# Effects of COVID-19 on the Gut and the Liver - A Case Series of 711 Patients in New York City

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**Research Article**

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# Abstract

**Background** As the COVID-19 epidemic is wreaking havoc with a staggering number of infections and fatalities worldwide, digestive symptoms are increasingly coming to the limelight. However, the data on the extent of gut and liver involvement has been variable and somewhat conflicting.

**Methods** We identified 711 adults who had tested positive for COVID-19 at Richmond University Medical Center in New York between March 13 and May 13, 2020. We analyzed their clinical and laboratory data from electronic medical records.

**Results** The average age of the patients was 60.5 years; 55% were men. 27.1% reported a gastrointestinal (GI) symptom and 56.9% had at least one abnormal liver enzyme. The most common was diarrhea with a frequency of 17.3% followed by nausea 16.2% and vomiting/anorexia 13.7%. Abdominal pain 5.6%, dysgeusia 3.2%, and GI bleeding 2.2% was the least common. Symptoms were mostly mild and lasted 3-5 days. The liver function was deranged in more than half of the patients. AST alone was elevated in 16.6%, both AST/ALT 15.7%, alkaline phosphatase 23%, and bilirubin 10%. Potential confounders were rare but included preexisting liver disease and hepatotoxic medications. Prothrombin time (PT) was mildly elevated in 13.4%. The lipase was elevated in 2.4% without upper abdominal pain. In 75%-90% of cases, liver test abnormalities were mild (1.5-3 x normal). Overall, 86.6% of patients were admitted primarily with respiratory failure and 28.5% died of their illness.

**Conclusions** 27% of COVID-19 patients experienced a digestive disturbance and >55% showed a predominantly mild degree of liver dysfunction and cholestasis.


# Introduction

### Reports of severe acute respiratory syndrome coronavirus 2

(SARS-CoV-2) related gastroenteritis and hepatitis are increasingly drawing medical attention. In some cases, digestive symptoms are the earliest or the only presenting complaints of the disease (1-2). However, the number of studies is still small to reliably estimate the rate, extent, and severity of the alimentary canal involvement. We aimed to retrospectively study 711 COVID-19 patients at a single center to determine the frequency of gastrointestinal (GI) and liver manifestations and their severity.

# Methods

### Study Population, Setting, And Data Collection

We identified 716 patients who had tested positive for Covid-19 at the Richmond University Medical Center or one of its ambulatory centers between March 13 and May 13, 2020, at the peak of the epidemic in New York City. We included 711 adults (18 years and over) in the study regardless of the reason for their visit. 641 patients had a positive result on a reverse-transcriptase–polymerase-chain-reaction (RT-

PCR) assay on a nasopharyngeal swab; 616 of them were admitted due to SARS CoV-2 related hypoxic respiratory failure. The remaining 71 patients had a positive result on the Abbott ID Now rapid test on a nasal specimen. They included pregnant women in the labor and delivery ward (n=44), patients in the psych unit (n=11), or outpatient clinic/endoscopy suite (n=16). Children (younger than 18 years of age) were excluded from the study. Informed consent was waived. We performed a retrospective electronic chart review to obtain demographic data, information on GI symptoms, and laboratory results. We looked for reports of dysgeusia, anorexia, nausea, vomiting, diarrhea, abdominal pain, and GI bleeding at or before the presentation or at any time during the course of hospital stay. Abnormal liver function tests (LFTs) were categorized as mild if 1.5-3 x upper limit of normal (ULN), moderate (3-9 x ULN), and severe (>10 x ULN). Results were carefully interpreted, considering any potential confounders. We specifically looked for preexisting liver disease (hepatitis C, chronic alcoholic liver disease, cirrhosis) and reviewed medication history, especially oral anticoagulants and anti-retroviral agents to account for deranged LFTs.

### Statistical Analysis

We summarized the categorical variables as counts and percentages.

