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Original Article

In-depth Analysis of the Discrepancy in Dengue Test Results and Association with Various Factors

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ABSTRACT

Introduction: *Dengue fever remains a significant public health challenge worldwide, especially in tropical and subtropical regions. Accurate and timely diagnosis is crucial for effective management and control. This study aims to explore the discrepancies in dengue test results and the association with demographic, symptomatic, and environmental factors.* ***Methods & Materials:*** *This observational study was conducted over six months at Dhaka Medical College, involving 77 participants presenting with symptoms suggestive of dengue. Data were collected on demographic details, clinical symptoms, laboratory parameters, and environmental risk factors. Dengue diagnosis was confirmed using NS1 antigen and IgG/IgM serological tests.* ***Result:*** *The study predominantly involved children aged 6-10 years (33.77%), with a mean age of 8.66±8.73 years, and a higher prevalence of males (55.84%) residing in urban areas (57.14%). A significant majority (89.61%) had no prior dengue infection. The NS1 antigen test was positive in 81.82% of cases, while serological responses varied, with 18.18% IgG positive, 14.29% IgM positive, and 12.99% positive for both. Environmental risk factors such as inadequate mosquito control measures were prevalent (55.84%). Notable laboratory variability suggested acute inflammatory responses, with high mean values in WBC count and serum ferritin levels. A strong inverse correlation was observed between lymphocyte and neutrophil percentages.* ***Conclusion:*** *The study highlighted significant discrepancies in dengue test results influenced by various factors, including environmental risks and laboratory parameters. These findings emphasize the need for comprehensive diagnostic strategies that incorporate both antigen and antibody testing to improve the accuracy of dengue diagnostics and enhance public health interventions.*

Keywords: *Dengue fever, NS1 Antigen, IgG/IgM, Serological Tests, Diagnostic Discrepancies, Environmental Factors, Laboratory Parameters*

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INTRODUCTION

Dengue fever, a mosquito-borne viral disease, poses a significant public health challenge globally, especially in tropical and subtropical regions. The disease is caused by the dengue virus (DENV), which comprises four serotypes that can cause a wide spectrum of symptoms, ranging from mild febrile illness to severe forms such as dengue hemorrhagic fever and dengue shock syndrome [1]. The global burden of dengue has been profound, with a dramatic increase in the number of cases over the past decades. Epidemiological data indicate that an estimated 390 million dengue infections occur worldwide each year, with a significant proportion leading to dengue-related illness [2]. Accurate and timely diagnosis of dengue is crucial for effective management and control of the disease. Currently, several diagnostic methods are employed, including virus isolation, nucleic acid detection, and serological tests for dengue virus-specific antibodies (IgM and IgG) and the non-structural protein 1 (NS1) antigen [3]. Among these, NS1 antigen detection has emerged as a vital tool for early diagnosis due to its presence during the acute phase of infection, often before seroconversion to IgM and IgG antibodies occurs [4,5]. Recent studies have reported that the sensitivity and specificity of NS1 antigen tests vary, with some assays demonstrating high diagnostic accuracy [6]. For example, the Panbio Dengue Early Rapid test combined with commercial IgM/IgG rapid tests has shown improved diagnostic sensitivity, suggesting that combining NS1 antigen detection with IgM and IgG serology could significantly enhance the sensitivity of acute dengue diagnosis [7]. This combination extends the possible window of detection, thereby improving the clinical utility of rapid immunochromatographic testing for dengue. Moreover, the use of NS1 antigen detection in conjunction with IgM/IgG serology is not only beneficial for diagnosing acute infections but also enhances the capability to detect secondary infections, which are often more severe [8]. A meta-analysis further supports the use of NS1 antigen-based tests, highlighting their high specificity and reasonable sensitivity, particularly when used in combination with IgM tests [9]. These findings underscore the importance of integrated diagnostic approaches that utilize both antigen and antibody detection to achieve accurate and early diagnosis. The timeline of effectiveness of these diagnostic tools is critical, as the NS1 antigen is detectable from day 1 up to day 9 post-onset of symptoms, whereas IgM antibodies appear later and remain longer in the bloodstream [10]. Therefore, the

