

# Are My Patients with Celiac Disease at Higher Risk of COVID-19 Virus?

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**Abstract** COVID-19, caused by severe acute respiratory syndrome coronavirus (SARS-CoV-2), is now a worldwide spreading pandemic. Most of the attention is directed to the upper and lower respiratory airways, however, it appears that the gastrointestinal tract is also inoculated and infected. In this regards, celiac disease patients are a potential high-risk group for the corona virus infection and the endoscopist communities should be aware of their professional risks.

**Keywords:** celiac disease, covid-19, SARS-CoV-2, corona virus, high risk, immune deficiency, gastrointestinal endoscopy

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## 1. Introduction

The COVID-19 pandemic is an outbreak of the novel respiratory disease COVID-19 that had first was noticed at the end of 2019 in the mega-metropolis of Wuhan in the Chinese province of Hubei. The epidemic in China started around January 2020 and finally spread worldwide and became a pandemic. The outbreak was caused by the previously unknown corona virus SARS-CoV-2 triggered. This virus is also known as a novel corona virus [1].

Multiple observations indicate that this infectious virus almost certainly originated from the zoonotic kingdom, although the précised reservoir is not yet completely delineated. Initially thought to come from bats or pangolin, passed on to humans directly or via an intermediate mammal [2]. Finally, it is suspected that a double infection of the virus species SARS-associated coronavirus led to recombination and that the SARS-CoV-2 virus is a new chimera from these earlier viruses [1]. The past epidemic origins: the Himalayan palm civet for SARS-CoV and the dromedary camel for MERS-CoV were identified, not yet for the corona virus SARS-CoV-2. It should be stress that the corona viruses are universally spread and span numerous mammals: bats, piglets, pigs, feline (cats), horses and swine [3-7].

Today, the globe is facing a very contagious Pandemic, transmit from person to person. It affects mainly the respiratory tract, but information is accumulating that the gastrointestinal tract is not resilient. In fact, the corona virus infection can involve and damage the gut and other organs like heart, vessels, liver and kidneys [8,9]. Animals, including bats harbor the virus in their intestine [10] and the covid-19 can be detected in stools of infected patients [11]. More so, the gastrointestinal tract can present a shedding rout for SARS-CoV-2 environmental contamination

[12]. The present review aims to highlight some aspects that might affect the celiac disease (CD) patients in face of the SARS-CoV-2 Pandemic that is currently globally spreading.

## 2. High Risk Aspects of Corona Virus Infection in Celiac Disease Patients

The following are CD features that might relay to the current SARS-CoV-2 infections

**A. Celiac disease is an immune dysregulated condition.** Being an autoimmune disease where loss of tolerance to gluten and gliadins is occurring, CD can be characterized as a mucosal immune dysregulated condition [13]. The innate as well as the reactive systems are engaged. Enterocyte-interepithelial lymphocytes-IL-15 cross talks, Toll-like receptors, regulatory T cells, mucosal mast cells, mucosal cytokines, Th1/Th2 balance, Reactive CD<sup>4</sup>T and activated B cells relationship are some of those derangements [14-20]. Most will attenuate and normalize on streaked gluten free diet, hence, few will persist, keeping long-term degree of mucosal inflammation. One wonder what will be the outcome if SARS-CoV-2 infects such a vulnerable mucosa.

**B. IgA deficiency** affects 2%–3% patients with CD, a frequency approximately 10–15 times higher than the general population [21]. It is the most common human immunodeficiency and is characterized by a serum IgA concentration of <7 mg/dL. Secretory IgA antibodies have various critical functions. Immune protection against infectious agents, establishment of a healthy microbiome and regulating host-commensal homeostasis are the most important. Most affected people are asymptomatic, some will present with infectious diarrhea. But approximately one third suffer from recurrent bacterial, enteroviral or protozoal infections of the respiratory and gastrointestinal

tracts [22]. Related to the subject of the present review, secretory IgA is important in protecting the respiratory and the gut mucosa against viruses, be it enteroviruses or pulmonary influenza. Since SARS-CoV-2 infects both of them and since IgA deficient CD patients are also deficient in secretory IgA in the respiratory tract, they might be prone to be infected. Interestingly, after acute infection with SARS-CoV-2, the median duration of the serum IgA antibody detection was 5 days, after symptom onset, with a positive rate of 92.7% [23]. Unfortunately, no studies are available on the enteric and respiratory secretory IgA status in the infected patients. Epidemiological surveys on the rate of Covid-19 infection in IgA deficient patients, compared to controls are lacking. Time will tell if the IgA deficient CD population is a risk group for corona virus infection.

**C. Immune deficiency conditions associated with celiac disease.** In addition to the IgA deficiency, other immune deficiencies are associated with CD. Common Variable Immune Deficiency, Chronic Granulomatous Disease and isolated IgM deficiency are some of them [24,25]. When associated with CD, those condition represent an additional potential risk for the current pandemic viral infection.

