

MESENTERIC ISCHEMIA AND COVID-19: A SYSTEMATIC REVIEW

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Abstract: Much has been discussed about the relationship between Covid-19 infection and mesenteric ischemia. The present study aims to conduct a systematic review of the literature on the subject. This is a systematic review of the literature where data collection was performed in the PubMed (NCBI), Virtual Health Library (VHL) and Google Scholar databases, during October/2021. During the research conducted in these databases, 23 articles were selected that met the eligibility prerequisites of which 16 of them had full text available online and were included in this study. It is evident that acute mesenteric ischemia in the context of patients with Covid-19, even though it is a rare condition, has high morbidity and mortality. The exact pathophysiology of the condition and the factors that lead to the emergence of extrapulmonary and ischemic manifestations is still poorly understood, requiring further studies and discussions on the subject in order to foster knowledge, and mesenteric ischemia should be suspected in patients with Covid-19 when they present sudden abdominal pain disproportionate to abdominal signs.

Keywords: Mesenteric ischemia, Covid-19, Pandemic.

INTRODUCTION

The pandemic caused by the SARS-CoV-2 of the coronavirus family has persisted in Brazil since March 2020, and the virus that was originated in China with first report in 2019 (BULUT *et al.* 2021). Currently, more than 21 million cases of COVID-19 have been confirmed throughout Brazil, leading to about 600,000 deaths by October 2021 (BRASIL, 2021).

Patients critically affected by Covid-19 often develop gastrointestinal complications during the course of the disease, including intestinal ischemia (EL MOHEB *et al.* 2020). Mesenteric ischemia is characterized as a syndrome of acute abdomen that

leads to hypoxemia and malnutrition of gastrointestinal organs due to sudden arterial obstruction being a rare surgical emergency and presenting as a clinical picture typically of sudden abdominal discomfort and strong intensity associated with nausea, vomiting and diarrhea (SANTOS, 2021).

Much has been discussed about the relationship between Covid-19 infection and mesenteric ischemia. The present study aims to conduct a systematic review of the literature on the subject.

METHODOLOGY

Data were collected in the PubMed (NCBI), Virtual Health Library (VHL) and Google Scholar databases in October/2021, through the combination of Boolean descriptors in English, Portuguese and Spanish:

#1 "Covid-19" OR "SARS-CoV-2" (Medical Subject Headers - (MeSH)) AND

#2 "Mesenteric Ischemia" (MeSH) AND

We selected: (1) articles that had at least one combination of two of the terms described in the search strategy and (2) articles with the full text available online. Additionally, textbooks, protocols from internationally recognized institutions such as the World Health Organization (WHO) were also consulted.

RESULTS AND DISCUSSION

During the research carried out in the databases, 23 articles were selected that met the eligibility prerequisites of which 16 of them had full text available online. Thus, 16 articles were included in this study and evaluated in an integral way. Of the selected articles, 1 is the type of quantitative study (ELMOHEB *et al.* 2020), 4 were systematic reviews (AVILA *et al.* 2021; PIROLA *et al.* 2021; KERAWALA, 2021; FAN, 2020) and 11 were case reports (DINOTO *et al.* 2021; HANIF *et al.* 2021; ALEMÁN, 2021; AMARAVATHI *et al.* 2021; AL MAHRUQI *et al.* 2021 NASSEH *et al.*

2021; HASSAN, 2021; BIANCO *et al.* 2020; FAN *et al.* 2020; NORSA *et al.* 2020; KARNA *et al.* 2020).

Acute mesenteric ischemia in the context of patients with Covid-19 is a rare condition with significant morbidity and mortality (AVILA *et al.* 2021; FAN *et al.* 2020). It is an extrapulmonary involvement (HANIF *et al.* 2021) of the disease that has been gaining progressive relevance and being described in a significant proportion of infected patients (PIROLA *et al.* 2021).