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diagnostic strategy might involve using NS1 tests during the early phase of the disease and antibody detection subsequently to confirm infection if initial tests are negative [11]. Despite the advantages of current diagnostic methods, discrepancies in test results and the factors influencing these outcomes are areas of ongoing research. Variability in test performance can be attributed to differences in the timing of sample collection, the serotype of the dengue virus involved, and whether the infection is primary or secondary [12]. Additionally, studies have suggested that individual patient factors, such as the immune status and the presence of cross-reacting antibodies from other flavivirus infections, may also impact diagnostic accuracy [13]. The complexity and variety of dengue diagnoses emphasize the necessity for constant review and optimization of diagnostic tests to respond to the dynamic epidemiology of the illness and the variable clinical presentations reported in different populations [14]. Ultimately, improving diagnostic tools and strategies will play a pivotal role in the global effort to control and reduce the burden of dengue [15]. In conclusion, while significant advances have been made in the development of diagnostic assays for dengue, challenges remain in ensuring their effectiveness across different settings and patient populations. Continued research and development to refine these diagnostic tools are essential to keep pace with the evolving landscape of dengue fever and its management.

METHODS & MATERIALS

This prospective observational study was conducted at the Outpatient Department of Dhaka Medical College, Dhaka, Bangladesh. The study duration was six months, from July 2023 to December 2023. The sample consisted of 77 patients who presented with fever and other clinical symptoms indicative of dengue. Inclusion criteria were patients showing signs of acute dengue infection, such as high fever, severe headache, pain behind the eyes, muscle and joint pains, and rash. Patients with other existing comorbidities, such as chronic liver or kidney diseases, as well as those undergoing any form of radiation treatment, were excluded from the study to avoid confounding the diagnostic outcomes. Upon confirmation of eligibility, detailed clinical information and blood samples were collected for diagnostic testing, which included NS1 antigen detection and IgM/IgG serological tests to confirm dengue infection. Statistical analysis was performed using SPSS software version 25. Descriptive statistics were used to summarize the demographic and clinical characteristics of the study population. Multivariate logistic regression models were used to identify factors significantly associated with discrepancies in test results, adjusting for potential confounders. Statistical significance was set at $p<0.05$ for all analyses.

RESULTS

Table – I: Distribution of participants by baseline characteristics (*n*=77)

Baseline Characteristics	Frequency	Percentage
Age		
<2 years	18	23.38%
2-5 years	12	15.58%
6-10 years	26	33.77%
11-20 years	15	19.48%
21-30 Years	3	3.90%
>30 years	3	3.90%
Mean±SD	8.66±8.73	
Gender		
Male	43	55.84%
Female	34	44.16%
Residence		
Urban	44	57.14%
Suburban	13	16.88%
Rural	20	25.97%
Occupation		
Businessman	1	1.30%
Office Woker	2	2.60%
Service Worker	2	2.60%
Housewife	4	5.19%
Unemployed	2	2.60%
Student	29	37.66%
Not Applicable	37	48.05%
Education		
Not Applicable	32	41.56%
No Formal Education	8	10.39%
Primary Education	30	38.96%
Secondary Education	6	7.79%
Undergraduate	1	1.30%
Monthly Family Income		
<=15,000	8	10.39%
150,01-25,000	13	16.88%
25,001-35,000	13	16.88%
35,001-45,000	17	22.08%
45,001-55,000	17	22.08%
>55,000	9	11.69%

The majority of the participants were children aged 6-10 years, accounting for 33.77% of the sample. Infants under two years of age represented 23.38%, and adolescents aged 11-20 years comprised 19.48% of the participants. Adults aged 21-30 years and those older than 30 each made up 3.90% of the sample. The Mean±SD age of participants was 8.66±8.73 years. In terms of gender distribution, males represented 55.84% of the study population. Participants primarily resided in urban areas (57.14%), with fewer from rural (25.97%) and suburban (16.88%) areas. Among the participants, 37.66% were students, making them the largest occupational group. Not applicable, referring to children, accounted for 48.05% of the participants. Educational levels varied among participants: 41.56% were children not yet of educational age, 38.96% had received primary education, and 7.79% had secondary education. A small fraction (1.30%) had undergraduate-level education. The monthly family income of participants was distributed across several brackets, with 22.08% each earning between 35,001-45,000 and 45,001-55,000, showing a middle-income trend.

