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RESEARCH LETTER

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Predominant dengue virus serotype in Dhaka, Bangladesh: A research letter on samples from 2022 outbreak

1 | INTRODUCTION

Dengue, an arthropod-borne viral disease transmitted by mosquitos *Aedes aegypti* and *Aedes albopictus*, has become a cause of global public health concern in recent years.[1–3] The impact of dengue disease, both from a health and economic standpoint, for a country could be devastating, as evidenced by recent epidemic outbreaks in different countries around the globe.[4,5] More than three fourth of the world's population is at an increased risk of dengue disease largely due to urbanization, climate change, and increased human mobilization.[6,7]

During a period spanning from 2000 to 2002, more than 5000 cases of hospitalization due to DENV-3 infection were reported in Bangladesh.[8–10] During the next 15 years, sporadic outbreaks of dengue were reported in Bangladesh with DENV-1 and DENV-2 being identified as the causative agent.[11,12] The next big outbreak of dengue was observed in 2018 with the re-emergence of DENV-3, and co-circulation of DENV-1 and DENV-2 thought to be responsible for the outbreak.[13,14] In 2019 dengue outbreak, there were 10 times as many dengue patients compared to the previous year, causing hundreds of fatalities in Dhaka, the capital of Bangladesh, and adjacent cities. This time DENV-3 was identified as the predominant circulating serotype. From 2019 each year Bangladesh has gone through a dengue outbreak with another 63,030 cases and 174 fatalities reported till December 2022.

In 2022, Bangladesh is experiencing the largest dengue outbreak in recent history with reports of highest morbidities and mortalities. According to an official press release, from January 1, 2023, more than 85,000 people have been infected with the virus resulting in 398 deaths. This is an alarming trend as the number of cases and fatalities have increased significantly compared to previous years. But up until now the predominant serotype for the 2022 outbreak has not been reported in relevant literature, which is an integral component of dengue prevention and treatment strategies. Therefore, in this brief report, we aimed to identify the DENV serotype responsible for the 2022 outbreak along with relevant clinical pictures of infected patients.

2 | MATERIALS AND METHODS

2.1 | Study population and sample collection

National Institute of Laboratory Medicine and Referral Centre, only reference center in Bangladesh. This institute's primary tasks include conducting research and facilitating high-quality laboratory services across the nation. Here, samples are received from Dhaka city, and nearly daily, 10–30 samples are tested for dengue NS1 and dengue IgG and IgM using immuno-chromatography test (ICT). This cross-sectional study conducted at Department of Virology, NILMRC from October 20, 2022 to January 15, 2023.

With all aseptic precaution blood samples (5 mL) were collected from febrile patients (H/O fever) enrolled. Approximately 723 blood samples were collected for dengue NS1 and dengue IgG and IgM testing. Among them, 232 dengue NS1 positive samples were preserved in −80°C.

2.2 | RNA extraction

Total RNA was extracted from samples obtained from patients who were dengue NS1 positive the Viral RNA Mini Kit (Qiagen), and samples were then stored at −80°C until real-time RT-PCR for serotyping was carried out.

2.3 | Dengue serotyping by multiplex real-time reverse transcriptase-polymerase reaction

We used Altona RealStar® dengue type RT-PCR Kit 1.0 (Hamburg) for the detection of DENV serotype. In multiplex reaction mixture, Master A contains specific primer for DENV1 and DENV4 and Master B contains specific primer for DENV2 and DENV3. Reverse transcription of 20 min at 55°C was followed by 45 cycles of amplification in a Quant studio-5 real-time Detection System. In case of PCR result interpretation, cycle threshold (*Ct*) less than 38 was evaluated as positive and *Ct* value more than 38 was considered negative.

