

# In COVID-19 Patients, the Identified Gastrointestinal Symptoms in Tertiary Care Center of India

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## ABSTRACT

**Aim:** This study aimed to assess the demographic details of coronavirus disease-2019 (COVID-19) patients, their comorbid conditions, preexisting illnesses such as tuberculosis (TB), the prevalence of gastrointestinal (GI) symptoms, duration of GI symptoms, gender-wise distribution of GI symptoms, age-wise distribution of GI symptoms, lab investigation, and computed tomography (CT) scanning was done to record the grading.

**Materials and methods:** In total, 956 COVID-19 patients admitted to an isolation ward of a tertiary care center were screened for 3 months. Patients were confirmed positive for SARS-CoV-2 virus by real-time polymerase chain reaction (RT-PCR) test with a throat swab. Patient's age, demographic details, preexisting illness, and GI symptoms such as fever, impairment of appetite, loss of taste, loss of smell, hiccups, nausea, vomiting, diarrhea, abdominal pain, symptom's duration, history of chronic drug intake, biological markers, CT scanning, and comorbidities were recorded. Based on the provided protocol, standard care management was given to the admitted COVID-19 patients.

Statistical analysis was performed using SPSS version 20.0. Frequencies with percentages, median (min, max), Chi-square test, and Mann-Whitney U test were used to test the statistical significance, and a  $p$ -value of  $<0.05$  was considered statistically significant.

**Results:** In our prospective study of 956 COVID-19 hospitalized patients, details were analyzed and the results are: the median age was 45 years, 70% of male, 60% were above 35 years, comorbidities like diabetes present in 42%, hypertension in 36%, asthma in 8%, cardiovascular diseases (CVD) in 5%, and history of chronic drug intake in 21%.

Among 956 COVID-19 patients, GI symptoms were loss of smell (29.2%), loss of taste (26.4%) for 3 days; nausea (10%), vomiting (7.1%), abdominal pain (12.7%), and fever (42.5%) were observed for 2 days among the 36–45 years of age-group; and the loss of appetite (19%) for 3 days among the age-group of 46–55 years.

The loss of appetite (23.7 vs 16.9%) ( $p = 0.014$ ), taste (32.4 vs 23.8%) ( $p = 0.005$ ), nausea (14.6 vs 8.2%) ( $p = 0.003$ ), and vomiting (10.8 vs 5.5%) ( $p = 0.004$ ) were higher in females than in males. No gender difference was observed in loss of smell ( $p = 0.057$ ), abdominal pain (12 vs 14.3%) ( $p = 0.491$ ), hiccups (4 vs 2.1%) ( $p = 0.132$ ), and fever (41.3 vs 45.3%) ( $p = 0.329$ ).

Females had significantly higher levels of C-reactive protein (CRP) than males (6.1 vs 3.8) ( $p = 0.002$ ). No gender difference was observed in neutrophil/lymphocyte ratio (NLR) ( $p = 0.772$ ), ferritin, and lactate dehydrogenase (LDH). CT-grade IV was higher in males than in females (1.7 vs 1.5%), but the rest of the CT grades were higher in females than in males.

**Conclusion:** In conclusion, GI symptoms are the onset of symptoms that are first expressed after being infected with the SARS-CoV-2 virus. Several studies showed the GI symptoms but did not analyze the age and gender that are risk factors for any disease, but our study showed all GI symptoms and their association with age and gender, which will shed light for our clinicians for early symptom identification, diagnosis, and appropriate treatment.

**Keywords:** Angiotensin-converting enzyme 2, COVID-19, Ferritin, GI symptoms, Loss of smell, Loss of taste, Loss of appetite, SARS-CoV-2.

*Euroasian Journal of Hepato-Gastroenterology* (2022): 10.5005/jp-journals-10018-1371

## INTRODUCTION

The 21st-century pandemic coronavirus disease-2019 (COVID-19) is caused by the most powerful virus that made the entire world follow social distancing and hygienic procedures such as proper handwashing and wearing masks. The World Health Organization has termed the SARS-CoV-2 virus COVID-19 based on the pandemic year 2019.<sup>1</sup> As per researcher Woolf et al., COVID-19 is the third leading disease that is accounting for 697.5 deaths per million, whereas heart diseases and cancer were accounting for 1287.7 deaths per million and 1219.8 deaths per million, respectively.<sup>2</sup>

According to CDC and other researchers, the virus invades the body through open surfaces like noses, infected hands, and other sources, and the virus affects multiple organs bringing failure of the organs starting from lungs, GI disorders, liver, heart, brain, blood vessels, kidneys, and leading to death.<sup>3,4</sup> The

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COVID-19 virus enters the host cells through multiple sources like noses, contaminated hands, and oral–fecal via the angiotensin-converting enzyme 2 (ACE2) receptor.<sup>5</sup> The ACE2 is expressed highly in the colon and ileum region, especially in the absorptive cells of the GI cells.<sup>6–8</sup>

The GI involvements in the COVID-19 patients were reported by a few researchers and they claim that the oral–fecal route of transmission of the SARS-CoV-2 virus may be the reason for GI infection and the COVID-19 infection may have caused bleeding and severe inflammation which would have to worsen the immune system of the COVID-19 patients, leading to immune suppression, failure in drug absorption, failure of organs, and finally causing death.<sup>9,10</sup> The causes of the death of COVID-19 patients with GI involvement were reported unclear by certain researchers,<sup>11–14</sup> and GI involvement was related to several factors such as the oral–fecal route of transmission, comorbid condition, SARS-CoV-2 virology, COVID-19 virus, and its pathogenesis. Hence, this research is carried out in both the qualitative method and the quantitative method. The oral–fecal route of transmission, SARS-CoV-2 virology, COVID-19 virus, and its pathogenesis were researched in the qualitative method by a systematic review, and GI symptoms, comorbid conditions, and investigation, including CT, were researched by the quantitative method involving patients with COVID-19 and GI symptoms.

