



COMMENTARY

Gut Feeling: The Plausible Faecal-Oral Transmission Route of Covid-19

Mohammad Khalid Parvez*

Department of Pharmacognosy, King Saud University College of Pharmacy, Riyadh, Saudi Arabia



*Corresponding author: Mohammad Khalid Parvez, PhD, Associate Professor, Department of Pharmacognosy, King Saud University College of Pharmacy, Riyadh 11451, Saudi Arabia, Tel: +966-14675132, Fax: +966-14677245

Abstract

The ongoing Covid-19 pandemic, caused by SARS-CoV-2 is taking a toll on public health. The spread of Covid-19 is confirmed through person-to-person direct contact, aerosolized nasal or oral droplets, and fomites. The clinical symptoms of Covid-19 are cough, headache, fever and breathlessness, including mild to severe pneumonia and death. In addition, a proportion of individuals experience vomiting, stomach ache or diarrhoea with or without respiratory disease. Recent clinical studies have reported detection of SARS-CoV-2 RNA in gut specimen and stool samples, suggesting another route of transmission in both symptomatic and asymptomatic cases. Therefore, occurrences of SARS-CoV-2 in human excreta and wastewater may further aggravate faecal-oral spread of Covid-19 in underdeveloped nations. Nonetheless, more studies are needed to show whether infectious as well as transmittable amounts of SARS-CoV-2 can be found in water sources.

Keywords

Covid-19, SARS-CoV-2, Clinical manifestation, Gastrointestinal shedding, Water contamination, Faecal-oral transmission

Background

The ongoing Covid-19 pandemic is taking a toll on public health, especially in underdeveloped countries with inadequate healthcare systems [1,2]. SARS-CoV-2, the etiological agent of Covid-19 is the third and most pathogenic human coronavirus after 2002-3 SARS-CoV-1 and 2012-13 MERS-CoV [2-4]. The SARS-CoV-2 is an enveloped, RNA virus genetically very close to bat SARS-like-CoV, suggesting its zoonotic origin [4,5]. The spread of Covid-19 is confirmed through person-to-person direct contact, inhalation of aerosolized nasal or

oral droplets, and fomites [6-8]. Though the high transmission and aggressive pathogenesis of SARS-CoV-2 still remain poorly understood, previous knowledge on the SARS-CoV-1 outbreak has helped understand these to some extent. SARS-CoV-2 has the incubation period of 2-14 days, and clinical symptoms include cough, headache, fever and breathlessness, including mild to severe pneumonia and death [9]. Some patients may also show rashes on toes (Covid toes), discolouration of skin, dizziness, burning sensation and loss of taste and smell. Notably, Covid-19 patients mostly in old age or with pre-existing medical conditions associated with lungs, heart, kidney or liver have shown higher mortality rate. Currently there is no specific treatment for Covid-19, except remdesivir that is approved as emergency antiviral and a couple of promising vaccines in clinical Phase I/II trials [1].

Gut Manifestation and Faecal Shedding of SARS-CoV-2

A proportion of Covid-19 patients also have nausea, vomiting, stomach aches or diarrhoea before the onset of respiratory symptoms [10-14]. Interestingly, the first case of Covid-19 in the United States had two days of nausea, vomiting and diarrhoea besides pneumonia [14]. In clinical analysis, SARS-CoV-2 RNA has been detected in anal or rectal swabs, blood and stool samples along with regular specimen like naso- or oro-pharyngeal swabs [14]. In addition, viral RNA has been identified in gut specimen from oesophagus, stomach, duodenum, and rectum of hospitalized patients [14-23]. Interestingly, higher viral loads are observed in the rectal swabs and stool samples than nasopharyngeal

swabs, collected at different time-points [19-23]. Very recently, detection of viral RNA is also reported in urine sample of a patient with severe pneumonia [24]. It appears that SARS-CoV-2 is detectable in the stool for several days even after the patient has cleared the virus from respiratory tract. Clearly therefore, patients who are asymptomatic or recovered from Covid-19 could be shedding high amount of virus into their faeces without knowing it. Taken together, it seems that shedding of SARS-CoV-2 in gastrointestinal tract and excreta is a common manifestation of Covid-19, which increases the risk of its community spread.