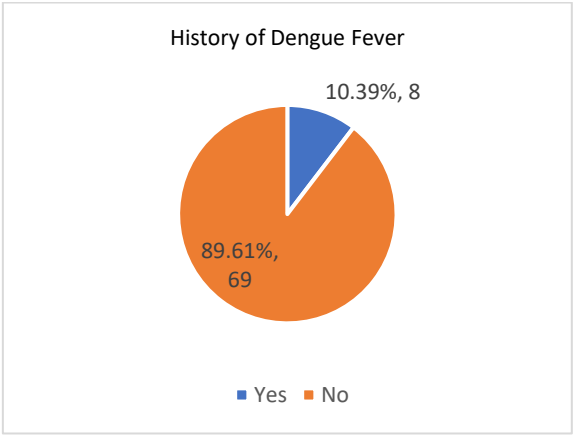

Figure – 1: Distribution of previous dengue infection among the participants (*n*=77)

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A significant majority of the study population, 89.61% (69 individuals), reported no prior incidents of dengue fever, while 10.39% of the participants had been previously affected by dengue fever.

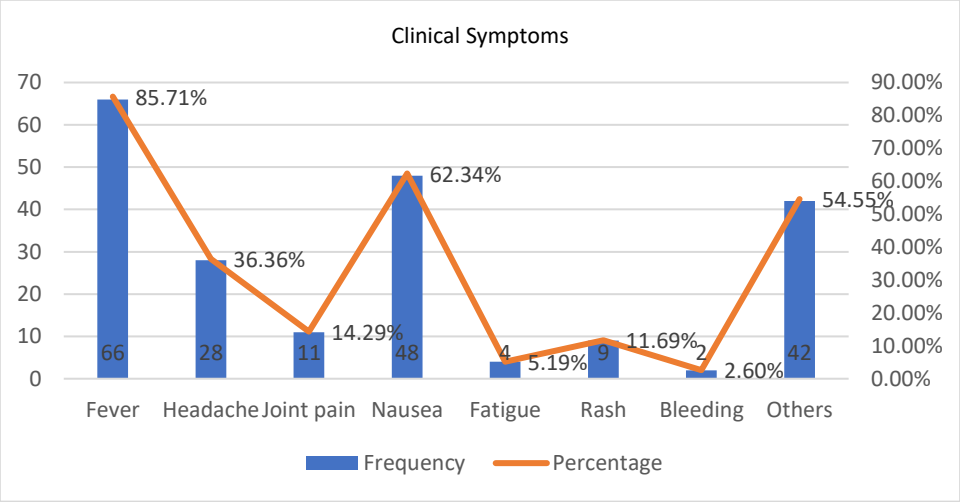

Figure – 2: Distribution of clinical symptoms among the participants (*n*=77)

Fever was the most common symptom, affecting 85.71% of participants, followed by fatigue at 62.34%, and joint pain at 36.36%. Less prevalent symptoms included nausea at 14.29%, rash at 11.69%, and bleeding, a more severe symptom, at 5.19%. The category labeled "Others" included various less common symptoms, representing 54.55% of reports.

Table – II: Distribution of dengue fever symptoms among the participants (*n*=77)

Duration of Dengue Symptoms	Frequency	Percentage
<1 weeks	57	74.03%
1-2 weeks	17	22.08%
>2 weeks	3	3.90%

The majority of patients, 74.03% (57 participants), experienced symptoms for less than one week. A smaller proportion, 22.08% (17 participants), reported symptoms lasting between one and two weeks. Only 3.90% (3 participants) had symptoms that persisted for more than two weeks.