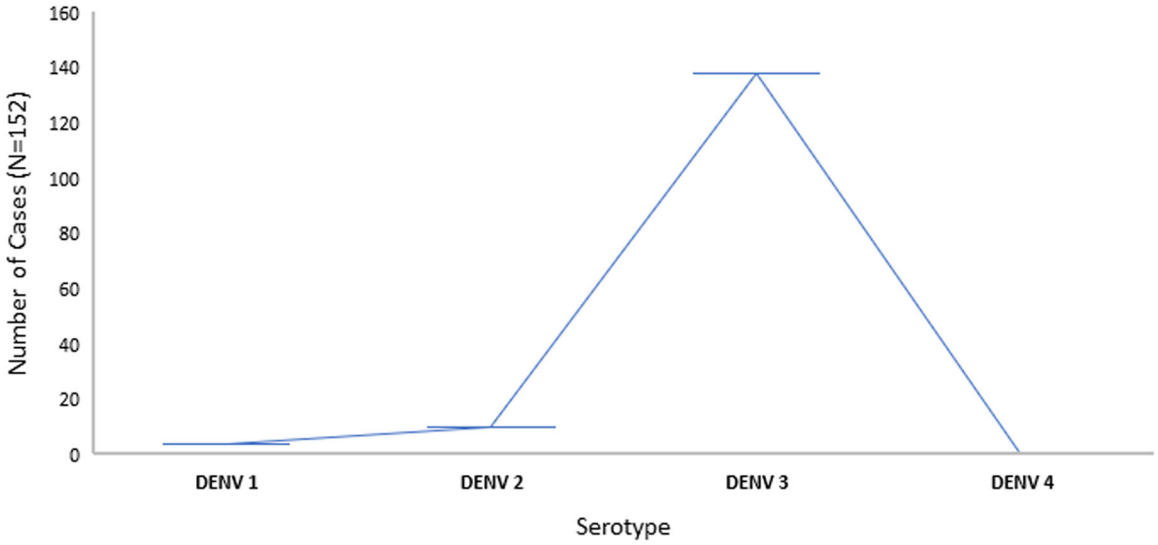

FIGURE 1 Distribution of dengue serotypes among all cases.

2.4 | Ethics approval and informed consent to participate

The Institutional Review Board (IRB) of the NILMRC granted ethical permission for the secondary analysis of conserved samples. All participants provided their written, fully informed consent, together with the parents of any minors. The doctors and the medical technologist collected personal information and other relevant medical data using a semistructured questionnaire. Each patient had an anonymous, numerical unique identifier assigned to them in the main database.

2.5 | Statistical analysis

Statistical analysis was performed by Statistical Package for Social Science (SPSS), versions 22.0 (IBM SPSS Statistics for Windows, Version 22.0: IBM Corp.).

3 | RESULT

3.1 | Dengue demographic data

For this study, 232 cases were identified as dengue NS1-positive in Dhaka city and adjacent areas. Among NS1-positive patients, serotyping could be performed in 152 patient samples. Among the patients, male and female accounted for 65% ($n = 100$) and 35% ($n = 52$), respectively. Around 50% ($n = 76$) of study patients were from the 16–26-year age group with 31.58% ($n = 48$) from the 27–36-year age group.

3.2 | Clinical course and serotype

Among the study participants, most were found to be infected with DENV-3 serotype ($n = 138$) with DENV-2 ($n = 10$) and DENV-1 ($n = 1$) also being reported. We could not find the DENV-4 serotype in any of the tested samples.

During the study period, the Dhaka metropolitan city in Bangladesh saw an overall distribution of the DENV-3, DENV-2, and DENV-1 serotypes of 91% ($n = 138$), 6.5% ($n = 10$), and 0.6% ($n = 1$), respectively. During that time, none of them tested positive for DENV-4 (Figure 1).

Besides fever ($n = 152$), common symptoms among study participants were headache ($n = 136$), myalgia ($n = 104$), arthralgia ($n = 94$), retro-orbital pain ($n = 94$), and diarrhea ($n = 50$). Severe symptoms such as lethargy were found in 50% of cases ($n = 76$). Other symptoms such as vomiting, abdominal pain, and epistaxis were also reported (Table 1).