## Results

### Demographic Characteristics

The study population comprised a diverse ethnic group including Whites (284), Blacks (180), Hispanics/Latinos (170), Asians (37), and mixed (40). The mean age of the patients was 60.5 years; 55% (n=395) were men. (Figure 1)

### Frequency of GI Symptoms in COVID-19

We found that GI symptoms were documented in 27% (n=193) of patients with COVID-19. Diarrhea was the most common complaint with a frequency of 17.3% (n=86) followed by nausea 16.2% (n=80), and vomiting/anorexia 13.7% (n=68). Except in very few cases (n=4), neither vomiting nor diarrhea was profound to cause any severe dehydration. Some patients had abdominal pain 5.6% (n=28) which was mostly described as cramps. The mean duration of symptoms was 3-5 days. The least commonly reported complaints were dysgeusia 3.2% (n=16) and GI bleeding 2.2% (n=11). (Figure 2). 4 patients with occult bleeding and 2 with overt bleeding had a hemoglobin drop above 2 g/dl and received transfusion therapy.

### Liver and Pancreatic Function Abnormalities

We found biochemical evidence of hepatopancreaticobiliary dysfunction in the majority of COVID-19 patients (Figure 3). 57% (n=405) had at least one abnormal result. AST alone was elevated in 16.6% (n=118), both AST/ALT 15.7% (n=112), alkaline phosphatase 23% (n=164), and bilirubin 10% (n=71). In a small number of patients (n=6), ALT alone was elevated. Overall, 33.5% had an abnormal ALT/AST (75%

were mild) and 21.4% had cholestasis with abnormal alkaline phosphatase (92% were mild). Some patients had chronic liver disease (n=9), notably cirrhosis, alcoholic hepatitis, and hepatitis C. Others had been taking HIV medications (n=9). However, the enzyme levels in these patients were found to be elevated > 2 times above their baseline values. PT/INR was mildly elevated in 13.4% (n=95) of patients. While 27 of these patients were on an oral anticoagulant, the rest could likely be attributed to COVID-19. The lipase level was elevated (1.5 to 4 x ULN) in 2.4% (12/502) of patients. However, there was no associated characteristic upper abdominal pain to suggest pancreatitis.

### The Bigger Outcome Picture

88.6% (n=630) of our patients were admitted with respiratory failure and 28.5% (n=203) died of their illness.

# Discussion

These findings reflect a significant impact of COVID-19 on the digestive system and liver function. Although diarrhea and vomiting were the most prevalent symptoms, neither was severe to solely cause end-organ damage e.g. acute kidney injury or hypotension. Studies have shown that GI symptoms of COVI-19 may precede respiratory symptoms (1). We found one patient who presented similarly. Up to 10% of patients may present only with GI symptoms without any respiratory symptoms (2). Both of these observations carry important clinical and public health implications and can help the clinicians in early diagnosis as well as infection control by timely isolation. Our results are concordant with other studies from the US and Europe, although researchers from China have reported a lower rate of GI symptoms in Wuhan patients (3). The average duration of the reported symptoms in our study subjects was between 3-5 days. However, studies have shown prolonged viral particle shedding in stools, in some cases weeks after the nasopharyngeal clearance of the virus (4). The clinical significance of this and the virulence of fecal viral RNA fragments is currently unknown.

The extent of aminotransferase enzymes elevation, especially in patients with chronic liver disease indicates that COVID-19 can add injury to insult by further hepatocellular damage. The proposed mechanisms are severe immune response syndrome, or direct viral cytotoxicity (5). Fortunately, none of the patients developed acute liver failure. Concomitant administration of any hepatotoxic medication should be avoided. Early data points to the role of angiotensin-converting enzyme-2 (ACE-2) receptors in enterocytes, cholangiocytes, and hepatocytes as the SARS-CoV-2 portal of entry to GI tract (6). Currently, there is no evidence of any correlation between the severity of the digestive and pulmonary symptoms of COVID-19. Nevertheless, more severe alterations in liver enzymes found in critical care patients may be associated with poorer outcomes (6). 13.5% (n=96) of patients in this case series had no symptoms despite a documented infection. They had tested positive after screening before same-day surgery, psychiatric admission, labor, and delivery, or discharge to a nursing home. The case fatality rate of 28.5% in this series is lower than what has earlier been reported by S Richardson et al in New York at the peak of

the epidemic (7). This is a grim public health reminder of the deadly nature of COVID-19 and the exorbitant toll on the hospital resources.