**Ethical Clearance**

Ethical clearance was obtained from the Ethical Committee of the Institutional review board.

**Inclusion Criteria**

All ages of patients admitted after a positive result of the SARS-CoV-2 virus.

**Exclusion Criteria**

Patients who are morbidly ill and moribund patients, pregnant patients, and unavailability of the results of SARS-CoV-2 testing.

**MATERIALS AND METHODS**

**Study Population**

In total, 956 (Male:Female 669:287) patients were admitted to a Government Hospital, Guindy, Chennai, Tamil Nadu, from 8th November, 2020 to 10th January, 2021 with symptoms of COVID-19.

**Methodology**

*Sample Collection and Analysis*

Patients with confirmed positive results for SARS-CoV-2 virus, diagnosed by throat swab of patients by RT-PCR tests were admitted to the isolation ward for further prognosis of COVID-19. Patient’s age, gender, demographic details, preexisting illness, and GI symptoms such as fever, impairment of appetite, loss of taste, loss of smell, hiccups, nausea, vomiting, diarrhea, and abdominal pain. The abdominal pain was categorized from mild to severe. The duration of each symptom was noted. History of chronic drug intake was also recorded. Biological markers, CT scanning, and the presence of comorbidities such as diabetes, hypertension, asthma, and cardiovascular diseases were also recorded. Serial charting of biological markers and CT grading were recorded. Based on the provided protocol, standard care management was given to the admitted COVID-19 patients.

**How to cite this article:** Murugesan M, Govindarajan R, Prakash L, et al. In COVID-19 Patients, the Identified Gastrointestinal Symptoms in Tertiary Care Center of India. *Euroasian J Hepato-Gastroenterol* 2022;12(1):24–30.

**Source of support:** Nil

**Conflict of interest:** None

*List of Tests Conducted*

Biological markers such as NLR, ferritin,<sup>15</sup> CRP,<sup>16</sup> and LDH<sup>17</sup> levels were done. CT scanning was performed for the admitted COVID-19 patients.<sup>18</sup>

*Quality Control*

To ensure the quality of the investigations, the tests were performed under standard operating procedures with quality control as provided along with the assay.

*Statistical Analysis*

Statistical analysis was performed using SPSS version 20.0. Frequencies with percentages are presented for categorical variables. Median (min, max) was reported for variables that showed skewed distribution. Chi-square test and Mann–Whitney *U* test were used to test the statistical significance. A *p*-value of <0.05 was considered statistically significant.

**RESULTS**

A total of 956 patients were hospitalized with confirmed COVID-19 during the study period.

Table 1 shows the demographic and presence of comorbidities details of the study population. The median age of the study population was 45 years and consisted of 70% male patients. Around 60% of the patients were aged above 35 years. A comorbid condition such as diabetes was present in nearly 42% of the patients,

**Table 1:** Demographic and comorbidities details of the study population

Variables	N	(%)
Age (in years)*	45	8.93
Gender		
Male	669	70
Female	287	30
Age categories (in years)*		
≤25	142	14.9
26–35	225	23.5
36–45	132	13.8
46–55	184	19.2
56–65	153	16.0
≥66	120	12.6
Comorbid conditions		
Diabetes mellitus	400	41.8
Hypertension	340	35.6
Asthma	76	7.9
CVD	43	4.5
TB	13	1.4
History of chronic drug intake	203	21.2

\*Median (min, max)