TABLE 1 Clinical manifestations of the enrolled cases.

Clinical features	*N* (%)
General symptoms	
Fever	152 (100)
Headache	136 (89.5)
Retro orbital pain	94 (61.8)
Joint pain	94 (61.8)
Diarrhea	52 (34.2)
Myalgia	104 (68.4)
Rash	88 (57.9)
Severe symptoms	
Abdominal pain, Tenderness	4 (2.6)
Vomiting	18 (11.8)
Bleeding from nose/epistaxis	6 (4)
Lethargy	76 (50)
H/O hospitalization	24 (15)

4 | DISCUSSION

In our analysis, DENV-3 (91%) was the most common serotype with no cases of DENV-4 identified in our samples. In contrast to this study, in samples tested and reported by the Institute of Epidemiology, Disease Control, and Prevention (IEDCR), DENV-4 was found in 11% (n = 13) of samples, DENV-3 was found in 89% (n = 110), and no other serotypes were found in 2022.[15]

All Participants of this study were NS-1 positive while attending our outdoor and suffered from an acute febrile illness lasting 2–7 days with at least two of the following symptoms: headache, retro-orbital discomfort, myalgia, arthralgia, rash, hemorrhagic signs, leucopenia, regardless of age or sex. According to the current study's findings, the age range of 16–26 years suffered the most, followed by the age range of 27–36 years. Men and women made up 65% and 35% of the patient population, respectively (Table 1). The few studies from Asia, such as those from Singapore, that have examined male and female dengue incidence have tended to find greater male incidence.[16–18]

In our study, the common general symptoms reported are fever (n = 152), headache (n = 136), myalgia (n = 104), arthralgia (n = 94), retro-orbital pain (n = 94), and diarrhea (n = 50) respectively. Another study in Asia reported severe fever (100%), body aches (93.1%), skin rashes (26%), nose and/or mouth bleeding (5.63%), and an enlarged liver (43.96%) as the predominant clinical features among dengue patients, which are similar to our study findings.[19] Interestingly, a higher proportion of dengue patients during the 2022 epidemic had diarrhea, vomiting, myalgia, anorexia, and retro-orbital pain compared to the previous outbreaks in neighboring country Nepal, which might be due to differences in sample size or even changes in properties of the infecting virion.[20,21] The fact that the current study did not account for disease severity was a limitation of our study because we solely focused on outpatient department. And, we could not analyze the risk of hospitalization and dengue hemorrhagic fever in case of DENV-3 infection.

5 | CONCLUSION

Three DENV serotypes were found to be in circulation during the severe 2022 outbreak in Bangladesh, with DENV-3 predominating. This points to instances of serotype displacement; in particular, DENV-1 returned to the country after a period and had substantial virus levels. Therefore, an urgent plan of action for evidence-based policymaking for dengue management and prevention should focus on the exact mapping of the DENV infection, the dynamics of population-level immunity, and virus evolution.

AUTHOR CONTRIBUTIONS

Tasnim Nafisa: Conceptualization; formal analysis; methodology; writing—original draft. **Arifa Akram**: Conceptualization; methodology; supervision; writing—original draft. **Mahmuda Yeasmin**: Conceptualization; formal analysis; methodology; writing—original draft. **Tania Islam Resma**: Writing—original draft. **Md Abu Baker Siddique**: Data curation; investigation; resources. **Nur Hosen**: Data curation; investigation. **Monirul Islam**: Data curation; investigation. **Golam Rabbani**: Data curation; investigation. **Monira Pervin**: Methodology; supervision. **Mohammad S. S. Shakil**: Writing—original draft. **Md Maruf Ahmed Molla**: Writing—review and editing.

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CONFLICT OF INTEREST STATEMENT

Coauthor Md Maruf Ahmed Molla is an editorial member at Health Science Reports, but will have no role in editorial decision making regarding this manuscript. The other authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

TRANSPARENCY STATEMENT

The lead author Arifa Akram affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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