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Letter to the Editor

Predominance of Dengue virus type 2-genotype II (Cosmopolitan) in Bangladesh, 2023: Presumptive sudden replacement of a prevailing virus strain

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Dear Editor

Dengue fever is the most prevalent arthropod-borne infectious disease caused by dengue virus (DENV) worldwide, affecting predominantly densely populated urban/semiurban areas in tropical and subtropical regions. In the last two decades, the global incidence of dengue increased, which poses a growing concern for public health. In Bangladesh, being presumably endemic since the 1960s, the dengue outbreak was recognized from 2000 to 2002, causing at least 2400–6200 cases each year. Thereafter, dengue was less prevalent with generally 1000 cases until 2014. However, large outbreaks occurred in 2018 and 2019 with more than 10,000 and 100,000 cases, respectively. The high prevalence of dengue has been persisting in 2022 causing more than 60,000 infected cases, which exponentially increased to 321,179 cases in 2023, representing a record largest outbreak (Director General Health Services, https://dghs.gov.bd/) [1]. This outbreak caused 1705 deaths with case fatality rate 0.53, which has been increasing gradually since 2018 (0.26 %). Every year, dengue is more prevalent from July to November, while being found all the year round.

DENV has four major serotypes (DENV-1 through DENV-4) which confer serotype-specific immunity in infected individuals. Circulating dominant DENV serotypes are different depending on countries/region and year. In Bangladesh, DENV-2 was predominant from 2013 to 2017. After the co-circulation of DENV-1, -2, and -3 in 2018, DENV-3 was described as being predominant in outbreaks from 2019 until 2022 [2–4]. However, there was a dearth of information of DENV serotype that caused the devastating outbreak in 2023. Accordingly, we conducted the present study to determine their serotype/genotype and phylogenetic features.

We collected a total of 282 blood samples from suspected dengue patients who admitted to two medical institutions (Mugda Medical College hospital, Dhaka, 208 samples; Mymensingh Medical College hospital, Mymensingh (approx. 100 km north of Dhaka), 74 samples), from September 2023 to January 2024. Inclusion criteria of patients were 1) sudden onset of fever with or without rash, joint pain, and 2) duration of fever of more than 7 days. Using the extracted RNA from the blood samples, DENV was detected by RT-PCR targeting *C-prM* gene. Sequences of *C-prM* and envelope (E) genes were determined by Sanger sequencing with RT-PCR products, and analyzed for their serotype, sequence identity and phylogenetic relatedness to global DENV strains by using BLAST search and MEGA software package.

C-prM gene was detected in 30 samples (18 and 12 in Dhaka and Mymensingh, respectively). Phylogenetic analysis of *C-prM* gene sequences revealed that all the viruses were DENV-2 belonging to genotype II (Cosmopolitan) (Fig. 1(a)). Similar finding was obtained for E gene sequence that could be determined for 3 samples (Fig. 1(b)). All the DENV-2 were classified into cluster C of genotype II [4], and mostly grouped into a subcluster 1 (SC1). The 2023 DENV-2 in Bangladesh were highly close (>99 % identity) to those in India (2021–2023), China (2022), UAE (2023), USA (2023), and Caribbean region (Martinique, Guadeloupe; 2023). However, they were slightly distant from those in Bangladesh in 2017 and 2018, within clade C. On the other hand, DENV-2 genotype II-clade C includes viruses from Asia (India, Thailand, China, etc.) reported since 2014. These observations suggest that the Bangladeshi DENV-2 in 2023 might be a virus strain that was genetically evolved from those prevailing previously in Asia, and emerged in the Indian subcontinent recently, showing a sign of global dissemination. It was also notable that the Bangladeshi DENV-2 diverged into two lineages in the phylogenetic tree of *C-prM* gene, suggesting further diversification of this virus.

Though the number of samples was limited, the present study revealed the presumptive sudden replacement of predominant serotype from DENV-3 (2019–2022) to DENV-2 (2023) in Bangladesh, without observing co-circulation of DENV-2 and DENV-3. Such change in DENV serotypes is suggested to increase the sequential infection event with different DENV serotypes in the population, associated with the occurrence of severe dengue disease. This may be one of the reasons for the highest mortality rate in 2023 during the past 6-year period. Recently, DENV-2 genotype II has been remarkably spreading globally [5]. Accordingly, it will be increasingly important to monitor the trend of DENV-2, and also early detection of serotype replacement for the control of dengue epidemic.