Table – III: Distribution of dengue test results among the participants (*n*=77)

Dengue Test Results	Frequency	Percentage
NS1 Antigen		
Positive	63	81.82%
Negative	14	18.18%
Dengue IgG and IgM		
IgG Positive	14	18.18%
IgM Positive	11	14.29%
IgG and IgM Positive	10	12.99%
IgG and IgM Negative	42	54.55%

The NS1 antigen test showed 81.82% (63 participants) testing positive, while 18.18% (14 participants) were negative. For serological tests, 18.18% (14 participants) tested positive for IgG only, and 14.29% (11 participants) for IgM only. Additionally, 12.99% (10 participants) were positive for both IgG and IgM, and 54.55% (42 participants) were negative for both antibodies.

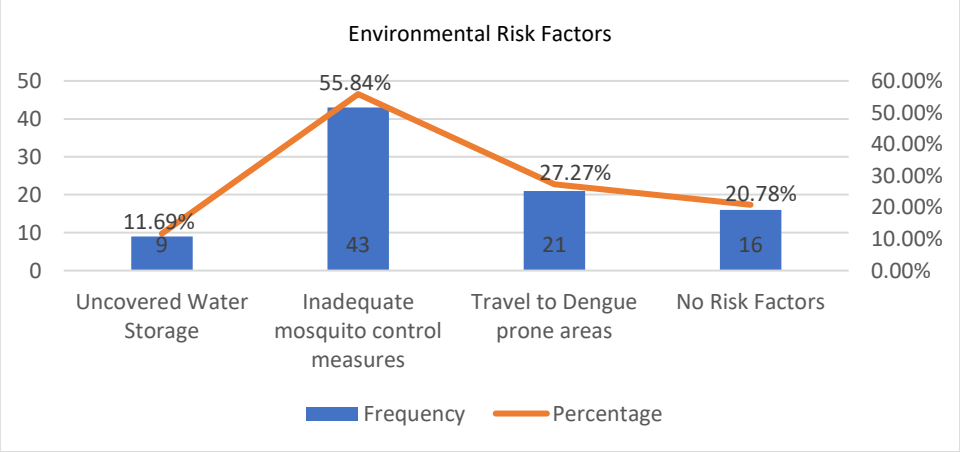

Figure – 3: Distribution of environmental risk factors of dengue among the participants (*n*=77)

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The most prevalent risk factor identified was inadequate mosquito control measures like not using mosquito nets, coils and sprays appropriately, reported by 55.84% (43 participants). Travel to dengue-prone areas was noted in 27.27% (21 participants), while uncovered water storage, a potential breeding site for mosquitoes, was present in 11.69% (9 participants). Notably, 20.78% (16 participants) reported no identifiable environmental risk factors.

Table – IV: Distribution of laboratory parameters among the participants (*n*=77)

Variables	Mean±SD
Hemoglobin (g/dL)	11.20±2.06
Hematocrit (%)	41.98±47.35
WBC	59285724.33±516176826.7
Platelet (µL)	147642.86±337815.86
Lymphocyte (%)	47.59±19.36
Neutrophil (%)	51.03±17.42
Serum Creatinine (mg/dL)	7.63±48.20
SGPT	91.57±135.15
SGOT	99.31±111.74
S. Ferritin	1026.53±1687.10
D Dimer	5.21±14.72

Table IV summarizes the laboratory parameters for the study participants. The Mean±SD hemoglobin was 11.20±2.06 g/dL, while the hematocrit percentage was notably variable at 41.98±47.35%. The WBC count was exceptionally high, with a Mean±SD value of 59,285,724.33±516,176,826.7, suggesting data anomalies. Platelet counts were also recorded with a high variance, at 147,642.86±337,815.86 per microliter. Lymphocyte and neutrophil percentages were 47.59±19.36% and 51.03±17.42%, respectively. Serum creatinine levels were 7.63±48.20 mg/dL, indicating a wide range in kidney function across participants. Liver enzyme levels showed SGPT at 91.57±135.15 U/L and SGOT at 99.31±111.74 U/L. Serum ferritin was significantly elevated at 1026.53±1687.10 ng/mL. D Dimer levels, indicative of blood clotting disturbances, were 5.21±14.72 µg/mL. These values highlight the clinical variability among participants with dengue fever.

