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Original Research Article

Gastrointestinal and hepatic manifestations of COVID-19 patients in tertiary care hospitals in Bangladesh

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ABSTRACT

Introduction: The worldwide pandemic of COVID-19 caused by the virus SARS-CoV-2 has continued to progress and increasing information is becoming available about the incidence of gastrointestinal symptoms as well as abnormal liver functions test of the patients who are infected. Patients with severe disease are more likely to developed gastrointestinal symptoms specially diarrhea and altered liver functions test.
Methods: This was a cross-sectional study carried out in COVID-19 inpatients department of BSMMU and DMCH, Dhaka. In total 140 patients, 95 male and 45 female were included in this study.
Result: About 42% patients belonged to mild COVID-19 group, 17% moderate and 41% severe COVID group. In our study 58 (41.4%) patients had diabetes mellitus, 47 (33.6%) had hypertension, 42 (30%) had ischemic heart disease, 11 (7.8%) had bronchial asthma, 8 (5.7%) was obese, 5 (3.5%) had hypothyroidism. Cough was the predominant symptoms in 114 (81%) patients followed by fever 110 (79%), shortness of breath 57 (41%), body ache 51 (36%), sore throat 33 (23%), anosmia 21(15%), others 10 (7%). Among gastrointestinal manifestations anorexia (32.1%) was most common symptoms followed by diarrhoea (29.3%), nausea (16.4%), vomiting (11.4%), abdominal pain (10%) and GI bleeding (2%). GI symptoms were the initial presentation in 18% patients.
Conclusion: This study revealed that gastrointestinal manifestations were present in a significant portion of patients. Diarrhoea was a common GI symptom. Gastrointestinal symptoms were the initial presentation of COVID-19.

Keywords: COVID-19, Gastrointestinal symptoms, Hepatic manifestations, Diarrhoea, Anorexia

INTRODUCTION

The worldwide pandemic of novel coronavirus (2019-nCoV) pneumonia initially developed in one of the largest cities, Wuhan, Hubei province of China since early December 2019. Later declared as the sixth public health emergency of international concern by the world health organization and subsequently named coronavirus disease 2019 (COVID-19).[1] According to WHO, till 05th October 2021, more than 2,34,609,003 confirmed cases

have been recorded with a death toll of 4,797,368 worldwide. Bangladesh reported its first confirmed COVID-19 case on 8th March 2020. On 5th October 2021 about 15,51,351 cases are detected and 27,414 patients died in Bangladesh.[2] The outbreak of COVID-19 caused by the virus SARS-CoV-2 has been continued to progress. Data from different study becoming available about the incidence of digestive symptoms as well as abnormal liver-associated enzymes in patients who were infected. Different studies revealed that respiratory symptoms of COVID-19 such as fever, dry cough, shortness of breath were the most common symptom at visit similar to severe acute respiratory syndrome (SARS) in 2003 and middle east respiratory syndrome (MERS) in 2012, which is firmly indicative of droplet transmission and contact transmission.

However, the prevalence of less common features like diarrhea, nausea, vomiting and abdominal pain varies significantly among different study populations, along with an early and mild onset frequently followed by typical respiratory symptoms. In a recent study showed that 61% of the patient developed GI symptoms, among them 11.6%develop before hospital admission and 49.5% during hospital admission.[3] GI manifestations are reported in 10-61.1% of individuals with COVID-19, with variable onset and severity. The majority gastrointestinal symptoms of COVID-19 were mild and self-limiting and include anorexia, diarrhoea, nausea, vomiting and abdominal pain/discomfort. A few patients presented with feature of acute abdomen with etiologies such as acute pancreatitis, acute appendicitis, intestinal obstruction, intestinal ischemia, hemoperitoneum or abdominal compartment syndrome.[4]

