

Worse impact of second wave COVID-19 pandemic in adults but not in children with inflammatory bowel disease: an Italian single tertiary center experience

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Abstract. – **OBJECTIVE:** From September 2020, a second wave of COVID-19 pandemic started. We aimed at exploring the impact of SARS-CoV-2 infection in IBD patients during the two waves.

PATIENTS AND METHODS: All IBD patients with a confirmed diagnosis of SARS-CoV-2 infection were enrolled. They were sorted into two groups (those infected before September 2020, and those from September 2020 to January 2021) and compared by demographic and clinical data.

RESULTS: Twenty-five patients (out of about 600 with a follow-up visit) were infected with SARS-CoV-2 (4.1%). Sixteen were male and the mean age was 46.5 ± 14.3 years (range 24-74). Six were smokers and 11 had comorbidities; 2 were on steroids and 17 on immunosuppressants or biologics. Three patients (12%) needed hospitalization and other three patients were treated with azithromycin, steroids and LMWH, all of them during the second wave. No patient died or developed any sequelae. Two subjects were infected during the first wave (0.3 vs. 3.83, $p < 0.0001$). Non-significant differences were found between the two groups.

CONCLUSIONS: A higher number of IBD patients were infected during the second wave. No patient developed a severe form of pneumonia, even those treated with immunosuppressants or biologics. No risk factor for hospitalization was found.

Key Words:

COVID-19, IBD, Epidemiology.

lockdown was introduced, a progressive reduction of incidence was observed, and the number of new cases dropped under 200 per day in July 2020¹. From September 2020, the daily number of SARS-CoV-2 infected people raised progressively reaching a peak on 13th November 2020, when about 40.000 new cases were registered in one day¹. During the second wave of COVID-19 outbreak the whole Italian territory was involved. The clinical characteristics of the COVID-19 disease were the same of the first wave with similar percentage of patients needing hospitalization and admission at intensive care unit (ICU)¹.

The Italian Group for the study of Inflammatory Bowel Disease (IG-IBD) published a case series of 79 IBD patients infected with SARS-CoV-2 during the first wave, but no data are available about the impact of COVID-19 second wave in IBD patients². A single center experience in Brescia did not show a significant impact of SARS-CoV-2 infection in IBD patients in a city with high circulation of the virus during the first wave³.

The aim of this observational study was to evaluate the impact of COVID-19 in IBD patients during the first and the second wave of COVID-19 outbreak in a single tertiary center, including both adult and pediatric patients.

Patients and Methods

This observational cohort study was performed at a single, tertiary, IBD center in San Giovanni Rotondo (Italy). All consecutive IBD patients with a diagnosis of SARS-CoV-2 infection (as confirmed by either a positive naso-pharyngeal

Introduction

The first COVID-19 infections in Italy date back to last February 2020¹, spreading predominantly in the Northern area of Italy. After a strict

Table I. Demographic and clinical data of infected patients.

Patients	25
Mean age \pm SD (range)	46.5 \pm 14.3 (range 24-74)
Male sex	16 (64%)
Current smokers	6 (24%)
Mean BMI \pm SD (range)	25.9 \pm 5.0 (19-41)
CD:UC	14:11
Mean disease duration in years (range)	14.5 \pm 8.3 (2-36)
Biologics or ISS	17 (68%)
Active disease	7 (28%)
Mean CCI (range)	0.8 (0-4)
Standard therapy for COVID-19*	6 (24%)
Hospitalization	3 (12%)
ICU	0
NIV	0

SD: Standard Deviation; CD: Crohn Disease; BMI: Body Mass Index; UC: Ulcerative Colitis; ISS: Immunosuppressants; CCI: Charlson Comorbidity Index; ICU: Intensive Care Unit; NIV: Non-Invasive Ventilation. *Azithromycin, steroids, low molecular weight heparin.

swab or a positive serological test) were enrolled. Infected patients were divided into two groups (those infected between February and August 2020, during the first wave, and those from September to January 2021 in the second wave) and compared by demographic (age, sex, smoking habit) and clinical data (type of IBD, treatments, clinical activity, comorbidities, BMI, and COVID-19 therapy and outcomes).

Statistical Analysis

We performed Mann-Whitney U test to compare quantitative data, Fisher's exact test for nominal variables and univariate analysis to identify possible risk factors of worse course.

Results

A total of 25 IBD adult patients (out of about 600 who had a follow-up visit since February 2020) were infected with SARS-CoV-2 (4.1%). Two of them were infected before September 2020 compared with 23 during the second wave ($p < 0.0001$). The demographic and clinical characteristics of infected patients are shown in Table I. No statistically significant differences were found between the characteristics of patients infected during the first vs. the second wave.

Among the infected patients, four of them were completely asymptomatic, whereas the others developed mild to moderate symptoms, mainly fever, cough, ageusia, anosmia and arthralgia. During the second wave, three patients (12% of infected patients) needed hospitalization for dyspnea and oxygen desaturation, yet none of them was admitted to ICU or received non-invasive ventilation. As for therapy, along with these hospitalized patients who received also low-flow oxygen supplementation, other three subjects were treated at home with azithromycin, oral steroids and low molecular weight heparin (LMWH). No patients died or developed any sequelae until now. We also compared the clinical and demographic features of hospitalized and non-hospitalized patients (Table II) and we did not evidence any difference between these two groups. At univariate analysis, no risk factors for hospitalization were found. Finally, we did not observe any case of COVID-19 in our IBD pediatric population, even after close contacts with positive subjects.