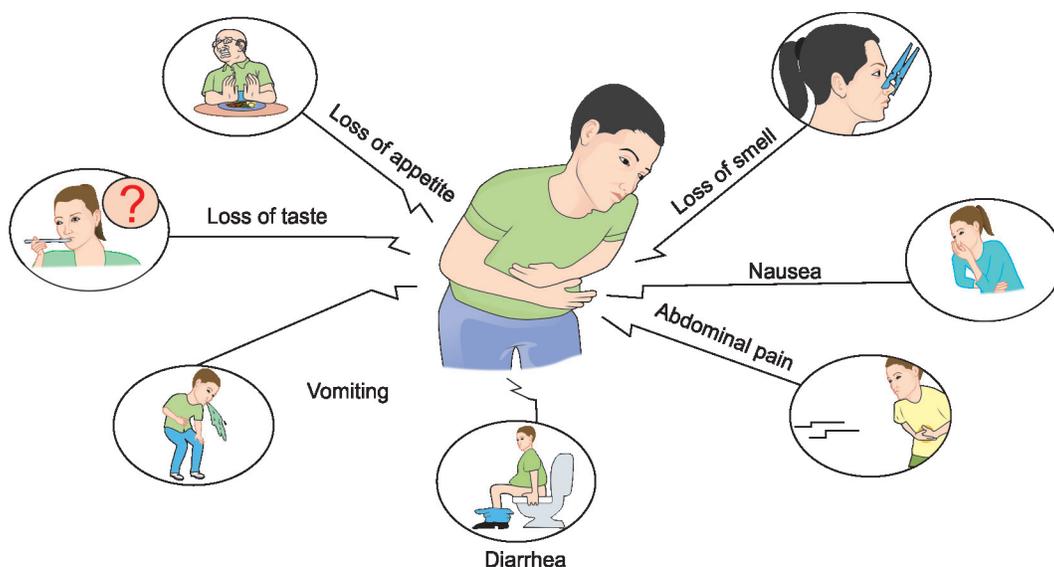


Fig. 1: GI symptoms of COVID-19 patients of tertiary care center

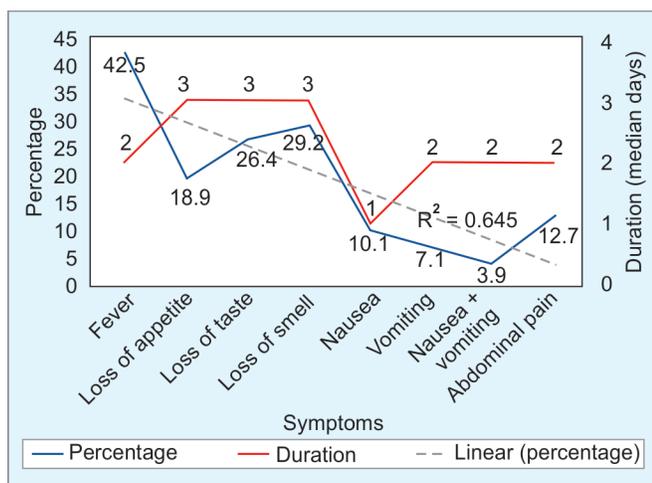


Fig. 2: Prevalence of GI symptoms in COVID-19 patients

hypertension in 36%, CVD in 5%, and asthma in 8%. The onset of GI symptoms was observed in approximately half of the study population at admission. A history of chronic drug intake was noted in 21% of the patients.

Figure 1 shows the GI symptoms of COVID-19 patients in the tertiary care center. The recorded GI symptoms in COVID-19 patients were loss of smell, nausea, abdominal pain, diarrhea, vomiting, impairment of taste, and loss of appetite. The clinicians further evaluated the degree of abdominal pain and duration of GI symptoms in COVID-19 patients and recorded it.

Figure 2 shows the prevalence of GI symptoms with a median duration of symptoms among the COVID-19 admitted patients. Fever was predominantly (42.5%) among the study participants. Impairment of smell (29.2%) was highly prevalent with a median duration of 3 days, followed by loss of taste (26.4%) for 3 days and loss of appetite in 19% of the patients for 3 days. Nearly, 10% of the patients had nausea for 1 day and 7.1% had vomiting for 2 days. Nausea and vomiting together were present in 3.9% of the patients for a median duration of 2 days. Abdominal pain was present in 12.7% of the patients for a median period of 2 days. The median duration of fever was 2 days in the study population, while the loss

Table 2: Grading of abdominal pain in COVID-19 hospitalized patients

Grading of abdominal pain	N = 139	(%)
Midnight pain	9	0.9
Mild pain	67	7.0
Severe pain	9	0.9
Continuous pain	10	1.0
Intermittent pain	44	4.6

of appetite, taste, and smell was present for 3 days among the study population. The presence of nausea was there for 1 day, and nausea and vomiting were there for 2 days, respectively.

Table 2 shows the grading of abdominal pain as one of the GI symptoms in COVID-19 patients. The degree of abdominal pain varied among the study population. Most of them had mild pain (7%) or intermittent pain (4.6). Continuous pain was observed in 1% of the patients, whereas severe pain and midnight pain were recorded in less than 1% of the COVID-19 patients with one of the GI symptoms of abdominal pain.

Table 3 shows the age-wise prevalence of GI symptoms in COVID-19 patients. Loss of appetite (26.6%) was found to be high among the age-group of 46–55 years. While impairment of taste (34.8%) and smell (38.6%) was highly present among people in the age-group of 36–45 years compared with other groups. The proportion of nausea (12.1%) and vomiting (10.6%) was also found to be high among the same age-group (36–45 years). Fever was present in nearly half of the hospitalized COVID-19 patients in all the age-groups, but more than 50% of the patients had a fever in the age-group of 36–55 years.

Table 4 shows the gender-wise prevalence of GI symptoms in COVID-19 patients. The loss of appetite was higher in females than in males (23.7 vs 16.9%) ( $p = 0.014$ ). Similarly, loss of taste was also higher in females (32.4 vs 23.8%) ( $p = 0.005$ ). There is no gender-wise difference noted in loss of smell ( $p = 0.057$ ). Nausea (14.6 vs 8.2%) ( $p = 0.003$ ) and vomiting (10.8 vs 5.5%) ( $p = 0.004$ ) were highly prevalent among female patients. The prevalence of abdominal pain (12 vs 14.3%) ( $p = 0.491$ ) and hiccups (4 vs 2.1%) ( $p = 0.132$ ) was similar between male and female patients. Fever was present

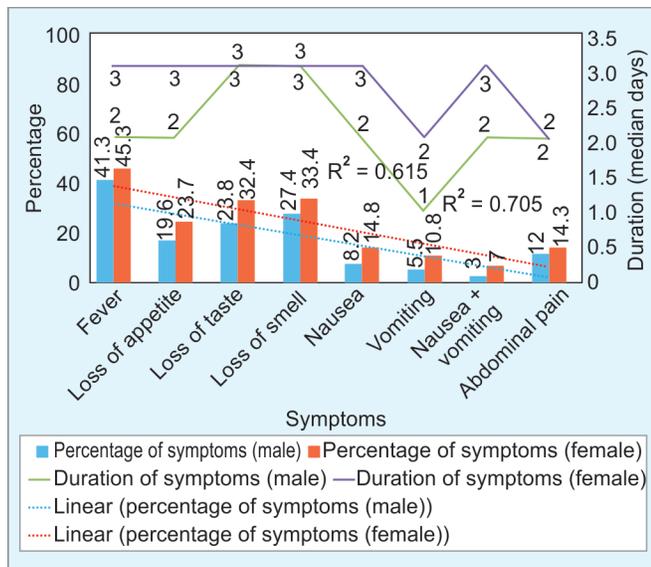
**Table 3:** Age-wise prevalence of GI symptoms in COVID-19 patients