**D. Immune suppressive therapy in refractory celiac disease.** Despite being rare, refractory CD is a very challenging diagnosis and therapy. Immune suppressive drugs are the main therapy, so far. Systemic steroids, budesonide, azathioprine, adenosine nucleoside analog cladribine, infliximab, campath (anti CD52), methotrexate, cyclosporine A, recombinant IL-10, anti IL-15 or hemopoietic stem cell transplantations were suggested to treat the condition and its morbid and lethal complications [26]. Once again putting CD patients in high risk for the Covid-19 infections.

#### **E. Pulmonary disease associated with celiac disease**

The list of respiratory conditions associated with CD is continuously expanding. Asthma [27], pulmonary Hemosiderosis [28], hemochromatosis [29,30], cystic fibrosis [31] and even respiratory syncytial virus [32], are some of them. It appears that Children with CD diagnosed during infancy were found to attended hospital for a prior respiratory syncytial virus infection or any other viral bronchiolitis more than other children. Even thought not celiac children, in Crohn's children, another intestinal inflammatory condition, Bronchial reactivity and lung functions are compromised [33]. It goes without saying that adults or elderly with chronic health diseases, including chronic lung debilitating conditions are at increased morbidity and mortality risk, when infected with Covid-19 virus. So, if a CD patient has such a condition, he/she is potentially at risk of corona virus infection and complications.

### **3. Potential Shared Aspect between Covid-19 High Risks Populations and CD Patients**

Table 1 lists the shared aspects between CD and potential risks for corona virus infection and complications.

**Table 1. SHARED aspects between CD and potential risks for corona virus infection and complications**

High risk populations	Covid-19 virus	References
Elderly	High risk	[34,35]
Chronic pulmonary diseases	High risk	[36]
hypertension, diabetes, heart diseases, decompensated cirrhosis, HIV with low CD4 counts, immunosuppression, solid organ transplant recipients and pregnancy	High risk	[36,37]
Smoking	High risk	[38]
Increased mortality and morbidity disease	More the in CD	[39,40]
Detrimental aspect of gluten ingestion: pro-inflammatory, cytotoxic, decreases cell viability and differentiation etc.	Gluten potential effects	[41]
Side effect of gluten free diet: nutritional deficiencies Toxicity, increased morbidity and mortality, mental health etc.	Gluten withdrawal potential effects	[42]
Low diagnosed/undiagnosed CD ratio	Low diagnosed asymptomatic patients	[43]

### **4. A Final Warning Message to the Endoscopic Gastroenterologists**

A final warning message to the endoscopic gastroenterologists in the current SARS-CoV-2 spreading Pandemic. Although it does not appear to be related to the topics of the current review, I feel responsible to highlight same recent observations concerning the gut effects of the corona virus. A lot of attention is given to medical communities' high risks, hence, not enough is given to the gastrointestinal endoscopist who operate in an infected compartment. SARS-CoV-2 RNA is resent in the feces of the infected patients [8,9,11]. Colonic biopsy samples positivity has been consistently documented. As mentioned above, stool's viral shedding is more prolonged then in respiratory compartments' secretions [12] and potential fecal-oral transmission was most recently suggested [44]. Above all, a plethora of other viruses are part of the enteric microbiome and affect the microbiota/dysbiota balance in health and disease [45] and the covid-19 effects on the gut homeostasis are yet unknown.

Since the covid -19 is highly infectious and can survive on surfaces for certain periods and since most of the infected people are a/hypo-symptomatic, the gastrointestinal endoscopists should be educated, warned and be aware of their high professional risk to be contaminated or infected, as is the case for the *helicobacter pylori*.

Reviewing the literature of the SARS-CoV1, a family member of the current SARS-CoV2, it spread through the intestinal tract, kidney and sweat glands to be excreted via feces, urine and sweat [46]. In this regard, the Spanish society of digestive pathology (SEPD) and gastroenterology (AEG) should be congratulated for their most recent recommendations [47]. Additionally, the current cleaning and disinfections procedures should be evaluated for SARS-CoV-2 survival on the endoscopes' surfaces and channels, during and after aspiration of oral and fecal material via endoscopes. Much more, specific focus on

personal protection equipment and dress code modalities should be implemented in community and hospital endoscopy suites. Those preventive measures are starting to appear in the adult medical and scientific literature [48,49], not yet in the pediatric endoscopy one. The high risks, warning and recommendations apply for CD since many of the patients need endoscopies for diagnosis or associated complications and diseases

No reports yet are available on corona virus transmissions during gastrointestinal procedures, however, those professional risk should be explored, preferably "an hour earlier".

## 5. Conclusions

The current SARS-CoV-2 Pandemic is spreading with more unresolved questions than answers. CD patients are potentially a high-risk group for many reasons as well as the gastrointestinal endoscopists. CD patients, professional treatment teams like nurses, physicians and dieticians and their societies should be aware of the potential risk of the covid-19 virus and act accordingly.

## Conflict of Interest

No potential conflicts of interest in authorship or publication

## Financial Declaration

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## Abbreviations List

CD-celiac disease, SARS-CoV-2-severe acute respiratory syndrome coronavirus-2.

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