ORIGINAL ARTICLE

Frequency and correlation of gastrointestinal symptoms with outcomes in hospitalized patients with COVID-19.

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ABSTRACT… Objective: To assess the frequency and correlation of GI manifestations with outcomes in hospitalized patients suffering from COVID-19. **Study Design:** Retrospective Cohort study. **Setting:** Tertiary Care Hospital, Gujrat. **Period:** April 1st, 2020 to March 31st, 2021. **Material & Methods:** Medical records were collected retrospectively from six hundred eighty eight COVID-19 patients having complete charts. Among them male were 364 (52.91%). Incomplete charts were excluded from the study. Multivariate logistic regression analysis was used after adjusting for co-morbidities and clinical demographics. **Results:** Most of the patients with COVID-19 presented with cough (38.44%), dyspnea (37.53%), and fever (34.34%), while GI symptoms were noted in 25.92% of patients. Among them diarrhea was in 12.83%, nausea and vomiting in 10.53%, diminished hunger 9.32%, and abdominal discomfort 3.83%. Mortality, admission to ICU and need for intubation was more common among patients with diarrhea. (p = 0.006). **Conclusion:** Gastrointestinal (GI) manifestations are common in patients with COVID-19. Among them patients with diarrhea were more prone to admission to intensive care unit, intubation and death so patients with COVID-19 should be questioned for GI symptoms also. Medical professionals should know that diarrhea may be an indicator of severity of disease and its effect on prognosis of patient.

Key words: COVID-19, Diarrhea, Hospitalized Patients, ICU, Intubation.

INTRODUCTION

Since December 2019, corona virus disease 2019 (COVID-19) has been devastating the entire globe. More than hundred million patients were infected with COVID-19 throughout the world till 30th January 2021.[1] Although manifestations due to respiratory tract involvement such as cough, fever and difficulty in breathing are commonly reported clinical features in patients infected with SARSCoV-2, extrapulmonary involvement resulting in variety of symptoms was also reported in many studies including GI complaints like nausea, vomiting and diarrhea in patients with COVID-19.[2,3,4] A large meta-analysis including 6686 patients of COVID-19 showed fifteen percent prevalence of gastrointestinal symptoms, in which most common were diarrhea, nausea, vomiting, and anorexia.[5] In addition, GI manifestations appeared to be associated with prolonged hospitalization and poor outcomes.

In a multicentre study from china 60% of patients without gastrointestinal symptoms improved and were discharged, while on the other hand only 34.3% of the patients suffering from GI symptoms showed recovery.[6]

Thus the co-relation between GI manifestations in patients with COVID-19 and their outcomes is very important to understand. Many studies were done in different countries to look this association[7,8], majority of studies were done on Chinese or European populations. In this study we tried to assess the frequency and correlation of GI manifestations with outcomes in Pakistani population.

MATERIAL & METHODS

It was retrospective cohort study. Complete charts of the patients with COVID-19 were included in study while patients with incomplete

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charts were excluded. Medical records were collected retrospectively from six hundred eighty eight patients with COVID-19 admitted in District Headquarter Hospital, Gujrat from April 1, 2020 to March 31, 2021 after informed consent and approval from ethical committee (NSMC/25/6).

Out of which 364 (52.91%) were male. Clinical history and presenting complaints were recorded (Table-I) Categorical data was expressed as proportions/ percentages for analysis while continuous data as median (interquartile range). Statistical Packages for Social Sciences 20 was used for data analysis. Specifically, analysis was done to assess the correlation between gastrointestinal symptoms and outcomes. The analysis was done on GI manifestations like nausea, vomiting, diarrhea and abdominal pain. Common symptoms like cough, fever and difficulty in breathing were also analyzed. Outcomes like discharge or death of the patients were recorded. Statistically P-values of < 0.05 were considered significant.