Symptoms	Age categories (in years) N (%)					
	≤25 (n = 142)	26–35 (n = 225)	36–45 (n = 132)	46–55 (n = 184)	56–65 (n = 153)	≥66 (n = 120)
Loss of appetite	15 (10.6)	27 (12)	25 (18.9)	49 (26.6)	37 (24.2)	28 (23.3)
Loss of taste	27 (19.0)	58 (25.8)	46 (34.8)	54 (29.3)	45 (29.4)	22 (18.3)
Loss of smell	29 (20.4)	74 (32.9)	51 (38.6)	57 (31)	41 (26.8)	27 (22.5)
Nausea	13 (9.2)	20 (8.9)	16 (12.1)	21 (11.4)	14 (9.2)	13 (10.8)
Vomiting	7 (4.9)	18 (8)	14 (10.6)	12 (6.5)	9 (5.9)	8 (6.7)
Abdominal pain	13 (9.1)	30 (13.3)	15 (11.4)	27 (14.7)	17 (11.1)	19 (15.8)
Fever	55 (38.7)	84 (37.3)	70 (53)	97 (52.7)	60 (39.2)	40 (33.3)
Hiccups	4 (2.8)	8 (3.6)	6 (4.5)	8 (4.3)	5 (3.3)	2 (1.7)

**Table 4:** Gender-wise prevalence of GI symptoms in COVID-19 patients

Symptoms	Male (n = 669) 70%	Female (n = 287) 30%	p-value
Loss of appetite	16.9%	23.7%	0.014*
Loss of taste	23.8%	32.4%	0.005*
Loss of smell	27.4%	33.4%	0.057
Nausea	8.2%	14.6%	0.003*
Vomiting	5.5%	10.8%	0.004*
Abdominal pain	12%	14.3%	0.491
Fever	41.3%	45.3%	0.329
Hiccups	4%	2.1%	0.132

\*Statistical significant



**Fig. 3:** Gender-wise prevalence of GI symptoms with median duration in COVID-19 patients

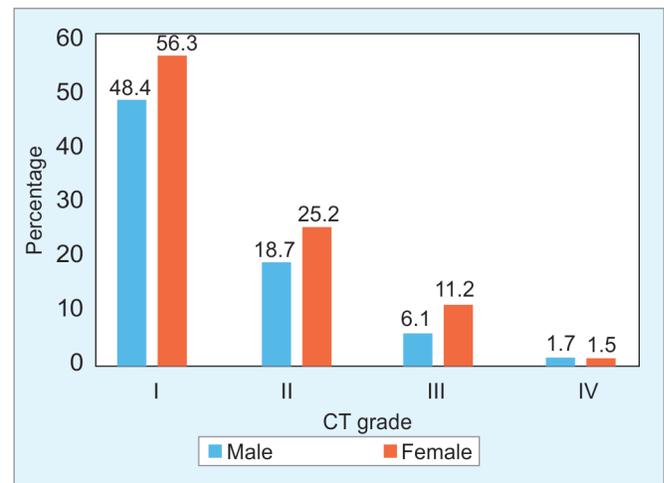
in more than 40% of the patients with no gender difference (41.3 vs 45.3%) ( $p = 0.329$ ).

Figure 3 shows the comparison of GI symptoms among males and females in COVID-19 admitted patients. The loss of appetite was higher in females than in males (23.7 vs 16.9%) ( $p = 0.014$ ). Similarly, loss of taste was also higher in females (32.4 vs 23.8%) ( $p = 0.005$ ). There is no gender-wise difference noted in loss of

**Table 5:** Gender-wise lab investigations details of the study population at the time of admission

Lab investigations	Male	Female	p-value
NLR	2 (0.4, 29)	2 (0.7, 22)	0.772
Ferritin	131 (1, 981)	109 (6, 494)	0.406
LDH	332 (24.2, 1921)	331.5 (35, 1689)	0.650
CRP	3.8 (0.0, 174)	6.1 (0.0, 92.7)	0.002*

\*Statistical significant values are in median (min, max)



**Fig. 4:** Gender-wise distribution of CT grades

smell ( $p = 0.057$ ). Nausea (14.6 vs 8.2%) ( $p = 0.003$ ) and vomiting (10.8 vs 5.5%) ( $p = 0.004$ ) were highly prevalent among female patients. The prevalence of abdominal pain (12 vs 14.3%) ( $p = 0.491$ ) and hiccups (4 vs 2.1%) ( $p = 0.132$ ) was similar between male and female patients. Fever was present in more than 40% of the patients with no gender difference (41.3 vs 45.3%) ( $p = 0.329$ ).

Table 5 shows the gender-wise lab investigations details of the study population at the time of admission. There was no statistically significant difference in NLR ( $p = 0.772$ ). Ferritin and LDH levels also did not differ between males and females. However, females had significantly higher levels of CRP than males (6.1 vs 3.8) ( $p = 0.002$ ).

