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Review article

Acute Abdomen in the ERA of COVID 19: Case Series and Literature Review

Jowhara Al-Qahtani [1], Haya Al-Kuwari [2], Mohammed Sameer [1], Mohammed Alobaidi [2], Syed Muhammad Ali [1], Rajvir Singh [3]

[1]Acute Care Surgery, Hamad Medical Corporation. Doha- Qatar.
[2]General Surgery, Hamad Medical Corporation. Doha- Qatar.
[3]Chief Medical Office, Hamad Medical Corporation. Doha- Qatar.

*Corresponding author: Syed Muhammad Ali, Department of Acute Care Surgery, Hamad Medical Corporation, Weill-Cornell Medicine Qatar, Doha, Qatar; *alismc2051@gmail.com*

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Abstract

The COVID-19 pandemic involved the globe and resulted in major mortalities mainly affecting the respiratory system. Initially thought to be respiratory disease it was later postulated and confirmed the involvement of gastro-intestinal tract (GIT) and its contribution to the complications and mortalities. Herein we present five cases of severe COVID-19 infection with GI involvement and their management with literature review.

Keywords: ***COVID-19, Acute abdomen***

Introduction

An outbreak of coronavirus 2019 (COVID-19) infection, caused by severe acute respiratory syndrome virus (SARS-CoV-2), has rapidly spread from China to almost all over the world. Unfortunately, the number of infected people is rising with increased mortality.

Patients can be asymptomatic or symptomatic with various degrees of severity. Gastro-intestinal (GI) involvement is documented in the literature, the incidence of which initially ranged from 3% to currently 20% with vague presentations like abdominal pain, nausea, and vomiting. Evidence is accumulating that GI symptoms are more; and SARS-CoV-2 can be detected in feces in about 50% of infected subjects [1]. It is reported that sometimes those GI symptoms may precede couple of days prior to the diagnosis of COVID-19 [2].

The prognosis of patients with COVID-19 with gastrointestinal symptoms is still largely unknown. Studies implied that these patients may have worse clinical outcome than those without digestive symptoms, emphasizing the importance of symptoms such as diarrhea to diagnose COVID-19 early [3]. Pan et al [4] also showed that as the severity of the disease increased, digestive symptoms became more pronounced. A multicenter and cross-sectional study demonstrated that approximately 50 % of patients experienced symptoms such as diarrhea, nausea, vomiting, and abdominal pain. Furthermore, the time from onset of gastrointestinal symptoms to hospital presentation is delayed compared to respiratory symptoms (9.0 vs. 7.3 days) [5].

Wang and colleagues found that patients admitted to the intensive care units (ICU) were more likely to have abdominal pain and loss of appetite compared with non- ICU patients [6]. Mao et al [3] did subgroup analyses to investigate the difference in gastrointestinal symptoms between patients with severe and non-severe COVID-19. They found a higher prevalence of abdominal pain in patients with severe COVID-19 than in those with non-severe group [3].

Here we present 5 patients who were diagnosed with COVID 19 and found to have surgical acute abdomen with perforated viscus. Literature review of reported cases in the world was done to investigate any correlation between COVID 19 and pneumoperitoneum and predict the outcome of such patients.

Patient cases

Case 1

38 Years old previously healthy male patient presented with respiratory symptoms, COVID-19 PCR was positive, the patient respiratory symptoms kept worsening and he required endotracheal intubation. 26 Days post ICU admission for COVID-19 pneumonia, the patient was found to have abdominal distension and sigmoid colon perforation diagnosed after CT Abdomen. He underwent exploratory laparotomy and Hartmann procedure. Patient showed full recovery and was discharged home.

Case 2

40 years old male known to have diabetes mellitus and hypertension was admitted to the medical intensive care unit as a case of COVID-19 pneumonia requiring intubation for ventilatory support. One week later, he was found to have abdominal distension and CT scan showed distension of the cecum and ascending colon (Pseudo-obstruction). The patient was treated conservatively, and the abdominal distension became significantly less. However few days later the patient succumbed due to respiratory complications.

