The Association between Stool Shedding of SARS-Cov-2, Microbiome Diversity and Intestinal Inflammation

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Introduction

- The transmission of the etiologic virus of COVID-19 (severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]) is thought to occur mainly via respiratory droplets.
- However, limited evidence has shown the virus can be found in feces and involve the gastrointestinal (GI) tract.
- The implications of these findings are unclear.

Aims

- The aim of this study was to assess if patients with COVID-19 present with fecal shedding of SARS-CoV-2.
- We also sought to assess intestinal inflammation and changes in their microbiota.

Methods and Materials

- **Design:** prospective cohort study that included outpatients preenting with symptoms of COVID-19 and were tested using a nasopharyngeal PCR test (NPT).
- **Inclusion criteria:** Two cohorts were selected: one with a (+) NPT and a control group with a (-) NPT. Stool and a clinical data were collected at baseline and then, days 14, 28 and 42.
- SARS-CoV-2 viral loads were measured in stool using PCR and stool microbiome was analyzed using 16S rRNA gene sequencing (V3/V4 region).
- Fecal calprotectin levels were also measured on each sample and used as a surrogate marker of intestinal inflammation.
- Primary Outcome: Detectable SARS-CoV-2 viral loads

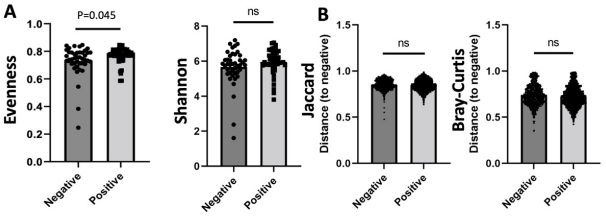
Results

- 101 patients were recruited (410 total samples).
- Of those, 55 had a (+) COVID-19 NPT.
- Most patients with a (+) COVID-19 NPT PCR had a detectable fecal viral load (71%).
- Among these patients, 23 (55%) had detectable viral stool loads only at baseline.
- Within the rest, 12 had detectable viral loads through day 14, 6 through day 28 and one through day 42.
- Only one patient had a (-) NPT but detectable SARS-CoV-2 in the baseline stool sample.
- Subjects with (+) NPT presented more commonly with myalgias (p=0.02), dysgeusia (p=0.019) and anosmia (p=0.03) when compared to those with (-) NPT.
- There were no differences in any other symptoms including GI manifestations.
- Within the group with a (+) NPT, those patient with detectable SARS-CoV-2 in the stool were younger but no differences were seen in other demographic variables, symptoms, or fecal calprotectin levels (**Table 1**).
- There was no correlation between fecal SARS-CoV-2 loads and fecal calprotectin levels (rho: 0.007 [p=0.95]).
- Patients with a (+) NPT PCR had higher evenness when compared to those that tested (-) for a NPT PCR.
- However, no differences were seen in other alpha or beta diversity (**Figures 1 A and 1B**, respectively).

Table 1

	(+) NP test (n=54)	(-) NPT (n=45)	P value
Age [Mean in years (SD)]	37 (10)	40 (13)	0.30
Female gender [n (%)]	41 (75.9)	38 (82.6)	0.41
Race [n (%)]			0.22
Caucasian	31 (56.4)	29 (63.0)	
Black	18 (32.7)	16 (34.8)	
Asian	1 (1.8)	1 (2.2)	
Hispanic ethnicity [n (%)]	3 (5.6)	1 (2.2)	0.39
Detectable stool SARS-Cov-2 [n (%)]	39 (70.9)	1 (2.2)	<0.0001*
Body Mass Index [Mean in Kg/m2 (SD)]	31.5 (8.4)	28.0 (6.8)	0.1
Oxygen saturation [Mean in % (SD)]	98.1 (1.5)	97.8 (1.9)	0.49
Fecal calprotectin [Median in µg/mg(IQR)]	30 (30-83)	30 (30-34)	0.92
Symptoms at presentation			
Fevers [n (%)]	14 (25.5)	11 (23.9)	0.86
Fatigue [n (%)]	34 (61.8)	22 (47.8)	0.16
Cough [n (%)]	32 (58.2)	22 (47.8)	0.30
Anorexia [n (%)]	1 (1.8)	1 (2.2)	0.9
Pharyngalgia [n (%)]	25 (45.5)	21 (45.7)	0.98
Myalgias [n (%)]	33 (60.0)	17 (37.0)	0.02*
Anosmia [n (%)]	12 (21.8)	3 (6.5)	0.03*
Dysgeusia [n (%)]	13 (23.6)	3 (6.5)	0.019*
Any gastrointestinal Symptoms [n (%)]	32 (58.2)	23 (50.0)	0.41
Diarrhea [n (%)]	15 (27.3)	11 (23.9)	0.7
Abdominal pain [n (%)]	2 (3.6)	6 (13.0)	0.08
Nausea [n (%)]	15 (27.3)	17 (37.0)	0.3
Blood in the stool [n (%)]	None	1 (4.4)	0.12

Figure 1



Conclusions

- Even though intestinal viral shedding of SARS-CoV-2 in patients with COVID-19 is common, these patients do not present with elevated fecal calprotectin.
- They also don't present with a significantly disrupted gut microbiome or a higher incidence of gastrointestinal symptoms when compared to patients with respiratory symptoms and no COVID-19.