Figure 4 shows the gender-wise distribution of CT grade among the study population. CT-grade I (56.3 vs 48.4%), II (25.2 vs 18.7%), and III (11.2 vs 6.1%) were higher in females than males, whereas

CT-grade IV was present in a higher percentage in males than in females (1.7 vs 1.5%).

## DISCUSSION

As per the aims of the study, clinicians observed and recorded the demographic details, comorbidities, preexisting illness, history of chronic drug intake, lab investigation, and CT, and GI symptoms in genders, age-groups, and its duration.

### Demographic Details and Comorbidities in COVID-19 Patients with GI Symptoms

The demographic details of the admitted COVID-19 patients were showing that the median age was 45 years and 70% of the hospitalized COVID-19 patients were males compared with 30% of females. Published researches show that the clinical outcomes in COVID-19 patients were influenced by certain factors such as age, gender, and the underlying medical conditions like comorbid illnesses. The research also explains that the reasons behind the gender-related differences are due to the immune responses such as chemokines and declined T-cell as age progresses, and plasma-intake immune cytokines were higher in males than in females.<sup>19,20</sup>

As per Guan et al., the confirmed COVID-19 patient's median age was 47, whereas our hospitalized COVID-19 patient's median age was 45,<sup>21</sup> and the other study conducted in COVID-19 patients presented with 56 years of median age.<sup>22</sup>

In our study, 872 (91%) patients were with comorbid conditions like diabetes mellitus, hypertension, asthma, CVD, and TB. Only 9% of hospitalized COVID-19 patients were without comorbid illnesses. About 41% of COVID-19 patients with GI symptoms were with diabetes followed by 35% of hypertension. The Chinese Centers for Disease Control and Prevention report shows that underlying illnesses like hypertension, diabetes, cancer, respiratory, and cardiovascular disease were found as associating risk factors in the death of the COVID-19 patients.<sup>23</sup> In our hospitalized COVID-19 patients, cardiovascular diseases were found in 4.5% of patients, whereas studies by Ielapi et al. and Madjid et al. showed that the reason for mortality for 20% of COVID-19 patients was cardiovascular disease as their underlying illness.<sup>24,25</sup> One UK study described that the COVID-19 patients with pulmonary, cardiac, cancer, and kidney diseases were at higher risk of death.<sup>26</sup> About 21% of screened population acquired COVID-19 in this study who had a long history of chronic drug intake. We searched any previous data available, and we found that none have reported COVID-19 and a history of chronic drug intake.

### GI Symptoms and their Duration in COVID-19 Patients

Approximately, half of the study patients had onset of GI symptoms at admission. The prevalence of GI symptoms such as loss of smell and loss of taste was higher among hospitalized COVID-19 patients with a median duration of these symptoms for 3 days.

Fever was present in half of the COVID-19-hospitalized patients with a percentage of 42%, and the median duration of fever was 2 days. Studies by Song et al. and Wang et al. found low-grade fever, and as per Wang's study, fever was present in COVID-19 patients after 1–2 days of diarrhea and nausea.<sup>27,28</sup>

In our study, loss of smell (29.2%) was highly prevalent with a median duration of 3 days followed by loss of taste (26.4%) for 3 days. Other researchers showed the occurrence of these symptoms such as temporary loss of smell and taste, loss of taste,

and loss of smell, but did not present the prevalence percentage and duration.<sup>29,30</sup> An Italian researcher Giacomelli et al. reported a disorder of taste, and Chen et al. from the United States also reported loss of smell and taste.<sup>31,32</sup> Our study also recorded the percentage of loss of appetite in 19% of the patients for 3 days. Few data described the presence of loss of appetite such as Yang et al. and Cholankeril et al. reported 25.3%.<sup>33,34</sup>

In the present study, nearly 10% of the patients had nausea for 1 day and 7.1% had vomiting for 2 days. Our data were compatible with Andrews et al. study with a median of 10.5% of nausea and 7% of vomiting, respectively. Our study also identified COVID-19 patients with both nausea and vomiting in 3.9% for a median duration of 2 days, but Andrews et al. did not report patients with both the symptoms of nausea and vomiting and its duration. About 4.9% of nausea was reported by Cholankeril et al.<sup>35,36</sup> compared with our study's 7.1% of patients with vomiting, Remes-Troche et al. study showed compatibility, whereas Fern et al. showed 10.2%.<sup>37,38</sup>

In our study, abdominal pain was found in 12.7% for a median period of 2 days, whereas studies by Redd et al. and Rokkas et al. reported that 14.5% and 6.9% of COVID-19 patients suffered from abdominal pain.<sup>39,40</sup>

Our study recorded even the abdominal pain grading and its nature. Out of the 12.7% of the COVID-19 patients with abdominal pain, mild pain was recorded in 7%, and intermittent pain in 4.6%. Continuous pain and severe and midnight pain was observed in 1% and less than 1% of COVID-19 patients.

Our study was the first to report the abdominal pain grading and its nature. Our study further reordered and analyzed the GI symptoms of COVID-19 patients' age differentiation. Age differentiation was discussed below.

### GI Symptoms in COVID-19 and their Age Differentiation

In our study, loss of appetite (26.6%) was found to be high among the age-group of 46–55 years.