Case 3

34 Years old previously healthy male patient presented to ED with respiratory symptoms due to COVID-19 pneumonia that required endotracheal intubation, 8 days later he was found to have

abdominal distension. Chest X- ray showed pneumoperitoneum and the patient was taken to the operating room for exploratory laparotomy which showed transverse colon perforation and was treated with primary repair. Few days later the patient was improving and was extubated and discharged home.

Case 4

53 years old previously healthy male patient admitted to the medical intensive care unit as a case of severe COVID-19 pneumonia requiring ventilatory support. Four days later, patient had increased abdominal distension and peak airway pressures. CT scan of the chest and abdomen showed multiple segmental pulmonary embolisms, pneumomediastinum and pneumo-retroperitoneum. The patient was managed non operatively. However, one month later, he expired due to COVID related complications and multi-organ failure.

Case 5

47 years old with severe COVID-19 pneumonia on mechanical ventilation developed increasing abdominal distension. Chest X-ray was significant for free air under the diaphragm whereas, CT scan of the abdomen with contrast showed pneumoperitoneum, pneumomediastinum as well as free fluid in all four quadrants of the abdomen. The patient was managed non operatively as the pneumoperitoneum was attributed to extension of pneumomediastinum possibly due to tracheo-bronchial tree injury. The patient remained hospitalized for two months and recovered completely from COVID pneumonia.

Method

Literature search was done using PubMed, Google Scholar, Cochrane, to look for articles that reported GI symptoms (acute abdominal pain) and COVID 19 in English language. Papers that reported positive COVID 19 and pneumoperitoneum or suspicion of perforated viscus were included.

Statistical methods

Descriptive statistics in the form of mean and standard deviations for interval variables such as age and frequency with percentages for categorical variables were reported. Student t tests were applied to see significant mean age difference according to gender and comorbidity. P value 0.05 (two tailed) was used statistically significant level. SPSS 26.0 statistical package was used for the analysis.

Results

We found 23 cases from 17 publications. All were COVID 19 positive and were of 54.1±19.3 years of age, 8 being females (34.8%) and 15(65.2%) male patients. 13 patients (56.5%) had at least one comorbidity. The mean age of the comorbid patients was more than those without any comorbidity (63.0±18.8 years vs female 42.0±15.3 years, p=0.008) whereas; there was no statistical difference between mean age according to gender (male 54.3±18.8 years) vs female (53.9±21.5 years, p=0.96).

CT abdomen was performed for 17 (73.9%) patients, X-ray for 16 (67.6%) and one patient had the US. Distention was the most common gastrointestinal symptom in 12 patients (52.1%), pain 8 (34.8%), incidental findings of pneumoperitoneum in 2(8.7%), and hemodynamic instability in 2 (8.7%). 18 patients (78.3%) had primary while 5 patients (21.7%) had secondary pneumoperitoneum. The most common perforated organ was colon 10 (43.4%), in the frequency of cecum 4(17.4%), and then right colon 2(8.7%), transverse colon 1(4.3%), left colon 1(4.3%), and sigmoid, rectum and not identified were 2 (8.7%) each. Small bowel perforation was less common and accounted for only 4(17.4%) patients, where duodenum, jejunum, and ileum were 1 (4.3%) each.

Conservative treatment was carried out in 9 patients (39.1%); however, surgery was performed in 14 patients (60.9%). Seven (30.4%) patients died, 12 (52.1%) were discharged, 3 (13%), with one patient was not described.

Patients' details are given below in Table 1 [7-22].