Table – V: Association Between Dengue NS1 antigen and IgG and IgM Antibody Test (*n*=77)

Variables	Dengue NS1 Positive (n=63)		Dengue NS1 Negative (n=14)		p-value
	n	%	n	%	
IgG Positive	10	15.87%	4	28.57%	<0.001
IgM Positive	5	7.94%	6	42.86%	
IgG and IgM Positive	8	12.70%	2	14.29%	
Negative	40	63.49%	2	14.29%	

Table V demonstrates the association between the Dengue NS1 antigen and the presence of IgG and IgM antibodies. Among the 63 participants who tested positive for the Dengue NS1 antigen, 15.87% (10 participants) were IgG positive, while only 7.94% (5 participants) were IgM positive, and 12.70% (8 participants) were positive for both IgG and IgM. Interestingly, 63.49% (40 participants) of those who were NS1 positive tested negative for both antibodies. In contrast, of the 14 participants who tested negative for the NS1 antigen, a higher percentage were antibody positive: 28.57% (4 participants) were IgG positive, 42.86% (6 participants) were IgM positive, and 14.29% (2 participants) were positive for both antibodies. Only 14.29% (2 participants) of the NS1 negative group tested negative for both antibodies. These results, marked by a statistically significant p-value of <0.001, indicate a stronger antibody response in NS1 negative individuals compared to those who are NS1 positive.

Table – VI: Bivariate correlation between dengue test and laboratory parameters (*n*=77)

Correlations		NS1 test Results	IgG and IgM	Hemoglobin (g/dL)	Hematocrit (%)	WBC	Platelet (µL)	Lymphocyte (%)	Neutrophil (%)
NS1 test Results	Pearson Correlation	1	-.355**	-.272*	-0.122	-0.055	-0.042	-0.19	0.205
	Sig. (2-tailed)		0.002	0.017	0.291	0.638	0.72	0.097	0.073
IgG and IgM	Pearson Correlation	-.355**	1	0.182	0.146	0.094	0.022	-0.163	0.103
	Sig. (2-tailed)	0.002		0.113	0.205	0.417	0.85	0.157	0.375
Hemoglobin (g/dL)	Pearson Correlation	-.272*	0.182	1	0.04	0.095	-0.05	-0.018	0.016
	Sig. (2-tailed)	0.017	0.113		0.73	0.414	0.663	0.878	0.887
Hematocrit (%)	Pearson Correlation	-0.122	0.146	0.04	1	-0.005	-0.041	-0.067	0.095
	Sig. (2-tailed)	0.291	0.205	0.73		0.963	0.723	0.563	0.41
WBC	Pearson Correlation	-0.055	0.094	0.095	-0.005	1	-0.004	-0.01	-0.043

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	Sig. (2-tailed)	0.638	0.417	0.414	0.963		0.973	0.933	0.71
Platelet (µL)	Pearson Correlation	-0.042	0.022	-0.05	-0.041	-0.004	1	0.003	-0.026
	Sig. (2-tailed)	0.72	0.85	0.663	0.723	0.973		0.981	0.821
Lymphocyte (%)	Pearson Correlation	-0.19	-0.163	-0.018	-0.067	-0.01	0.003	1	-.834**
	Sig. (2-tailed)	0.097	0.157	0.878	0.563	0.933	0.981		<0.001
Neutrophil (%)	Pearson Correlation	0.205	0.103	0.016	0.095	-0.043	-0.026	-.834**	1
	Sig. (2-tailed)	0.073	0.375	0.887	0.41	0.71	0.821	<0.001	

Table VI provides a bivariate correlation analysis between dengue test results and various laboratory parameters among the participants. The NS1 test results showed a significant negative correlation with both IgG and IgM antibodies, with Pearson correlation coefficients of -0.355 (p=0.002) and hemoglobin levels at -0.272 (p=0.017). These correlations suggest that higher NS1 antigen levels are associated with lower levels of IgG and IgM antibodies and hemoglobin. Other correlations were less significant. Hematocrit, WBC, and platelet counts showed no significant correlations with NS1 test results. Lymphocyte percentage negatively correlated with NS1 antigen levels, with a Pearson coefficient of -0.190 (p=0.097), though this was not statistically significant. However, a strong negative correlation was found between lymphocyte and neutrophil percentages, with a coefficient of -0.834 (p<0.001), indicating an inverse relationship between these two cell types in the context of dengue infection.

