Gastrointestinal symptoms in COVID-19 could be associated with severe lung involvement and increased readmission rates

Hüseyin S Bozkurt¹ and Ömer Bilen²

Abstract

Introduction: SARS-CoV-2 virus manifests itself with primary lung damage but also has intestinal involvement. In this study, we aimed to investigate the frequency of gastrointestinal symptoms (GIS) and the relationship of GIS with readmission to the hospital within 30 days in SARS-CoV-2 infected patients who were hospitalized in a specified pandemic hospital.

Materials and Methods: Symptomatic patients diagnosed with rapid antibody positivity with real-time polymerase chain reaction and typical thorax computed tomography findings were included in this retrospective cohort observational study. Demographic and clinical data were obtained from electronic medical records. Hospital-associated GIS were considered as experiencing at least one of the GIS such as gas, bloating, diarrhea, and constipation developing within 72 h after hospital admission.

Results: The mean age of the patients was 58 ± 14.4 years and 60.7% were men. 82% of hospitalizations were a moderate and severe disease. 71.4% of patients without GIS had at least one of the GIS after hospitalization. As the severity of the disease increased, the frequency of the severity of gastrointestinal symptom increased. GIS bowel disorders were more prominent in patients with moderate and severe disease. Antibiotic and specific treatment (anti-IL-1, anti-IL-6) contributed to the occurrence of gastrointestinal symptom in SARS-CoV-2 inpatients.

Conclusion: According to our observations of the second wave of the pandemic, the presence, frequency, and severity of gastrointestinal symptom in inpatient is associated with severity of lung disease and increased readmission rate after discharge.

Keywords
SARS-CoV-2, gastrointestinal symptom, pneumonia

Introduction
SARS-CoV-2 virus which emerged in Wuhan, China, in 2019 caused severe damage as a result of uncontrolled adaptive immune response in the lungs but also in the bowels. Although the genomic and physiological mechanisms of the virus have been resolved to a great extent, uncertainties regarding multi-organ involvement persist.

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The fact that the virus involves the gastrointestinal system, as well as the lung system, is important in terms of showing the close relationship of the virus with the intestinal immune system. Although SARS-CoV-2 often manifests itself only with upper respiratory tract symptoms and signs of lung damage, the presence of gastrointestinal symptoms (GIS) which might be associated with intestinal dysbiosis affects mortality and morbidity. The finding of whole genome sequencing in the stools gives an insight that damages in the gut is a possibility. Dysbiosis of the gut microbiota leads to immune disturbance in the respiratory epithelium and mucosa, which can trigger impaired immune responses to respiratory viral infections. Because of the involvement of the intestinal system, hospital-associated causes of GIS may play an important role in the management of SARS-CoV-2. Despite the important roles of the gut–lung axis in antiviral immunity, only limited information is currently available concerning SARS-CoV-2 specific changes in the intestinal symptoms and there are very limited studies on the effect of hospital-associated GIS on the prognosis and follow-up of SARS-CoV-2.

In our study, we aimed to investigate the frequency of GIS such as gas, bloating, diarrhea, and constipation and the relationship of GIS with readmission to the hospital within 30 days in inpatients who had no previous GIS.

Method

Patients

This retrospective single-center cohort study included 28 mild/moderate/severely ill adult inpatients (≥18 years old), who were admitted to Istanbul Maltepe University Medical Faculty Hospital, the designated hospital for COVID-19 patients, 2020 from 1 November 2020, to 15 December 2020. All patients were diagnosed as COVID-19 positive according to WHO interim guidance and the treatment was in line with the Turkish management guidelines for COVID-19. It has been scanned retrospectively from the hospital registry system by following per under the Helsinki Declaration principles. The patients were followed up on 15 January 2021.

Inclusion criteria

Hospital-associated GIS was considered as experiencing at least one of the GIS such as gas, bloating, diarrhea, and constipation that developed 72 h after hospital admission. Patients with a previous diagnosis of COVID-19, a history of vaccination, and GIS were not included in the study (Table 1).

Procedures

The epidemiological and clinical characteristics and medication of confirmed mild/moderate/severe cases of SARS-CoV-2 were collected from electronic medical records by a standardized case report form. The method used for laboratory confirmation of SARS-CoV-2 is to perform real-time reverse-transcriptase polymerase chain reaction assay tests using throat swab specimens that were obtained from upper respiratory tracts every other day after clinical remission of symptoms, including fever, cough, and dyspnea.