Table: 1

No	Study	Age Gender	Initial COVID status	Intub-ated	Initial GI symptom	Image finding	Perforated organ	Duration from COVID positive to GI Symptoms	COVID Treat-ment Y=1 N=0	Diagnosis	Conser-vative=0 Surgery=1	ASA	Surgery/Outcome
1	Al-Qahtani	38 Male	Positive	Yes	Abdominal distension	Pneumo-peritoneum and free fluid	Sigmoid	26 days	1	Sigmoid perforation	1	Life saving	Exploratory Laparotomy and Hartmann procedure/ **Discharge**
2	Al-Qahtani	33 Male	Positive	Yes	Abdominal distension	Pneumo-peritoneum	Transverse colon	8 days	1	Transverse Colon perforation	1	III E	Exploratory Laparotomy, primary repair/**Discharge**
3	Al-Qahtani	47 Male	Positive	Yes	None	Pneumo-peritoneum with pneumo-mediastinum	None	34 days	1	Pneumo-mediastinum	0	-	None
4	Al-Qahtani	53 Male	Positive	Yes	None	Pulmonary embolism, Surgical emphysema, pneumo-mediastinum with pneumo-retroperitoneum	None	15 days	1	Pneumo-mediastinum	0	-	None
5	Al-Qahtani	46 Male	Positive	Yes	Abdominal Distension	Extensive surgical emphysema, extensive pneumo-mediastinum extending intra-abdominal and pre-peritoneally	None	15 days	1	pneumo-mediastinum	0	-	None Spread of pneumomediastinum leading to presence of air preperitoneal, intra and retro peritoneal
6	Paramyth iotou [7] et al 2020	50 Female	Positive	Yes	None	Pneumo-peritoneum	Lung	45 days	1	Respiratory failure	0	-	presence of a large quantity of free air in the peritoneum attributed to spreading of air from the lung/ **Expired**

7	Gartland et al [8], 2020	47 Male DM	Positive	Yes	Abdominal Distension	Small bowel ischemia and perforation, patent mesenteric vessels	Ileum	14 days	1	Bowel necrosis and terminal ileal perforation	1	Life saving	Exploratory laparotomy, bowel Ischemia and perforation/ **Expired**
8	Kangas-Dick et al [9] 2020	74 Male	Positive	Yes	Abdominal distension	Pneumo-peritoneum and free fluid	Proximal GI tract perforation	5 days	1	Bowel perforation	1	-	No surgery/**Expired**
9	Giuffre et al [10], 2020	87 Female with polymyalgia rheumatica, giant cell arteritis	Positive	No	Abdominal distension and rectal bleeding	wall thickening of the lower third of the rectum with free perivisceral air	Perforated rectum	Same day	1	Perforated rectum	0	-	No surgery/**Expired**
10	De Nardi et al [11], 2020	53 Male, Hypertension, paroxysmal supraventricular tachycardia	Positive	No	Abdominal pain and distension, Diarrhea	Massive pneumo-peritoneum	Ascending colon	13 days	1	Cecal distension and perforation	1	Life-saving	Exploratory Laparotomy, right Hemicolectomy/ Discharged
11	Neto et al [12], 2020	80 Female, Hypertension	Positive	Yes	Diffuse abdominal pain and stiffness	Pneumo-peritoneum, free fluid in abdomen	Sigmoid	Same day	1	reduced visceral perfusion in the entire gastrointestinal tract and four punctate lesions in the sigmoid colon, with fecal content into the cavity	1	Life-saving	Exploration Laparotomy, recto-sigmoidectomy terminal Colostomy/ **Expired**
12	Parhar et al [13], 2020	36 Female Hypertension	Positive	Yes	Fever and elevated White cell count	Free air under diaphragm	Cecum and ascending colon perforation	Few days	1	Cecum and ascending colon perforation	1	Life saving	Exploration Laparotomy Right hemicolectomy and loop ileostomy were performed
13	Rojo et al [14], 2020	54 Female DM, HTN	Positive	Yes	Hemodynamic instability	Active bleeding from cecum and free air	Cecal perforation	15 days	1	Cecal ulceration with perforation	1	Life Saving	Right hemicolectomy/ **Expired**
14	Winnicka and Shenoy M [15], 2020	73 Male CAD, PVD, DM, Obesity	Positive	Yes	no GI symptoms, incidental findings of air under diaphragm	Free air under diaphragm	Unknown	16 days	1	-	0	-	No surgical procedure/ **Discharge**
15	Guo et al [16], 2020	40 Female	Un-known then positive	Yes	Nausea, vomiting, epigastric pain	Pneumo-peritoneum	Posterior duodenal wall perforation	Not mentioned	1	Duodenal perforation	1	-	Laparotomy, closure of perforation, **Discharged**
16	Lotti et al [17], 2020	72 Male, HTN, Diverticulosis	Positive	No	Abdominal pain	Pneumo-peritoneum	Jejunal diverticulum perforation	Same day presentation	1	Jejunal diverticulum perforation	1	-	Laparotomy Jejunal resection/ **Discharge**
17	Sharma et al [18], 2020	47 Male, DM, HTN	Positive	Yes	no GI symptoms, incidental findings of free air	Pneumo-peritoneum, Pneumo-mediastinum and subcutaneous emphysema	None	10 days	1	-	0	-	No surgical intervention/ **Discharge**
18	Bhattacharjee et al [19], 2020	45, Male HTN	Un-known than positive	No	Abdominal pain and distension	Free air under diaphragm	Unknown	initial presentation with GI symptom, diagnosed with covid on routine swab	1	Sealed hollow viscus perforation	0	-	No surgical intervention/ **Discharge**
19	Verma et al [20], 2020	60 Female Hypo-thyroidism	Positive	No	Abdominal pain and distension, generalised peritonitis	Free air under diaphragm	Upper third of rectum	11 days	1	Rectal perforation	1		laparotomy and transverse colostomy/ **Discharge**
20	Verma et al [20], 2020	24 Female Post C-section	Un-known than positive	No	abdominal pain, vomiting and distention of abdomen	Massive pneumo-peritoneum	Anterior wall of cecum	Same day	1	Cecal perforation	1	-	Laparotomy, primary closure with loop ileostomy/ **Discharge**
21	Verma et al [20], 2020	21 Male	Positive	No	vomiting and distention of abdomen	Pneumo-peritoneum	Anterior wall of stomach	Same day	1	Gastric perforation	1	-	laparotomy, Graham's patch closure of perforation/ **Discharge**