As per Elliott et al. age-stratified analyzed data, loss of appetite was found in 18–55 years of age in COVID-19 patients.<sup>41</sup>

COVID-19 patients of our study showed lack of smell (anosmia) in 38.6% in the age-group of 36–45 years, but Renaud et al. reported impairment of smell in 27.5% of patients in the age-group of 38 years.<sup>42</sup> In the present study, we found loss of taste (ageusia) was 34.8%, which is high in the age-group of 36–45 years compared with other age-groups. Researcher Shelton et al. did their study in two GI symptoms such as taste and smell in that they reported that both losses of taste and smell were found higher in the age-group of 26–35 years with 27%.<sup>43</sup> Our study shows that 12.1% of patients with the age-group of 36–45 years were presented with nausea and 10.65 of COVID-19 patients had vomiting during their hospitalization. Fever was present in 53% and hiccups were also high with 4.55 in the age-group of 36–45 years. Published research by Wong et al. showed the presence of hiccups as GI symptoms but not related with age correlation.<sup>44</sup>

Several published data showed the presence and percentages of GI symptoms in COVID-19 patients, but no studies were done with age association and all the GI symptoms in COVID-19 patients.

Our study wanted to record all the details in regard to GI symptoms in COVID-19 patients, thus, a further analysis sheds light on the association of gender and GI symptoms in COVID-19 patients, which we discussed in our next section of this research article.

## GI Symptoms in COVID-19 Patients and their Association with Gender Differentiation

As per our study, male COVID-19 patients were observed with higher GI symptoms compared with females with the percentages of 70% and 30%, respectively. The loss of appetite (23.7 vs 16.9%) ( $p = 0.014$ ) and lack of taste (32.4 vs 23.8%) were higher in females than in males with the statistical significance of  $p = 0.005$ . No gender-wise difference was observed for loss of smell. Researcher Hopkins et al. reported that women than men have complained highly on the loss of olfaction (loss of smell) during the occurrence of COVID-19.<sup>45</sup>

In this study, nausea (14.6 vs 8.2%) ( $p = 0.003$ ) and vomiting (10.8 vs 5.5%) ( $p = 0.004$ ) were higher in females than in males with the statistical significance of  $p = 0.004$ , and no gender association was observed as association for GI symptoms such as abdominal pain (12 vs 14.3%) ( $p = 0.491$ ), hiccups (4 vs 2.1%) ( $p = 0.132$ ), and fever (41.3 vs 45.3%) ( $p = 0.329$ ).

There were several studies on the male and the female ratio of COVID-19 occurrence, but no data were presented on the association of all the GI symptoms and gender.

In our study, all the findings were analyzed, including the lab investigations, to have the best knowledge on GI symptoms in COVID-19 patients, which we will discuss in the last section of this article.

## Lab Investigation and CT in COVID-19 Patients with GI Symptoms

In our study, females had significantly higher levels of CRP than males (6.1 vs 3.8) ( $p = 0.002$ ), and the study by Wu J et al. also found elevation of CRP in their COVID-19 patients.<sup>46</sup> No statistical significance was observed in NLR ( $p = 0.772$ ), ferritin, and LDH between males and females. A study by Abbasinia et al. showed that CRP and LDH were elevated by 50% and 39.9% of COVID-19 patients.<sup>47</sup> Habibzadeh et al. reported that the serum ferritin was elevated in some COVID-19 patients in their study,<sup>48</sup> but no gender association with biomarkers was provided by these publications.

In our present study, CT-grade I, II, and III were higher in females than males, whereas CT-grade IV was present that was slightly higher in males than in females (1.7 vs 1.5%). The study by Saeed et al. showed a significant correlation between males and the CT with the  $p$ -value  $< 0.05$ , and described the severity score of CT as CT-I – 1–5% or less involvement (ground-glass opacification), CT-II – 5–25% (bilateral involvement), CT-III – 26–49% (posterior distribution), CT-IV – 50–75% (multilobar involvement), and CT-V –  $> 75\%$  (consolidation).<sup>49</sup>

## CONCLUSION

In conclusion, GI symptoms are the symptoms of onset in COVID-19 patients (i.e., GI symptoms are the first symptoms expressed once an individual is infected by SARS-CoV-2 virus), hence, the early diagnosis of patients with GI symptoms can further reduce the organ failures such as lung, liver, and kidney failure, leading to a reduction of the mortality rate of COVID-19 patients.

Several studies showed the GI symptoms but did not analyze the age and gender (which are important variables and risk factors for any diseases both clinically and physiologically) correlation with GI symptoms in COVID-19 patients, but our study showed all GI symptoms and their association with age and gender, hence, our study will bring a powerful impact on clinicians who diagnose

and provide treatment for COVID-19 patients based on their GI symptoms and age differentiation.

## Authors' Contribution

Corresponding Author: Narayanasamy Krishnasamy – *Authorization Approval, and Overall supervision.*

First Author: Malarvizhi Murugesan – *Study design, and Manuscript supervision.*

Second Author: Ramkumar Govindarajan – *Review of literature and supervision.*

Third Author: Lakshmi Prakash – *Critical revision and approval.*

Fourth Author: Chandra Kumar Murugan – *Data collection and proofreading.*

Fifth Author: J Janifer Jasmine – *Analysis, interpretation of the data, manuscript preparation.*