The illness severity of SARS-CoV-2 was defined according to the clinical and thorax CT radiological criteria:

Mild Disease/Pneumonia: Patients who are in the clinic of fever, cough, and fatigue, who do not need oxygen and shortness of breath, and who have a normal lung or slightly ground glass appearance on tomography.

Moderate Disease/Pneumonia: Patients who describe shortness of breath in addition to clinical findings, SpO2 > 90 and above, need intermittent nasal oxygen, and with ground-glass, uncommon local or multi-focal infiltration findings on tomography.

Severe Disease/Pneumonia: In addition to clinical findings, patients with significant shortness of breath, SpO2 < 90 and in need of oxygen with a continuous nasal and/or mask, and diffuse ground glass in tomography, diffuse multi-focal infiltrations, and consolidated areas.

The criteria for discharge were the absence of fever for at least 3 days, substantial improvement in both lungs on chest CT, clinical remission of respiratory symptoms, and two throat-swab samples negative for the SARS-CoV-2 test obtained at least 24 h.

The specific treatment consists of monoclonal antibodies [anti-Il6(TCZ), anti-Il1] and immune plasma therapies.

Outpatient readmission means further inpatient admission rather than presenting for follow-up and as a criterion for readmission to the hospital in 30-day return; it was symptomatic such as cough, dyspnea, weakness 1 month after discharge.

Statistical analysis

Chi-square independence test was used to get the dependency relation between variables which are at nominal and/or ordinal scale. If the prerequisite of the chi-square independence test was not provided, Fisher’s exact test was used for 2*2 contingency tables. To test the mean equality for two groups, the Mann Whitney U test was used because of the normality condition. Frequency distribution and percentage were used as descriptive statistics for nominal and ordinal scale variables. Mean, standard deviation, and frequency
Table 1. Clinic features of SARS-CoV-2 inpatients.