This study sheds some light on the propensity of the novel coronavirus to affect the digestive system. It shows a significant frequency of GI symptoms and considerable liver injury, albeit rather mild in severity. We believe that the actual numbers may be higher given the physicians' emphasis on the more critical respiratory manifestations of the disease and consequently, under-reporting of GI symptoms by providers and/or patients. This tendency is one of the limitations of our study. Second, we could not follow-up on the patients who were discharged from the emergency room to obtain additional history about any new GI symptoms after the discharge. Larger, conclusive studies are needed to better understand the GI pathogenesis of COVID-19. Other important and challenging aspects for gastroenterologists that call for definitive answers are the risk of exposure during endoscopies, the risk of the fecal-oral transmission, and the safety of fecal microbiota transplantation.

## Declarations

All human studies at our institution are approved by the hospital ethics committee.

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## Figures

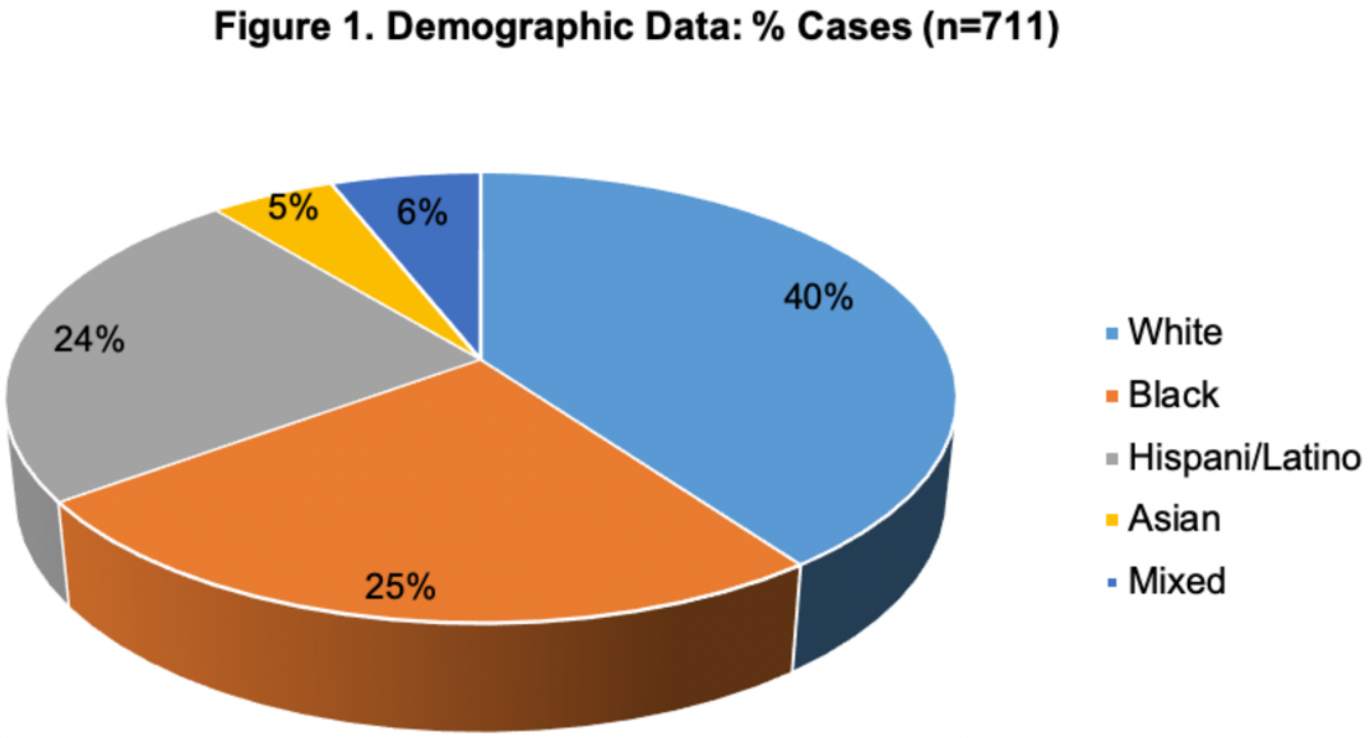


**Figure 1**

Demographic Data: % Cases (n=711)

