Prevalence of Gastrointestinal Sequelae among Previously Hospitalised Patients due to COVID-19 and its Association with Computed Tomography Chest Severity: A Cross-sectional Study

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ABSTRACT

Introduction: Coronavirus Disease 2019 (COVID-19) is a highly infectious disease primarily characterised by respiratory symptoms. While respiratory symptoms initially predominated during the pandemic, there has been an increase in Gastrointestinal (GI) manifestations in the later phase. Moreover, reports have highlighted the presence of chronic GI symptoms following COVID-19 infection.

Aim: To determine the prevalence of GI sequelae after COVID-19 hospitalisation and its association with Computed Tomography (CT) chest severity scores.

Materials and Methods: The present cross-sectional study was conducted at a COVID-19 designated tertiary care hospital, Indira Gandhi Medical College and Research Institute, Puducherry, India, from April 2022 to December 2022. Patients admitted with COVID-19 illness between January 2021 and June 2021 were included in the study. Socio-demographic details, CT chest severity scores, and chronic GI symptoms (nausea, vomiting, diarrhoea, abdominal pain, etc.) were collected from patients' medical records and through telephonic interviews. The data were analysed using Statistical Package for Social Sciences (SPSS) version 26.0 Qualitative variables were expressed as frequencies and percentages. The association of CT severity with GI symptoms was assessed using the Chi-square test, with a p-value of <0.05 considered significant.

Results: A total of 1,903 patients who met the inclusion criteria were included in the study. Among the participants, 1142 (60%) were males and 761 (40%) were females. The majority of patients belonged to the age group of 41-60 years, followed by 21-40 years. The mean age of the patients was 48.88±1.72 years. The prevalence of chronic GI symptoms was observed in 26% of patients, with 36.6% experiencing abdominal pain and 19.6% having gastroesophageal reflux. Diarrhoea was reported by 15.8% of patients. Patients with severe CT severity scores showed a lower prevalence of GI symptoms.

Conclusion: Chronic GI symptoms were observed in nearly one-fourth of the patients hospitalised for COVID-19. Interestingly, patients with severe CT chest severity scores exhibited a lower prevalence of GI symptoms. Further experimental studies are needed to understand the pathogenesis of GI symptoms and their association with CT severity, which could contribute to the development of effective treatment strategies.

INTRODUCTION

An outbreak of pneumonia initially originated in Wuhan, Hubei province of China had quickly spread to other parts of the world in 2020, leading to the emergence of COVID-19 [1]. The World Health Organisation (WHO) declared this outbreak as a pandemic in March 2020, causing significant disruptions to global health and the economy [2]. While respiratory symptoms are the hallmark of COVID-19 illness, GI symptoms such as diarrhoea, anorexia, abdominal pain, and vomiting have also been reported. The presence of abundant Angiotensin Converting Enzyme-2 (ACE-2) receptors in the intestines, which facilitate viral entry into intestinal cells, could explain the occurrence of GI symptoms in COVID-19 patients [3]. Studies have also indicated that COVID-19 can impact the gut microbiota, leading to GI symptoms [4-6]. Specifically, COVID-19 patients have shown a lower abundance of anti-inflammatory bacteria and an increase in opportunistic pathogens in their gut microbiomes, which may contribute to GI symptoms [5,6]. Furthermore, some patients continue to experience these GI symptoms as chronic sequelae even after recovering from COVID-19 illness [7]. Therefore, this study was conducted to assess the prevalence of GI sequelae following COVID-19 hospitalisation and its association with CT chest severity scores in the South Indian population.

MATERIALS AND METHODS

This cross-sectional study was conducted at Indira Gandhi Medical College and Research Institute, a COVID-19 designated tertiary care hospital in Puducherry, India, from April 2022 to December 2022. Approval for the study was obtained from the institute's research and ethics committee (IEC No.370/IEC-33/IGMC&RI/PP-04/2022). Demographic data, presenting symptoms, and CT chest severity scores were collected from patient records in the medical records department The study included patients admitted with COVID-19 illness between January 2021 and June 2021.

Inclusion criteria: Patients who were tested positive for COVID-19 through Reverse Transcription Polymerase Chain Reaction (RT-PCR) and presented with fever, respiratory symptoms, or GI symptoms were included in the study.

Exclusion criteria: Patients with known digestive diseases such as gastroesophageal reflux disease or irritable bowel syndrome, those admitted for observation for less than 24 hours, and pregnant women were excluded from the study.

CT chest severity scores were determined based on the percentage of lung lobe involvement. The scores were classified as follows: Score-1 (<5% area involved), Score-2 (5-25% area involved),

Score-3 (25-50% area involved), Score-4 (50-75% area involved), and Score-5 (>75% area involved), with a total score of 25. Scores less than 8 were considered mild, 9-15 as moderate, and greater than 15 as severe [8].

Patients included in the study were contacted via phone, and a detailed history of GI symptoms was obtained. With patients' permission, the conversations were recorded over the phone and considered as informed consent for the study. Some patients were assessed during their follow-up visits to the hospital. GI symptoms persisting for more than 30 days after infection were classified as GI sequelae [9]. Socio-demographic details (gender, age group), CT severity scores, and gastrointestinal symptoms such as nausea, vomiting, diarrhoea, and abdominal pain were recorded.