It is defined as a sudden interruption in the supply of blood within the mesenteric circulation (AL MAHRUQI *et al.* 2021) being characterized as a rare life-threatening abdominal emergency (KERAWALA, 2021).

Clinical symptoms may involve abdominal pain, vomiting and diarrhea (AVILA *et al.* 2021). This form showed itself in several of the case studies analyzed and was often the only manifestation of virus infection reported by the patient.

The exact pathophysiology of the condition and the factors that lead to the emergence of extrapulmonary and ischemic manifestations is still little understood (AMARAVATHI *et al.* 2021). It is known that angiotensin-converter enzyme 2 (ECA2) receptors are the gateway to the virus in cells (PIROLA *et al.* 2021; EL MOHEB *et al.* 2020).

The high expression of these receptors along the epithelial lining of the intestine may explain the involvement of diseases in abdominal organs (PIROLA *et al.* 2021; KERAWALA, 2021; MOHEB *et al.* 2020). These receptors are also present on the endothelial surface, which can result in a direct viral toxicity with endothelial dysfunction through inflation and thrombosis (AL MAHRUQI *et al.* 2021; KERAWALA, 2021; HANIF *et al.* 2021; FAN, 2020). Endothelial damage can induce massive release of Von Willebrand factor, further increasing the risk

of thrombosis (PIROLA *et al.* 2021).

It has been widely reported that SARS-CoV-2 infection is associated with an increased risk of various thromboembolic complications (PIROLA *et al.* 2021). Although the exact mechanism of thromboembolism associated with Covid-19 is unclear, the Virchow triad is by far the most common explainable mechanism of thromboembolism in these patients (HANIF *et al.* 2021).

Four common main causes of mesenteric arterial ischemia include acute mesenteric artery thrombosis, acute mesenteric artery embolism, acute mesenteric vein thrombosis, and non-occlusive mesenteric ischemia secondary to vasoconstriction (PIROLA *et al.* 2021; FAN, 2020). Possible hemodynamic instability in severe Covid-19 infection leads to hypotension and shock that may be a possible mechanism of non-occlusive mesenteric ischemia observed in these patients (KERAWALA, 2021).

Laboratory tests may demonstrate a very high D-dimer and C-reactive protein (CRP) (AVILA *et al.* 2021; AL MAHRUQI *et al.* 2021). Although nonspecific, the presence of elevated D-dimer along with elevated serum lactate and acute abdominal symptoms should raise a high rate of suspected mesenteric ischemia (ANA, 2020).

Computed tomography angiography is the modality of choice for the diagnosis of mesenteric ischemia and presents sensitivity and specificity of 89.4% and 99.5%, respectively (KERAWALA, 2021; AMARAVATHI *et al.* 2021).

Recently, the role of contrast ultrasound has been described to detect abdominal microcirculation disorders in severe cases of COVID-19 (PIROLA *et al.* 2021). Findings of thickening of the bowel wall on ultrasound, intestinal pneumatosis on radiological examination and direct damage to the mucosa to histological analysis may be present in these

patients (PIROLA *et al.* 2021).

Treatment usually includes systemic anticoagulation and evaluation by the surgical team due to the need for invasive approach (AVILA *et al.* 2021) and the majority of patients underwent laparotomy and intestinal resection (KERAWALA, 2021).

El Moheb (2020) in a study that analyzed 486 patients with acute respiratory distress syndrome of whom 244 were negative for Covid-19 and 242 were positive for the disease showed that patients with Covid-19 were more likely to develop gastrointestinal complications compared to those without the disease and among the diseases of the gastrointestinal tract enunciated 4% of them presented with intestinal ischemia. The pathological findings of patients with Covid-19 and mesenteric ischemia submitted to surgery demonstrated fibrin thrombi in the underlying areas of microvasculature necrosis (EL MOHEB *et al.* 2020).

