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Research Article

COVID-19 and IBD: Medical Unit Experience

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Abstract

Aim and Introduction: In the era of the COVID-19 pandemic, it is legitimate to ask whether there is a higher risk of developing a COVID-19 infection or a more severe infection in patients with inflammatory bowel disease compared to the general population. On the other hand, it is advisable to study the impact of the different treatments on the risk of developing a severe form of COVID-19, as well as the factors of bad evolution of the infection.

Materials and Methods: A prospective descriptive study was conducted during the period from March 2020 to January 2021 on 13 IBD patients with COVID-19 infection.

Results and Conclusion: At the end of our study, SARS-Cov-2 infection does not seem to have an impact on the evolution of IBD, and conversely the presence of an underlying IBD does not seem to increase the risk of Covid-19 infection. However, some therapies could be a risk factor for severe SARS-Cov-2, especially if they are associated with other risk factors.

Keywords: *Inflammatory Bowel Diseases (IBD); Crohn's Disease (CD); Ulcerative Colitis (UC); SARS-Cov-2; Covid-19*

Introduction

Chronic Inflammatory Bowel Diseases (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), are pathologies whose pathogenesis would involve a deregulation of the intestinal immune system, thus in the era of the COVID pandemic, the question of the risk of developing a COVID-19 infection, or a more severe infection in these patients may be raised.

Aim of the Study

Our study aimed to report the impact of COVID-19 infection on patients with IBD.

Methods

Study design

This was an observational analytic prospective study from March 2020 to January 2021 enrolling all patients with IBD and had developed a COVID-19 infection within a Hepato-gastroenterology department.

Outcomes

The primary outcomes of this study were the impact of COVID-19 infection on the evolution of IBD, the severity of the infection on these patients, and the impact of the different treatments on the risk of developing a severe form of COVID-19. The secondary outcomes were the epidemiological profile of IBD patients with COVID-19 infection during the pandemic.

Data collection and ethical considerations

The patient data were anonymously collected from a uniform structured reporting used in our department for patients with IBD and the study protocol was conducted following the Helsinki declaration.

Statistical analysis

Variables reported as mean ± standard deviation for parametric data and as frequencies (Percentage) for categorical variables. Statistical analyses were performed using SPSS v23 (IBM Corp, NY, USA).

Results

Among the 1,494 cases followed for IBD, we reported 13 confirmed cases that were infected with Covid-19. Our series was included 8 women and 5 men with a mean age of 32.9 years.

All patients were of urban origin, 7.6% of them were smokers, 23% had an antecedent (one had adrenal insufficiency on hydrocortisone, one had sterility, and one had portal hypertension on Porto-sinusoidal vascular disease), and 61.5% had already underwent surgery for their IBD. It was a CD in 12 cases and a UC in 1 case. The CD localization was colic in 25% of cases and ileocolic in 75%. The phenotype was luminal in half of the cases (n = 6), stenosing in 33.3% of cases, and fistulizing in 16.7% of cases. It was associated with ano-perineal manifestations in 33.3% of cases.

The patients were already on Anti-TNF in 46.2% of cases (38.5% on Infliximab and 7.7% on Adalimumab), 7.7% on Anti-Interleukin (Ustekinumab), 15.4% were on oral corticosteroids, 23% on 5-ASA, 7.7% were in therapeutic abstention and none of our cases were under on Azathioprine. The symptomatology of patients with COVID-19 was summarized in table 1.

Symptomatology	Percentage (%)
Anosmia	53,8%
Ageusia	23%
Dry cough	23%
Chills-fever	38.5%
Aches and pains	30.7%
Asthenia	38.5%
Diarrhea	7.7%
Vomiting	7.7%
Shortness of breath	15.4%

Chest CT-scan was performed in 38.4% of cases which was normal in all patients. The CRP level was high in all our patients with a mean of 30.5. D-dimer and fibrinogen were performed in 15.3% of our patients and were elevated in 50 and 100% of cases respectively. No lymphopenia was noted in our patients.

The treatment administered was based on zinc and vitamin C combined with Azithromycin alone in 46.2% of cases, combination of with Chloroquine -Azithromycin in 46.2% of cases. Low-molecular-weight heparin was administered in 30.8% of cases, aspirin in 15.4% of cases, and corticosteroid therapy in 15.4% of cases. None of them had developed a severe form of COVID-19.

A therapeutic window in 50% of patients was made among patients who were on Anti-TNFa and Ustekinumab. The median treatment delay in these patients was of 0 days (0;8). However, despite the delay in treatment in these patients, there was no impact of COVID-19 on the progression of IBD and none of them had developed a relapse.

The activity of the disease according to the CDAI score was moderate to severe activity in 33.4% of patients, and the COVID-19 had no impact on their underlying disease.

Discussion

On March 11, 2020, the WHO declared a global pandemic due to the COVID-19 virus that originated in an outbreak in Wuhan, China. The severity of this virus is variable, which is why special attention has been paid to the most vulnerable people, namely the elderly and those with pre-existing medical conditions or those undergoing treatments that compromise the immune system.

IBD is considered to be a disease of immune dysfunction, and the vast majority of drugs effective against IBD for moderate to severe disease are immunosuppressive [1-3].

IBD itself is not considered to increase the risk of non-gastrointestinal infectious diseases [4]. However, SARS CoV-2 acts by invading cells through interactions with the ACE2 receptor (Angiotensin-Converting Enzyme 2), which is found in particular on enterocytes, which is why some studies suggest that patients with IBD may be at increased risk of COVID-19 [5,6]. Nevertheless, IBD carriers may have a higher soluble form of ACE2, which would limit the binding of SARS CoV-2 to cell surfaces [7].

