

Diarrhoea in COVID-19 with Emphasis on Non Respiratory Presentation: A Case Series

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ABSTRACT

Coronavirus Disease 2019 (COVID-19) infection can have myriad presentations ranging from non specific constitutional symptoms to respiratory failure and extrapulmonary manifestations. As COVID-19 is viewed predominantly as an illness of the respiratory tract, extrapulmonary manifestations are often overlooked. The case series is of seven COVID-19 diagnosed patients who presented with diarrhoea, without respiratory symptoms. Clinicodemographic characteristics, hospital course and outcome of these patients are described here. Median age of the patients was 42 years. There were four males and three females. One patient had diabetes mellitus and hypertension, one had hypothyroidism and one had Hodgkin's lymphoma along with tuberculosis. Five patients had fever while all had diarrhoea as the predominant presenting complaint. Median duration of symptoms was four days before admission. Laboratory abnormalities included anaemia (n=5; 57.1%), lymphopenia (n=3; 42.9%) and elevated inflammatory markers i.e., ferritin and C-reactive protein (n=2; 28.6%). Most patients did not require any specific treatment other than supportive care. All patients were successfully discharged after a median hospital stay of 10 days. Isolated diarrhoea without respiratory symptoms can be presenting complaint of COVID-19 and should be considered by clinicians in current pandemic scenario.

Keywords: Coronavirus 2019, Gastrointestinal manifestations, Outcomes, Prognosis

INTRODUCTION

An outbreak of pneumonia of unknown cause in Wuhan, China occurred in December 2019. Investigation into the outbreak led to the identification of new virus, Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) [1]. This virus primarily spreads through respiratory droplets and the virus has also been detected in blood and stool [2]. Common symptoms include systemic symptoms like fever, myalgias or respiratory symptoms like throat pain, cough and breathlessness. Gastrointestinal symptoms have been reported in a minority of patients and may include nausea, vomiting, anorexia and diarrhoea [3,4].

There is limited literature on gastrointestinal manifestations of COVID-19. Herein, the clinical features, hospital course and outcomes of admitted COVID-19 patients presenting with diarrhoea are reported from analysis of initial cohort.

The patients presented at All India Institute of Medical Sciences-National Cancer Institute, Jhajjar (National Capital Region). The institute has been conducting an observational study on all the admitted COVID-19 patients from May 2020 to July 2020. Total 800 patients of the cohort were analysed. In a previously reported clinicoepidemiologic characteristic study, there were 144 COVID-19 patients admitted at the study centre, of which 4 (2.8%) had diarrhoea and 3 (2.1%) had nausea or vomiting; however, none of them had isolated gastrointestinal manifestations [4]. Subsequently, it was encountered that some patients had isolated diarrhoea as the only manifestation of COVID-19. This case series describes seven patients who presented to hospital with diarrhoea as the predominant manifestation of COVID-19 infection, without any respiratory symptoms. [Table/Fig-1] shows the outline of all described cases.

CASE SERIES

Case 1

A 56-year-old female presented with history of fever and diarrhoea of four days duration, along with myalgias. She was a known case of hypothyroidism was on thyroid hormone replacement therapy and thyroid hormone levels. She had history of contact with a confirmed

case of COVID-19 (husband) who was already in quarantine. Her symptoms started with three to four episodes of loose watery stool per day which did not contain any blood or mucous. She also developed fever which was intermittent and associated with chills and rigours. She denied any history of throat pain, cough or breathlessness.

On examination, patient was febrile, while other vitals being stable and systemic examination was non contributory. Her Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) of nasal and pharyngeal swab was positive for COVID-19.

She was managed with oral and intravenous (IV) fluid rehydration and other supportive measures. Her symptoms resolved in four days and she was discharged to home quarantine after 10 days of hospitalisation.

Case 2

A 48-year-old female presented with fever and diarrhoea of five days duration. She was a known case of diabetes mellitus for eight years and hypertension for two years. She was already on medication Telmisartan 40 mg once a day, and tablet Metformin 1 gm twice a day. She had history of contact with a confirmed case of COVID-19 (husband). She had loose watery stools, seven to eight episodes per day without any blood or mucous. She also had intermittent fever with chills and rigours. Her oral intake was poor.

On admission, she had mild tachycardia with other vitals being normal (Pulse Rate (PR)- 120/min, blood pressure- 110/64 mmHg, SpO₂ (Saturated Oxygen)-97% on room air). Systemic examination did not reveal anything else. Her RT-PCR of nasal and pharyngeal swab was positive for COVID-19.

She was managed with IV fluids while antihypertensive medications were stopped. Insulin was given as per sliding scale for blood sugar control while in view risk of severe disease, patient was given tab. Hydroxychloroquine (HCQ) according to standard protocol (400 mg twice daily, on day 1 followed by 400 mg once a day, for next four days). She made a complete recovery over next five days with complete resolution of symptoms and was discharged on 12th day of admission.

