rate of 82.3% (n=241). In contrast, the serological markers showed much lower yield during the acute phase, with Dengue IgM and Dengue IgG being positive in only 13.0% (n=38) and 9.2% (n=27) of cases, respectively. This highlights the necessity of prioritizing antigen detection for early triage during rapid surges. Diagnostic triage relied heavily on the Dengue NS1 antigen.

Table 2: Diagnostic markers and key laboratory findings (n=292).

Laboratory parameter	Positive/Raised, N (%)
Dengue NS1 antigen	241 (82.3)
Dengue IgM antibody	38 (13.0)
Dengue IgG antibody	27 (9.2)
Platelet count (low)	207 (70.9)
CRP level (raised)	234 (80.1)
SGPT (raised)	147 (50.3)

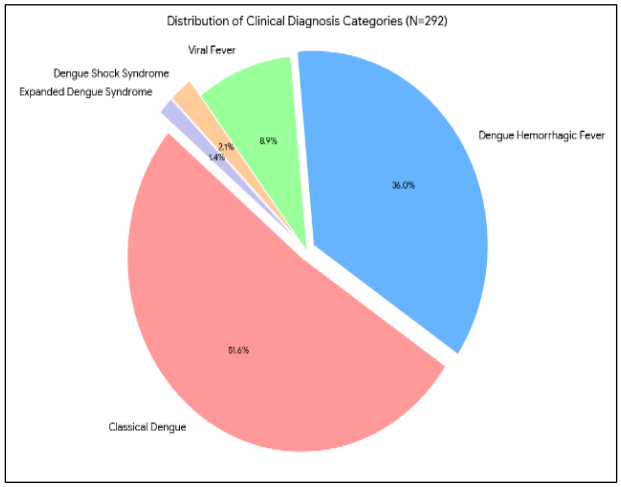

Figure 1: Distribution of clinical diagnosis categories (n=292).

Hematological analysis revealed pervasive thrombocytopenia in 70.9% of patients. Furthermore, systemic inflammation and hepatic involvement were evident through elevated C-Reactive Protein (CRP) levels in 80.1% and raised Serum Glutamic Pyruvic Transaminase (SGPT) in 50.3% of the cases.

Disease progression and outcomes by glycemic status

The clinical diagnosis distribution (pie chart) at figure 2 provides a clear breakdown of the clinical severity observed among the 292 patients. The majority of the cohort presented with classical dengue fever (51.7%) and dengue hemorrhagic fever (36.0%). More severe manifestations, including dengue shock syndrome (2.1%) and expanded dengue syndrome (1.4%), were also identified, underscoring the multisystemic nature of the outbreak. Systemic complications occurred in 14.38% of patients, with Acute Kidney Injury (AKI) being the most frequent major complication (7.2%).

The study found that glycemic control significantly influenced clinical trajectories. Patients with uncontrolled glycemia (HbA1C>6.5%) experienced a significantly higher incidence of systemic complications (26.2% vs. 12.4%, p=0.018) and a higher frequency of clinical deterioration (7.7% vs. 0.4%, p=0.010) compared to those with controlled glycemic status.

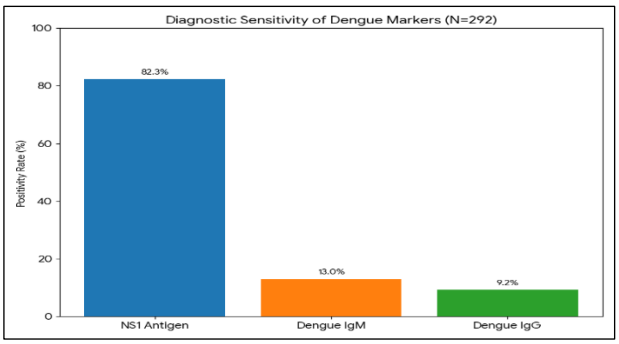

Figure 2: Diagnostic sensitivity of dengue markers (n=292).

Table 3: Clinical outcomes and complications stratified by glycemic status (n=292).