RESULTS
Baseline characteristics of included 688 patients are shown in Table-I. Mostly hospitalized patients had cough (38.45%), difficulty in breathing (37.54%), and fever (34.35%), while gastrointestinal symptoms were found in 25.92% of the patients. Among them diarrhea was most common presentation (12.8%), nausea/ vomiting in (10.5%), loss of appetite (9.3%), and pain abdomen (3.8%). Almost twenty six percent patients were died. Study concluded that older age, male gender and patients with diarrhea had significantly high mortality (p < 0.001). Similarly patients with cough and difficulty in breathing were more likely to die (p < 0.001). Among the hospitalized patients 34.3% were shifted to intensive care unit (ICU). Table-III summarizes the baseline features of these patients. Study concluded that men, patients with diarrhea and difficulty in breathing had more tendency to admit in ICU (p < 0.001).As also mentioned in Table 3, 22.14% of patients were put on mechanical ventilation, intubation was 1.928 times more common in males than females. Our study also showed that intubation was more common in patients with cough, diarrhea and dyspnea p (< 0.001).

	Median (IQR) or n (%)
	All Patients, n = 688
Age (year)	59 (49–73)
> 60 (year)	314 (45.6%)
Sex	
Men	364 (52.91%)
Women	324 (47.14%)
Diabetes mellitus	300 (43.64%)
Hypertension	490 (71.24%)
Chronic obstructive pulmonary disease	62 (9.05%)
Hepatitis C Virus infection	28 (4.15%)
Malignancy / Tumour	28 (4.16%)
GI Symptoms	
Any Gastrointestinal (GI) symptom	178 (25.93%)
GI symptoms without respiratory symptoms	70 (10.23%)
Exclusively GI symptoms	24(3.54%)
Nausea or vomiting	72 (10.54%)
Diarrhea	88 (12.83%)
Abdominal pain	26 (3.83%)
Decreased appetite	64 (9.35%)
Other Symptoms	
Fever	236 (34.35%)
Cough	264 (38.44%)
Dyspnea	258 (37.51%)
Table-I. Baseline characteristics of hospitalized COVID-19 patients	

	Median (IQR) or n (%)		
	Alive at Discharge n=508	Death, n = 180	P-Value
Age (year)	60 (47–72)	68.5 (59.8–81.3)	<0.001*
Sex			
Men	250 (49.2%)	114 (63.3%)	0.001*
Women	258 (50.8%)	66 (36.7%)	0.001*
Gastrointestinal Symptoms			
Any GI symptom	122 (24%)	56 (31.1%)	0.331
Exclusively GI symptoms	20 (3.9%)	4 (2.2%)	0.173
Nausea or vomiting	52 (10.2%)	20 (11.1%)	0.863
Diarrhea	50 (9.8%)	38 (21.1%)	0.006*
Abdominal pain	20 (3.9%)	6 (3.3%)	0.593
Decreased appetite	26 (14.4%)	38 (7.5%)	0.296
Other Symptoms			
Fever	168 (33.1%)	68 (37.8%)	0.474
Cough	182 (35.8%)	82 (45.6%)	0.013*
Shortness of breath	158 (31.1%)	100 (55.6%)	<0.001*
No GI symptoms	386 (76.0%)	124 (68.9%)	0.331
Table-II. Survived vs. deceased patients admitted with COVID-19			

COVID-19 patients admitted to the intensive care unit

	Median (IQR) or n (%)		
	Medicine Floor only, n = 452	ICU, n = 236	P-Value
Age (year)	62.5 (48–76)	63 (53–70)	0.380
Sex			
Men	220 (48.7%)	144 (61%)	0.009*
Women	92 (39%)	232 (51.3%)	0.009*
Gastrointestinal Symptom			
Any gastrointestinal symptoms	106 (23.5%)	72 (30.5%)	0.169
GI symptoms without respiratory symptoms	52 (11.9%)	16 (6.8%)	0.130
Exclusively GI symptoms	18 (4.0%)	6 (2.5%)	0.332
Nausea or vomiting	42 (9.3%)	30 (12.7%)	0.464
Diarrhea	44 (9.7%)	44 (18.6%)	0.019*
Abdominal pain	14 (3.1%)	12 (5.1%)	0.617
Decreased appetite	40 (8.8%)	24 (10.2%)	0.692
Other Symptoms			
Fever	154 (34.1%)	82 (34.7%)	0.689
Cough	162 (35.8%)	102 (43.2%)	0.214
Shortness of breath	130 (28.8%)	128 (54.2%)	<0.001*
No GI symptoms	246 (76.5%)	164 (69.5%)	0.169
Table-III. COVID-19 patients admitted to the ICU and requiring intubation.			

