

Gastrointestinal Symptoms And Outcomes In Hospitalized Covid 19 Patients During Second Wave In India In Esic Hospital Okhla Phase I New Delhi.

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Abstract

Introduction: COVID 19 is new pandemic disease .it mainly affects respiratory system but can affect many other system in human body. Gastrointestinal system has been found to be affected in many patients. Gastrointestinal (GI) symptoms were very common in patients with coronavirus disease 2019 (COVID-19). It is unclear if the presence of GI symptoms is associated with poor outcomes in COVID-19. We aim to assess GI symptoms and their outcome and severity in covid 19 patients. it could be used for prognostication in hospitalized patients with COVID-19.

Methods:

We retrospectively analyzed patients admitted to Esic hospital okhla phase 1 new delhi from April 18 2021 to 10th may 2021 . The patient's case sheets were reviewed for the presence of GI symptoms like nausea, vomiting, dyspepsia, loose stool, abdominal discomfort, abdominal pain, passage of mucus or blood in stool etc at time of admission and during hospital stay. COVID-19 patients having Gastrointestinal symptoms (cases) were compared with COVID-19 patients who have no gastrointestinal symptoms (control).

Results: A total of 185 patients suffering from covid 19 disease who were admitted in this hospital were included, of which 45 (20.6%) covid positive patients had minimum 1 or more then one of the GI symptoms (cases). These patients were compared with the 140 COVID-19 patients who don't have GI symptoms (controls). The average age of cases was 57.6 years (SD 17.2) and that of control was 63.3 years (SD 14.6). No statistically significant difference was noted in comorbidities and laboratory findings. The primary outcome was mortality, which did not differ between cases and controls (42.5 vs 37.85%, $p = 0.68$). No statistically significant differences were noted in secondary outcomes, including the length of stay (LOS, 7.8 vs. 7.9 days, $p = 0.87$) and need for mechanical ventilation (29 vs. 26.9%, $p = 0.82$).

Discussion: In our study, the presence of GI manifestations in COVID-19 at the time of admission and during stay in hospital was not associated with increased mortality, LOS, or mechanical ventilation. The novel coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was started as an epidemic in Wuhan, [Ramachandran/Gajendran/Perisetti/Goyal] China. It was later declared as a global pandemic with New York as the current epicenter [2]. The SARS-CoV-2 mainly spreads through direct exposure (droplets, person to person). However, it is also assumed to be transmitted by fomite transmission, airborne transmission, and feco-oral transmission [1]. The COVID-19 is predominantly a respiratory disease manifested by fever, fatigue, dry cough, anorexia, myalgia, and dyspnea [5]. However, gastrointestinal (GI) manifestations such as nausea, vomiting, diarrhea, and abdominal pain are increasingly being recognized as important manifestations of COVID-19 [4–8]. Other symptoms such as dysgeusia and anosmia are also gaining attention as important symptoms of COVID-19 [9, 10]. The spectrum of COVID-19 infection ranges from mild to critical. Most of the patients (81%) have mild disease, 14% of the patients have severe disease, and 5% of the patients have a critical disease [2, 7]. The factors associated with morbidity and mortality or (severe COVID-19 infection) include advanced age >65 years, chronic respiratory diseases, hypertension, diabetes mellitus (DM), malignancy, and cardiovascular disease or any immunocompromised state [12–14]. In a recent study published from the USA, about 12% of the patients required mechanical ventilation, and the mortality rate of patients on mechanical ventilation was 88% [15]. In a study by Pan et al. [11], the presence of GI symptoms was associated with higher liver enzymes, lower monocyte count, and longer prothrombin time. The overall pooled prevalence of GI symptoms in COVID-19 based on a systematic review

was reported to be 18% [16]. The most common GI symptom reported is diarrhoea (10.27%), followed by nausea or vomiting (7.56%) and abdominal pain [16]. SARS-CoV-2 has also been found in the fecal samples of COVID-19 patients even after the complete resolution of symptoms [13, 17]. Therefore, the fecal-oral transmission is also considered as a potential mode of transmission [17]. The occurrence of GI symptoms is probably from the intestinal tropism of the SARS-CoV-2 [18]. Moreover, GI symptoms can coexist or even precede respiratory manifestations [19]. Rarely, COVID-19 patients can present with only GI symptoms without respiratory symptoms [11]. Hence, there has been an increasing interest in whether GI symptoms are associated with severe disease. There are conflicting reports in terms of whether GI symptoms are associated with severe COVID-19 or not [11, 20]. Therefore, in this study, we aimed to analyze if the presence of GI symptoms at the time of hospitalization is associated with early use of mechanical ventilation or mortality i.e severity of disease when compared to those who did not have GI symptoms.