In the most COVID-19 affected countries, till April 2020, namely Wuhan and Bergamo, no cases of COVID-19 had been identified in the respective cohorts of IBD patients [8,9]. Similarly, in a center in Lombardy, Italy, which at that time had the world's highest rates of COVID-19 cases [9], of the 522 IBD patients, no case of COVID-19 had been reported [10]. A recent study in Spain compared the results of the 40 COVID-19 cases in the IBD cohort with the rates observed in the general population in Madrid found a significantly lower risk of COVID-19 for IBD than in the general population [11]. In our series, 0.9% of IBD carriers presented an infection with COVID-19, while the rate of COVID-19 infection in the Moroccan general population was 1.3% [12,13], with no difference statistically significant (p-value = 0,11).

The same Spanish comparative study evaluated the mortality risk of COVID-19 in IBD patients matched to the general population and concluded that was no significant difference in the case fatality rate of COVID-19 in IBD patients [11].

A study by Mao., *et al*. the IBD Elite Union, and a consortium of the seven largest Chinese reference centers that treat more than 20,000 IBD patients noted that there is no impact of COVID-19 on IBD patients [8,10].In our series, COVID-19 had no impact on IBD patients.

However, according to a study carried out in Italy on a set of 24 IBD reference centers that reported the highest number of cases (79 patients), there was a significant association between active IBD and pneumonia-related to COVID-19, and deaths related to both active IBD and COVID-19 [14]. In our series 33.4% of our IBDs were active and COVID-19 had no impact on their underlying diseases.

Concerning IBD therapies, there is ample evidence of an increased risk of non-gastrointestinal opportunistic infections associated with it [15-19]. However, according to the British Society of Gastroenterology (BSG) and the American Gastroenterological Association (AGA), there is no evidence of an increased risk of COVID-19 infection associated with these drugs [20].

However, while these treatments may not increase the risk of COVID-19 infection, some treatments may increase the risk of developing a severe form of COVID-19 as shown in some studies [21]. A study based on the SECURE-IBD database (Surveillance Epidemiology of Coronavirus Under Research Exclusion) studied the impact of different therapeutic classes on the risk of developing a severe form of COVID-19, concluded that thiopurine monotherapy and combination therapy would present a higher risk compared to anti-TNF monotherapy [21]. The impact of combination therapy on increasing the severity of COVID-19 disease appears to be mainly due to thiopurines. This was consistent with previous studies that observed a higher risk of viral infections in patients treated with thiopurines alone or in combination therapy [22]. In some high-risk cases (elderly or people with multiple co-morbidities) in stable remission on combination therapy, discontinuation of thiopurine during the COVID-19 pandemic may be warranted [21].

The same study suggests the possibility that anti-TNF could have a protective effect against the development of severe COVID-19. Moreover, the use of anti-TNF as a COVID-19 treatment has been advocated by some experts to mitigate the strong inflammatory response observed in severe diseases [23]. At least one clinical trial has been planned in China to study the use of biosimilar adalimumab as a treatment for COVID-19. However, studies with larger sample sizes are needed to confirm safety across all classes of biologics.

Mesalamine and sulfasalazine appear to be associated with a form of serious COVID-19 infection in many of the comparisons in this study. However, this causal relationship cannot be considered until more supporting evidence is available. It is also possible that is not mesalamine and sulfasalazine that increase the risk of serious COVID-19, but rather other drugs such as anti-TNFs that confer relative protection in comparison. However, these findings may be an additional reason to avoid or defuse mesalamine therapy in clinical situations where they are of limited value [21].

As for corticosteroids, they can either have deleterious effects or induce an immune response if administered at the time of the onset of cytokine storm, whereas in patients with severe onset, they may play a role in the attenuation of a hyperimmune response [24].

In our series, none of our patients were on thiopurines and none of them developed severe forms, which is consistent with the data from this study. However, those who were on 5-ASA did not develop severe forms of COVID-19. It should be noted that 66.7% of the patients who were on 5-ASA received chloroquine treatment, so this is a bias that does not allow us to know if it is the effect of chloroquine.

Currently, as of January 26, 2021, through the SECURE-IBD database, there are 4578 cases of COVID-19 in patients monitored for IBD in 66 countries. 17% were hospitalized, of which 3% were in intensive care units and with a death rate of 4%. Seven percent of patients who died were on 5-ASA, 7% on Azathioprine monotherapy, 7% on Budesonide, 14% on oral/parenteral corticosteroids. The other therapies had a lower percentage of deaths. Thirty-four percent of patients who died had more than 3 comorbidities, 16% had 2 comorbidities, and 6% had one comorbidity, and 2% of patients who died had no comorbidity [25].

Concerning the risk factors for poor progression of SARS-CoV-2, an Italian study, there was no association between corticosteroid or anti-TNF use and death due to COVID-19 [14]. Age > 65 years was the strongest predictor of death related to COVID-19. Multivariate analysis from the SECURE-IBD registry of the first 525 patients from 33 countries had identified the following risk factors associated with the worst course of COVID-19: advanced age, the presence of at least two comorbidities, and the use of systemic steroids or sulfasalazine/5-aminosalicylate [20]. In our series, no patient was older than 65 years, 15.4% had only one comorbidity, which would probably explain the good outcomes of SARS-CoV-2 in our patients.

Conclusion

The SARS-CoV-2 infection may not seem to have an impact on the evolution of IBD, and conversely, the presence of underlying IBD does not seem to increase the risk of Covid-19 infection. However, certain therapies could be a risk factor for severe forms of Covid-19, especially if they are associated with other risk factors.

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