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SUPPLEMENT ARTICLE

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Impact of COVID-19 in immunosuppressive drug-naïve autoimmune disorders: Autoimmune gastritis, celiac disease, type 1 diabetes, and autoimmune thyroid disease

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Abstract

Few conflicting data are currently available on the risk of SARS-CoV-2 infection in patients with autoimmune disorders. The studies performed so far are influenced, in most cases, by the treatment with immunosuppressive drugs, making it difficult to ascertain the burden of autoimmunity *per se*. For this reason, herein we assessed the susceptibility to COVID-19 in immunosuppressive drug-naïve patients with autoimmune diseases, such as autoimmune gastritis (AIG), celiac disease (CD), type 1 diabetes (T1D), and autoimmune thyroid disease (AITD). Telephone interviews were conducted on 400 patients—100 for each group—in May 2021 by looking at the positivity of molecular nasopharyngeal swabs and/or serology for SARS-CoV-2, the need for hospitalization, the outcome, and the vaccination status. Overall, a positive COVID-19 test was reported in 33 patients (8.2%), comparable with that of the Lombardy general population (8.2%). In particular, seven patients with AIG, 9 with CD, 8 with T1D, and 9 with AITD experienced COVID-19. Only three patients required hospitalization, none died, and 235 (58.7%) were vaccinated, 43 with AIG, 47 with CD, 91 with T1D, and 54 with AITD. These results seem to suggest that autoimmunity *per se* does not increase the susceptibility to COVID-19. Also, COVID-19 seems to be mild in these patients, as indicated by the low hospitalization rates and adverse outcomes, although further studies are needed to better clarify this issue.

KEYWORDS
autoimmune gastritis, autoimmune thyroid disease, autoimmunity, celiac disease, COVID-19, immunosuppressive drugs, type 1 diabetes

Coronavirus disease 2019 (COVID-19), caused by a novel virus named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is an acute infectious disease the symptomatic spectrum of which varies from flu-like symptoms to interstitial pneumonia with respiratory failure and death.[1] Given the high mortality from COVID-19, many studies have been conducted so far to assess the risk of infection in frail individuals, including patients with pre-existing chronic conditions, and the need to optimize their clinical management.

To date, few and conflicting data are available concerning the infectious risk and prognosis of COVID-19 associated with autoimmune diseases.[2] While some studies focused on patients with rheumatological and gastroenterological autoimmune disorders have not shown an increased risk of COVID-19,[3,4] others have shown the opposite.[5,6] It should be noticed that some of the studies mentioned above, particularly those investigating patients with rheumatic diseases and inflammatory bowel disease, have been influenced by immunomodulatory therapy. Thus, it is difficult to establish whether the autoimmunity *per se* or rather the immunosuppression may increase the susceptibility to COVID-19 and severity.

For these reasons, between May 1 and May 21, 2021, telephone interviews were carried out in 400 patients with autoimmune disorders not requiring immunosuppressive therapies and regularly followed up at the University Hospital of Pavia, Lombardy (Fondazione IRCCS Policlinico San Matteo). We contacted 100 patients with autoimmune gastritis (AIG), 100 with celiac disease (CD), 100 with type 1 diabetes (T1D), and 100 with autoimmune thyroid disease (AITD)—precisely 80 with autoimmune thyroiditis and 20 with Graves' disease. All patients with overlapping autoimmune conditions and undergoing therapy with steroids or other immunosuppressants and biologics were excluded.

Through a questionnaire administered by telephone, demographic and clinical characteristics were investigated (Table 1).

Key Message

Patients with pre-existing autoimmune disorders, such as autoimmune gastritis, celiac disease, type 1 diabetes, and autoimmune thyroid disease, and naïve to immunosuppressive therapy, appear to have a similar risk of COVID-19 compared to the general population.

The median age of the study population was 48 years (range 15–90 years), with a female predominance (284, 71%). All patients with AIG were taking vitamin B12 supplementation, all those with CD had been on a strict gluten-free diet (GFD) for at least 12 months, all those with T1D were on insulin therapy, while patients with AITD were on either hormone replacement therapy or anti-thyroid drugs.

When we assessed the COVID-19 positivity through molecular nasopharyngeal swabs and/or serology for SARS-CoV-2, we found that 33/400 patients (8.2%) tested positive, of whom 7 with AIG, 9 with CD, 8 with T1D, and 9 with AITD. This figure is comparable to that reported in the general population in the same geographical area in Lombardy (8.2%; data from the Italian Ministry of Health, as of May 21, 2021).[7]

Only 3/33 COVID-19 patients (9.1%) required hospitalization due to severe infection course, while the remaining were asymptomatic (8/33 patients, 24.2%) or complained of mild symptoms (22/33 patients, 66.7%), and thus were treated at home. None of the 33 patients had a fatal outcome.