Stability and Infectivity of SARS-CoV-2 in Faecal Environment

The duration of SARS-CoV-2 shedding in stools with means of 14-21 days as well as the amount of detectable viral RNA has been observed to vary among patients [16,19,20,25,26]. Furthermore, though isolation of viable virus particles from faeces collected at later time points has been unsuccessful, results for RNA tests are shown positive. In view of this, shedding of SARS-CoV-2 in stool confirmed by RNA detection does not necessarily vouch for its viability several hours after defecation. And, whether the contaminated excreta are infectious and can be considered as another potential source of Covid-19 transmission, remain to be proven. Nonetheless, similar to enteric enveloped viruses that are shed in faeces as infectious particles, the SARS-CoV-2 virion should also remain stable and viable in environmental conditions *ex vivo*. To support this hypothesis, a very recent study has reported the infectious nature of faeces-derived SARS-CoV-2 in cultured cells [23]. However, a conclusive data on electron microscopic detection of viable SARS-CoV-2 particles in stools would be further required. To achieve this, multiple stool samples from several Covid-19 patients, and possibly at different time-points should be collected and stored at 4 °C, and analyzed shortly. Additionally, the physicochemical studies on the stability and viability of the virus particles at different environmental conditions, such as pH, temperature and disinfectant would be needed.

The Faecal-Oral or Aerosol-Nasal Transmission of SARS-CoV-2

Considering the cell culture based data that presents an experimental proof of infectivity of faeces-derived SARS-CoV-2 [23], the potentiality of water/food- or aerosol-borne transmission of Covid-9 is plausible. In general, enteric or diarrhoeal viruses have been well associated with various sources of contaminated water, including supply pipelines, wells, streams, lakes, swimming pools, and waste water. The raw eaten green vegetables such as salads and fruits, which are irrigated with untreated sewage or gray water, are a major source of such infections. Shellfish that grows in faeces-contaminated water is known to potentially transmit enteric

viruses. Moreover, inhalations of aerosolized or splattered infectious virus particles have been implicated in their community spread. Previously, a study on hundreds of infected residents of a private housing society in Hong Kong showed that building's faulty drainage significantly contributed to the aerosolization and respiratory spread of faecal SARS-CoV-1 [27].

Water Surveillance for SARS-CoV-2

In view of the hypothesised faecal contamination of water sources and water-borne spread of Covid-19, several surveillance studies have reported detection of SARS-CoV-2 RNA in wastewater [28-33]. Recently, occurrence of SARS-CoV-2 RNA in Spanish wastewater treatment plants in a low prevalence area has confirmed viral shedding in stools even before the first cases of Covid-19 were reported [34]. Therefore, water testing has been further suggested as a non-invasive early-warning instrument for monitoring the community spread of COVID-19 [35-37]. Even though there is a plausible high faecal-oral transmission of Covid-19 in regions with either poor sanitation or wastewater mismanagement, the role of human excreta is not widely endorsed.

Concluding Remarks

In the present health crisis, individuals with symptoms of vomiting or diarrhoea without respiratory or other explanation may be infected with Covid-19. The reports on detection of SARS-CoV-2 in human gastrointestinal specimen and excreta, verily suggest them as potential source of transmission in both symptomatic and asymptomatic cases. Thus, occurrences of SARS-CoV-2 in human excreta and wastewater under unhygienic practices or poor sanitation conditions may further aggravate faecal-oral spread of Covid-19 in underdeveloped nations. Moreover, detection of SARS-CoV-2 in wastewater highlights the relevance of water surveillance as an early indicator of Covid-19 within a community. Therefore, covid-19 surveillance could be implemented in wastewater treatment plants as an important tool to help municipalities to coordinate with healthcare authorities. Nonetheless, more experimental and clinical studies are needed to show whether infectious as well as transmittable amounts of SARS-CoV-2 can be found in water sources.

