

Opinion Paper

Are the Consequences of Gastrointestinal Infections of SARS-CoV-2 Underestimated?

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With more than 7.8 million confirmed cases and over 430,000 deaths COVID-19 has had an impact on the whole world (16.06.2020). In many countries the peak of the first wave seems to be passing and strict lockdown measures are being eased gradually. It is important to implement risk mitigation procedures to ensure the safety of those people returning to the workplace and participating in "public life". Despite mounting evidence that faeces are infectious there seems to be little discussion of this, no public awareness of risk, or implementation of potential mitigation strategies. In addition, lasting alterations in the gut microbiome of patients infected with SARS-CoV-2 have been observed in at least two pilot studies. Dysbiosis in the gut microbiome influences different biochemical functions and is associated with diverse diseases, effecting the immune system, metabolic states and mental health. In consequence, there could be unidentified long-term health risks of SARS-CoV-2 infections in the gut.

In a meta-analysis of 60 studies, comprising 4243 COVID-19 patients Cheung et al. showed that the pooled prevalence of any gastrointestinal symptoms was 17.6% (95% CI: 12.3-24.5%), with 11.8% occurring with non-severe COVID 19 symptoms and 17.1% with severe symptoms [1]. Not all studies reported all individual gastrointestinal symptoms, consequently the pooled prevalence of anorexia was 26.8% (95% CI: 16.2-40.8), diarrhoea 12.5% (95% CI: 9.6-16.0), nausea/vomiting 10.2% (95% CI: 6.6-15.3), and abdominal pain/discomfort 9.2% (95% CI: 5.7-14.5).

Using immunofluorescent staining, Xiao et al. showed expression of the ACE2 protein in the glandular cells of gastric, duodenal, and rectal epithelia [2]. They also demonstrated staining of viral nucleocapsid protein in the same epithelia cell populations. In addition, the authors showed that of 73 hospitalized patients in the study, 53% tested positive for SARS-CoV-2 RNA in stool. Wu et al. confirmed these findings and went a step further and followed the patients over time showing that respiratory samples remained positive for SARS-CoV-2 RNA for a mean of 16.7 days (SD 6.7) and faecal samples remained positive for a mean of 27.9 days (SD 10.7) after first symptom onset [3]. These findings have been repeated and verified in a number of additional studies, in adults and children, asymptomatic, mild and severe COVID-19 patients. In addition, Wu et al. showed that from 60 patients that were released from hospital after clinical recovery 10% were still positive for SARS-CoV-2 RNA in anal swab [4]. At least four independent studies have been published reporting the isolation of infectious SARS-CoV-2 from stool samples. For example, Wang et al. reported the isolation of live SARS-

CoV-2 from stool samples (non-diarrhoea) from two patients [5]. This is of particular interest since various studies have shown the production of bioaerosols during toilet flushing [6]. That is significant since new data shows that airborne transmission plays a major role for the spread of SARS-CoV-2 [7]. Indeed, in a report Liu et al. studied the potential aerosol transmission of SARS-CoV-2 in two Wuhan hospitals [8]. The authors reported elevated levels of viral RNA in the patient toilet areas and recommended proper disinfection and ventilation. In addition, Van Doremalen et al. showed that viable SARS-CoV-2 could be detected in aerosols up to 3 hours after aerosolization, and up to 2-3 days on plastic and stainless steel [9].

First studies of the gut microbiome of COVID-19 patients showed a significant decrease in diversity and abundance compared to healthy control (HC) [10]. This was combined with the increased relative abundance of opportunistic pathogens like *Streptococcus* and *Rothia*. The study showed significant disease-specific shifts in the overall microbiota composition between COVID-19 and H1N1 patients and HC. Changes in the gut microbiome have been shown to associate with various diseases, for example IBS, IBD, type 2 diabetes, cardiovascular condition and depression. Further studies are needed to evaluate the long term effects on SARS-CoV-2 infections in the gut and possibly a restorative treatment regime needs to be developed.

Taken together these results strongly indicate that SARS-CoV-2 infections in the gut have short- and long-term effects. The short-term effects are gastrointestinal symptoms and in about 50% of the patients viral shedding in stool occurs. Toilet flushing can create infectious bioaerosols that are a potential risk factor for oral/nasal-faecal transmission of SARS-CoV-2. Cleaning procedures of toilets in hospitals, care facilities, schools, nurseries, work places, restaurants, trains, busses, airplanes and public spaces will need to be looked at and perhaps improved.

Conflict of Interest

I am a founder, director and shareholder of TiKa Diagnostics Ltd., however the company is specialized in diagnostics of Mycobacteria (for example TB) in humans and animals, and has not provided funding or any other support/influence for this review.

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