Patients who were admitted with GI symptoms showed a higher risk of complications, including acute respiratory distress syndrome, myocardial infraction, acute renal failure, intensive care unit (ICU) admission and high case fatality rate.[5] 23 (20.5%) patients reported at least one gastrointestinal symptom at the onset of the SARS-3 CoV-2 infection and the most common manifestations were diarrhea (17.8%), abdominal pain (9.8%), and vomiting (7.1%). Gastrointestinal symptoms were the only manifestation of COVID-19 in 6.25% of the cases. About 16.9%patients had elevated SGOT and 15.2% had elevated SGPT.[6] Indeed, the index case of COVID-19 in the United States presented with gastrointestinal symptoms like nausea and vomiting in addition to systemic and respiratory symptoms, and subsequently developed abdominal discomfort and diarrhea.[7]

GI symptoms were more common in severe disease (17.1%).8 In some cases GI symptoms may be present before respiratory symptoms, with some patients only presenting with digestive symptoms in the absence of respiratory symptoms. These presentations can potentially lead to delay in diagnosis if clinicians were unaware with GI presentation of COVID-19.[9] Multicenter study done in Bangladesh showed that 61.4% patients had gastrointestinal symptoms with diarrhoea about 35% cases.[10] Large study done in admitted patients in China showed that 11.4%patients had at least one GI symptoms ,GI symptoms associated with increasing age, severe disease, 41% patients took antibiotics.[11] Abnormal liver function test were consistently shown to be more prevalent in severe disease. SARS-CoV-2 shares 82% genome sequence similarity to SARS-CoV and 50% genome sequence homology to middle east respiratory syndrome coronavirus (MERS-CoV) all three coronaviruses are known to cause severe respiratory symptoms. Liver function impairment has been reported in up to 60% of patients with SARS and has also been reported in patients infected with MERS-CoV.[12] The objective of this study was to determine the prevalence and characteristics of gastrointestinal and hepatic manifestations in COVID-19 patients admitted to tertiary care hospitals in Bangladesh.

METHODS

This cross-sectional study was conducted in the COVID-19 units of Bangabandhu Sheikh Mujib Medical University (BSMMU) and Dhaka Medical College Hospital (DMCH), Dhaka, Bangladesh, from June 2020 to May 2021. The study included 140 purposively sampled COVID-19 patients confirmed by RT-PCR. Inclusion criteria were symptomatic patients aged≥18 years, while exclusion criteria included pregnant or lactating women, and those with chronic liver disease, chronic kidney disease, gastrointestinal malignancy, chronic G.I.T. infections or inflammations, and malabsorption syndromes. Data collection involved demographic information, clinical symptoms (e.g., fever, cough, diarrhea, nausea, vomiting, abdominal pain, jaundice, GI bleeding), drug history, BMI, SpO2, and respiratory rates.

Laboratory investigations included CBC, bilirubin, AST, ALT, ALP, and PT, performed according to COVID-19 management protocols. Disease severity was classified based on WHO guidelines. Socio demographic and lifestyle factors such as age, gender, smoking status, and alcohol consumption were assessed through questionnaires. Data were processed and analyzed using SPSS version 25.0, with means calculated for continuous variables and frequencies and percentages for quantitative observations. Chi-Square and ANOVA tests were used for categorical and continuous variables, respectively, with significance set at $p<0.05$. Ethical considerations included informed consent, confidentiality, and Institutional review board (IRB) approval. Data quality was ensured through regular supervision, random checks, and scheduled progress meetings with the guide.

RESULTS

Table I shows that 96 (68.5%) patients belonged to age group over 50 years. The mean age was found 55.14±13.5 years with range from 25 to 95 years. Two

third 95 (67.8%) of the patients were male and 45 (32.2%) were female. Male female ratio was 2:1.

Table 1: Incidence of different types of asterion.

Socio-demographic characteristics	Number of patients (N)	(%)
Age (years)		
19-29	04	2.8
30-39	15	10.8
40-49	25	17.9
>50	96	68.5
Mean±SD	55.14±13.5	
Range (min-max)	25-95	
Sex		
Male	95	67.8
Female	45	32.2

Table 2: Distribution of the study patients according to co-morbidities (n=140).

Co-morbidities	Number of patients (N)	(%)
Diabetes mellitus	58	41.4
Hypertension	47	33.6
Ischemic heart disease	42	30
Bronchial asthma	11	7.8
Obesity	08	5.7
Hypothyroidism	05	3.5

Table II shows that 58 (41.4%) patients had diabetes mellitus, 47 (33.6%) had hypertension, 42 (30%) had ischemic heart disease, 11 (7.8%) had bronchial asthma, 8 (5.7%) was obese, 5 (3.5%) had hypothyroidism.

