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LETTER TO THE EDITOR

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Stool samples versus nasopharyngeal specimens for the initial diagnosis of SARS-CoV-2 infection

Dear Editor,

We read with a great interest the article by Fumian et al.,[1] entitled "SARS-CoV-2 RNA detection in stool samples from acute gastroenteritis cases, Brazil" and published in the *Journal of Medical Virology* on January 2021. Indeed, their work and several others have reported the detection SARS-CoV-2 RNA in the feces of COVID-19 patients, which had suggested the possibility of SARS-CoV-2 transmission via the fecal-oral route. Clinical spectrum of the disease can be very heterogeneous,[2] and rapid and accurate diagnosis is essential for, early reporting, early quarantine, early treatment, and cutting off epidemic transmission. Gastrointestinal symptoms such as diarrhea, abdominal pain, and vomiting have been reported in patients with COVID-19, and have been correlated with SARS-CoV-2 RNA detection in stool samples of these patients.[3] With such data, some practionners are tempted to use stool samples, as an easier alternative to nasopharyngeal samples (NPS) for initial diagnosis of COVID-19.

We here describe a comparison between stool and nasopharyngeal specimens for the initial detection of SARS-CoV-2 RNA in patients with suspected COVID-19.

This retrospective analysis included consecutive patients who underwent COVID-19 testing on a NPS, with a stool sample collected within ±48 h of NPS collection. Samples were tested using a SARS-CoV-2 RT-PCR in-house assay developped by the Institut Pasteur Paris, or the Realstar SARS-CoV-2 RT-PCR Kit1.0 (Altona Diagnostics).

Data were compared using the Mann–Whitney test or the Fisher's exact test.

This study was based on medical records, in strict compliance with the French reference methodology MR-004 established by French National Commission on Informatics and Liberties, and approved by the Institutional data protection authority of CHU Lille.

A total of 197 patients were included in this study. The female/male sex-ratio was 0.93, and the median age was 53 years old (range from 0 to 96 years old). Most of stool samples (62.4%) were collected the same day as the NPS, and the others within ±48 h.

As shown in Figure 1, SARS-CoV-2 RNA was detected in 27 NPS (13.7%). Only 12 fecal samples corresponding to these NPS were found positive, giving a positive agreement of 44.4%. The median time since symptoms onset was similar in patients with a negative result in stools as compared to those with a positive result (8 vs. 6 days, $p = .88$). Similarly, the proportion of patients with gastrointestinal symptoms was not statistically different between both groups (50% vs. 40%, $p = .7$). The viral load in NPS seemed to be higher in patients with a detection of SARS-CoV RNA in stool samples, with a median cycle threshold (C_t) value at 22.7 (interquartile range = 16.4; 27.2) versus 25.6 (22.4; 30.4) in NPS of patients with a negative result in stools, but the difference did not reach statistical significance ($p = .1$). In patients with a positive result in stools, only a low correlation was observed between C_t values in NPS and in stool samples (Spearman's rank correlation coefficient = .32).

On the other hand, the negative agreement was 98.8%. Indeed, virus RNA was detected in two stool samples among those corresponding to negative NPS. In one patient, the stool sample was collected 2 days postsymptoms onset, and the COVID-19 diagnosis was confirmed with a positive sputum sample. In the other patient, the stool sample was collected 20 days post symptoms onset. No other respiratory sample was available, but anti-SARS-CoV-2 IgM and IgA antibodies were detected in a serum sample collected 4 days later.

Our results confirm that SARS-CoV-2 RNA is detected in stool only in a proportion of patients with positive respiratory samples. In their recent meta-analysis, Cheung et al.[3] reported that virus RNA was detected in stool samples from 48.1% of COVID-19 patients during the course of the illness, even in stool collected after respiratory samples tested negative. The duration of SARS-CoV-2 detection was reported to be significantly longer in stool samples than in respiratory samples[4] and can reach up to 47 days after first symptoms onset.[5] However, viral RNA was detectable in the stool of only 15.3% of patients on presentation.[3]

Otherwise, it is currently well-known that NPS can yield false negative results, probably due to sample quality, or to the time of collection, and this type of sample should be repeated or supplemented with other types of samples such as LRT specimens in patients with pneumonia, or stool samples in patients with gastrointestinal symptoms.

In conclusion, stool samples cannot be used as alternative to NPS for the initial diagnosis of COVID-19; however, they can represent an additional tool in patients presenting with gastrointestinal symptoms.

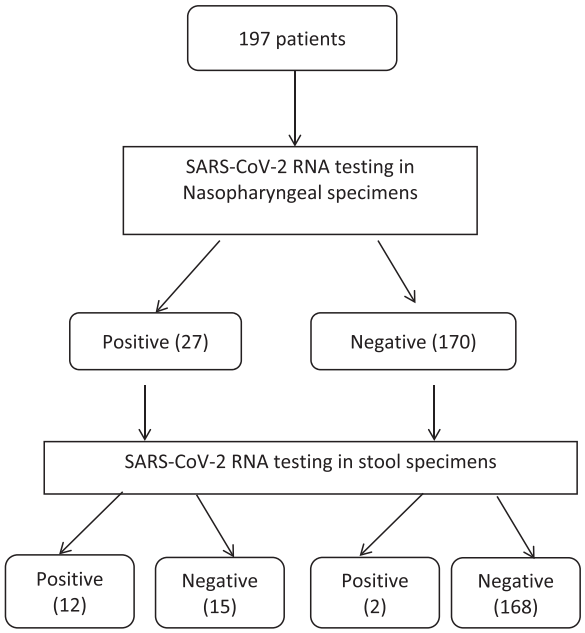

FIGURE 1 Detection of SARS-CoV-2 RNA in stool and nasopharyngeal specimens

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AUTHOR CONTRIBUTION STATEMENT

Enagnon Kazali ALIDJINOU designed the study and contributed to data collection, data analysis and manuscript drafting; Laurine MILLIERE contributed to data analysis and manuscript drafting; Ilka ENGELMANN, Claire TINEZ, Youssef BOUAROURO, Mahdi OUAFI, Mouna LAZREK, Brigitte PREVOST, Didier HOBER and were involved in specimen analysis and data collection. All Authors contributed to critical revision of manuscript.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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