S. No.	Age/ Sex	Symptoms apart from diarrhoea	Co-morbidities	Chest X-ray	Severity	Reason for testing	COVID specific Treatment given	Duration of symptoms before admission (days)	Duration of hospital stay (days)	Hemoglobin (g/dL)	Total leucocyte count (per mm ³)	Differential leucocyte count, percent	Serum ferritin (ng/mL)	Serum C reactive protein (mg/L)	Laboratory investigation abnormality	Outcome
1	56/ F	Fever, myalgia	Hypothyroidism	Normal	Mild	Household contact	Nil	4	10	12.2	8680	Neutrophils 64%; Lymphocytes 23%	21.5	0.5	Nil	Discharged
2	48/ F	Fever, decreased oral intake	Diabetes mellitus, hypertension	Normal	Mild	Household contact	Hydroxy-chloro-quine	5	12	11.9	4640	Neutrophils 67%; Lymphocytes 23%	69.5	0.9	Anaemia	Discharged
3	41/ M	Nausea	No	Normal	Mild	Household contact	Nil	4	10	12.5	4190	Neutrophils 71; Lymphocytes 14%	224	1.5	Anaemia, Lymphopenia	Discharged
4	42/ M	Fever	No	Normal	Mild	Household contact	Nil	3	10	9.9	7710	Neutrophils 82%; Lymphocytes 10%	112	12	Anaemia, Lymphopenia, elevated CRP	Discharged
5	36/ M	Fever, headache	No	Normal	Mild	Household contact	Nil	3	10	13.4	7320	Neutrophils 52%; Lymphocytes 31%	128	1.5	Nil	Discharged
6	26/ F	Fever, nausea	No	Normal	Mild	Healthcare worker, high risk contact	Nil	2	10	11.6	6100	Neutrophils 50; Lymphocytes 36%	222	2	Anaemia	Discharged
7	57/ M	Poor oral intake, easy fatiguability	Hodgkins Lymphoma (in remission) Lymph node TB (near completion of treatment)	Normal	Mild	No exposure history	Hydroxy-chloro-quine, anti-tubercular therapy	7	11	9.4	4220	Neutrophils 77%; Lymphocytes 9%	1540	28	Anaemia, Lymphopenia, hypokalemia, elevated CRP, elevated ferritin	Discharged

[Table/Fig-1]: Demographic characteristics, symptomatology, laboratory abnormalities and outcomes of patients included in the study (n=7).

Case 3

A 41-year-old male presented with history of diarrhoea of four days duration. He also complained of nausea on and off. He had no known co-morbidities. He had history of contact with a confirmed case of COVID-19 (wife) who was already in quarantine. His symptoms started with four to five episode of loose watery stool per day which did not contain any blood or mucous. He denied any history of fever, throat pain, cough or breathlessness. Patient was vitally stable. His RT-PCR of nasal and pharyngeal swab was positive for COVID-19.

He was managed with oral rehydration solution and made complete recovery in four days and was discharged in 10 days.

Case 4

A 42-year-old male presented with history of fever and diarrhoea of three days duration. He had no known co-morbidities. He had history of contact with a confirmed case of COVID-19. His symptoms started with three to four episode of loose watery stool per day which did not contain any blood or mucous. He gave history of intermittent fever not associated with chills for six days. Patient was vitally stable with normal systemic examination. His RT-PCR of nasal and pharyngeal swab was positive for COVID-19.

He was managed with oral rehydration solution and made complete recovery in three days and was discharged in 10 days.

Case 5

A 36-year-old male presented with history of fever for three days along with diarrhoea for two days. He also had headache for last two days. He had no known co-morbidities. He had history of contact with a confirmed case of COVID-19 (flatmate) who was already in quarantine. He had seven episodes of diarrhoea over 24 hours. Stools did not contain any blood or mucous. There was no history of breathlessness. Patient was vitally stable and systemic examination

was non-contributory. His RT-PCR of nasal and pharyngeal swab was positive for COVID-19.

He was managed with oral rehydration and made complete recovery in three days and was discharged in 10 days.

Case 6

A 26-year-old female presented with history of fever, nausea and diarrhoea of two days duration. She had no known co-morbidities. She was a health care worker and was working at a designated COVID-19 hospital. Her symptoms started with intermittent fever with chills and loose watery stool of two days duration. She had five episodes over 24 hours. Stools did not contain any blood or mucous. Patient was vitally stable and systemic examination was non-contributory. Her RT-PCR of nasal and pharyngeal swab was positive for COVID-19.

She was managed with oral rehydration and she made complete recovery in four days. She was discharged in 10 days.

Case 7

A 57-year-old male presented with loss of appetite, diarrhoea and easy fatiguability of seven days duration. He was a known case of Hodgkin's lymphoma (in remission) and Lymph node tuberculosis in continuation phase of Antitubercular Therapy (ATT). He underwent testing for COVID-19 in view of him being symptomatic and having risk to severe disease. He had loose watery stools to 8 to 10 episodes per day without any blood or mucous. He had poor oral intake and easy fatiguability also.