STATISTICAL ANALYSIS

The collected data were analysed using descriptive and inferential statistics with the help of SPSS version 26. Qualitative variables were presented as frequencies and percentages. The association between CT severity and GI symptoms was assessed using the Chi-square test. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 1,903 patients who met the inclusion criteria were included in the study. Among the participants, 1142 (60%) were males and 761 (40%) were females. The majority of patients 715 (37.6%) were in the age group of 41-60 years, followed by 21-40 years 613 (32.2%) [Table/Fig-1]. The mean age of the patients was 48.88±1.72 years.

Regarding CT chest severity scores, 30% of patients had a normal chest CT scan, while 15.7% had a severe CT severity score [Table/Fig-2].

Age group (years)	n (%)
< 20	34 (1.8)
21-40	613 (32.2)
41-60	715 (37.6)
61-80	507 (26.6)
> 80	34 (1.8)
Total	1903 (100)

[Table/Fig-1]: Distribution of patients according to age group.

CT severity	n (%)
Normal	570 (30.0)
Mild	538 (28.3)
Moderate	497 (26.0)
Severe	298 (15.7)
Total	1903 (100)

[Table/Fig-2]: Distribution of patients according to CT chest severity.

Gastrointestinal symptoms were observed in 495 (26%) patients. Among the various GI symptoms, 36.6% experienced abdominal pain, followed by 19.6% with GI reflux, and 15.8% with diarrhoea [Table/Fig-3].

GI symptoms	n (%)
Abdominal pain	181 (36.6)
Vomiting	57 (11.5)
Diarrhoea	78 (15.8)
Gastroesophageal reflux	97 (19.6)
GI bleed	67 (13.5)
Constipation	39 (7.9)

[Table/Fig-3]: Distribution of patients according to GI symptoms (n=495).

Interestingly, 28.8% of patients with a normal CT chest developed GI symptoms. For patients with mild CT severity scores, 25.6% had GI symptoms, and for patients with moderate CT severity scores, 28% had GI symptoms. However, only 18% of patients with severe CT severity scores developed GI symptoms. This finding was statistically significant [Table/Fig-4].

CT chest severity	GI symptoms		Chi-square value	p-value
	No (%)	Yes (%)		
Normal	406 (28.9)	164 (28.8)	12.922	0.005*
Mild	400 (28.4)	138 (25.6)		
Moderate	358 (25.4)	139 (28)		
Severe	244 (17.3)	54 (18)		

[Table/Fig-4]: Association of CT severity with GI symptoms.

DISCUSSION

COVID-19 viral infection manifests as fever, dry cough, dyspnoea, headache, and weakness [10]. While respiratory symptoms are common, some patients also experience GI symptoms. Recent research articles on COVID-19 have shown that the Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2) virus RNA can be detected in stool specimens and rectal swabs [11,12]. Patients with diarrhoea have a higher proportion of virus RNA in their stool compared to those without diarrhoea. The elimination of SARS-CoV-2 from stool takes longer than elimination from the nose and throat [13], leading to concerns about GI infections and the possibility of faecal-oral transmission.

SARS-CoV-2 can directly or indirectly affect the digestive system by causing an inflammatory response. The ACE-2 receptor, used by the virus for entry, is highly expressed in GI epithelial cells such as the ileum, duodenum, caecum, and colon [14]. Studies have shown a decrease in anti-inflammatory bacteria and an enrichment of opportunistic pathogens in the gut microbiome of COVID-19 patients, which persists even after recovery [5]. Furthermore, opportunistic fungal pathogens have been observed in the faeces of COVID-19 patients during hospitalisation and recovery [6]. Alterations in the gut microbiota and the expression of ACE-2 receptors in intestinal cells may contribute to GI symptoms in COVID-19 patients [4].

Extrapulmonary symptoms, including GI symptoms, can mislead physicians, as they may appear before respiratory symptoms. These symptoms can also persist as chronic conditions after recovery from COVID-19 in some patients. GI symptoms have been reported as the initial manifestation of COVID-19, even before fever and respiratory symptoms [15]. The prevalence of GI symptoms varies across studies, with some reporting low prevalence, while others report higher rates ranging from 30-50% [16-21].

Among the GI symptoms, diarrhoea and anorexia have been commonly reported, while abdominal pain is less prevalent [22-27]. The severity of GI symptoms does not necessarily correlate with the severity of COVID-19 illness [3]. However, some studies suggest a higher proportion of GI symptoms in severe cases [25,28]. In present study, patients with severe COVID-19 illness had a lower prevalence of GI symptoms, indicating less involvement of the GI tract compared to the chest.

Limitation(s)

The main limitation of the study design was that the information obtained through telephonic conversation might not be as accurate compared to in-person interviews. Another limitation of the study was the inability to determine the reason for the lower prevalence of GI symptoms in patients with a severe CT chest severity score.

CONCLUSION(S)

Chronic GI symptoms were observed in nearly a quarter of patients who were hospitalised for COVID-19. Patients with a severe CT chest severity score exhibited a lower prevalence of GI symptoms after recovering from COVID-19 illness. Further epidemiological studies with a large sample size are recommended to confirm present study

findings. Additionally, experimental and animal studies should be conducted to gain a better understanding of these extrapulmonary symptoms of COVID-19. This will aid in the development of new guidelines for managing GI symptoms in COVID-19 patients.

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