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Letter: SARS-CoV-2-induced gastrointestinal inflammation

We read with great interest the study of Taxonera et al on diarrhoea in IBD patients with COVID-19.[1] One potential link between SARS-CoV-2 infection and intestinal inflammation may be the ACE2 receptor.[2] However, it remains unclear to what extent active SARS-CoV-2 replication occurs in enterocytes.[3] A recent study in postmortem examinations found high viral loads in the upper gastrointestinal tract and ileum compared to those in the colon[4] without relevant histological abnormalities. Thus, the gradient between the viral load in the oesophagus and in the colon could be a result of swallowed viruses from the respiratory tract.

Therefore, we sought to differentiate intestinal inflammation in COVID-19 from detection of SARS-CoV-2RNA as a non-inflammatory epiphenomenon. All hospitalised patients received SARS-CoV-2 PCR of sputum, nasopharyngeal swabs, stool samples and rectal swabs as well as measurement of faecal calprotectin as a non-invasive marker of intestinal inflammation.[5] The study was approved by the local ethics committee (2020-1711).

We included 26 patients. The patients did not differ regarding age, sex, comorbidities or symptoms. SARS-CoV-2 PCR was positive in the rectal swab and/or stool sample in 10, including five stool samples, three rectal swabs and two patients with both a stool sample and rectal swab. Only three patients presented with ongoing diarrhoea at the time of admission, all without detection of SARS-CoV-2RNA in faecal samples. Faecal calprotectin was significantly higher in patients with detection of SARS-CoV-2 in either stool samples or rectal swabs (median 61.6 vs 240.5 ng/ml, $P = 0.001$; Figure 1). This association also held true when analysing only positive stool samples (75.8 vs 257 ng/ml, $P = 0.029$) or rectal swabs (64.9 vs 224 ng/ml, $P = 0.042$). A higher faecal calprotectin was associated with higher CRP and IL-6, indicating more severe systemic inflammation. However, this correlation failed to reach statistical significance (both Spearman's rho = 0.403, $P = 0.051$). Patients with detection of SARS-CoV-2 in faecal samples had a higher inflammatory response as indicated by IL-6 (89.6 vs 21.8 ng/ml, $P = 0.048$). As faecal calprotectin is an established surrogate marker of gastrointestinal inflammation, our results may hint towards relevant inflammation in patients with COVID-19 and detection of SARS-CoV-2 in faecal samples.

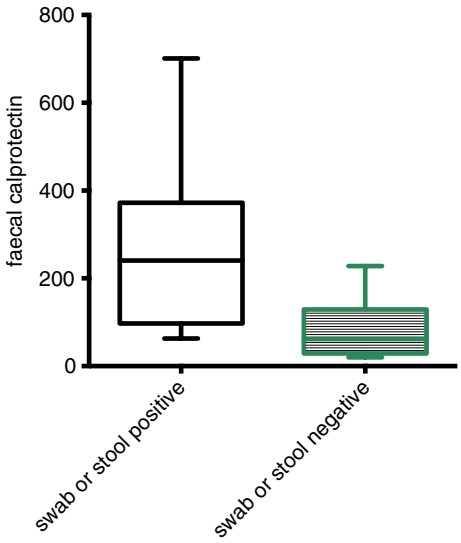

FIGURE 1 Boxplots of faecal calprotectin in patients with positive and negative rectal swabs or stool samples

In conclusion, the presence of SARS-CoV-2 in the gastrointestinal tract is associated with greater intestinal inflammation. Our results support the thesis that the presence of SARS-CoV-2 in the GI tract is not (only) a result of swallowed viruses but of gastrointestinal inflammation. This is supported by the fact that systemic markers of inflammation increase with increasing faecal calprotectin. This correlation was not statistically significant in this sample of 26 patients.

The concept of intestinal infection with SARS-CoV-2 and replication is also supported by a recent study from Hong Kong, which observed viral transcription activity in stool samples even after respiratory clearing.[6] This is important for faecal microbiota transplantation (FMT) for recurrent *Clostridioides difficile*. SARS-CoV-2 RNA should be tested for to ensure reliable patient access to FMT while maintaining the safety and quality of procedures.

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LINKED CONTENT

This article is linked to Taxonera et al and Taxonera & Alba papers. To view these articles, visit https://doi.org/10.1111/apt.15804 and https://doi.org/10.1111/apt.16117

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REFERENCES

1. Taxonera C, Sagastagoitia I, Alba C, Mañas N, Olivares D, Rey E. 2019 novel coronavirus disease (COVID-19) in patients with inflammatory bowel diseases. *Aliment Pharmacol Ther*. 2020;52:276-283.
2. Garg M, Royce SG, Lubel JS. Letter: intestinal inflammation, COVID-19 and gastrointestinal ACE2-exploring RAS inhibitors. *Aliment Pharmacol Ther*. 2020;52:569-570.
3. Zhou J, Li C, Liu X, et al. Infection of bat and human intestinal organoids by SARS-CoV-2. *Nat Med*. 2020;26:1077-1083.
4. Early postmortem mapping of SARS-CoV-2 RNA in patients with COVID-19 and correlation to tissue damage. bioRxiv [Internet]. https://www.biorxiv.org/content/10.1101/2020.07.01.182550v1
5. Magro F, Lopes J, Borralho P, et al. Comparison of different histological indexes in the assessment of UC activity and their accuracy regarding endoscopic outcomes and faecal calprotectin levels. *Gut*. 2019;68:594-603.
6. Zuo T, Liu Q, Zhang F, et al. Depicting SARS-CoV-2 faecal viral activity in association with gut microbiota composition in patients with COVID-19. *Gut*. 2020.(0):1–9.