Keywords- COVID-19, Gastrointestinal manifestations, Severe-acute-respiratory-syndrome coronavirus, Outcomes- Mortality- Length of stay

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I. Methods

This is a retrospective cohort study conducted in a cohort of COVID-19 patients who were admitted ESIC Hospital Okhla Phase 1 New Delhi. This study is approved according institutional Review Board as minimal-risk research while utilizing anonymized and de-identified retrospective data collection and waived the requirement for informed consent. We included patients who were admitted to the hospital with a confirmed diagnosis of COVID-19 on rapid antigen test and on rt/pcr test for covid from april 18, 2021, to may 1st, 2021. Patients younger than 18 yrs, those positive pts who were not hospitalized and treated on opd basis and pregnant pts were excluded. Data related to patients' clinical symptoms, comorbidities, medications received, vitals at time of admission and at time of presentation lab tests treatment and medications received and their outcome were collected (Table 1). Demographic variables like age, sex, race, smoking status, and BMI were obtained. Data on various comorbid conditions like hypertension, dyslipidemia, coronary artery disease, DM, history of any cancer, chronic obstructive pulmonary disease, and asthma were obtained. Medication history of the use of various drugs like angiotensin-converting enzyme inhibitor/angiotensin receptor blocker, non-steroidal anti-inflammatory drugs, aspirin, or statin use was collected., initial laboratory investigations like haemoglobin level, WBC, absolute lymphocyte count, platelet count, ferritin, C-reactive protein (CRP), d dimer, lactic acid, aspartate aminotransferase, and alanine aminotransferase were noted. The GI symptoms were defined as the presence of nausea, vomiting, dyspepsia, diarrhoea/passage of mucus in stool, or abdominal pain at the time of admission. The study cohort was divided into 2 groups one group having GI symptoms(cases) other group having no GI Symptoms (control) The primary outcome was death from any cause. Secondary outcomes were total length of stay, Need for mechanical ventilations during hospitalization.

Table 1. Prevelence of gastrointestinal (GI) system in study group

GI SYMPTOMS	N (%)
No gastrointestinal symptoms	140(75..67%)
Nausea/vomiting	14(7.56%)
Diarrhoea	19(10.27%)
Nausea/vomiting+diarrhoea	12(6.48%)
Nausea/vomiting + abdominal pain	6(3.24%)

Table 2. Prevelence of individual gastrointestinal (GI) symptoms In study group with gi symptoms(cases)

GI SYMPTOMS	N (%)
Nausea/vomiting	08(17.77%)
Diarrhoea	19(42.22%)
Nausea/vomiting+diarrhoea	12(26.6%)
Nausea/vomiting+abdominal pain	06(13.33%)

Statistical analysis was performed using IBM SPSS software version 26 (SPSS Inc., Armonk, NY, USA). Descriptive summary statistics are presented as means and SD for continuous variables and frequencies with percentages for categorical variables. Categorical and continuous variables were tested for statistical significance using χ^2 tests and t tests, respectively. If the continuous variable is not normally distributed, we utilized the nonparametric test such as the Mann-Whitney U test to compare the groups.

II. Results

Study Population and Baseline Demographics

A total of 200 patients were hospitalized with confirmed COVID-19 during the study period. 15 patients were excluded based on the exclusion criteria. A total of 185 patients met the inclusion criteria and formed our final study population. Of these, 45 (24.32%) patients had GI symptoms (cases), and 140 patients had no GI symptoms (controls) (Table 1). Diarrhea was the most common GI symptom, which was reported in 10.27% of the cohort, followed by nausea or vomiting, reported in 6.48% of the patients, and only 3.24% of the patients had abdominal pain (Table 2). Demographic variables are noted in Table 3. The mean age was 57 years ($SD \pm 17$) in cases as compared to 63 years ($SD \pm 15$ years) in controls. The mean BMI was 31.7 and 30.7 in cases and controls, respectively. Comorbidities such as hypertension, dyslipidemia, chronic obstructive pulmonary disease, asthma, coronary artery disease, DM, and cancer were similarly distributed between 2 groups (Table 3). There was no difference in the presence of other symptoms such as fever, cough, dyspnea, fatigue, and myalgia between the 2 groups. Laboratory Data There was no statistical difference between the 2 groups in values of laboratory data such as mean haemoglobin, WBC, lymphocyte, and platelet counts. The mean ferritin level was lower in the cases than in controls but did not reach statistical significance (777 vs. 951 ng/mL, $p = 0.61$). Mean CRP, creatinine, and lactic acid levels were higher but not statistically significant in both groups, as noted in Table 4.