Table II. Comparison of clinical and demographic data between hospitalized and non-hospitalized patients.

	Hospitalized pts	Non hospitalized pts	<i>p</i>
Patients	3	22	
Male sex	2 (66.7%)	14 (63.6%)	1
Mean age \pm SD (range)	47 \pm 13 (32-55)	46.4 \pm 14.7 (24-74)	0.84
Mean BMI \pm SD (range)	33 \pm 7.6 (25.5-40.6)	25.1 \pm 3.9 (19-33.2)	0.11
Current smokers	0	6 (27.3%)	0.55
CD:UC	2:1	12:10	1
Mean disease duration in years (range)	16.7 \pm 11.6 (9-30)	14.2 \pm 8.0 (2-36)	1
Active disease	1 (33%)	7 (31%)	1
Biologics or ISS	2 (66.7%)	15 (68.2%)	1
Steroids	0	2 (9%)	1
Mean CCI (range)	0.7 (0-1)	0.8 (0-4)	1

SD: Standard Deviation; CD: Crohn Disease; BMI: Body Mass Index; UC: Ulcerative Colitis; ISS: Immunosuppressants; CCI: Charlson Comorbidity Index.

Discussion

To our knowledge, this is the first study focusing on the impact of SARS-CoV-2 infection in patients with IBD during the second wave of COVID-19 outbreak.

Starting from September 2020, Italy faced with a second wave of COVID-19 with a larger virus spread, likely because of the lifting of some lockdown restrictions⁴. Compared to the first months of this pandemic, the second phase involved the entire national territory and Southern Italy (where our Hospital is located) registered a remarkable increase of SARS-CoV-2 cases^{1,5}. However, the clinical impact of this second wave was not too different from the first one, as the rate of hospitalized patients and of those requiring ICU admission remained the same¹. As a consequence, a higher number of IBD patients followed at our tertiary center was infected with SARS-CoV-2 and, in most cases, developed a symptomatic form of COVID-19.

Since September 2020, twenty-three patients contracted SARS-CoV-2 infection and three of them (12%) required hospitalization for dyspnea and desaturation and were treated with standard therapy (azithromycin, oral steroids and LMWH) plus oxygen supplementation. All of them were dismissed after few days without any complication. During this second wave, seventeen of our patients (including two hospitalized subjects) were on biologic or immunosuppressant therapy, and the treatment was temporarily stopped in all of them. None of our patients died or developed any sequelae. Moreover, we did not witness any case of pediatric IBD patients with COVID-19.

In the previous study of IG-IBD, age over 65 years, UC diagnosis, active disease, and a higher CCI score were significantly associated with COVID-19 related death². A preliminary report of SECURE-IBD registry on the initial 525 patients from 33 countries identified advanced age, the presence of at least 2 comorbidities, the use of systemic steroids or sulfasalazine/5-aminosalicylate as risk factors associated to worst course of SARS-CoV-2⁶. Currently, the SECURE-IBD registry reports 4,578 cases of SARS-CoV-2 infections among IBD patients with 17% of them requiring hospitalization and 3% admitted to ICU⁷.

In our cohort, the low mean age of infected patients and the low CCI score could explain why no deaths or cases requiring ICU were observed. We did not observe any risk factors for hospital-

ization at the univariate analysis, although there is a trend for higher BMI in hospitalized patients, which is a well-known risk factor of poor outcome of COVID-19 in the general population⁸.

As suggested by the International Organization for the study of IBD (IOIBD) recommendations⁹, we did not discontinue therapies with immunosuppressants or biologics during this pandemic and a reorganization of the biologic drug infusions' administration was done in order to minimize the risk of infection¹⁰. Moreover, in two previous studies, a concomitant biologic therapy neither enhanced the risk of contracting SARS-CoV-2 nor influenced the outcome of the disease^{11,12}.

However, a relevant number of infected patients have been found during this second wave at our center compared to the study by Norsa et al³ who did not report any case of COVID-19 during the first wave in an area with the highest incidence of disease. The percentage of IBD patients who required hospitalization (12% of all IBD infected patients) is quite higher than that reported in the Italian general population (4.8%)¹³. Moreover, a higher prevalence of infection in IBD patients was observed in our cohort compared with general population of the Puglia (the region where our Hospital is located). In fact, 25 out of 600 IBD patients followed up during 2020 contracted the infection (4.1%), compared with a total of 115,156 infected individuals out of the 4,029,000 Apulian citizens (2.8%)¹⁴.

Conclusions

Although this second wave caused a higher number of SARS-CoV-2 cases in our cohort and quite relevant number of hospitalized patients, we do not report a worst outcome of COVID-19, even in patients with known risk factors for a poorer prognosis of COVID-19. However, the higher prevalence of SARS-CoV-2 infection in IBD patients compared to the general population and the higher risk of hospitalization need more studies to confirm these preliminary data.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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Data Request

Data cannot be shared for ethical/privacy reasons. The data underlying this article cannot be shared publicly due to the privacy of individuals that participated in the study. The data will be shared on reasonable request to the corresponding author.

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