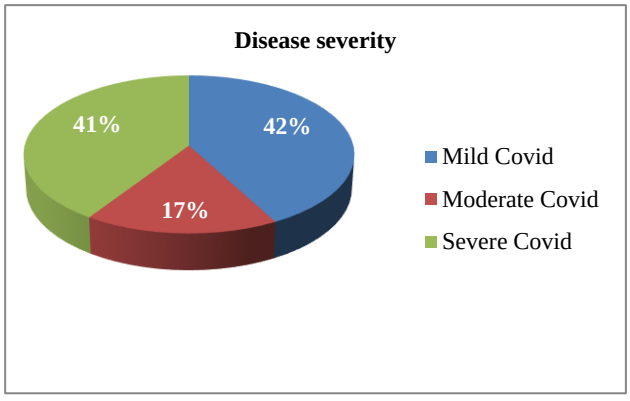

Figure 1: Pie chart showing distributions of patients according to disease severity.

Figure 1 illustrate the distribution of COVID-19 patients according to disease severity. Among the study population, 59 patients (42%) had mild COVID-19, 24 patients (17%) had moderate COVID-19, and 57 patients (41%) had severe COVID-19.

Table 3, shows that cough was the predominant symptoms in 114 (81%) patients followed by fever 110 (79%), shortness of breath 57 (41%), body ache 51 (36%), sore throat 33 (23%), anosmia 21 (15%), others 10 (7%).

Table 3: Distribution of the study patients according to non-GI symptoms (n=140).

Symptoms	Number of patients (N)	(%)
Fever	110	79
Cough	114	81
Shortness of breath	57	41
Body ache	51	36
Sore throat	33	23
Anosmia	21	15
Runny nose	5	3.5
Headache	5	3.5

Table 4: Distribution of the study patients according to GI symptoms (n=140).

Symptoms	Number of patients (N)	(%)
Anorexia	45	32.1
Nausea	23	16.4
Vomiting	16	11.4
Diarrhoea	41	29.3
Abdominal pain	14	10
GI bleeding	03	02
Hematemesis	01	0.7
Melaena	03	02
GI symptoms as initial presentation	25	18

Table 4, shows the association of socio demographic, lifestyle, clinical, severity of COVID-19 patients with the occurrence of hepatic manifestations. Among the patients who had hepatic manifestations, 35 (41.7%) were overweight, 7 (8.3%) were obese and 39 (46.4%) had severe COVID-19 disease. Among the patient who do not have hepatic manifestations, 7 (12.5%) was overweight, 1 (1.8%) was obese and 18 (32.1%) had severe disease. This difference is statistically significant indicating that increasing BMI and severity can be considered as an associated risk factor for the development of hepatic manifestations in COVID-19 patients.

Table 5 shows the association of socio demographic, lifestyle, clinical, severity of COVID-19 patients with the occurrence of GI manifestations. Among the patients who had GI manifestations, 29 (52.8%) had severe disease and among the patient who do not have GI manifestations, 28 (32.9%) had severe disease and the difference is statistically significant (p=0.002) indicating that severe disease associate with GI manifestations.

Table 5: Association of gastrointestinal manifestations with sociodemographic, lifestyle and clinical characteristics of COVID-19 patients (n=140).

	With GI symptoms N (%)	Without GI symptoms N (%)	P value
Gender			
Male	38 (69.1)	57 (67.1)	0.801
Female	17 (30.9)	28 (32.9)	
Age (years)			
19-29	1 (1.8)	3 (3.5)	
30-39	4 (7.3)	11 (12.9)	0.440
40-49	8 (14.5)	17 (20)	
50 or more	42 (76.4)	54 (63.5)	
Smoking			
Non-smoker	42 (76.4)	70 (82.4)	0.387
Smoker	13 (23.6)	15 (17.6)	
Antibiotics			
Yes	14 (25.5)	27 (31.8)	0.079
No	41 (74.5)	58 (68.2)	
Antiviral			
Yes	4 (7.3)	4 (4.7)	0.523
No	51 (92.7)	35 (94.6)	
BMI			
Underweight	1 (1.8)	2 (2.3)	
Normal	33 (60)	54 (63.5)	0.472
Overweight	18 (32.7)	24 (28.2)	
Obese	3 (5.5)	05 (5.9)	
Severity			
Mild	13 (23.6)	46 (54.2)	0.002
Moderate	13 (23.6)	11(12.9)	
Severe	29 (52.8)	28 (32.9)	

P value reached from chi square test

Table 6: Association of hepatic manifestations with socio demographic, lifestyle, and clinical characteristics of COVID-19 patients (n=140).

