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Mechanism and risk factors of ischemic bowel in COVID 19 patients

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Abstract
Introduction: SARS-CoV-2 is an abbreviation for severe acute respiratory syndrome-coronavirus-2 that started after the emergence of coronavirus disease-2019 (COVID-19). This condition is presented initially with a severe form of pneumonia, but many patients show extra-pulmonary complications, one of them being the development of ischemic bowel secondary to hypercoagulation status.
Aim: This review aimed to find the common risk factors observed in COVID 19 patients who develop bowel ischemia and mechanism related to this disease.

Keywords: the major keywords are COVID 19, bowel ischemia, SARS-CoV-2, gastrointestinal complications (GI), and risk factor

Introduction

SARS-CoV-2 is an acronym for severe acute respiratory syndrome-coronavirus-2, which started after the arrival of coronavirus disease-2019 (COVID-19) that was initially reported in Wuhan China. Based on genome analysis, COVID 19 belongs to the Betacorona virus genus. Also, it is included in SARS (severe acute respiratory syndrome) and MERS (Middle East respiratory syndrome), and Gastrointestinal Complications (GI) present in one-third of admitted patients [1] However, it is regularly presented by infectious pneumonia. Above all, the major signs depicted among such patients are fever, cough, and shortness of breath, while some develop gastrointestinal (GI) and hepatic symptoms. Further, the most common GI symptoms presented are fever, vomiting, abdominal pain and abdominal distention, and hematochezia [2]. Most importantly, liver function abnormalities are regular and entail elevation of AST, ALT, and total bilirubin. Most studies have reported that the incidence rate of gastrointestinal symptoms in COVID 19 patients ranges from 2%-79.1% [3]. Concurrently, COVID-19 RNA has been found in stool specimens of COVID-19 patients, suggesting the addition of fecal-oral transmission to droplet transmission

Materials and method

Search strategies

A search on PUBMED and EMBASE of all the published readily accessible, peer-reviewed, full articles written in English was conducted (between March 2020 to June 2021) about thromboembolic complications seen in COVID -19 before writing this review. Most of the articles included retrospective, observational, single or multicenter studies, case reports, and correspondences. Consequently, acute mesenteric ischemia called sudden blood flow disruption within the mesenteric circulation, and estimated rate of mortality in the literature up to 80 % [4], which can be presented in thrombosis/emboli 60-70%, non-occlusive up to 30% or venous occlusion 5-10%, an embolism can affect the SMA more due to small take-off angle [5]. Therefore, Covid 19 is predisposing for thrombo-embolic complications for both arterial and venous. Essentially, the incidence of thrombosis in COVID 19 patients with systemic thromboprophylaxis in the literature is 31%, where 4% is for atrial thrombotic events, which tend to have severe complications [5, 6]. The findings indicated that mortality related to Atrial Thrombosis in one cohort study is 20 % [7]. From this number, the patients with chronic COVID 19 complicated AMI may show severe abdominal pain, abdominal distention, vomiting, diarrhea, and sepsis [7]. From this search, the researcher discovered that many case reports were published about the venous and atrial thrombosis in Covid 19 patients, which led to bowel ischemia, limb ischemia and stroke, splenic infarction linked to severe Covid 19 cases [6, 8, 9].

Furthermore, from the obtained studies, the majority of the patients with arterial thrombotic events were male, which is considered a risk factor. The reported age of these patients ranged from 29 to 86 years. The majority of the AT patients had pre-existing conditions, such as hypertension, cardiovascular disease, atrial fibrillation, chronic kidney disease, chronic obstructive lung disease, obesity, hyperlipidemia, diabetes mellitus, asthma, leukemia, and renal tubular acidosis. Only five studies reported AT in patients with no comorbid conditions [8] Nevertheless, the exact mechanism of development of AMI in Covid-19 patients is unknown. Some theories have been developed to explain this concept. For instance, hypercoagulability stated that COVID 19 patients develop these complications due to the level of von Willebrand factor. Concurrently, the model highlight that there is the expression of ACE-2 receptor on the enterocyte of the small bowel that tends to be targeted by COVID 19 virus (protein S), leading to direct bowel damage and inflammation [5, 9, 10] and pneumatosis intestinalis [11]. The final mechanism explained was the presence of shock and hemodynamic compromise, which is commonly associated with severe COVID 19 pneumonia [12, 13]. In the literature, the outcomes indicated that the high level of D

dimer and fibrinogen is associated with a thromboembolic event [14, 6, 4]. Also, the CT finding is sensitive to 95% finding of intestinal pneumatosis, portal venous gas, lack of wall enhancement, presence of organ ischemia raise the suspicions of AMI [4]. One case about bowel ischemia in negative nasopharyngeal swab for COVID 19 was found in resected small bowel back as positive for two spikes of mRNA protein of the virus [15]. There is the importance of recognizing that since the COVID-19 pandemic, clinicians and researchers try to find any new information about the disease or the virus. Based on the obtained studies, this pandemic affects the respiratory system and other systems such as the gastrointestinal tract [4]. One of the various ways COVID-19 affects other parts of the body, apart from the respiratory, is its hypercoagulable state [5]. In this review article, the investigator tried to collect the most prominent risk factors leading to a hypercoagulable state and mesenteric ischemia reported and listed accordingly.