| Case | Gender | Age (y/o) | Mild pneumonia | Steroid and LMWH | Inpatient day | Specific treatment (IL-1, IL-6, plasma) | Specific Treatment type | >1 GIS | Gastronestinal symptom type | Gastronintestinal symptom type | Antibiotic type | Antibiotic type | Died | Readmission on hospital after first month | Treatment type of readmission | Unit |
|------|--------|-----------|----------------|-----------------|---------------|------------------------------------------|------------------------|--------|-----------------------------|-----------------------------|-----------------|-----------------|------|----------------------------------------|--------------------------|------|
| 1    | F      | 45        | No             | No              | 6             | No                                       | No                     | No     | No                          | No                          | No              | No              | No   | No                                     | No                      |      |
| 2    | F      | 47        | Yes            | No              | 5             | No                                       | No                     | No     | No                          | No                          | No              | No              | No   | No                                     | No                      |      |
| 3    | M      | 51        | Yes            | No              | 8             | No                                       | No                     | No     | No                          | No                          | No              | No              | No   | No                                     | No                      |      |
| 4    | F      | 36        | Yes            | No              | 4             | No                                       | No                     | No     | No                          | No                          | No              | No              | No   | No                                     | No                      |      |
| 5    | M      | 41        | Yes            | No              | 7             | No                                       | No                     | No     | No                          | No                          | No              | No              | No   | No                                     | No                      |      |
| 6    | M      | 81        | Moderate        | Yes             | 14            | No                                       | Yes                    | Constipation | No                          | No                          | No              | No              | No   | No                                     | No                      |      |
| 7    | F      | 40        | No             | Moderate        | 13            | No                                       | No                     | No     | No                          | No                          | No              | No              | No   | No                                     | No                      |      |
| 8    | F      | 61        | No             | Moderate        | 11            | No                                       | No                     | No     | No                          | No                          | No              | No              | No   | No                                     | No                      |      |
| 9    | F      | 45        | No             | Severe          | 12            | Yes                                      | Yes                    | Tobramab | Yes                         | Gas                          | Blasting         | Yes             | No   | Yes                                    | Gastrointestinal         |      |
| 10   | M      | 66        | No             | Moderate        | 14            | Yes                                      | Yes                    | Yes     | No                          | No                          | Gastrointestinal         | No              | Yes   | No   | Yes                                    | Gastrointestinal         |      |
| 11   | M      | 44        | No             | Severe          | 10            | Yes                                      | Yes                    | TCZ     | Yes                         | Gas                          | Blasting         | Yes             | Yes   | No                                     | Pulmonologist            |      |
| 12   | F      | 50        | No             | Severe          | 10            | Yes                                      | Yes                    | Gas      | Blasting                    | Yes                          | Gastrointestinal         | No              | Yes   | No   | Yes                                    | Pulmonologist            |      |
| 13   | F      | 50        | No             | Severe          | 10            | Yes                                      | Yes                    | Constipation | Gas                          | Yes                          | Gastrointestinal         | No              | Yes   | No   | Yes                                    | Pulmonologist            |      |
| 14   | M      | 65        | No             | Severe          | 14            | Yes                                      | Yes                    | TCZ     | Yes                         | Gas                          | Diarrhea                 | Yes             | No    | Yes   | Yes                                    | Pulmonologist            | Cardiology |
| 15   | F      | 45        | No             | Moderate        | 13            | No                                       | Yes                    | Yes     | Gas                         | Blasting                    | Yes                          | Yes             | No    | No   | Yes                                    | Pulmonologist            | Outpatient Internal medicine |
| 16   | M      | 44        | No             | Severe          | 12            | Yes                                      | Yes                    | TCZ     | Yes                         | Gas                          | Blasting         | Yes             | No    | No   | Yes                                    | Gastrointestinal         | Pulmonologist |
| 17   | M      | 73        | No             | Severe          | 11            | Yes                                      | Yes                    | TCZ     | Yes                         | Gas                          | Blasting         | Yes             | No    | No   | No                                    | Pulmonologist            | Outpatient Internal medicine |
| 18   | M      | 80        | No             | Severe          | 22            | Yes                                      | Yes                    | TCZ     | Yes                         | No                          | No              | No              | No    | No   | Yes                                    | Pulmonologist            | Pulmonologist |
| 19   | M      | 49        | No             | Severe          | 10            | No                                       | Yes                    | NO      | No                          | No                          | No              | No              | No    | No   | No                                    | Pulmonologist            | Pulmonologist |
| 20   | M      | 87        | No             | Severe          | 13            | Yes                                      | Yes                    | Immune plasma | Deterhia                    | Yes                          | Ceftriaxone | No              | No    | No   | No                                    | Pulmonologist            | Pulmonologist |
| 21   | M      | 61        | No             | Severe          | 23            | Yes                                      | Yes                    | TCZ     | No                          | Deterhia                    | Yes                          | Meropenem | Yes   | No   | No                                    | Pulmonologist            | Pulmonologist |
| 22   | M      | 80        | No             | Moderate        | 11            | Yes                                      | Yes                    | Anti-IL-1 | Yes                         | Gas                          | Blasting         | Yes             | Yes   | No   | No                                    | Ceftriaxone             | Pulmonologist |
| 23   | M      | 48        | No             | Severe          | 17            | Yes                                      | Yes                    | TCZ     | No                          | Deterhia                    | Yes                          | Ceftriaxone | No    | No   | No                                    | Pulmonologist            | Pulmonologist |
| 24   | F      | 70        | No             | Severe          | 14            | Yes                                      | Yes                    | TCZ     | No                          | Deterhia                    | Yes                          | Meropenem | Yes   | No   | No                                    | Pulmonologist            | Pulmonologist |
| 25   | F      | 70        | No             | Severe          | 17            | Yes                                      | Yes                    | TCZ     | No                          | Gas                         | Blasting         | Yes                          | Meropenem | No    | No   | No                                    | Pulmonologist            | Pulmonologist |
| 26   | M      | 76        | No             | Severe          | 10            | Yes                                      | Yes                    | Anti-IL-1 | Yes                         | Gas                          | Blasting         | Yes                          | Ceftriaxone | No    | Yes   | No                                    | Pulmonologist            | Outpatient Internal medicine |
| 27   | M      | 49        | No             | Severe          | 8             | Yes                                      | No                     | TCZ     | No                          | Deterhia                    | Yes                          | Ceftriaxone | No    | No   | No                                    | Pulmonologist            | Outpatient Internal medicine |
| 28   | M      | 50        | No             | Severe          | 24            | Yes                                      | Yes                    | Anti-IL-1 | Yes                         | Gas                          | Blasting         | Yes                          | Ceftriaxone | No    | Yes   | No                                    | Pulmonologist            | Outpatient Internal medicine |

| Gender | Frequency | Percent |
|--------|-----------|---------|
| Male   | 17        | 60.7    |
| Female | 11        | 39.3    |
| Total  | 28        | 100.0   |