Regarding the COVID-19 vaccination status, 235/400 patients (58.7%) received at least the first vaccination dose at the time of the interview, including 43 patients with AIG, 47 with CD, 91 with T1D, and 54 with AITD.

TABLE 1 Demographic and clinical characteristics of patients with autoimmune gastritis, celiac disease, type 1 diabetes, and autoimmune thyroid disease

Variables	Autoimmune gastritis	Celiac disease	Type 1 diabetes	Autoimmune thyroid disease
Overall population, n	100	100	100	100
Median age, years (range)	60 (15–86)	40 (19–87)	43 (17–73)	54 (24–90)
Male/female, n	28/72	37/63	39/61	12/88
BMI, kg/m^2 (range)	26 (17–35)	21 (15–34)	24 (15–38)	26 (18–43)
Smoking habit, n (%)	34 (34%)	9 (9%)	12 (12%)	12 (12%)
Comorbidities				
None, n (%)	10 (10%)	30 (30%)	60 (60%)	33 (33%)
Hypertension, n (%)	76 (76%)	9 (9%)	14 (14%)	31 (31%)
Diabetes, n (%)	13 (13%)	2 (2%)	-	10 (10%)
Cardiovascular disease, n (%)	20 (20%)	5 (5%)	6 (6%)	10 (10%)
Others, n (%)	60 (60%)	40 (40%)	13 (13%)	40 (40%)
COVID-19 infection, n (%)	7 (7%)	9 (9%)	8 (8%)	9 (9%)
Hospitalization for COVID-19, n (%)	1 (1%)	0 (0%)	1 (1%)	1 (1%)
Vaccination for SARS-CoV–2, n (%)	43 (43%)	47 (47%)	91 (91%)	54 (54%)

Abbreviations: BMI, body mass index; COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Our results regarding susceptibility to COVID-19 and outcome of CD, T1D, and AITD are in line with those obtained by previous studies,[8-10] even if some critical differences in clinical settings must be mentioned. First, this study was conducted in the main Italian region hit by the pandemic and in one of the highest risk areas.[11] Despite this, we did not find an increased apparent prevalence of COVID-19 in this selected population. One possible explanation may be that most of these patients are young adults. Also, we have encompassed a relatively long time-lapse, which includes both the first and the second peak waves of the pandemic, thus providing a more comprehensive figure of the entity of the problem. We have here also provided the very first data regarding COVID-19 in patients with AIG, which is a relatively common disorder, often associated with other autoimmune conditions.[12] Regarding COVID-19 severity, the relatively favorable outcome found in the present study is comparable to that reported in previous research of ours, looking at the outcome of COVID-19 patients treated in a primary care setting.[13] Finally, the vaccination status is in line with the Italian situation, which prioritized elderly patients and those with T1D, regardless of the presence/absence of complications.

Indeed, our study has many limitations that must be mentioned. Our analysis was limited by the relatively small number of patients interviewed and its observational and retrospective nature. In particular, we cannot draw any firm conclusion regarding the prevalence of asymptomatic COVID-19 in this population and the risk of passing on the infection.

In conclusion, our study suggests that autoimmunity *per se* is not associated with increased susceptibility to COVID-19 compared to the general population. Further studies are needed to assess better the COVID-19 risk associated with autoimmune disorders to establish the best diagnostic and therapeutic management of these patients during the pandemic era and their actual need for vaccine prioritization. Also, the hypothetic bidirectional relation of autoimmune disorders affecting COVID-19 course and SARS-CoV-2 increasing the risk of developing autoimmunity remains elusive.[14]

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AUTHOR CONTRIBUTIONS

Giovanni Santacroce: Writing-review the original article & editing (equal). **Marco Vincenzo Lenti**: Conceptualization (equal); Methodology (equal); Writing-review & editing (equal). **Nicola Aronico**: Writing-review & editing (equal). **Emanuela Miceli**: Writing-review & editing (equal). **Elisabetta Lovati**: Writing-review & editing (equal). **Pietro Carlo Lucotti**: Writing-review & editing (equal). **Luigi Coppola**: Writing-review & editing (equal). **Antonella Gentile**: Writing-review & editing (equal). **Mario Andrea Latorre**: Writing-review & editing (equal). **Francesco Di Terlizzi**: Writing-review & editing (equal). **Simone Soriano**: Writing-review & editing (equal). **Chiara Frigerio**: Writing-review & editing (equal). **Ivan Pellegrino**: Writing-review & editing (equal). **Ivan Pellegrino**: Writing-review & editing (equal). **Alessandra Pasini**: Writing-review & editing (equal).

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