Resurgence and predominance of G3P[8] human rotaviruses in north-central Bangladesh, 2018–2019

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Abstract

Predominance of genotype G3P[8] rotavirus was revealed for children and adults with diarrhoea in north-central Bangladesh for a 1-year period from September 2018. The G3P[8] rotaviruses were phylogenetically close to recent Indian strains, having antigenic variation in VP7 and VP4 compared with old Bangladeshi strains.

Keywords: Antigenic drift, Bangladesh, G3P[8], phylogenetic analysis, rotavirus

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Rotavirus A (RVA) is a major aetiological agent of human diarrhoeal diseases primarily in children worldwide, and is classified into G genotypes (VP7) and P genotypes (VP4) based on sequences of the outer capsid proteins. Most human RVA are classified into G1–4, G9 and G12 combined with P[4] or P[8]. P[8] is genetically classified into two subtypes, P[8]a and P[8]b, with P[8]a being predominant among RVA [1]. In Bangladesh, G1P[8] has been reported to be a dominant genotype since 2004 [2], whereas a temporary increase was observed for G2, G9 and G12 compared with previous findings [3]. In contrast, G3 RVA has been scarcely detected since 1988, despite sporadic detection in Dhaka in 2005 [4]. In recent surveillance, G1P[8] and G12P[8] have been described as the most widespread genotypes [5,6], with G2P[4] occasionally being dominant [7]. However, emergence of G3P[8] was noted in 2016, and this genotype accounted for 3%–7% of all RVA genotypes until 2017 in Dhaka and other main cities [6,8], so its potential spread has been suggested.

During a 1-year period from September 2018 to August 2019, a total of 681 stool samples were collected from individuals with diarrhoeal illness (558 and 123 from children and adults, respectively) in two hospitals in Mymensingh, located in north-central Bangladesh. RVA genomic dsRNA segments were detected by polyacrylamide gel electrophoresis and silver staining in 73.3% and 17.1% of stool samples from children and adults, respectively. Among a total of 430 RVA-positive samples, 50 samples were randomly selected from each month, and analysed for their G and P types by semi-nested RT-PCR. The most common genotype was G3P[8]a (56%), followed by mixed types, i.e. G1/G3 with P[8]a/P[8]b/P[4] (26%), G3 with P[8]a/P[4] (4%). Samples with G3, including mixed type, accounted for 92%. Full-length open-reading frames of VP7, VP4 and VP6 genes were determined for eight RVA samples by RT-PCR and Sanger sequencing, and deposited in GenBank [9] under Accession numbers MN414253 to MN414276.

Phylogenetic analysis of VP7, VP4 and VP6 genes was performed using MEGA.7 software [10]. VP7 genes of all the G3P[8]a RVA in the present study in Mymensingh (G3RVA-MMC) were grouped into a G3a lineage (Fig. 1a), which contains globally spreading G3 RVA strains since the middle of the 2000s, and is most closely related to G3 RVA in India from 2015 to 2017. In contrast, G3RVA-MMC VP7 genes showed slightly lower identity (97.9%) with the Bangladeshi G3 rotavirus reported in 2005. VP4 genes of G3RVA-MMC were assigned into the 3c cluster of the P[8]a-3 lineage, which is closely related to recent Indian strains, but distinct from the 3a cluster with P[8] RVA in Bangladesh in the 2000s (Fig. 1b). VP6 genes of G3RVA-MMC were typed as I genotype 1 and clustered with RVA from India and South-East Asian countries (1a cluster), and were distant from the 1b cluster containing old Bangladeshi strains (Fig. 1c).

Alignment of full-length VP7 and VP4 deduced amino acid sequences revealed that the G3RVA-MMC and some recent Indian G1/G3 strains have common amino acids that were caused by non-synonymous substitution and distinct from older strains with the same genotype, at positions within or near their antigenic sites (VP7, amino acid 221; VP4, amino acids 162, 586, 600) (see Supplementary material, Fig. S1). These findings suggested that antigenically similar G3 RVA were distributed in Bangladesh and India.

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FIG. 1. Phylogenetic dendrogram of G3-VP7 gene (a), P[8]-VP4 gene (b), and I genotype 1-VP6 gene (c) of human rotavirus A (RVA). Closed circles indicate G3P[8] RVA analysed in the present study, diamonds denote old RVA studied in Bangladesh (2001–2005). As outgroup, RVA strains Wa (VP7) and DS-1 (VP4, VP6) were used. Dendrograms were constructed by maximum likelihood method using the MEGA.7 software package. Trees were statistically supported by bootstrapping with 1000 replicates, and genetic distances were calculated using the Kimura two-parameter model. The variation scale is described at the bottom. Percentage bootstrap support is indicated by the values at each node (values <80 are omitted). Lineages and sub-lineages are shown on the right in accordance with those described previously (VP7 and VP6 [11]: VP4 [12]).

