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Co-circulation of three recombinant norovirus genogroup II genotype 4 variants, 2014-2016, Hong Kong, China

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Background: Norovirus is a leading cause of acute gastroenteritis and food-borne illnesses worldwide. All age groups are affected but certain groups, including infants, young children, the elderly, and the immunocompromised are particularly vulnerable to severe clinical outcome. Norovirus is genetically diverse and one genotype known as GII.4 has been globally-circulating in the past two decades. New variants of norovirus GII.4 emerged every 2 to 4 years and usually associated with surge in norovirus outbreaks and hospitalizations. The most recent pandemic GII.4 variant was called Sydney 2012 that has emerged for over 4 years. Close molecular surveillance of norovirus gastroenteritis is important to detect the next pandemic GII.4 variant.

Material/methods: Hong Kong is a coastal city in southern part of China. Starting from March 2014, our team has established a molecular surveillance of in-patients with laboratory-confirmed norovirus infections in our hospitals. All norovirus GII.4 cases were subjected to partial RNA-dependent RNA polymerase (RdRp) gene genotyping and full-length capsid (VP1) gene was determined by Sanger sequencing. Virus genotype and variant assignment were performed using RIVM's online Norovirus Genotyping Tool. Phylogenetic inference was performed using the neighbour-joining statistical model.

Results: From March 2014 to September 2016, a total of 850 stool samples were collected from 836 patients. The median age was 3 years (interquartile range: 1-52 years). Norovirus VP1 genotype was determined from 742 (88.8%) cases, in which 401 (54.0%) belonged to GII.4. All GII.4 strains belonged to VP1 Sydney 2012, except for two strains that were classified into New Orleans 2009. RdRp genotyping of VP1 Sydney 2012 revealed 3 genotypes: GII.Pe (n=383; 96.0%), GII.P16 (n=11; 2.8%), and GII.P4 New Orleans 2009 (n=5; 1.3%). GII.P16 was first detected in January 2016 whilst GII.P4 New Orleans 2009 was detected sporadically throughout the study period. Phylogenetic

analysis of VP1 showed that GII.4 strains in 2016 containing GII.P4 New Orleans 2009 were most distant from the prototype strain of GII.4 Sydney 2012.

Conclusions: We report co-circulation of three recombinant norovirus GII.4 variants from 2014-2016 in Hong Kong. The predominant variant was GII.Pe_GII.4 Sydney 2012. Strains of GII.P16_GII.4 Sydney 2012 that emerged in the winter of 2015/16 and accounted for a majority of outbreaks in the US remained a minority in Hong Kong. Strains of GII.P4 New Orleans 2009_GII.4 Sydney 2012 that emerged in Australia in mid-2016 was found to have most amino acid changes in VP1 from the prototype. Close monitoring of the two emergent recombinant GII.4 variants is needed.

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