Outcome variable	Controlled glycemia (n=250), N (%)	Uncontrolled glycemia (n=42), N (%)	P value
Systemic complication	31 (12.4)	11 (26.2)	0.018*
Disease deterioration	1 (0.4)	3 (7.7)	0.010*
Hospital stay >3 days	122 (48.8)	28 (66.7)	0.032*
Improved status	249 (99.6)	39 (92.9)	0.010*

*p<0.05 considered statistically significant using Chi-square test

DISCUSSION

This study provides a comprehensive overview of the clinico-demographic and laboratory characteristics of dengue patients admitted to BIRDEM General Hospital during the severe 2023-2024 outbreak in Bangladesh. The findings demonstrate a predominance of young adult male patients from urban areas, highlighting the continuing concentration of dengue transmission in densely populated metropolitan settings. Similar demographic trends have been reported in previous studies conducted in Bangladesh and other South Asian countries.[16,17]

The mean age of the participants in the present study was 35.63±15.22 years, with most patients belonging to the economically productive age group. This observation is comparable to findings reported by Prattay et al, where the majority of dengue cases occurred among adults aged 18-40 years.[16] The increasing involvement of adults may be associated with occupational exposure, mobility, and changing epidemiological patterns of circulating dengue serotypes.[18] Male predominance was also observed in this study, consistent with previous regional reports suggesting higher outdoor exposure among men and greater healthcare-seeking behavior in male populations.[19]

Urban residence was identified in the majority of patients, reflecting the strong association between dengue transmission and rapid urbanization. Poor waste disposal systems, water stagnation, overcrowding, and climate variability create favorable breeding environments for *Aedes* mosquitoes in urban Bangladesh.[20] Similar associations between urban density and dengue transmission have been documented in previous epidemiological studies.[21]

Fever, body ache, headache, and vomiting were the most common presenting symptoms in this study. These findings are consistent with established clinical patterns of dengue infection described in earlier studies.[17,22] Thrombocytopenia and elevated liver enzymes were also highly prevalent among patients, indicating significant hematological and hepatic involvement during acute infection. Hepatic dysfunction in dengue has been linked to direct viral injury, immune-mediated inflammation, and circulatory compromise.[23]

One of the major findings of this study was the significantly higher positivity rate of NS1 antigen compared with IgM and IgG antibody tests. NS1 antigen positivity was detected in more than four-fifths of patients, confirming its value as an early diagnostic marker during the acute febrile phase. Previous studies have similarly demonstrated that NS1 antigen detection offers high sensitivity during the first few days of illness before antibody seroconversion occurs.[24] Early diagnosis through NS1 testing can facilitate prompt clinical monitoring and reduce progression to severe dengue complications.

Another important observation was the association between uncontrolled diabetes mellitus and adverse clinical outcomes. Patients with elevated HbA1c levels experienced significantly higher rates of systemic complications and prolonged hospitalization. Diabetes has been recognized as an important risk factor for severe dengue due to endothelial dysfunction, impaired immune response, and increased inflammatory activity.[25] These findings emphasize the importance of careful monitoring of dengue patients with metabolic comorbidities during outbreaks.

Despite most patients recovering with supportive management, severe manifestations including dengue hemorrhagic fever, dengue shock syndrome, and expanded dengue syndrome were observed in a subset of cases. These findings reinforce the need for early diagnosis, risk stratification, and appropriate supportive care to reduce dengue-related morbidity and mortality in resource-limited healthcare settings.

This study has several limitations. Being a single-center hospital-based study, the findings may not fully represent the overall dengue situation across Bangladesh. The relatively limited sample size and observational design may restrict the generalizability of the results. Additionally, long-term follow-up of patients was not performed, limiting assessment of delayed complications and outcomes. Some clinical data were dependent on hospital records, which may have introduced information bias. Despite these limitations, the study provides important insights into the diagnostic utility of NS1 antigen testing and the clinical characteristics of dengue patients during a major outbreak.

CONCLUSION

While most of our patients (98.6%) improved, the emergence of severe manifestations like DHF (36%) and DSS (2.1%) serves as a stark reminder of the disease's potential lethality. The results of this study can guide clinicians at all levels to facilitate early diagnosis and intervention, particularly using NS1 testing and vigilant monitoring of metabolic and hepatic markers. Strengthening public awareness and vector control programs remains the most effective long-term strategy to mitigate the morbidity and mortality of future outbreaks in Bangladesh.

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