	With altered LFT N (%)	Without altered LFT N (%)	P value
Gender			
Male	59 (70.2)	36(64.3)	0.460
Female	25 (29.8)	20 (35.7)	
Age (years)			
19-29	3 (3.6)	1 (1.8)	
30-39	8 (9.5)	7 (12.5)	0.824
40-49	14 (16.7)	11 (19.6)	
50 or more	59 (70.2)	37 (66.1)	
Smoking			
Nonsmoker	67 (79.8)	45 (80.4)	0.931
Smoker	17 (20.2)	11 (19.6)	
Antibiotics			
Yes	25 (29.8)	16 (28.5)	0.879
No	59 (70.2)	40 (71.4)	
Antiviral			
Yes	7 (8.3)	1 (1.8)	0.144
No	77 (91.7)	55 (98.2)	
BMI			
Underweight	2 (2.4)	1 (1.8)	
Normal	40 (47.6)	47 (83.9)	0.001

Continued.

	With altered LFT N (%)	Without altered LFT N (%)	P value
Overweight	35 (41.7)	7 (12.5)	
Obese	7 (8.3)	1 (1.8)	
COVID severity			
Mild	27 (32.1)	32 (57.2)	0.01
Moderate	18 (21.4)	6 (10.7)	
Severe	39 (46.4)	18 (32.1)	

DISCUSSION

This was a cross-sectional study conducted at COVID unit, BSMMU and DMCH during June 2020 to May 2021. Patients admitted in COVID unit of BSMMU and DMCH were screened for eligibility and offered inclusion into the study if eligible and 140 patients (117 from BSMMU and 23 from DMCH) were eventually enrolled into the study. The aim of this study is to see the gastrointestinal and hepatic manifestation of Covid-19 patients. It was observed in this study that the majority (68.5%) patients belonged to age >50 years. The mean age was found 55.14±13.5 years with range from 25 to 95 years.

Ahmed et al, reported that the most prevalent affected age groups were in 26-35 years 71 (35.5%), in 16-25 years 54 (27%), in 35-45 years 49 (24.5%) and mean age was 32.2±2 years. Study by Ramachandran et al. showed that the mean age was 57.6 years (SD±17.2).[13] In another study, it was reported that the median age of patients 61 years (50-70) and with diarrhoea was 59 years (44 to 64 years).[14] According to Paul et al, age range was from 9 to 80 years and mean age was 43 years that was similar to mean age in China and India.[15] Median age was 43.5 years in a Indian study conducted by Bhandari et al., where Chen et al, found it was 55.5 years.[16,17]

But studies from America conducted by Richardson et al, showed median age of 63 years.[18] This study showed that almost two third (67.8%) patients were male and 45 (32.2%) was female and male female ratio was 2.1:1. Huang et al, found that 73% were male, Wang et al., reported 54.3% were male.[19,20] Regarding socio demographic data of our study, male were predominant as in other studies. This study showed diabetes mellitus is the major comorbid condition present in 58 (41.4%) patients followed by hypertension 47 (33.3%), ischemic heart disease 42 (30%), bronchial asthma 11 (7.8%), obesity 8 (5.7%), hypothyroidism 5 (3.5%). Paul et al, reported that common comorbidities were diabetes (21%), hypertension (17%), chronic kidney disease (CKD) (11%), asthma (8%), stroke (3%) and ischemic heart disease (IHD) (2%). In this study we found that 59(42%) patient had mild, 24 (17%) patients had moderate and 57 (41%) patients had severe group of COVID-19 infection.[15] In a Bangladeshi study Paul et al, reported that the mild, moderate and severe cases were 53%, 31%, 13% respectively.[15] Among the reported cases worldwide, 80% has mild to moderate diseases, (non-pneumonia/pneumonia), 13.8% severe diseases and 6.1% were critical case throughout the world.[21] In this study we found that 28 (20%) patients were smoker. None of the patients gave history of alcohol. There was no significant association found between smoking and nonsmoking group for elevated transaminase and diarrhoea. Study done by Ramachandran et al, showed there was no significant association found between smoking and nonsmoking group for gastrointestinal symptoms.[13]