Conflict of Interests

The author has no conflict of interests and funding to declare.

References

- WHO (2020) Coronavirus disease (COVID-19) outbreak situation.
- Wu F, Zhao S, Yu B, Chen YM, Wang W, et al. (2020) A new coronavirus associated with human respiratory disease in China. *Nature* 579: 265-269.

3. Ren LL, Wang YM, Wu ZQ, Xiang ZC, Guo L, et al. (2020) Identification of a novel coronavirus causing severe pneumonia in human: A descriptive study. *Chin Med J (Engl)* 133: 1015-1024.
4. Gorbatenko AE, Baker SC, Baric RS, de Groot RJ, Drosten C, et al. (2020) The species severe acute respiratory syndrome-related coronavirus: Classifying 2019-nCoV and naming it SARS-CoV-2. *Nature Microbiol* 5: 536-544.
5. Chan JF, Kok KH, Zhu Z, Chu H, To KK, et al. (2020) Genomic characterization of the 2019 novel human-pathogenic coronavirus isolated from a patient with atypical pneumonia after visiting Wuhan. *Emerg Microbes Infect* 9: 221-236.
6. Chan JF, Yuan S, Kok KH, To KK, Chu H, et al. (2020) A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: A study of a family cluster. *Lancet* 395: 514-523.
7. Seto WH, Tsang D, Yung RW, Ching TY, Ng TK, et al. (2003) Effectiveness of precautions against droplets and contact in prevention of nosocomial transmission of severe acute respiratory syndrome (SARS). *Lancet* 361: 1519-1520.
8. van Doremalen N, Bushmaker T, Morris DH, Holbrook MG, Gamble A, et al. (2020) Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1. *N Engl J Med* 382: 1564-1567.
9. Huang C, Wang Y, Li X, Ren L, Zhao J, et al. (2020) Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 395: 497-506.
10. Gu J, Han B, Wang J (2020) COVID-19: Gastrointestinal manifestations and potential fecal-oral transmission. *Gastroenterology* 158: 1518-1519.
11. Wang D, Hu B, Hu C, Zhu F, Liu X, et al. (2020) Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *J Am Med Assoc* 323: 1061-1069.
12. Chen N, Zhou M, Dong X, Qu J, Gong F, et al. (2020) Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: A descriptive study. *Lancet* 395: 507-513.
13. Chang D, Lin M, Wei L, Xie L, Zhu G, et al. (2020) Epidemiologic and clinical characteristics of novel coronavirus infections involving 13 patients outside Wuhan, China. *JAMA* 323: 1092-1093.
14. Holshue ML, DeBolt C, Lindquist S, Lofy KH, Wiesman J, et al. (2020) First case of 2019 novel coronavirus in the United States. *N Engl J Med* 382: 929-936.
15. Zhang W, Du RH, Li B, Zheng XS, Yang XL, et al. (2020) Molecular and serological investigation of 2019-nCoV infected patients: Implication of multiple shedding routes. *Emerg Microbes Infect* 9: 386-389.
16. Xu Y, Li X, Zhu B, Liang H, Fang C, et al. (2020) Characteristics of pediatric SARS-CoV-2 infection and potential evidence for persistent fecal viral shedding. *Nature Med* 26: 502-505.
17. Tang A, Tong ZD, Wang HL, Dai YX, Li KF, et al. (2020) Detection of novel coronavirus by RT-PCR in stool specimen from asymptomatic child, China. *Emerg Infect Dis* 26: 1337-1339.
18. Young BE, Ong SWX, Kalimuddin S, Low JG, Tan SY, et al. (2020) Epidemiologic features and clinical course of patients infected with SARS-CoV-2 in Singapore. *JAMA* 323: 1488-1494.