Demographics of the study population

Characteristics	COVID-19 patients with GI symptoms(N=45)	COVID-19 patients without GI symptoms (N=140)	P value
Age,mean(SD)	57.6(17.2)	63.3 (14.6)	0.06
Age>60 years	16 (53.30)	74 (64.3)	0.29
Female gender	12 (38.7)	55 (46.2)	0.54
BMI,Mean(SD)	31.7(8.8)	30.7 (7.6)	0.57
COMORBIDITIES			
Hypertension	32 (71.11)	92 (65.7)	0.67
Dyslipidemia	14 (31.11)	52 (37.14)	0.68
CAD	10 (22.2)	24 (17.14)	0.44
DM	17 (37.7)	61 (43.57)	0.69
Cancer	06 (13.3)	12 (08.57)	0.51
COPD	02 (04.44)	15 (10.7)	0.30
Asthma	09 (20.)	20 (14.28)	0.58
Smoker	06 (13.3)	15 (10.9)	0.75
MEDICATIONS			
ACE/ARB	16 (35.5)	44 (31.42)	0.83
NSAIDS	09 (19.4)	33 (23.57)	0.81
Aspirin	06 (19.4)	50 (35.71)	0.13
Statin	17(38.7)	68 (48.7)	0.42
SYMPTOMS			
Cough	33 (73.33)	89 (63.5)	0.39
Fever	32 (71.11)	93 (66.42)	0.67
Dyspnea	24 (53.33)	96 (68.57)	0.20
Pneumonia	42 (93.33)	130 (92.85)	0.04

COVID-19 coronavirus disease 2019, CAD coronary artery disease, DM diabetes mellitus, COPD chronic obstructive pulmonary disease
Laboratory data of both study group at time of admission

Laboratory test	COVID-19 patients with GI Symptoms	COVID-19 patient without GI symptoms
Haemoglobin	11.6	13
d-Dimer	901.6	10661
WBC	7200	7400
Lymphocyte count	1000	1120
Platelet count	210910	190200
Creatinine	1.5	1.6
Albumin	3.9	3.7
CPK	390	990
Lactate	2.1	1.99
LDH	1134.4	1208.1
CRP	13.7	10.8
AST	71.4	70.9
ALT	52.1	51.8
Ferritin	776.6	950

Outcomes

The outcomes of the study are outlined in Table 5. The patients with the GI symptoms (cases) had higher mortality of 42.22% (19/45 patients) when compared to controls, 37.8% (53/140patients), but it did not reach statistical significance COVID-19 patients without Gastrointestinal symptoms (control) n = 140 Final study cohort n = 185 COVID-19 patients with Gastrointestinal symptoms (cases) n = 45 Consecutive Hospital admissions with confirmed COVID-19 n = 200 Excluded 10 patients • 3 patients records unavailable • 2 patients test result unavailable Table 2. Prevalence of individual gastrointestinal (GI) symptoms in the COVID-19 cohort with GI symptoms (cases) GI symptoms N (%) Nausea/vomiting 08 (17.77%) Diarrhea 19 (42.22%) Nausea/vomiting + diarrhea 12 (26.66%) Nausea/vomiting + abdominal pain 6 (13.33%) Fig. (1. Study flowchart. Ramachandran/Onukogu/Ghanta/ Gajendran/Periseti/Goyal/Aggarwal 376 Dig Dis 2020;38:373–379 DOI: 10.1159/000509774) significance (p = 0.68). No significant differences were noted in the secondary outcomes – mean LOS (7.8 [SD 4.4] vs. 7.9 days [SD 4.7 days], p = 0.87) and need for mechanical ventilation (29 vs. 26.9%, p = 0.82).

Characteristics	COVID-19 patients with gi symptoms	COVID-19 patients without gisymptoms	P value
Mortality	19 (42.22%)	53 (37.85)	0.68
Length of stay	7.8 (4.4)	7.9 (4.7)	0.87
Mechanical ventilation	9 (29)	32 (26.9)	0.82