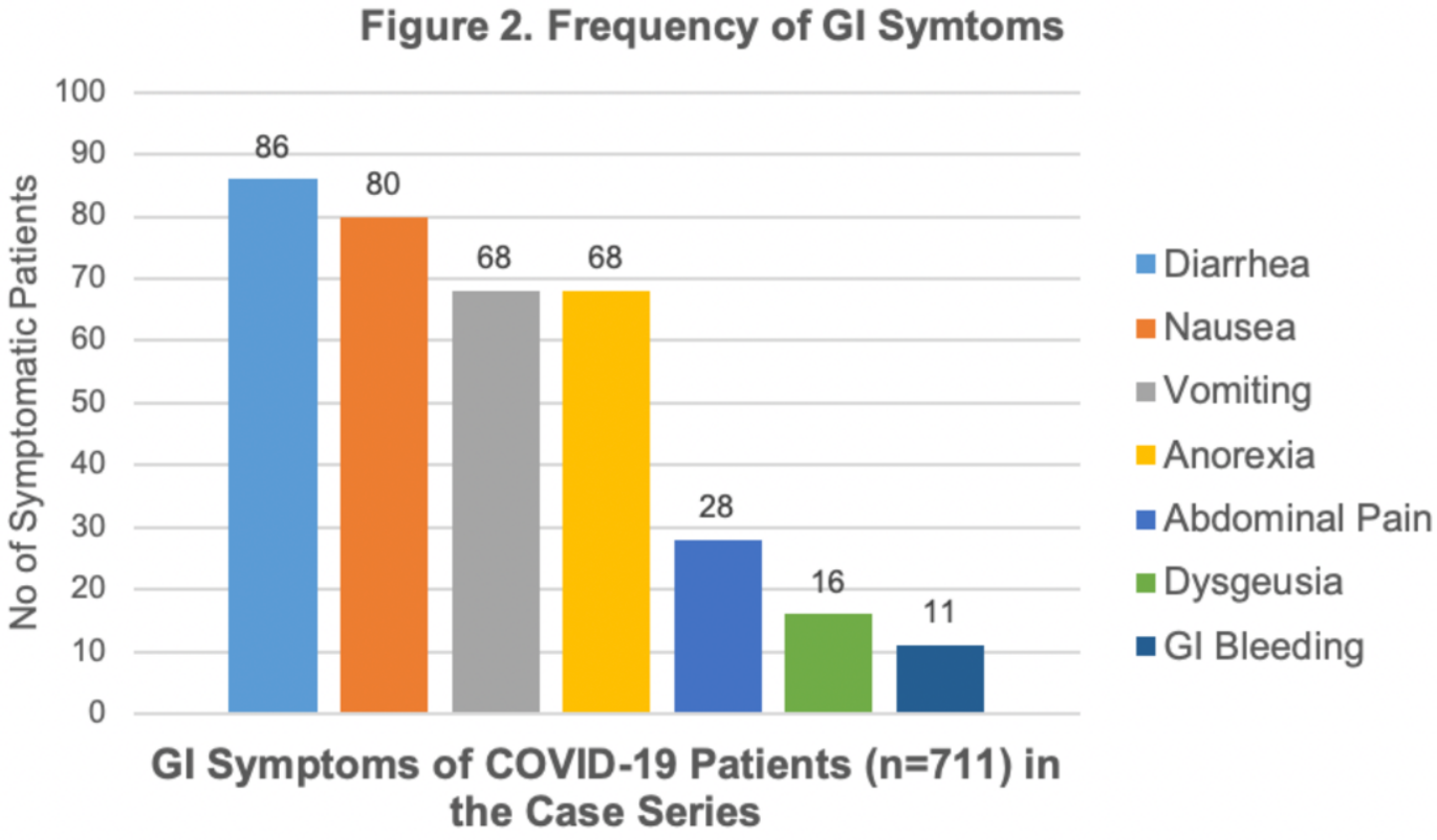


**Figure 2**

GI Symptoms of COVID-19 Patients (n=711)