In present study fever was present in 110 (79%), cough 114 (81%), shortness of breath in 57 (41%), body ache 51 (36%), sore throat 33 (23%), anosmia 21(15%), headache 5 (3.5%), runny nose 5 (3.5%) which are similar to that reported by Kang et al, that there were 77 (65.3%) patients with fever or chills, 84 (71.2%) with cough or sputum production, 49 (41.5%) with dyspnea, 47 (39.8%) with myalgia, 43 (36.4%) with headache. Wu et al, reported cough (41.4%) was the most common symptom at onset of illness, followed by fever (39.7%) and fatigue (36.2%).

Paul et al, founded among the 100 patients, fever (91%), dyspnea (41%), cough (33%) were the most frequent symptoms.[15] Other symptoms were sore throat (12%), diarrhoea (12%), myalgia (12%), rectal bleeding (2%). Common symptoms included fever 98.6%, fatigue 70%, and dry cough 59.4% in a study by Wang et al.[20] All these data are almost similar to that of our study. Among GI manifestation anorexia was predominant symptom present in 45 (32.1%) patients followed by diarrhoea 41 (29.3%), nausea 23 (16.4%), vomiting 16 (11.4%) abdominal pain 14 (10%), GI bleeding 03 (2%). About 25 (18%) patients had GI symptoms as the initial presentations. No patient was found clinically icteric.

In present study we found that 14 (10%) patients had abdominal pain. Most of the pain is mild epigastric pain. Two patients with abdominal pain had GI bleeding. There are multiple causes of abdominal pain in COVID-19 patients such as acute pancreatitis, acalculous cholecystitis, mesenteric ischemia, acute colonic pseudo-obstruction. High BMI, presence of DM increase the risk acute pancreatitis.[22] Acute colonic obstruction usually present with diffuse abdominal pain, neutrophilic leukocytosis, imaging showed thickened gut wall ,patient usually improved after conservative management.[23] Mesenteric ischemia develop in critically ill patients ,some of them develop paralytic ileus.[24] Acalculous

cholecystitis develop in crically ill patients related to gall bladder hypomotility and may require surgical intervention.[25] Some patient with COVID-19 may present with acute abdomen without any identifiable cause.[26] This study showed that gastrointestinal bleeding occur only 3 (2%) of patients, only one patients had hematemesis, all the patients had melaena. Majority of the patients presented with GI bleeding were over 50years age group and had abdominal pain.

One of the patients received rivaroxaban and antiplatelet who presented with hematemesis and melaena. Gastrointestinal bleeding may occur in hospitalized patients due to stress ulcer.[27] Gastrointestinal bleeding may be caused by ischemic colitis in COVID-19 patients. COVID-19 associated coagulopathy are often seen evidence by high d-dimer and fibrinogen which may predispose to thrombosis.[28] Point prevalence of GI bleeding is 3%, no identifiable risk factor was found, GI bleeding is not associate with the use of antiplatelet or anticoagulant.[29] Compilation of data from our study with data of previous study conducted in other countries collectively showed that diarrhoea has significant association with severity of COVID-19.

The limitations of this study include its short duration, relatively smaller sample size, and the inability to exclude nonalcoholic fatty liver disease. A similar prospective study with a larger sample size is recommended to validate the findings of the present study.

CONCLUSION

This study revealed that gastrointestinal manifestations were present in a significant portion of patients. Diarrhoea was a common GI symptom. Elevated transaminases were also noted and gastrointestinal symptoms were sometimes the initial presentation of COVID-19. Increasing age and severe disease were significantly associated with the occurrence of diarrhoea.

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