22	Nahas et al [21] 2020	92 Male HTN, CKD, Colonic malignancy	Positive	No	Diffuse abdominal pain	Pneumo-peritoneum with no collection and distended bowel loops	Descending colon	Same day	1	Descending colon perforation 5 cms from previous colostomy site	1	-	Laparotomy, resection and terminal-colostomy/ **Expired**
23	Persiano et al [22], 2020	73 Male IHD, CKD, NIDDM HTN	Un-known than Positive	No	fever and Diarrhea, abdominal distention and tenderness	Pneumo-peritoneum with no collection and distended bowel loops	Ascending colon	11 days	1	Ascending colon perforation	1	-	Laparotomy and right Hemicolectomy/ **Discharged**

Discussion

Almost 20% of COVID-19 patients have abdominal symptoms ranging from mild generalized pain, nausea, vomiting, to significant and acute surgical abdomen. The proportion of acute abdominal pathologies has increased from 32.7% to 50.5%, and demonstrated an increase in the severity of these pathologies 7.9% to 19.7%, and an associated trend for increased need for surgical intervention 26.3% to 47.6% in one study [23].

The most common perforated organ was the colon as one would assume small bowel would be the most common organ. 60% of patient had surgical intervention with high mortality reaching to 30%. This could be explained partially to the fact that some had late diagnosis, or they were in septic shock and poor outcomes to start with. However, 52% of patient who underwent surgery had good outcome and sent home after prolonged hospital course [3].