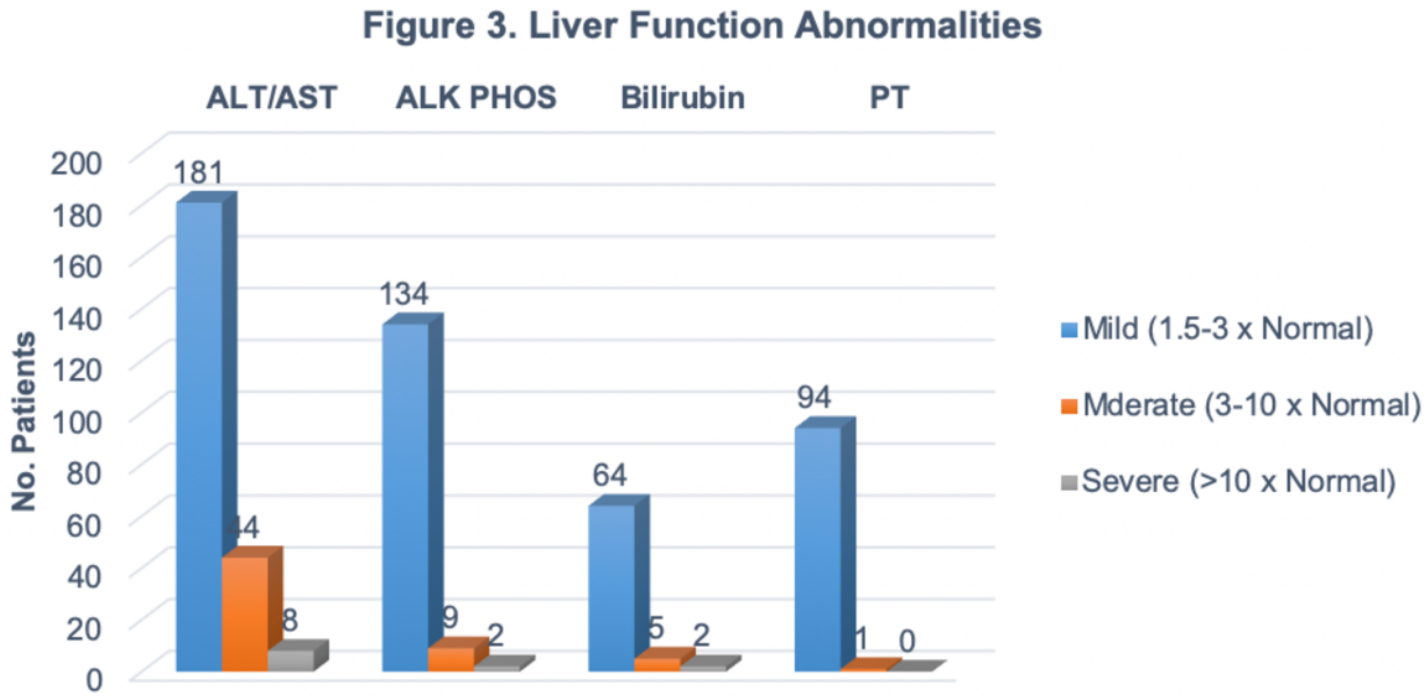


**Figure 3**

Liver Function Abnormalities in 711 COVID-19 Patients