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Symptom Profiles and Risk Factors for Hospitalization in Patients With SARS-CoV-2 and COVID-19: A Large Cohort From South America

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The pandemic caused by a novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can cause several gastrointestinal (GI) symptoms. A recent systematic review showed a prevalence of GI symptoms in 17.6%. The most frequent manifestations were anorexia (26.8%), diarrhea (12.5%), nausea/vomiting (10.2%), and abdominal pain (9.2%),¹ and recent reports showed the detection of viral RNA in stools for prolonged periods (70.3%).¹

We established the frequency and impact of GI symptoms, and viral presence in stools among Chilean patients infected with SARS-CoV-2.

Methods

We used information available from the Chilean Ministry of Health. SARS-CoV-2 infection was confirmed by a quantitative real-time reverse transcription-polymerase chain reaction from nasopharyngeal swab (NPS).

We analyzed a convenience cohort (2 hospitals, Faculty-of-Medicine, Pontificia Universidad Católica de Chile/FM-PUC) of SARS-CoV-2-infected patients, including their sociodemographic and clinical data, and biological samples (nasopharyngeal swab, sputum, and stools), which were collected for quantitative real-time reverse transcription-polymerase chain reaction analyses, and used the cycle threshold (C_T) as a surrogate marker of viral load. The protocol was approved by the FM-PUC Scientific Ethics Committee.

Results

In Chile, there were 82,271 tests performed to detect SARS-CoV-2, and 7213 (8.8%) were positive by April 11, 2020, accounting for an incidence of 37.1 cases per 100,000 inhabitants. We included 7016 in the analysis (97.3% of patients confirmed nationally). The median age was 40 years, and 50% were female individuals.

The most common symptoms were cough (53.4%), myalgia (56.4%), and fever (43.9%) (Figure 1). Diarrhea was reported in 7.3%, and 3.7% had abdominal pain. A total of 1155 patients were hospitalized (16.5%): 716 (62%) were in a general ward, 439 (38%) were in an intensive care unit, and 328 (28.4%) required mechanical ventilation. At the end of this study, 80 deaths had occurred (mortality rate 1.1%).

The presence of diarrhea was associated with a higher risk of hospitalization, with a relative risk of 1.31 (95% confidence interval 1.1–1.57; $P < .01$), but abdominal pain was not (relative risk 1.25, 95% confidence interval 0.98–1.60; $P < .076$).

In the convenience cohort ($n = 28$), the median age was 43.6 years (23–83); 11 (39.3%) were female individuals, and 12 (42.9%) were hospitalized. None of our patients died at the end of this study. Twelve (42.9%) patients referred to GI symptoms, including diarrhea (32.1%), nausea (14.3%), abdominal pain (3.6%), and vomiting (3.6%). Viral RNA was detected in 23 patients (83.1%) with respiratory secretions, and 6 (50%) patients with stool samples available were positive. Of these, 4 (66.7%) presented GI symptoms (Figure 1). No differences were observed in viral load in stools from patients with or without gastrointestinal symptoms, based on C_T values (C_T : 37.06 vs 35.47; $P = .800$, respectively). Interestingly, patients with diarrhea presented a trend toward higher viral detection in stools (odds ratio 6.8 (0.95–48.69); $P = .056$).

Discussion

In Chile, 7.3% of patients with SARS-CoV-2 reported diarrhea and 3.7% abdominal pain. A significant percentage of our population required hospitalization, reaching a low mortality rate of 1.1%. The presence of diarrhea was associated with a higher risk of hospitalization, increasing the risk by 31%; however, abdominal pain was not associated with a higher risk of hospitalization. In our convenience cohort, we determined that 50% of patients had detectable stool viral RNA during illnesses, and patients with diarrhea had higher stool RNA positivity than those without diarrhea.

The overall frequency of GI symptoms was similar to other populations.^{1–3} Recent publications showed that the frequency of GI symptoms is higher in severe patients,

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Abbreviations used in this paper: C_T , cycle threshold; GI, gastrointestinal; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