On admission, had tachycardia (heart rate 124 beats per minute), and dry tongue; other vitals were normal (blood pressure-100/62 mmHg, oxygen saturation 96% on room air). Other systemic examination was normal. His RT-PCR of nasal and pharyngeal swab was positive for COVID-19.

He was managed with IV fluids, ATT and HCQ. He made a complete recovery over next seven days with complete resolution of symptoms and was discharged on 11th day of admission.

DISCUSSION

Diarrhoea is not a common symptom of COVID-19 infection, and its frequency has been documented to range from 2-50%, with a pooled prevalence of around 12% [6]. SARS-CoV-2 uses host Angiotensin Converting Enzyme 2 (ACE2) receptor for entry. ACE 2 receptor is expressed in human intestine in proximal and distal enterocytes and can control inflammation and diarrhoea [7]. Xiao F et al., performed oesophageal, gastric, duodenal, and rectal biopsies in patient with COVID-19 induced Acute Respiratory Distress Syndrome (ARDS) having features of gastrointestinal bleeding. Authors did not find any mucosal damage during endoscopy, but histological examination revealed high percentage of ACE2 protein in the glandular cells of all examined segments, except for oesophagus [8]. Median symptom duration was four days in the present series, which was similar to a study in published literature [6].

Treatment described in literature is mainly supportive in absence of any approved specific treatment. Supportive treatment in form of rehydration is recommended. Various drugs that are being studied for a role in COVID-19 include chloroquine, HCQ, lopinavir-ritonavir, remdesivir and immunomodulators [7]. As per the institute policy, HCQ was used in patients who were at risk for severe disease (Diabetes, Malignancy, Age >65 years). HCQ was given after Electrocardiogram (ECG) was done and corrected QT interval (QTc) was normal.

In contrast, some studies have shown greater requirement of mechanical ventilation in patient with gastrointestinal symptoms, this series did not report any need for intensive care admission [6,7]. In fact, all patients had symptoms which were mild in severity. Infact, diarrhoea was also mild, most patients did not have signs of dehydration either, except for couple of cases requiring IV fluids. Thus, severity of diarrhoea might also be a factor in determining severity of disease, while its corollary might also hold true; that severe disease tend to have severe diarrhoea while diarrhoea per se might not be a risk factor for severe disease.

Importantly, five of the seven patients had fever (71.4%) and none had any respiratory symptoms, thereby stating the importance of testing in patients who present with diarrhoea at onset, especially from hotspot areas and have had high risk contacts. It highlights is the possibility of orofaecal transmission amongst household contacts, which can be seen from the patients having only gastrointestinal symptoms and no respiratory symptoms, these patients should also be subjected to testing of stool samples for viral Ribonucleic Acid (RNA) [9]. While vomiting and diarrhoea are included in the World Health Organisation (WHO) definition of suspect COVID-19, the Indian testing strategy places the onus on discretion of evaluating physician in case of non respiratory symptoms [10,11]. Thus, one should be aware of this non respiratory presentation of COVID-19, to avoid missing the diagnosis.

Another interesting feature highlighted from the patients is presence of anaemia in five of the seven patients (71.4%), which was higher than what is reported in other studies where anaemia has been found in up to 51% patients [12-15]. Lower haemoglobin has been associated with severe disease in few studies while its significance has been questioned in others [13-15]. Various mechanisms have been attributed to anaemia in COVID-19 patients like bone marrow dyserythropoiesis in which patients tend to have high Red-cell Distribution Width {(RDW) greater than 14.5%}, and secondary to interleukins causing

hepcidin like mechanism and increasing serum ferritin, while decreasing serum iron [16]. In couple of the reported patients, anaemia was present despite serum ferritin levels not being raised and normal RDW, which can be explained secondary to poor nutrition in a developing country. Interesting feature is that despite anaemia, all included patients had mild severity and did not have respiratory complaints. Possible explanation can be that patients had orofaecal transmission and because of anaemia which is not owing to systemic immune reaction, they had a milder and a localised gastrointestinal disease, as it has been postulated that iron deficiency may interfere with viral replication. One of the postulated mechanisms of HCQ is also by acting through iron haemostasis mechanism [17].

The present case series describes initial observation of diarrhoea as presenting complaint of COVID-19. Limitations include a small sample size, and lack of long term follow-up. Also, no microbiologic evaluation of stool samples could be done, due to scarcity of resources. Though this was a part of observational study and data was prospectively collected, it may not correctly estimate the proportion of this presentation in COVID-19 patients. Detailed anaemia work-up was not possible, except for serum ferritin and peripheral smears, in view of short stay and clinical improvement with treatment. Nevertheless, this case series highlights an important consideration for clinicians, in the current pandemic situation, to suspect COVID-19 in patients presenting with predominantly non respiratory symptoms.

CONCLUSION(S)

COVID-19 is a novel infection, and its clinical presentations, diagnostic markers and treatment are evolving. Although diarrhoea is documented in literature as a symptom of this infection, the emphasis on the same in real world scenario is lacking. It is essential that gastrointestinal symptoms of COVID-19 be studied in further detail and physicians should be sensitised to the presence of these symptoms as a presentation for COVID-19.

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