19. Pan Y, Zhang D, Yang P, Poon LLM, Wang Q (2020) Viral load of SARS-CoV-2 in clinical samples. *Lancet Infect Dis* 20: 411-412.
20. Wu Y, Guo C, Tang L, Hong Z, Zhou J, et al. (2020) Prolonged presence of SARS-CoV-2 viral RNA in faecal samples. *Lancet Gastroenterol Hepatol* 5: 434-435.
21. Wang W, Xu Y, Gao R, Lu R, Han K, et al. (2020) Detection of SARS-CoV-2 in different types of clinical specimens. *JAMA* 323: 1843-1844.
22. Zheng S, Fan J, Yu F, Feng B, Lou B, et al. (2020) Viral load dynamics and disease severity in patients infected with SARS-CoV-2 in Zhejiang province, China, January-March 2020: Retrospective cohort study. *British Med J* 369: m1443.
23. Xiao F, Sun J, Xu Y, Li F, Huang X, et al. (2020) Infectious SARS-CoV-2 in feces of patient with severe COVID-19. *Emerg Infect Dis* 26.
24. Sun J, Zhu A, Li H, Zheng K, Zhuang Z, et al. (2020) Isolation of infectious SARS-CoV-2 from urine of a COVID-19 patient. *Emerg Microbes Infect* 9: 991-993.
25. Lescure F-X, Bouadma L, Nguyen D, Parisey M, Wicky PH, et al. (2020) Clinical and virological data of the first cases of COVID-19 in Europe: A case series. *Lancet Infect Dis*.
26. Wölfel R, Corman VM, Guggemos W, Seilmaier M, Zange S, et al. (2020) Virological assessment of hospitalized patients with COVID-2019. *Nature* 581: 465-469.
27. Yu IT, Li Y, Wong TW, Tam W, Chan AT, et al. (2004) Evidence of airborne transmission of the severe acute respiratory syndrome virus. *N Engl J Med* 350: 1731-1739.
28. Ahmed W, Angel N, Edson J, Bibby K, Bivins A, et al. (2020) First confirmed detection of SARS-CoV-2 in untreated wastewater in Australia: A proof of concept for the wastewater surveillance of COVID-19 in the community. *Sci Total Environ* 728: 138764.
29. La Rosa G, Iaconelli M, Mancini P, Ferraro GB, Veneri C, et al. (2020) First detection of SARS-CoV-2 in untreated wastewaters in Italy. *medRxiv*.
30. Lodder W, de Roda Husman AM (2020) SARS-CoV-2 in wastewater: Potential health risk, but also data source. *Lancet Gastroenterol Hepatology* 5: 533-534.
31. Medema G, Heijnen L, Elsinga G, Italiaander R, Brouwer A (2020) Presence of SARS-CoV-2 in sewage. *medRxiv*.
32. Rimoldi SG, Stefani F, Gigantiello A, Polesello S, Comandatore F, et al. (2020) Presence and vitality of SARS-CoV-2 virus in wastewaters and rivers. *medRxiv*.
33. Wu F, Xiao A, Zhang J, Gu X, Lee WL, et al. (2020) SARS-CoV-2 titers in wastewater are higher than expected from clinically confirmed cases. *medRxiv*.
34. Randazzo W, Truchado P, Cuevas-Ferrando E, Simón P, Allende A, et al. (2020) SARS-CoV-2 RNA in wastewater anticipated COVID-19 occurrence in a low prevalence area. *Water Res* 181: 115942.
35. Daughton C (2020) The international imperative to rapidly and inexpensively monitor community-wide Covid-19 infection status and trends. *Sci Total Environ* 726: 138149.
36. Mallapaty S (2020) How sewage could reveal true scale of coronavirus outbreak. *Nature* 580: 176-177.
37. Naddeo V, Liu H (2020) Editorial Perspectives: 2019 novel coronavirus (SARS-CoV-2): What is its fate in urban water cycle and how can the water research community respond? *Environ Sci Water Res Technol*.