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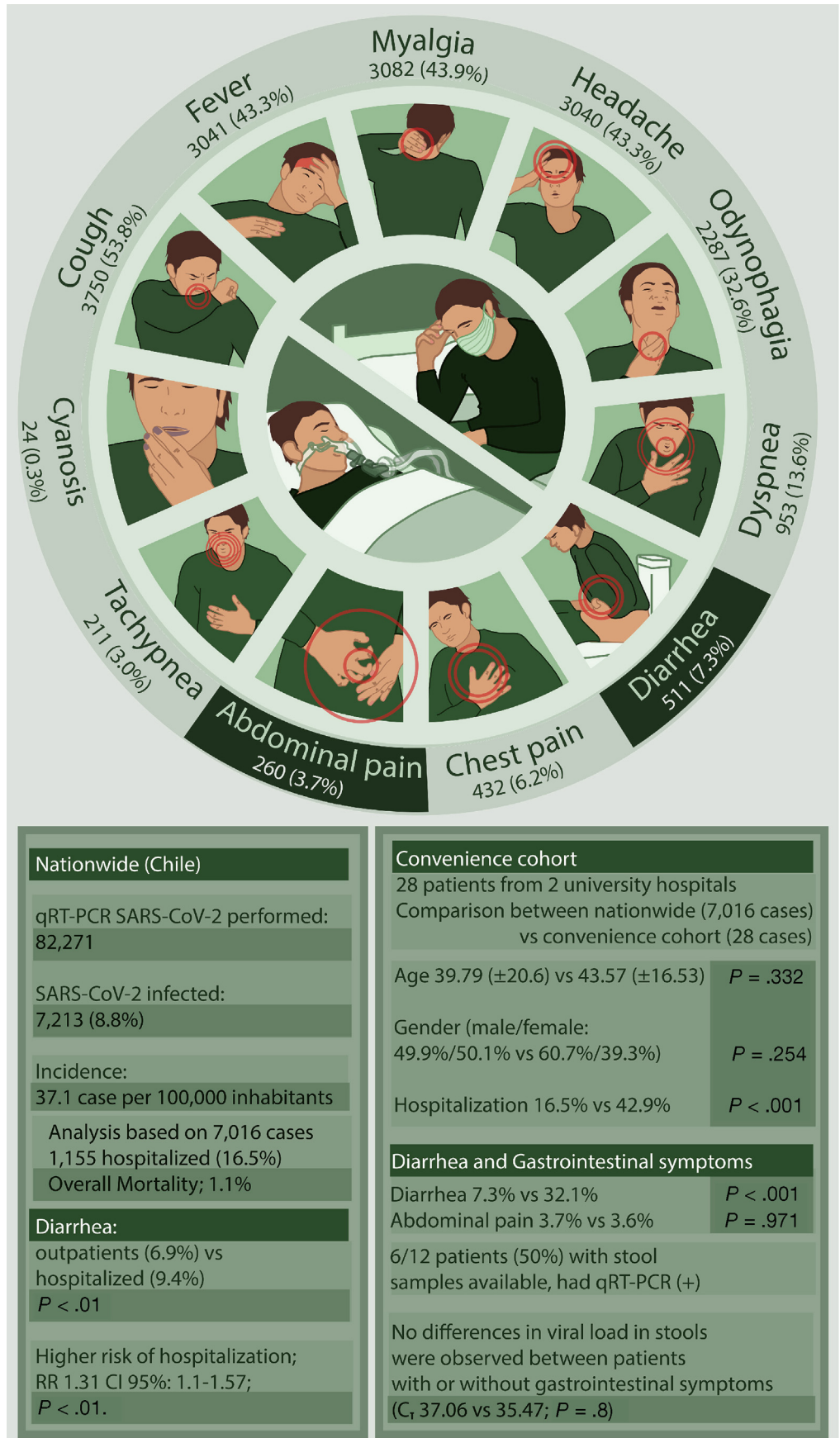


Figure 1. Clinical manifestations of SARS-CoV-2-infected patients in Chile.

becoming more pronounced with an increase in disease severity.^{1,2} However, the specific symptoms associated with higher risk had not been characterized. In this study, diarrhea and nausea were the most prevalent symptoms, highlighting and confirming the diverse clinical manifestations.^{1,3-5}

The mean C_T value was similar between patients with and without GI manifestations. We could obtain stool samples only from a subset of our recruited patients; hence, further studies are warranted to accurately assess the proportion of individuals with viral shedding in stools.

It has been widely proposed that SARS-CoV-2 could enter cells using the angiotensin-converting enzyme-2 as a receptor.⁶ Angiotensin-converting enzyme-2 modulates intestinal inflammation, and recent evidence showed that intestinal epithelium also supports SARS-CoV-2 replication, suggesting that the fecal-oral route could provide a source of potential transmission.^{7,8}

In conclusion, the presence of diarrhea was associated with a higher risk of hospitalization in Chilean patients diagnosed with SARS-CoV-2. The frequency of GI manifestations in our population is similar to previous reports. Fifty percent of patients have detectable SARS-CoV-2 RNA in stools. The fecal-oral route might be an underestimated mechanism of transmission. Preventive measures focused on this pathway could potentially decrease transmission.

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Conflict of interest

The authors disclose no conflicts.

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