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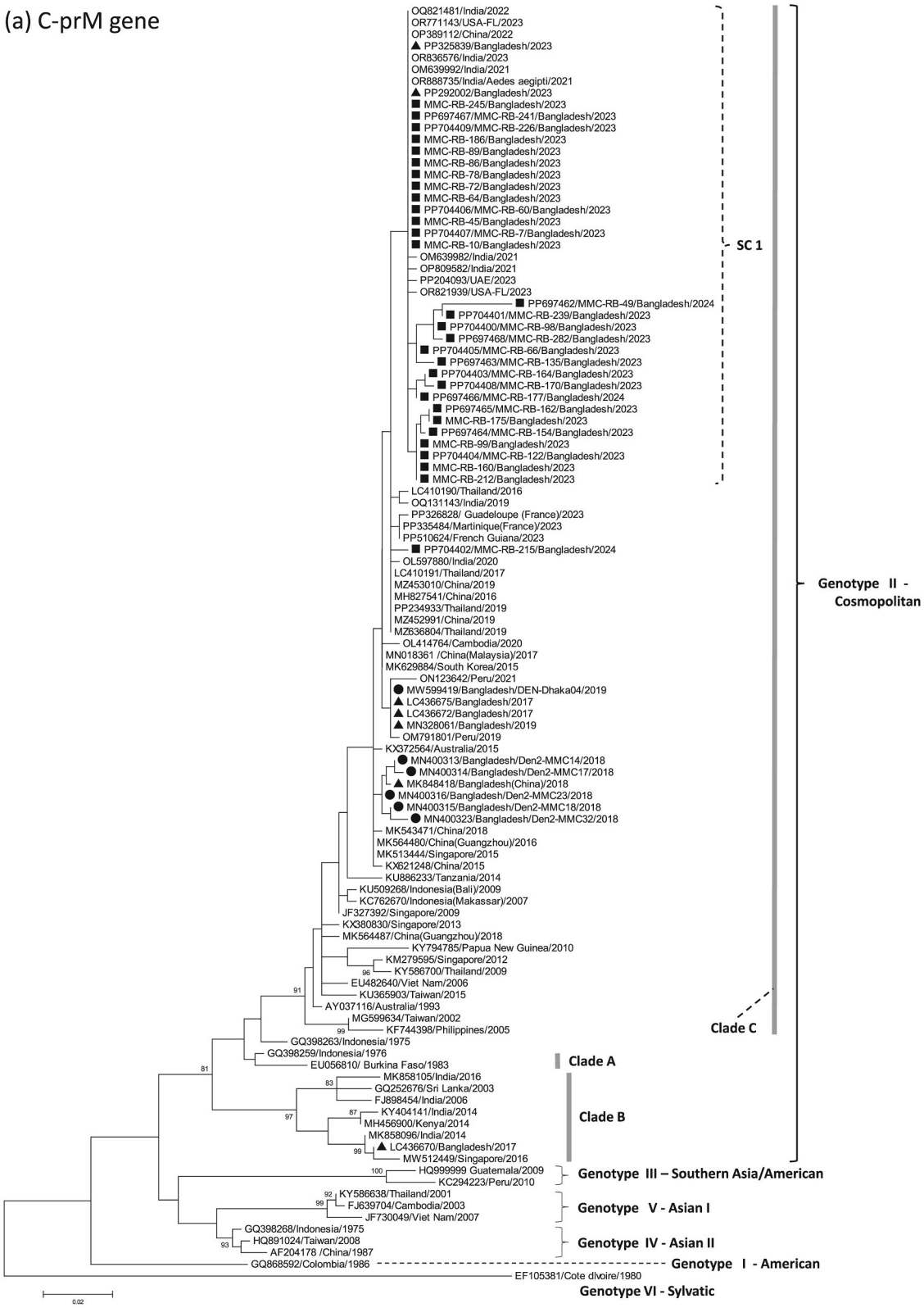

Fig. 1. Phylogenetic dendrogram of *C-prM* gene (a) and Envelope (E) gene (b) of DENV-2 in Bangladesh in 2023 and 2024, and other representative DENV-2 from diverse geographical locations, constructed by the maximum-likelihood method with the MEGA6 software package. Variation scale is described at the bottom. Percentage bootstrap support is indicated by the values at each node (values < 80 were omitted). Closed squares and circles indicate DENV-2 in the present study (2023–2024) and those in Dhaka in our previous studies (2018, 2019) [2], respectively. Triangles show also DENV-2 in Bangladesh that had been published previously elsewhere and those available in GenBank database. Genotypes of DENV-2 (I-VI) are shown on the right, and three clades A-C of genotype II (Cosmopolitan) assigned by Rahim et al. [4] are also indicated with vertical lines. Right dotted bracket shows subclade 1 (SC1) within clade C of genotype II, which includes DENV-2 in Bangladesh in 2023–2024.