| Inpatient day | N | Mean | Standard deviation | Minimum | Maximum |
|---------------|---|------|-------------------|---------|---------|
| 28            | 28| 12.25| 4.995             | 4       | 24      |

| Age | N | Mean | Standard deviation | Minimum | Maximum |
|-----|---|------|--------------------|---------|---------|
| 28  | 28| 58.00| 14.409            | 36      | 87      |

| Mild pneumonia | N Mean | Standard deviation | Minimum | Maximum |
|----------------|--------|--------------------|---------|---------|
| Yes            | 179    | 80.1               | 17.9    | 50.0    |
| Steroid and LMWH | 82.1 | 17.9               | 50.0    | 50.0    |
| Specific treatment (anti-IL-1, IL-6, plasma) | 5.0 | 5.0 | 5.0 | 5.0 |
| >1 GIS | 6.79 | 32.1 | 39.3 | 53.6 |
| Gastronintestinal symptom type | 6.07 | 32.1 | 39.3 | 53.6 |
| Antibiotic | 1.79 | 80.1 | 17.9 | 50.0 |
| Died | 1.79 | 80.1 | 17.9 | 50.0 |
| Readmission on hospital after first month | 6.07 | 32.1 | 39.3 | 53.6 |
were used as descriptive statistics for interval/ratio scale variables. SPSS version 25 was used for analysis.

**Results**

**Outcome**

The current study described 28 mild/moderate/severely ill adult inpatients (≥18 years old), who were admitted to Istanbul Maltepe University Medical Faculty Hospital during the second wave of the pandemic, the designated hospital for COVID-19 patients, 2020 from 1 November 2020, to 15 December 2020. The patients were followed up on 15 January 2021. The mean age of the patients was 58 ± 14.4 years and 60.7% were men. 82% of hospitalizations were a moderate and severe disease. 71.4% of patients without gastrointestinal symptom had at least one of the GIS after hospitalization, and as the severity of the disease increases, the frequency of development of GIS increases. While gas was the predominant symptom in patients with mild disease, it was found that more than one gastrointestinal symptom is more prominent in patients with moderate and severe disease. Gastrointestinal symptom occurrence is dependent on specific treatment (Il-1, Il-6, and plasma therapy) (\( p = 0.033 \)). While the mean procalcitonin level were 0.5 ng/mL in patients with severe disease and GIS, they were within normal limits in other patients. The occurrence of GIS is dependent on the use of antibiotics (\( p = 0.000 \)). Mortality is not dependent on experiencing the GIS. > 1 gastrointestinal symptom is dependent on the severity of pneumonia (\( p = 0.041 \)). Readmission to the hospital is dependent on having >1 symptom (\( p = 0.023 \)). Although the presence of GIS increases the length of hospital stay, the difference is not statistically significant (\( p = 0.173 \)).

**Clinical features**

GIS and following up inpatients. > 1 gastrointestinal symptom is dependent on the severity of pneumonia at a 95% confidence level. While the rate of having >1 symptom is 0.0% in those with mild pneumonia, this rate is 39.1% in those who have moderate and severe pneumonia (chi-square = 6.087, df = 1, \( p = 0.041 \)) (Table 2).

**Antibiotic/specific treatment and GIS in inpatients**

The occurrence of gastrointestinal symptom is dependent on the use of antibiotic at a 99% confidence level (chi square = 17.309, SD = 1, \( p = 0.000 \)).

While all those who use antibiotics experience GIS, this rate decreases to 27.3% in those who do not use an antibiotic (Table 3).

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**Table 2.** Pneumonia severity and GIS association.

| Mild pneumonia * >1 GIS crosstabulation |  |  | Total |
|----------------------------------------|---|---|-------|
|                                        | Yes | No |       |
| Mild pneumonia                         |     |    |       |
| Yes                                    | 0   | 5  | 5     |
| % within mild pneumonia                | 0.0%| 100.0%| 100.0%|
| No                                     | 14  | 9  | 23    |
| % within mild pneumonia                | 60.9%| 39.1%| 100.0%|
| Total                                  | 14  | 14 | 28    |
| % within mild pneumonia                | 50.0%| 50.0%| 100.0%|

**Table 3.** Antibiotic and GIS in inpatients.

| Antibiotic                          | Yes | No | Total |
|-------------------------------------|-----|----|-------|
| Gastrointestinal symptom            |     |    |       |
| Yes                                 | 17  | 3  | 20    |
| % within antibiotic                 | 100.0%| 27.3%| 71.4%|
| No                                  | 0   | 8  | 8     |
| % within antibiotic                 | 0.0%| 72.7%| 28.6%|
| Total                               | 17  | 11 | 28    |
| % within antibiotic                 | 100.0%| 100.0%| 100.0%|
Gastrointestinal symptom occurrence is dependent on specific treatment at a 95% confidence level (chi-square = 6.30, SD = 1, \( p = 0.033 \)). While the rate of experiencing GIS is 92.9% in those who receive specific treatment (TCZ, anti-IL1 treatment), this rate decreases to 50.0% in those who do not receive specific treatment (Table 4).

