



# Gastrointestinal tract diseases as a risk factor for SARS-CoV2 rectal shedding? An Italian report on 10 COVID-19 patients

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Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection has spread all over the world, with Italy being one of the most affected countries. Pandemic's serious consequences prompted researchers to clarify the possible transmission modes. To the best of our knowledge, no study from Italy has investigated SARS-CoV-2 rectal shedding, with the exception of a report describing a paucisymptomatic Italian who had been infected in China.<sup>1</sup>

SARS-CoV-2 rectal shedding would imply several consequences, e.g., the possibility of a genital contamination, arising concerns about the sexual transmission route and the obstetric management of coronavirus disease 2019 (COVID-19) pregnant women.<sup>2,3</sup>

Thus, we conducted a prospective study enrolling adult (age > 18 years) patients of both sexes with SARS-CoV-2 infection, who consecutively attended the Infectious Diseases Unit of the Azienda Ospedaliera Universitaria (A.O.U.) Federico II of Naples, from March through April 2020. SARS-CoV-2 infection

was defined by rhino-oropharyngeal swab positivity for SARS-CoV-2 RNA by reverse polymerase chain reaction (rRT-PCR). A rectal swab was collected from each subject on the same day the SARS-CoV-2 infection was diagnosed, performing an RT-PCR on these samples.

Ten patients were enrolled (7 males, 3 females; average age: 65 years). Six subjects had pneumonia, 1 was asymptomatic, and the others had mild to moderate symptoms. None was hospitalized in intensive care unit. Seven out of the 10 patients showed comorbidities: 3 were suffering from cardiovascular diseases, 1 from anxiety-depressive syndrome, 1 from cognitive decline and 2 from intestinal diseases. Two out of 10 patients (20%) showed a positive rectal swab for SARS-CoV-2. They were 75 and 67 years, respectively. Both were males, hypertensive and smokers, with the younger one having a history of chronic obstructive pulmonary disease. Interestingly, both patients had previously been hospitalized for their digestive pathologies (gallstone pancreatitis and colon adenocarcinoma, respectively) and then transferred to the Infectious Diseases Unit due to COVID-19 diagnosis. Here, they were treated with hydroxychloroquine, lopinavir/ritonavir, azithromycin and low-weight heparin for 14 days. All 10 patients achieved clinical healing and virological clearance according to 2 consecutive negative PCR tests on rhino-oropharyngeal swabs. Informed consent for the study was obtained from the patients. The study complied with the Declaration of Helsinki.

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Our study proposal was approved by the Scientific Ethics Committee of the University of Naples Federico II through an intra-departmental meeting on March 3, 2020 (protocol number: 213).

SARS-CoV-2 enters human cells through attachment to both angiotensin-converting enzyme 2 (ACE2) receptor (by S1-part of spike) and membrane (by S2-part of spike). Serine proteases, as the transmembrane serine protease 2 (TMPRSS2), can change S-spike configuration for a successful viral attachment.<sup>4</sup> ACE2 and TMPRSS2 are expressed in the intestinal epithelium.<sup>5</sup> To date, both viral RNA and live viruses have been detected in stools, indicating that digestive tract might be a site of viral replication.<sup>6-10</sup> The evidence that on the whole of our cases only the 2 patients suffering from preexisting digestive diseases showed a positive rectal swab, may not be a mere coincidence. Indeed, we hypothesize that digestive pathologies could facilitate infection of intestinal epithelium by SARS-CoV-2 and its replication, due to inflammation-related increase in ACE2 expression<sup>5</sup> and altered gut microbiome. Nowak et al.<sup>5</sup> demonstrated that inflammatory environment impacts on ACE2 and TMPRSS2 expression in patients with inflammatory bowel disease. The same authors suggested that active inflammatory bowel disease may enhance viral particle production and uptake in the colon.<sup>5</sup> Moreover, COVID-19 patients showed an imbalanced intestinal microbiota, with a reduced bacterial diversity and a higher relative abundance of opportunistic pathogens.<sup>9</sup> It is noteworthy that a close relationship exists between the gastrointestinal and respiratory tract, the so-called gut-lung axis. For example, influenza infection alters intestinal microbiota, and intestinal microflora disorders reduce host antiviral immune response.<sup>9</sup>

Our study shows a rate of 20% of positive rectal swabs (2/10) in a sample of COVID-19 patients. Previous studies indicated SARS-CoV-2 positive testing by stool samples, rectal swab or anal swab in up to 86% of patients with positive rhino-oropharyngeal swab, especially in children.<sup>8</sup> The lower percentage detected in our study could be due to the absence of pediatric patients, to the erratic viral rectal shedding,<sup>10</sup> and to the small sample size. We did not verify the duration of rectal swab positivity after respiratory clearance. However, there is evidence that viral shedding in the stool may continue for up to 10 weeks after initial symptoms.<sup>10</sup>

In conclusion, in our study the patients showing a positive rectal swab (20%, 2/10) had a preexisting gastrointestinal disorder. Thus, we speculate that such a comorbidity, inducing an inflammatory milieu with an imbalanced gut microbiome,

could provide a substrate facilitating the intestinal viral replication and the subsequent SARS-CoV-2 rectal shedding. Moreover, the diagnostic accuracy of rectal swab versus fecal material for SARS-CoV-2 detection needs further evaluation in larger studies.

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### Conflict of Interest

No potential conflict of interest relevant to this article was reported.

### Author Contribution

Conceptualization: all authors. Data curation: Patrì A, Pinchera B, Spirito L, Gentile I, Fabbrocini G. Formal analysis: Gentile I. Investigation: Pinchera B, Imbimbo C, Gentile I, Fabbrocini G. Methodology: Pinchera B, Gentile I. Supervision: Spirito L, Delfino M, Imbimbo C, Salvatore P, Gentile I, Fabbrocini G. Validation: Gentile I, Fabbrocini G. Writing-original draft: Patrì A. Writing-review & editing: all authors. Approval of final manuscript: all authors.

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