Theory

There are many hypotheses why COVID-19 appears to cause digestive symptoms, but, the exact molecular mechanism needs to be further investigated. A study conducted by Xiao et al [24], demonstrated results favoring gastrointestinal viral replication with potential fecal-oral route of transmission. Upon endoscopy and biopsy, the study also found that SARS-CoV-2 RNA was detected with positive staining of the viral nucleocapsid protein in gastric, duodenal, and rectal epithelium. These findings further support the evidence of replication of infectious virions occurring within the gastrointestinal tract [24].

It is postulated the role of angiotensin converting enzyme 2 (ACE-2) receptor in the pathogenesis of abdominal pain [25]. The virus binds to the ACE-2 receptor, which can be found in the lungs and various GI system including intestine, by which the virus gains cellular entry and create the potential for viral replication5. Zhang et al found that successful virus entry of SARS-CoV-2 depends not only on the presence of ACE-2 cell receptor; but also, the cellular serine protease, transmembrane protease serine 2 (TMPRSS2), which cleaves the S protein of human coronaviruses on the cell membrane) [26]. Both of these protein molecules are critical for fusion of viral and the cellular membranes [26]. ACE-2 and TMPRSS2 are co-expressed in lung alveolar type 2 cells and esophageal upper epithelial type II cells. It is also highly expressed in the ileum and colon which suggests that the virus can invade enterocytes of the digestive tract [1], and cause primary damage to GI tract. Davidson et al found that the binding affinity of ACE-2 to the outer domain of SARS-CoV-2 is ~10–20 times higher than that of SARS-CoV [27]. It is postulated that binding of SARS-CoV-2 with ACE-2 receptors in the gastrointestinal tract reduces the level of available receptors, which affects the absorption of tryptophan, and ultimately destroys the steady state of the intestinal flora [28,29].

There could be a direct injury of the gastrointestinal system due to a chain of inflammatory response. Villapol showed that any changes in intestinal dysfunction would induce changes in intestinal microbes, hence, an increase in inflammatory cytokines [29]. Once within a cell, the virus activates the intracellular immune system, which causes immune and non-immune cells to release large amounts of pro-inflammatory cytokines that activate a cytokine storm and result in damage to the host [30]. Huang et al found that the plasma cytokine and chemokine levels of COVID-19 patients were higher than those of healthy people [31]. The plasma level of certain cytokines such as IL-2, IL-7, IL-10, granulocyte colony stimulating factor (GSCF), and recombinant human interferon-induced protein-10 (IP-10), MCP-1, macrophage inflammatory protein-1A (MIP-1A), and TNF were high in levels of patients with severe disease than the level of cytokines of patients without severe disease [31].

Bhayana et al [32] suggested a role of ACE2 receptor and the possibility of direct vascular invasion by the virus or occlusion resulting from the microthrombus formation and causing mesenteric vessel ischemia (occlusive or non-occlusive), renal vessels infarcts, appendagitis, and omental infarcts [33]. Other Non-thrombotic events cause peritonitis, colonic distension, and colitis, and pancreatitis which have been reported in association with COVID-19 [5].

In general, presence of co-morbidities is associated with poor outcomes in patients with COVID-19. This may have implications for the management of patients with pre-existing digestive diseases [3]. Autopsy studies are important to help investigate histopathological changes in the gastrointestinal tract in patients with COVID-19. Only one autopsy report with details of gastrointestinal pathology has been published in an 85-year-old man with COVID-19, which showed segmental dilatation and stenosis in the small intestine [34]. Further studies are needed to clarify whether this finding is secondary to COVID-19 or a pre-existing gastrointestinal comorbidity [3].

Conclusion

There is evidence of COVID-19 involving the gastrointestinal tract and increases the morbidity and mortality if intestinal perforation ensues. A high grade of suspicion should be kept in mind as the sick patients are already ventilated and the GI pathology further aggravates the precarious condition. Although surgical intervention carries high mortality but provides the only chance of cure if carried out judiciously.

Data Availability

The data is available with corresponding author and all the references have been mentioned in the “Reference Section.”

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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Supplementary Materials

No supplementary material used.

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