The studies of Dinoto *et al.* 2021, Hanif *et al.* 2021, Alemán, 2021, Amaravathi *et al.* 2021, Al Mahruqi *et al.* 2021, Nasseh *et al.* 2021, Hassan, 2021, Bianco *et al.* 2020, Fan *et al.* 2020, Norsa *et al.* 2020, Karna *et al.* 2020 reported cases of patients with Covid-19 who developed mesenteric ischemia. Of those, the vast majority of patients were 45 years of age or older (NORSA *et al.* 2020; DINOTO *et al.* 2021; BIANCO *et al.* 2020; AMARAVATHI *et al.* 2021; NASSEH *et al.* 2021; AL MAHRUQI *et al.* 2021; KARNA *et al.* 2021).

Among the main comorbidities reported hypertension and diabetes were in most patients (NORSA *et al.* 2020; DINOTO *et al.* 2021; BIANCO *et al.* 2020) cannot be considered, however, as a risk factor given the high prevalence of these diseases mainly in older patients.

Complaints of abdominal pain, nausea, vomiting and fever were present in most of the cases described (NORSA *et al.* 2020; DINOTO

et al. 2021; BIANCO *et al.* 2020; FAN, 2020; HANIF *et al.* 2021; AMARAVATHI *et al.* 2021; NASSEH *et al.* 2021; ALEMÁN, 2021; KARNA *et al.* 2021), some of these patients presented gastrointestinal symptoms as the only manifestation of Covid-19 (NORSA *et al.* 2020; FAN, 2020; AMARAVATHI *et al.* 2021; NASSEH *et al.* 2021).

Computed tomography or ct angiography were performed in almost all cases described, showing findings suggestive of mesenteric ischemia (NORSA *et al.* 2020; DINOTO *et al.* 2021; BIANCO *et al.* 2020; FAN, 2020; HANIF *et al.* 2021; AMARAVATHI *et al.* 2021; NASSEH *et al.* 2021; AL MAHRUQI *et al.* 2021; ALEMÁN, 2021; KARNA *et al.* 2021). The presence of leukocytosis, increased CRP and D-dimer values were present in most studies (NORSA *et al.* 2020; DINOTO *et al.* 2021; BIANCO *et al.* 2020; FAN, 2020; NASSEH *et al.* 2021; AL MAHRUQI *et al.* 2021; ALEMÁN, 2021).

Among the therapies used the prescription of heparin as a drug treatment was performed in most patients (DINOTO *et al.* 2021; FAN, 2020; AMARAVATHI *et al.* 2021; NASSEH *et al.* 2021; ALEMÁN, 2021; KARNA *et al.* 2021) and laparotomy resulted in resection of the affected structures. Among the reported cases, many of the patients succumbed to the disease and died due to complications (NORSA *et al.* 2020; DINOTO *et al.* 2021; BIANCO *et al.* 2020; AL MAHRUQI *et al.* 2021; KARNA *et al.* 2021) reflecting the severity of the

evolution of the disease and its high morbidity and mortality.

Norsa (2020) reported the case of a 62-year-old male patient who presented three days before hospitalization with a bilious abdominal pain and vomiting, with computed tomography (CT) of the abdomen suggestive of mesenteric ischemia and a negative Covid-19 test. Histological examination of the dried small intestine showed complete ischemic necrosis of the mucosal layer and acute perivisceral inflammation and the presence of the virus was only documented with the performance of the ISH RNA assay (in situ hybridization), which reveals that even in the presence of a negative Covid-19 test, mesenteric ischemia as a complication of SARS-CoV-2 infection cannot be ruled out.

FINAL CONSIDERATIONS

Knowing all that, it is evident that acute mesenteric ischemia is present in the context of patients with Covid-19, even though it is a rare condition with high morbidity and mortality. The exact pathophysiology of the condition and the factors that lead to the emergence of extrapulmonary and ischemic manifestations is still poorly understood, requiring further studies and discussions on the subject in order to foster knowledge, and mesenteric ischemia should be suspected in patients with Covid-19 when they present sudden abdominal pain disproportionate to abdominal signs.

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