## REFERENCES

- Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. *New Engl J Med* 2020;382(8):727–733. DOI: 10.1056/NEJMoa2001017.
- Woolf SH, Chapman DA, Lee JH. COVID-19 as the leading cause of death in the United States. *JAMA* 2021;325(2):123–124. DOI: 10.1001/jama.2020.24865.
- CDC. Coronavirus (COVID-19) 2020. Accessed <https://www.cdc.gov/coronavirus/2019-ncov/index.html>.
- Zhang J, Garrett S, Sun J. Gastrointestinal symptoms, pathophysiology, and treatment in COVID-19. *Genes Dis* 2021;8(4):385–400. DOI: 10.1016/j.gendis.2020.08.013.
- Coronavirus 2019-nCoV. Coronavirus 2019-nCoV global cases by Johns Hopkins CSSE. Accessed <https://gisanddata.maps.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6>.
- Burgueño JF, Reich A, Hazime H, et al. Expression of SARS-CoV-2 entry molecules ACE2 and TMPRSS2 in the gut of patients with IBD. *Inflamm Bowel Dis* 2020;26(6):797–808. DOI: 10.1093/ibd/izaa085.
- Xiao F, Tang M, Zheng X, et al. Evidence for gastrointestinal infection of SARS-CoV-2. *Gastroenterology* 2020;158(6):1831–1833.e3. DOI: 10.1053/j.gastro.2020.02.055.
- Du M, Cai G, Chen F, et al. Multiomics evaluation of gastrointestinal and other clinical characteristics of COVID-19. *Gastroenterology* 2020;158(8):2298–2301.e7. DOI: 10.1053/j.gastro.2020.03.045.
- Lin L, Jiang X, Zhang Z, et al. Gastrointestinal symptoms of 95 cases with SARS-CoV-2 infection. *Gut* 2020;69(6):997–1001. DOI: 10.1136/gutjnl-2020-321013.
- Effenberger M, Grabherr F, Mayr L, et al. Faecal calprotectin indicates intestinal inflammation in COVID-19. *Gut* 2020;69(8):1543–1544. DOI: 10.1136/gutjnl-2020-321388.
- Han C, Duan C, Zhang S, et al. Digestive symptoms in COVID-19 patients with mild disease severity: clinical presentation, stool viral RNA testing, and outcomes. *Am J Gastroenterol* 2020;115(6):916–923. DOI: 10.14309/ajg.0000000000000664.
- Holshue ML, DeBolt C, Lindquist S, et al. First case of 2019 novel coronavirus in the United States. *New Engl J Med* 2020;382(10):929–936. DOI: 10.1056/NEJMoa2001191.
- Young BE, Ong SW, Kalimuddin S, et al. Epidemiologic features and clinical course of patients infected with SARS-CoV-2 in Singapore. *JAMA* 2020;323(15):1488–1494. DOI: 10.1001/jama.2020.3204.
- Pan Y, Zhang D, Yang P, et al. Viral load of SARS-CoV-2 in clinical samples. *Lancet Infect Dis* 2020;20(4):411–412. DOI: 10.1016/S1473-3099(20)30113-4.
- Cook JD, Lipschitz DA, Miles LE, et al. Serum ferritin as a measure of iron stores in normal subjects. *Am J Clin Nutr* 1974;27(7):681–687. DOI: 10.1093/ajcn/27.7.681.
- Tillett WS, Francis T. Serological reactions in pneumonia with a non-protein somatic fraction of pneumococcus. *J Exp Med* 1930;52(4):561–571. DOI: 10.1084/jem.52.4.561.

