Digestive Diseases

COVID-19: Don't Neglect the Gastrointestinal Tract!

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Infection with SARS-CoV2 affects predominantly the upper airways and the respiratory tract, but it frequently extends to the extrapulmonary system and can show manifestation in other organ systems. A series of clinical reports released during the last weeks indicate also a significant involvement of the gastrointestinal tract by the infection with SARS-CoV2.

There are 2 main aspects of concern: one being related to gastrointestinal symptoms (GIS) and their influence on the course of disease; the other being related to excretion of the virus (or its RNA fragments) in the patient's faeces and a possible role for faecal-oral transmission. Scientific assessment of both aspects is likely to provide important insights into the disease process and will emphasize the need for awareness of the involvement of the GI tract and help improve clinical management.

GIS in the context of COVID-19 include loss of appetite (anorexia), nausea, vomiting, diarrhoea, and abdominal pain. Available reports show a wide range regarding the prevalence of these symptoms, best explained by the retrospective nature of these studies. The prevalence of GIS was 11.4% among 651 included patients in Hangzhou [1], but was 50% among 204 patients in Hubei [2]. Cheung et al. [3] published a meta-analysis including more than 4,000 patients, reporting a prevalence of GIS of 17%. This was different from data from their local patient cohort in Hong Kong (59 patients) in which the prevalence was 25% [3]. In less than 10% of adult patients, GIS were the initial symptoms of COVID-19, with the frequency being higher in children. Recent experience has shown that GIS are frequently associated with a more severe course of the disease. Certainly, anorexia is rated as the most common symptom, but it is also the most unspecific among GIS and may primarily be related to systemic inflammation and malaise (fatigue) induced by the viral infection rather than to a substantial pathology within the gastrointestinal tract.

Diarrhoea represents the most relevant clinical aspect of gastrointestinal involvement. The prevalence of diarrhoea reported in 3 studies varied from 11 to 17% [1–3], but was as high as 31% in a group of healthcare workers with SARS-CoV2-induced pneumonia [4]. Apart from its impact on the patient's general condition, diarrhoea contributes to aggravation of the clinical course of COVID-19. Essential treatment of severe diarrhoea such as fluid and electrolyte replacement needs to be accompanied by the use of anti-diarrhoeic medication. Different mechanisms may contribute to diarrhoea in patients with COVID-19, and these have to be taken into account when choosing therapeutic measures. The latter includes stopping the administration of antibiotics (if such are administered) or switching to a different type, the administration of substances modulating the gut microbiome (e.g., probiotics and rifaximin) to help recover from dysbiosis, and the administration of conventional anti-diarrhoeic remedies to antagonize the damage to intestinal epithelia.

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In specific cases, the use of biologicals to modulate the immune system may also be considered.

Patients with chronic inflammatory bowel disease and other autoimmune diseases in the digestive system belong to the high-risk group for COVID-19 as these patients are often on immune-suppressive or immune-modulatory treatment. The pathophysiological impact of the infection and the cellular interaction of the virus with the intestinal mucosa have recently been reviewed elsewhere [5].

The other important feature of gastrointestinal issues in COVID-19 patients is the higher proportion of stool samples that are positive for virus RNA in patients with diarrhoea than in those without [4]. Of great concern is the prolonged SARS-CoV2 excretion in faeces which may persist after throat swabs turn negative. This could lead to persistent infectiousness beyond the time point at which patients are generally considered to be no longer at risk of transmitting the infection. Studies looking into this aspect report the persistence of faecal viral RNA in 23–82% for up to 11 days after oro-pharyngeal and sputum tests became negative [6]. Some patients retain the viral RNA for more than a month. Obviously, this could have an important impact on possibilities of viral transmission and the need and extent of hygienic measures to be taken. There remains major uncertainty as to whether SARS-CoV2 is viable in faeces or if the respective analyses report non-viable viral RNA fragments shed together with intestinal epithelial cells. For now, these data are obtained in retrospective, small-scale studies and are inconclusive.

Nevertheless, based on the information that is available, it is crucial to implement appropriate hygienic and medical strategies:

- Members of households of infected patients have to be informed about the possible routes of transmission of SARS-CoV2, in order to take special precautions such as the use of separate toilets where possible, careful and frequent hand washing, and regular washing of individual towels.
- Routine (elective) endoscopic examinations should be carefully planned in COVID-19 patients, and special precautions for protection of patients and the examining team should be taken.
- Faecal microbiota transplantation has become a very sensitive aspect in times of COVID-19. To prevent faecal SARS-CoV-2 transmission, a group of experts proposed assessing potential donors for the presence of typical COVID-19 symptoms within 30 days prior to donation. There is also the need for a detailed history including close contact with individuals with proven or suspected infection within the previous 30 days,

and, most importantly, extensive and dedicated testing for SARS-CoV2 in stool and upper airways [7]. (In our opinion, the use of faecal microbiota transplantation should remain maximally restrictive with the exception of refractory cases of *C. difficile* colitis, not responding to all novel medical options.)
- Considerations should be given to medication that might potentially prolong infectiousness either by modulation of gastric pH (i.e., acid suppressants) or by interfering with mucosal immunology (i.e., antibiotics).

The agenda for clinical research on COVID-19-related aspects in the gastrointestinal tract offers multiple opportunities. It certainly demands for studies on (a) the pathogenesis and impact of direct viral damage of the whole digestive system; and (b) factors contributing to COVID-19-associated diarrhoea with special emphasis on the gut microbiome and anti-diarrhoea management. A special focus should be directed on the role of the digestive system in transmitting the infection, on how to reduce the length of infectiousness, and on which precautions to be taken with regard to this matter.

Disclosure Statement

None of the authors have a conflict of interest.

Author Contribution

All authors have equally contributed in writing this editorial.

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