COVID-19 patients admitted to the hospital requiring intubation

	Median (IQR) or n (%)		
	Medicine Floor Only, n = 536	ICU, n = 152	P-Value
Age (year)	63.50 (50.25–76)	60 (46.5–68)	0.466
Sex			
Men	272 (50.7%)	92 (60.5%)	0.028*
Women	264 (49.3%)	60 (39.5%)	0.028*
Gastrointestinal Symptoms			
Any gastrointestinal symptom	130 (24.3%)	48 (31.6%)	0.266
GI symptoms without respiratory symptoms	62 (11.6%)	8 (5.3%)	0.133
Nausea or vomiting	50 (9.3%)	22 (14.5%)	0.507
Diarrhea	52 (9.7%)	36 (23.7%)	0.002*
Abdominal pain	18 (3.4%)	8 (5.3%)	0.952
Decreased appetite	50 (9.3%)	14 (9.2%)	0.876
Other Symptoms			
Fever	144 (32.5%)	62 (40.8%)	0.688
Cough	184 (34.3%)	80 (52.6%)	0.023*
Shortness of breath	262 (30.2%)	96 (63.2%)	<0.001*
No GI symptoms	406 (75.7%)	104 (68.4%)	0.266

DISCUSSION

Our study exhibits a clear predominance of gastrointestinal symptoms among COVID-19 patients which were admitted in hospital. Results were in accordance with another study which was done on 138 COVID-19 patients;[9] clinical features were fever (98.65%), malaise (69.61%), cough (59.45%), body aches (34.82%) and shortness of breath (31.22%), while GI manifestations like abdomen pain (3.63%), loose stool (10.12%) and nausea/ vomiting (3.61%). Fourteen patients had diarrhea first before onset of fever.[9] In another study it was found that incidence of diarrhea was associated with severity of COVID-19[5] However according to the WHO and China collaborative report on more than 50,000 COVID-19 patients, the incidence of GI symptoms was quite low and diarrhea was reported in only 3.7% of patients.[10] A study concluded after collecting data from 3 reports that the link between COVID-19 and diarrhea may be underestimated.[11-14] In another study on 1141 COVID-19 patients 16% of patients were presented with gastrointestinal symptoms only.[15]

According to results of our study, among GI symptoms diarrhea was interlinked closely with disease outcomes like admission in intensive care units, mechanical intubation and expiry. This study supplements an earlier review in which there was an increase in admission of patients with gastrointestinal manifestation. A study from New York showed that patients with GI problems had 70% more chances to have COVID-19.[2,16] Different studies showed clashing conclusions on negative outcomes of GI manifestation on patients with COVID-19.[17,18] Our study and many other studies demonstrate that overall GI symptoms have no significant relationship with mortality.[19,20] However after stratification we noticed that diarrhea is interlinked with poor outcomes. A meta-analysis showed 17.6% prevalence of GI manifestations.[21] While we found that 25.9% patients had GI symptoms. The difference may be due to timing of recording of symptoms, we documented prevalence of symptoms only at the time of hospitalization, which was not followed in that meta-analysis.

Limitations of study include lack of generalizability, as the study was done in single center and was retrospective cohort. Secondly it was conducted in beginning of pandemic when testing required more time and treatment was limited.

Gastrointestinal symptoms especially diarrhea may be caused by different medications used to treat COVID-19 like remdesivir, antibiotics, and

steroids. In our patients, proper history was taken before start of treatment and none of the patient was taking any drug like steroids or antibiotics that can cause diarrhea.

CONCLUSION
Gastrointestinal (GI) manifestations are common in patients with COVID-19. Among them patients with diarrhea were more prone to admission to intensive care unit, intubation and death so patients with COVID-19 should be questioned for GI symptoms also. Medical professionals should know that diarrhea may be an indicator of severity of disease and its effect on prognosis of patient. More studies are required to explore the connection between COVID-19 and gastrointestinal system.

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2	Shama Iqbal	Concept and study design revision and final approval of the study.	
3	Adnan Qadir	Data collection, Critical review, Statistical analysis.	
4	Muhammad Shahid	Data analysis and interpretation and drafting of the manuscript.	