ICU

COVID-19 can be extremely aggressive to patients, and some of them must be admitted into an ICU. While admitting the victims of this illness into an ICU could improve their state of respiratory and cardiovascular complications, this situation could increase the chances of hypercoagulability and maybe cause mesenteric ischemia. Therefore, ICU admission and immobilization are considered a risk for developing thrombotic events in COVID 19 patients [10, 16]. This situation implies that severe critical COVID19 patients and hypercoagulation have strong relation [17].

Diabetes Mellitus (DM)

For the past decades, DM has been a factor for thrombosis [6]. Similarly, COVID-19 patients with diabetes have a greater chance of developing thrombosis and may cause mesenteric ischemia. In that connection, the studies have revealed a recurring event of mesenteric ischemia in COVID-19 patients who have diabetes. Although this situation is not common as ICU admission, it may be the second most common risk factor.

Hypertension

A study was conducted in New York using 49 patients, having COVID 19 with arterial thromboembolism complications. In this research, a total of 12,639 patients with coronavirus were used. The findings portrayed that hypertensive patients have the highest effect of developing Ischemic bowel complications by 53% [5].

Gender

Based on COVID-19 studies, males have a more severe presentation and a comparably worse outcome than females [7]. Further, one study focusing more on the bowel ischemia presentation of COVID-19 found that males have more bowel ischemia presentation of COVID-19 prevalence than females. Simultaneously, this review found that males have a worse outcome than their counterparts. Generally, males are more affected by the arterial thromboembolic event [6].

Age

Pedram Keshavarz's review exposed that the mean age affected ranged between 28-80 years, and the majority were male [18] However, in this study, the median age was 67 years, and 76 % were male [5]. Besides, 62 years was the median age [6].

Old age is one seen consistently. In this regard, as age increases, the likelihood of having a clot rises, and the mortality worsens. Also, obesity and hypertension are seen in these patients, as they already contribute to the increase of clotting than the general population [14].

Time

The reported case mentioned that the time after admission to ICU is 18 days, where the patients start developing abdominal pain and tenderness, indicating the presence of bowel ischemia. This condition was detected after carrying out CT and intraoperatively, where the patient depicted gangrenous ascending colon and markedly distended colon from the cecum to rectosigmoid junction. Despite giving her admission heparin prophylaxis and ileostomy [19], the time to develop the artiralthrombembolic event, in general, was 11 days (7-13) days [6]. Based on the Northwell Covid survival calculator, the median predicted mortality at the time of vascular evaluation was 37%. The bowel ischemia diagnosis time of 27 % implied that such patients were severely ill and intubated in ICU before the onset of ischemia, but the noted high D- Dimer was more than 1000 ng/ml. Twenty-two patients (45%) presented with bowel ischemia and were diagnosis with COVID 19. Consequently, patients at 55 % developed ischemia during the hospital admission after an average of 4.5-6 days [5].

Associated thrombosis

Hypercoagulability state was observed in patients of COVID 19; thus, it is considered the predictor for poor prognosis [5]. A study done by Abdomehsen MA shows that many patients presented with mestric ischemia are associated with pulmonary embolism and splenic infarction [2]. The presence of other patients showed inflammation in the rectosigmoid area [2]. Also, the data of patients who died from COVID 19 complications showed a high level of D-Dimer (more than 5000 ng/dl) and a high level of Fiberin degradation product levels with longer Prothrombin time [5].

Conclusion

COVID0-19 pandemic has been a fast-expanding subject and an interest for most clinicians and researchers. It was mostly focused on the respiratory symptoms, but it was found that COVID-19 can cause a hyper-coagulable state and may bring clots in different parts of the body. This review found that one of the sites that could get clotted in the bowel manifesting most commonly in the superior mesenteric artery. Therefore, when COVID-19 patients have abdominal symptoms, even minor symptoms, they should be investigated for bowel ischemia, especially if they have one of the risk factors; ICU admission or Diabetes mellitus. This early investigation could prevent complications and decrease the mortality rate, reaching up to 22-50% [5].

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