DISCUSSION

The demographic characteristics of our study population primarily included younger participants, specifically children aged 6-10 years, which constituted the largest group (33.77%). This finding aligns with global observations where dengue tends to affect younger populations significantly, particularly in urban settings [16]. The mean age of our participants was 8.66±8.73 years, with a higher prevalence of males (55.84%), which is consistent with findings from other studies showing a slight male predominance in dengue cases [17]. This could be attributed to greater exposure to mosquito breeding sites in urban environments, which comprised 57.14% of our study setting. Regarding the clinical presentation, a vast majority (89.61%) of our participants had no prior dengue infections, underscoring the continual risk and exposure to dengue in endemic regions. The predominant symptoms were fever (85.71%), fatigue (62.34%), and joint pain (36.36%), mirroring the symptom profile reported in similar studies, where fever is typically the most common presenting symptom [18]. These symptoms reflect the acute inflammatory nature of dengue, corroborated by our finding that most symptoms (74.03%) resolved within one week. Laboratory diagnostics revealed an NS1 antigen positivity rate of 81.82%, which is higher compared considerable variability in parameters such as WBC count and serum ferritin levels, indicating acute inflammatory responses and potential complications. These findings are consistent with other research, which has documented significant hematological changes during dengue infection [22]. The variability in WBC and serum ferritin not only underscores the inflammatory response but also highlights potential markers for disease severity. The association between NS1 antigen positivity and lower rates of antibody positivity (IgG 15.87%, IgM 7.94%) compared to NS1 negative participants (IgG 28.57%, IgM 42.86%) suggests that the NS1 antigen is a crucial marker for early dengue diagnosis before seroconversion. This differential pattern of serological response emphasizes the importance of combining NS1 antigen detection with antibody testing to enhance diagnostic accuracy [5]. Furthermore, the strong inverse correlation between lymphocyte and neutrophil percentages (-0.834, p<0.001) reflects significant shifts in white blood cell types during infection, likely related to the immunopathological changes in dengue [23]. This aspect, coupled with the negative correlations between NS1 antigen levels and both IgG and IgM antibodies, as well as hemoglobin, suggests a nuanced relationship between disease severity and immune response, where NS1 antigen might serve as an indicator of disease progression and severity [20]. These findings collectively enhance our understanding of dengue pathophysiology, emphasizing the complex interplay between viral factors and host responses, which are crucial for improving disease management and intervention strategies in endemic areas.

Limitations of The Study

The study was conducted in to other regions as reported by Kulkarni et al., who documented a lower positivity in a similar setting [19]. The serological response varied, with lower rates of IgG (18.18%) and IgM (14.29%) positivity among NS1 positive participants, suggesting that NS1 antigen testing may be more effective during the acute phase before seroconversion. This phenomenon of delayed antibody response or variability based on disease stage has been noted in other studies, emphasizing the complexity of immune responses in dengue [20]. Environmental risk factors such as inadequate mosquito control measures (55.84%) and exposure to dengue-prone areas (27.27%) were prevalent in our study, similar to findings from Moi et al., who identified these factors as significant contributors to dengue transmission. This reinforces the importance of effective public health strategies to mitigate these risks [21]. Laboratory findings showed a single hospital with a small sample size. So, the results may not represent the whole community.

CONCLUSION

The current study has provided comprehensive insights into the factors influencing the variability of dengue diagnostic outcomes. The results revealed a predominantly young demographic primarily residing in urban areas, with the majority of participants presenting with acute symptoms such as fever, fatigue, and joint pain, which typically resolved within a week. Notably, the NS1 antigen test proved to be highly effective, showing positive results in a significant majority of the cases. However, the serological responses, as evidenced by the IgG and IgM tests, varied, suggesting a potential delay in antibody response or differences in immune response depending on the stage of the disease. Environmental factors, particularly inadequate mosquito control measures, were identified as major contributors to the transmission of dengue, highlighting the importance of enhanced preventive strategies in urban settings.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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