**Inpatient day**

Although the presence of GIS increases the length of hospital stay, the difference is not statistically significant (Table 5) (\( \mu_{\text{Yes}} = 13.57, \mu_{\text{No}} = 13.57, p = 0.173 \)).

**Readmission in the first month between GIS and non-GIS groups**

Readmission to the hospital is dependent on having >1 gastrointestinal symptom at a 95% confidence level. While 71.4% of those who were readmitted to the hospital had >1 symptom, this rate was 28.6% in those who did not re-admit to the hospital (chi-square = 5.143, df = 1, \( p = 0.023 \)) (Table 6).

The gastrointestinal symptom is dependent on having >1 GIS at 95% confidence level. While 65.0% of those who experienced GIS had >1 symptom, this rate was 12.5% in

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**Table 4.** Specific treatment and GIS in inpatients.

| Gastrointestinal symptom (72 h of hospitalization) | Specific treatment (anti-IL-1, anti-IL-6, plasma) | Yes | No | Total |
|-----------------------------------------------------|-----------------------------------------------|-----|----|-------|
| Yes Count 13 % within specific treatment 92.9% 50.0% 71.4% | | 13 | 7 | 20 |
| No Count 1 % within specific treatment 7.1% 50.0% 28.6% | | 1 | 7 | 8 |
| Total Count 14 % within specific treatment 100.0% 100.0% 100.0% | | 14 | 14 | 28 |

**Table 5.** Inpatient day between GIS and non-GIS group.

| >1 GIS | N | Mean | Standard deviation | Standard error mean | Mann U | Z | p |
|--------|---|------|--------------------|---------------------|---------|---|---|
| Inpatient day | Yes | 14 | 13.57 | 4484 | 1.199 | 68,500 | 0.173 |
| No | 14 | 10.93 | 5196 | 1389 | 1363 |

**Table 6.** Readmission rates between GIS and non-GIS groups.

| Readmission hospital * >1 GIS crosstabulation | Yes | No | Total |
|-----------------------------------------------|-----|----|-------|
| Yes Count 10 % within readmission 71.4% 28.6% 100.0% | | 10 | 4 | 14 |
| No Count 4 % within readmission 28.6% 71.4% 100.0% | | 4 | 10 | 14 |
| Total Count 14 % within readmission 50.0% 50.0% 100.0% | | 14 | 14 | 28 |
those who did not readmit to the hospital (chi-square = 6.300, df = 1, p = 0.033) (Table 7).

### Antibiotic and specific treatment on readmission

Readmission to the hospital is not dependent on antibiotic use (chi-square = 0.150, df = 1, p = 0.699). Antibiotic use is 64.3% for those who were readmitted to the hospital, while this rate is 57.1% for those who do not apply to the hospital again (Table 8).

Readmission to the hospital is not dependent on specific therapy (chi-square = 0.000, df = 1, p = 1.000). Specific therapy usage rate is 50% for those who return to the hospital and those who do not (Table 9).

### Discussion

SARS-CoV-2 infection usually presents itself with respiratory symptoms such as cough, shortness of breath, and fever. On the other hand, gastrointestinal symptom manifests itself in a very wide distribution rate of 3–70%. The rate of SARS-CoV-2 presenting with primary GIS is around 10%. SARS-CoV-2 has been shown to use the receptors of angiotensin-converting enzyme-2 (ACE-2) as

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**Table 7.** Hospitalization and GIS association.

| Gastrointestinal symptom (72 h from hospitalization) * >1 GIS crosstabulation |
|------------------------------------------------|
| **>1 GIS** | **Yes** | **No** | **Total** |
| Gastrointestinal symptom | Count | 13 | 7 | 20 |
| % within gastrointestinal symptom | 65.0% | 35.0% | 100.0% |
| No | Count | 1 | 7 | 8 |
| % within gastrointestinal symptom | 12.5% | 87.5% | 100.0% |
| Total | Count | 14 | 14 | 28 |
| % within gastrointestinal symptom | 50.0% | 50.0% | 100.0% |

