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EDITORIAL

Waterborne Enteric Coronaviruses and the SARS-CoV-2 Disease

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ABSTRACT

Enteric or diarrheal viruses are primarily transmitted through contaminated water, and cause self-limiting gastroenteritis, diarrhea or jaundice. The human coronaviruses (CoV), including the severe acute respiratory syndrome CoV (SARS-CoV-1) and Middle-East respiratory syndrome CoV (MERS-CoV) which are inherently respiratory viruses, also manifest in gastrointestinal tract. Similarly, the novel SARS-CoV-2 also causes diarrhea and liver disorder as well as shed in stool in a proportion of SARS-CoV-2 diseases (COVID-19) patients. This is well supported by detections of SARS-CoV-2 RNA in gut specimen, rectal swabs and stool samples. Recent data on its occurrence in wastewater provides a warning on further spread of COVID-19 in resource-poor countries. Therefore, laboratory test of COVID-19 patients stool along with nasopharyngeal specimen as

well as implementation of water surveillances could be very useful in protecting community health.

Key words: Enteric coronaviruses; SARS-CoV-2; COVID-19; Gastrointestinal manifestation; Fecal shedding; Water surveillance

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INTRODUCTION

Enteric or diarrheal rotaviruses, enteroviruses, noroviruses, astroviruses and adenovirus etc. generally cause self-limiting gastroenteritis, diarrhea or respiratory symptoms^[1]. Because these are waterborne pathogens, their gastrointestinal (GI) and fecal shedding further increases the risk of fecal-oral transmission. Coronaviruses (CoV) are inherently respiratory viruses, but they are also known for GI manifestations and stool shedding^[2-4]. In humans, six species of CoV (HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-HKU1, Severe Acute Respiratory Syndrome CoV or SARS-CoV-1, and Middle-East Respiratory Syndrome CoV or MERS-CoV) primarily cause common cold, flu, cough or pneumonia^[5]. In clinical studies, a proportion of HCoV-OC43, HCoV-NL63 and HCoV-NL63 infected patients have shown GI symptoms and high amounts of fecal shedding^[6-9]. Notably, though HCoV-HKU1 is commonly associated with acute respiratory infection, it has been also linked to GI issues^[10,11]. Similarly, diarrhea and other digestive manifestations, including stool shedding have been also reported in SARS-CoV-1 and MERS-CoV infected individuals^[12-19].

SARS-COV-2 AND COVID-19

The newly emerged SARS-CoV-2 is the seventh human CoV and third highly pathogenic CoV after the SARS-CoV-1 and MERS-CoV^[20,21]. The ongoing pandemic of the SARS-CoV-2 disease (COVID-19) is the most devastating health crisis ever, which has affected nearly 137 million people, with >2.9 million death^[20]. SARS-CoV-2 is an enveloped virus with plus-sense single-

stranded RNA genome (~30 kb), classified together with HCoV-OC43, HCoV-HKU1, SARS-CoV-1 and MERS-CoV within the genus *Betacoronavirus*^[21,22]. The origin of SARS-CoV-2 and its first source of human contact still remain debated. Nonetheless, genome sequencing and phylogenetic analysis have suggested its very close similarity (~96%) with bat SARS-like-CoV (Bat-SL-CoV), and potential zoonosis in bats^[22]. The human-to-human direct transmission of COVID-19 has been confirmed through multiple modes, such as naso-oral droplets, aerosols and fomites^[21]. SARS-CoV-2 has an incubation period of 2-14 days with symptoms of cough, fever, headache, breathlessness, rashes, burning sensation, mild-to-severe pneumonia or death^[21,23]. During a year of its outbreak, we have a better understanding of COVID-19 epidemiology, clinical presentations, treatments and intervention strategies. Worldwide, hundreds of therapeutics and interventions such as, antiviral drugs, cytokine antagonists, convalescent plasma and vaccine candidates are in clinical Phase-I/II/III trials^[24]. Notably, while few repurposed drugs have been granted emergency use approval, at least seven vaccine candidates have been recently approved in some countries.

GI MANIFESTATIONS OF COVID-19

Similar to SARS-CoV-1 and MERS-CoV cases, a proportion of COVID-19 patients are also presented with vomiting, abdominal pain, diarrhea or liver dysfunction, evidenced by virus shedding in GI biopsy-specimen such as esophagus, duodenum, stomach and rectum, including stool and urine^[25-34]. Notably, higher amount of SARS-CoV-2 RNA has been detected in patients' rectal swabs and stool samples than nasopharyngeal specimen^[32-36]. Notably therein, the SARS-CoV-2 RNA remains detectable in COVID-19 patients' stool samples for several days even after their respiratory specimen are tested negative.

DETECTION OF INFECTIOUS SARS-COV-2 IN STOOL

The duration of SARS-CoV-2 shedding in COVID-19 patients stool with means of 2-3 weeks, and the amount of detectable viral RNA has been observed to vary from case to case^[32,34,36]. Notably, a recent study has demonstrated the infectivity of stool-derived SARS-CoV-2 to cultured cells^[37]. In view of this, inadequate sanitation and wastewater management in most of the low-income countries, potentially aggravate the risks of its fecal-oral transmission^[38].

SARS-COV-2 AND WATER CONTAMINATION

There has been quantitative survey of enteroviruses, noroviruses, and adenoviruses in in raw and treated wastewaters, downstream river waters, and drinking waters^[39,40]. However, we have very limited information on the occurrence of the novel SARS-CoV-2 in water sources. Very recently, environmental viability and infectivity of stool-derived SARS-CoV-2 using cultured cells have been reported^[37]. Like enteric CoVs, SARS-CoV-2 contamination of water sources may occur through various pathways. The surface water, such as ponds, lakes and rivers where wastewater is often discharged directly without proper treatment, can further transport the virus into the communities. Several recent surveillance studies have reported detection of SARS-CoV-2 RNA in raw and treated wastewater samples collected from various water-treatment plants, rivers and hospital septic tanks^[41-55]. Notably, wastewater surveillance in a Spanish low-prevalence area has supported the enteric and stool shedding of SARS-CoV-2 even before the first cases of COVID-19 were reported^[47]. In addition,

higher titers of SARS-CoV-2 have been also found in wastewater samples than clinically confirmed cases^[48]. In addition, a French surveillance study showed the increase of SARS-CoV-2 RNA surge units in raw water accurately followed the increase of COVID-19 cases, which could be even detected before the spread of epidemic. Notably therein, a marked decline in the viral RNA units was also observed with the reduction in new cases following the lockdown^[49]. Very recently, a quantitative survivability assessment of SARS-CoV-2 in water sources and the risk of fecal-oral infection within 39 countries has been conducted^[50]. This has demonstrated the virus stability in water with high infection rates (>100 RNA copies/100 ml) for up to 25 days, and country-specific relative risk of transmission via contaminated rivers, waterways and community water systems. Nonetheless, more experimental and clinical studies are further needed to show whether infectious as well as transmittable amounts of SARS-CoV-2 can be found in water sources.

CONCLUSION AND FUTURE PERSPECTIVES

As for enteric human CoVs, SARS-CoV-2 is also manifested in GI tract, including shedding of infectious virus in stool samples of COVID-19 patients. Detection of SARS-CoV-2 RNA in water sources thereby, provides a cautionary warning that COVID-19 can be spread through fecal-oral routes in resource-poor countries. Therefore, laboratory test of COVID-19 patients stool along with nasopharyngeal specimen as well as implementation of water surveillances could be very useful in protecting community health.

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