FIG. 1. (*continued*).

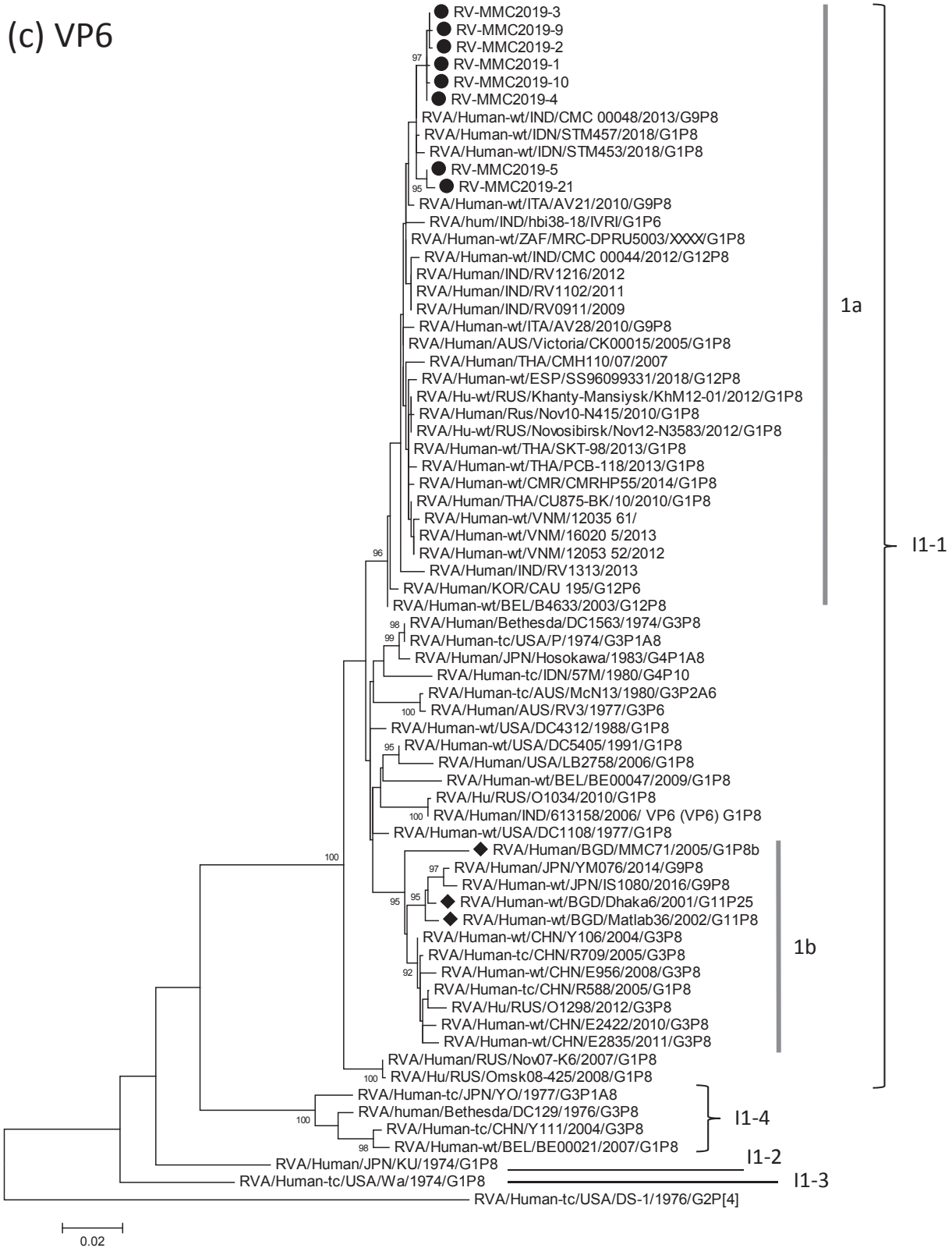

FIG. 1. (*continued*).

Our study revealed a higher current prevalence of RVA in children and adults in Mymensingh than in 2004–2006 (26.4% and 10.1% in children and adults, respectively) [2], associated with the predominance of G3P[8] RVA (92%), whereas G3 was undetected in our previous study [2]. In Bangladesh, rotavirus vaccine has not yet been introduced as routine immunization for children, although its efficacy has been evaluated by many clinical trials. Because the present vaccination rate in children is thought to be minimal, predominance of G3P[8] RVA may not be due to the result of selective pressure by rotavirus vaccine, but is more likely a natural fluctuation. Although the reason for the high prevalence of RVA in the present study is uncertain, re-emergence of G3P[8] RVA after its absence for a long period might have been involved. Further surveillance may be necessary to monitor the upsurge and prevalence of G3 RVA, and its impact on public health.

Conflicts of interest

The authors have no conflicts of interest to declare.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.nmni.2019.100621.

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