**Table 8.** Antibiotic in inpatients and readmission rates.

| Readmission * antibiotic crosstabulation |
|-----------------------------------------|
| **Antibiotic** | **Yes** | **No** | **Total** |
| Readmission | Count | 9 | 5 | 14 |
| % within readmission | 64.3% | 35.7% | 100.0% |
| No | Count | 8 | 6 | 14 |
| % within readmission | 57.1% | 42.9% | 100.0% |
| Total | Count | 17 | 11 | 28 |
| % within readmission | 60.7% | 39.3% | 100.0% |

**Table 9.** Specific treatment in inpatients and readmission rate.

| Readmission * specific therapy crosstabulation |
|-----------------------------------------------|
| **Specific treatment** | **Yes** | **No** | **Total** |
| Readmission | Count | 7 | 7 | 14 |
| % within readmission | 50.0% | 50.0% | 100.0% |
| No | Count | 7 | 7 | 14 |
| % within readmission | 50.0% | 50.0% | 100.0% |
| Total | Count | 14 | 14 | 28 |
| % within readmission | 50.0% | 50.0% | 100.0% |
the cellular receptor system in the upper respiratory tract, and although the expression of ACE-2 in the gastrointestinal system is quite high,\textsuperscript{9,10} the presence of GIS at varying rates and its effects on disease prognosis are still not fully explained.\textsuperscript{11}

In our study, it was observed that 71.4% of patients without GIS showed at least one of the symptoms after hospitalization and the frequency of development of intestinal disorders such as diarrhea–constipation increased as the disease severity increased. These findings suggest that the presence of GIS, which has a variable effect on the prognosis of the disease, may develop due to various factors (hospital infection, intensive antibiotic use, common proton pump inhibitor use, and specific treatments) rather than primary gastrointestinal system involvement of SARS-CoV-2 infection.

Tocilizumab (TCZ) is a type of monoclonal antibody that prevents hyperinflammation caused by IL-6 by binding to the IL-6 receptor and used for COVID treatment. TCZ has been reported to cause gastrointestinal damage, dysbiosis, and systemic infections.\textsuperscript{12,13} Alberto et al. reported that due to the competitive feature of anti-IL-1, it has the potential to increase viral replication with the target of rapamycin (mTOR) pathway,\textsuperscript{14} as well as gastrointestinal adverse effects with the mTOR pathway.\textsuperscript{15} Furthermore, it has been clearly shown that long-term, widespread use of proton pump inhibitor causes dysbiosis by disrupting the intestinal microbiota due to gastric hypoacidity.\textsuperscript{16} Widespread antibiotic use is the most common cause of intestinal dysbiosis in hospital admissions and SARS-CoV-2 is frequently used in patients. Antibiotic use should not be included in the management of COVID-19 unless the presence of bacterial infection is proven.\textsuperscript{17} Although antibiotic use is 64.3% for those who were readmitted to the hospital in our study, bacterial co-infection cannot be reliably ruled out.

Another interesting result of our study is the emergence of a linear relationship between GIS and SARS-CoV-2 lung injury. Since most of the GIS in our study occurred after hospitalization, it should be kept in mind that hospital-associated GIS may increase lung damage of SARS-CoV-2.

Although we found 47.82% in our study, Banerjee et al. showed that the 30-day return hospital admission rate was 8.5% with pneumonia.\textsuperscript{18} This can be explained by the fact that GIS can affect hospital admissions rates. However, it should be cited that patients with more severe disease are much more likely to be readmitted to hospital, either due to persistent symptoms, complications of COVID-19, or because of pre-existing co-morbidities and viral immunopathological research is needed for the prognosis of hospital-associated GIS. Our observational cohort study group was small and our initial results must further be supported by large cohort randomized studies. There is also a need for more comprehensive analytic calculation studies by confirming gut microbial analysis methods in those with dysbiosis in large cohort randomized studies.

**Conclusion**

Since the relationship between SARS-CoV-2 disease and gastrointestinal findings is very close, hospital-associated GIS contributes to the severity of lung disease and increases readmission to the hospital. These results must further be supported by large randomized studies.

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**Ethics approval**

The study was approved by Turkish Ministry of Health with 2021-08-31T10_28_04 number and was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

**Informed consent**

Written informed consent was obtained from all subjects before the study.

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