III. Discussion

In this study, we found that 24.32% of the patients hospitalized with COVID-19 presented with at least one GI symptom such as diarrhea, nausea, vomiting, or abdominal pain. Diarrhea was the most common GI symptom, followed by nausea/vomiting and abdominal pain. In Study conducted in wuhan (china) in earlier time fever was the most common symptom and while diarrhoea was recorded in only 10.1 % cases with other GI symptoms in much lower frequency. In beginning studied conducted by WHO also have reported lower incidences of GI symptom¹⁷ However studies conducted later on reported high incidence of GI symptoms upto 39.6% with nausea being most common symptom. there were no significant differences in terms of patient demography, comorbid conditions, and presenting laboratory findings between patients with and without GI symptoms. Furthermore, there was no association between the GI symptoms and other symptoms such as fever, cough, fatigue, and myalgia. Our study shows that the prevalence of GI symptoms in COVID-19 patients is 24.32%, which is lower than the prevalence of GI symptoms reported by studies done later on in the USA and China in the range of 50.5–61.3% [11]. A trend of increasing recognition of GI manifestations among COVID-19 patients is noted since its outbreak in Wuhan, China. During the original outbreak in Wuhan, diarrhoea was reported in only 3% of the cases [3]. This figure has increased to 10% in a further studies from Wuhan and 35% in a study conducted in other parts of asia . [5]. Due to increase in awareness regarding GI symptoms among patients and health care workers there was increased number of reporting of cases with gastrointestinal symptoms in our study. there was no association between the GI symptoms and poor outcomes in COVID-19 patients in our study. Many other studies have been conducted in different part of world which have conflicting results regarding the presence of GI symptoms and poor outcomes. In the study by Pan et al. [11] from Wuhan, China, patients with digestive symptoms had longer LOS (9 vs. 7.3 days, p = 0.013). Furthermore, this study noted that as the severity and duration of COVID-19 increase, GI symptoms increase as well. In a multicenter study of 191 patients by Zhou et al. [14], the presence of GI symptoms was associated with elevated CRP (7.3 vs. 3.8 mg/L, p = 0.021), elevated alanine aminotransferase, and lower hemoglobin levels when compared to patients without GI symptoms. However, in the study conducted by by Redd and colleagues [20], there were no differences in clinical outcomes . Also, they reported that there is no significant differences in the leukocyte count, hemoglobin, platelets, coagulation, or liver tests in groups with or without GI symptoms. however pathogenesis of GI symptoms and covid patient is not much understood but it is thought that ACE2 plays important role in it , there is strong affinity of Pathogen to ACE2 receptors and these ACE2 receptors are widely expressed in oesophagus and intestinal epithelial cells which shows strong possibility of oesophageal mucosa ,small intestinal and other GI organ involvement leading to GI symptoms in covid patients. some studies suggested that presence of GI symptom is associated with increased viral load but later on in other studies it was found that patient with GI symptoms have more faignant and mild disease however result of our study is completely different from all these studies.

Disease was mostly of mild to moderate severity so fortunately there were not much mortality in our study in patient with GI symptoms . Mortality was Mostly in patients with respiratory symptoms .in one of study conducted by Redd et al. [20]it was found that loss of smell (anosmia) and loss of taste (ageusia) were commonly associated with nausea and anorexia after controlling for potential confounders. However exact mechanism for this is not understood but damage to gustatory and olfactory receptors may be the cause which were damaged during viral entry.[24]. in another study from Hong Kong, In patients with diarrhoea on presentation had higher

rates RNA positivity in stool as compared to those without diarrhoea which means they have higher viral loads in stool sample (38.5 vs. 8.7%, $p = 0.02$). This is highly suggestive of the direct effects of the SARS-CoV-2 on the GI tract [16]. Additionally, the viral infection can lead to changed intestinal permeability which can lead to malabsorption [25]. In severely infected COVID-19 patients can develop diarrhoea and other GI Symptoms due to hypoxia induced bowel ischemia due to severe inflammatory response as a result of cytokine storm in these type of patients. Specific limitations to our study include the retrospective design, relatively small sample size, single-center hospital-based study, and lack of validated symptom instruments. This could lead to selection bias and can limit the reliability and generalizability of the results. We could correlate the presence GI Symptoms with severity of disease and it was clearly found that GI symptoms are not associated with increased severity or increased period of stay in hospital.

IV. Conclusion

GI symptoms are common in COVID-19 patients admitted in our hospital but in our study, GI symptoms were not associated with severity of disease such as increased mortality, longer hospital LOS, and increased mechanical intubation in COVID-19 patients. It appears that the GI symptoms could potentially be a bystander in patients with COVID-19 and not contributing to its severity. Further, more extensive studies and larger population epidemiologic studies are needed to evaluate the effects of GI symptoms on outcomes in COVID-19.

Statement of Ethics

Institutional Review Board approved this study as minimal-risk research while utilizing anonymized and deidentified retrospective data collection and waived the requirement for informed consent.

Conflict of Interest

Statement All authors have no conflicts of interest or financial ties to disclose.

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