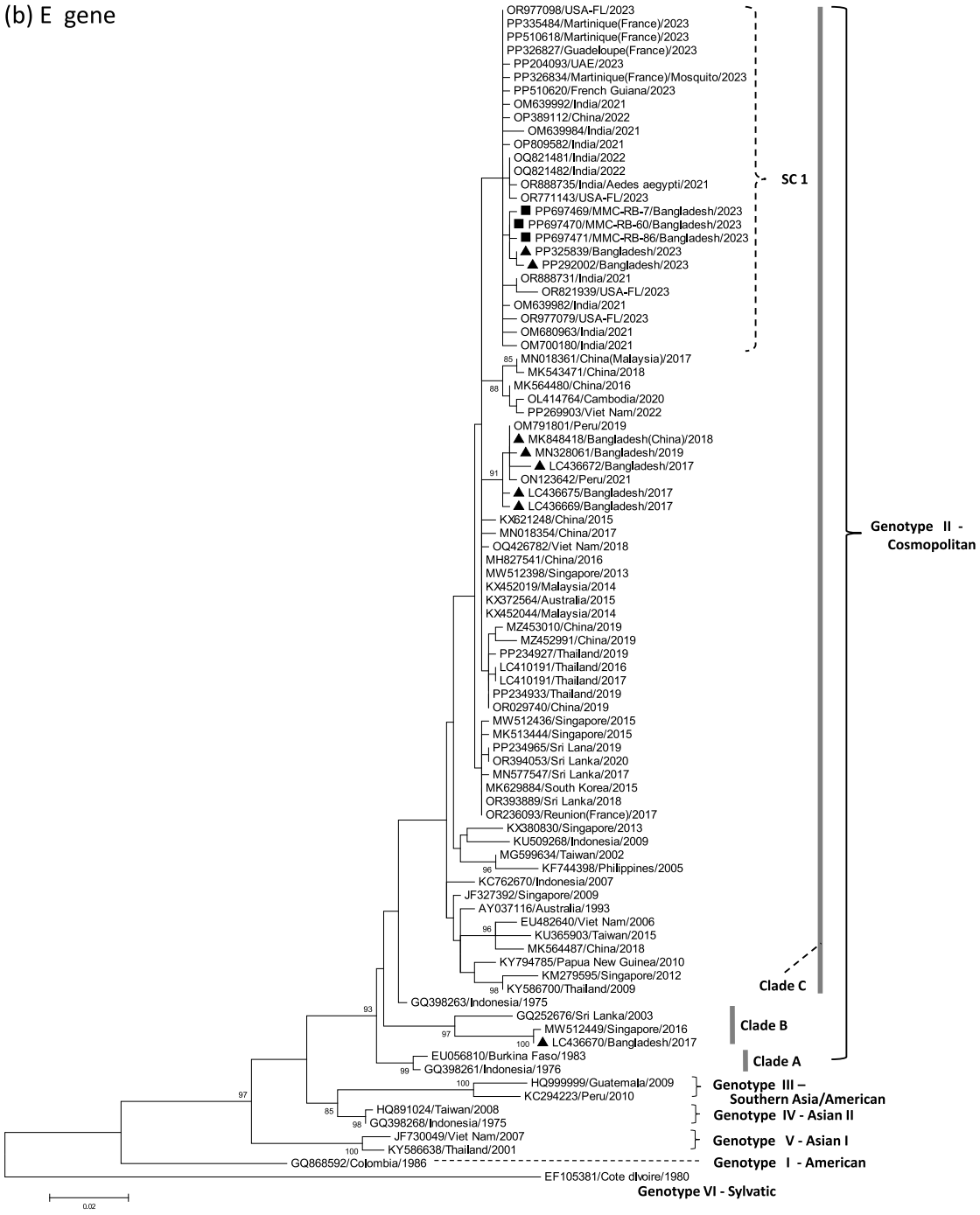

Fig. 1. . (*continued*).

Availability of data and materials

Nucleotide sequences of C-prM/E genes determined in this study were deposited to GenBank under accession numbers PP697462-PP697471, PP704400-PP704409.

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Patient consent statement

This study was approved by Institutional Review Board of Mymensingh Medical College (MMC/IRB/2024/641). Written informed consent was obtained from all the patients who participated in this study.

CRediT authorship contribution statement

Rahima Begum: Conceptualization, Formal analysis, Investigation, Methodology. **Shyamal Kumar Paul:** Conceptualization, Formal analysis, Supervision. **Meiji Soe Aung:** Data curation, Formal analysis, Investigation. **Nazia Haque:** Resources, Supervision. **Salma Ahmed:**

Resources, Supervision. **Arup Islam:** Resources. **Sultana Shabnam Nila:** Resources. **Sangjukta Roy:** Resources. **Afsana Jahan:** Resources. **Fardousi Akter Sathi:** Resources. **Abdullah Al Mamun:** Resources. **Joy Prokas Biswas:** Resources. **Nobumichi Kobayashi:** Investigation, Supervision, Writing – original draft.

Declaration of competing interest

The authors declare no competing of interest.

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