17. Bhagavan NV. CHAPTER 27-nucleotide metabolism. Medical Biochemistry (4th ed.), Academic Press,- Cambridge, Massachusetts. US 2002:1016 pp. 615–644. <https://doi.org/10.1016/B978-012095440-7/50029-9>.
18. Richmond, Caroline. "Obituary-Sir Godfrey Hounsfield". *BMJ* 2004;329(7467):687. DOI: 10.1136/bmj.329.7467.687.
19. Cevik M, Bamford CCG, Ho A. COVID-19 pandemic—a focused review for clinicians. *Clin Microbiol Infect* 2020;26(7):842–847. DOI: 10.1016/j.cmi.2020.04.023.
20. Cevik M, Kuppalli K, Kindrachuk J, et al. Virology, transmission, and pathogenesis of SARS-CoV-2. *BMJ* 2020;371:m3862. DOI: 10.1136/bmj.m3862.
21. Guan W-J, Ni Z-Y, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. *New Engl J Med* 2020;382(18):1708–1720. DOI: 10.1056/NEJMoa2002032.
22. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *The Lancet* 2020;395(10229):1054–1062. DOI: 10.1016/S0140-6736(20)30566-3.
23. Deng G, Yin M, Chen X, et al. Clinical determinants for fatality of 44,672 patients with COVID-19. *Crit Care* 2020;24(1):1–3. DOI: 10.1186/s13054-020-02902-w.
24. Ielapi N, Licastro N, Provenzano M, et al. Cardiovascular disease as a biomarker for an increased risk of COVID-19 infection and related poor prognosis. *Biomark Med* 2020;14(9):713–716. DOI: 10.2217/bmm-2020-0201.
25. Madjid M, Safavi-Naeini P, Solomon SD, et al. Potential effects of coronaviruses on the cardiovascular system: a review. *JAMA Cardiol* 2020;5(7):831–840. DOI: 10.1001/jamacardio.2020.1286.
26. Docherty AB, Harrison EM, Green CA, et al. Features of 20 133 UK patients in hospital with Covid-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study. *BMJ* 2020;369:m1985. DOI: 10.1136/bmj.m1985.
27. Song Y, Liu P, Shi XL, et al. SARS-CoV-2 induced diarrhoea as onset symptom in patient with COVID-19. *Gut* 2020;69(6):1143–1144. DOI: 10.1136/gutjnl-2020-320891.
28. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. *JAMA* 2020;323(11):1061–1069. DOI: 10.1001/jama.2020.1585.
29. Wiersinga WJ, Rhodes A, Cheng AC, et al. Pathophysiology, transmission, diagnosis, and treatment of coronavirus disease 2019 (COVID-19): a review. *JAMA* 2020;324(8):782–793. DOI: 10.1001/jama.2020.12839.
30. Graham CW, Dela CC, Cao B, et al. Novel Wuhan (2019-NCov) coronavirus. *Am J Respir Crit Care Med* 2020;201(4):7–8. DOI: 10.1164/rccm.2014P7.
31. Giacomelli A, Pezzati L, Conti F, et al. Self-reported olfactory and taste disorders in patients with severe acute respiratory coronavirus 2 infection: a cross-sectional study. *Clin Infect Dis* 2020;71(15):889–890. DOI: 10.1093/cid/ciaa330.
32. Chen A, Agarwal A, Ravindran N, et al. Are gastrointestinal symptoms specific for coronavirus 2019 infection? A prospective case-control study from the United States. *Gastroenterology* 2020;159(3):1161–1163.e2. DOI: 10.1053/j.gastro.2020.05.036.
33. Yang L, Tu L. Implications of gastrointestinal manifestations of COVID-19. *Lancet Gastroenterol Hepatol* 2020;5(7):629–630. DOI: 10.1016/S2468-1253(20)30132-1.
34. Cholankeril G, Podboy A, Aivaliotis VI, et al. High prevalence of concurrent gastrointestinal manifestations in patients with severe acute respiratory syndrome coronavirus 2: early experience from California. *Gastroenterology* 2020;159(2):775–777. DOI: 10.1053/j.gastro.2020.04.008.
35. Andrews PLR, Cai W, Rudd JA, et al. COVID-19-19, nausea, and vomiting. *J Gastroenterol Hepatol* 2021;36(3):646–656. DOI: 10.1111/jgh.15261.
36. Cholankeril G, Podboy A, Aivaliotis VI, et al. Association of digestive symptoms and hospitalization in patients with SARS-CoV-2 infection. *Am J Gastroenterol* 2020. DOI: 10.14309/ajg.00000000000000712.
37. Remes-Troche JM, Ramos-de-la-Medina A, Manríquez-Reyes M, et al. Initial gastrointestinal manifestations in patients with severe acute respiratory syndrome coronavirus 2 infection in 112 patients from Veracruz in southeastern Mexico. *Gastroenterology* 2020;159(3):1179–1181. DOI: 10.1053/j.gastro.2020.05.055.
38. Ferm S, Fisher C, Pakala T, et al. Analysis of gastrointestinal and hepatic manifestations of SARS-CoV-2 infection in 892 patients in Queens, NY. *Clin Gastroenterol Hepatol* 2020 1;18(10):2378–2379.e1. DOI: 10.1016/j.cgh.2020.05.049.
39. Redd WD, Zhou JC, Hathorn KE, et al. Prevalence and characteristics of gastrointestinal symptoms in patients with severe acute respiratory syndrome coronavirus 2 infection in the United States: a multicenter cohort study. *Gastroenterology* 2020;159(2):765–767.e2. DOI: 10.1053/j.gastro.2020.04.045.
40. Rokkas T. Gastrointestinal involvement in COVID-19: a systematic review and meta-analysis. *Ann Gastroenterol* 2020;33(4):355–365. DOI: 10.20524/aog.2020.0506.
41. Elliott J, Whitaker M, Bodinier B, et al. Predictive symptoms for COVID-19 in the community: REACT-1 study of over 1 million people. *PLoS Med* 2021;18(9):e1003777. DOI: 10.1371/journal.pmed.1003777.
42. Renaud M, Thibault C, Le Normand F, et al. Clinical outcomes for patients with Anosmia 1 year after COVID-19 diagnosis. *JAMA Netw Open* 2021;4(6):e2115352. DOI: 10.1001/jamanetworkopen.2021.15352.
43. Shelton JF, Shastri AJ, Fletez-Brant K, et al. The UGT2A1/UGT2A2 locus is associated with COVID-19-related loss of smell or taste. *Nat Genet* 2022;54(2):121–124. DOI: 10.1038/s41588-021-00986-w.
44. Wong SH, Lui RN, Sung JJ. COVID-19 and the digestive system. *J Gastroenterol Hepatol* 2020;35(5):744–748. DOI: 10.1111/jgh.15047.
45. Hopkins C, Surda P, Kumar N. Presentation of new onset anosmia during the COVID-19 pandemic. *Rhinology* 2020;58(3):295–298. DOI: 10.1111/jgh.15047.
46. Wu J, Liu J, Zhao X, et al. Clinical characteristics of imported cases of coronavirus disease 2019 (COVID-19) in Jiangsu province: a multicenter descriptive study. *Clin Infect Dis* 2020;71(15):706–712. DOI: 10.1093/cid/ciaa199.
47. Abbasinia M, Hormati A, Hossaini SKE, et al. Clinical manifestations of gastrointestinal symptoms in COVID-19 patients: an integrative review. *Gastroenterol Nurs* 2021;44(1):E1–E10. DOI: 10.1097/SGA.0000000000000584.
48. Habibzadeh P, Stoneman EK. The novel coronavirus: a bird's eye view. *Int J Occup Environ Med* 2020;11(2):65–71. DOI: 10.15171/ijoom.2020.1921.
49. Saeed GA, Gaba W, Shah A, et al. Correlation between chest CT severity scores and the clinical parameters of adult patients with COVID-19 pneumonia. *Radiol Res Pract* 2021; 6697677. DOI: 10.1155/2021/6697677.