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ORIGINAL ARTICLE

No COVID-19 pandemic impact on incidence and clinical presentation of celiac disease in Italian children

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Abstract

Aim: We aimed to evaluate the impact of Coronavirus Disease-19 (COVID-19) pandemic on the incidence and clinical presentation of celiac disease (CD) in children.

Methods: The diagnoses of CD were compared between the COVID-19 pandemic (from April 2020 to March 2022) and the pre-pandemic period (from April 2018 to March 2020) in three Italian Paediatric Gastroenterology centres (Varese, Como, Catanzaro). Electronic patient records were reviewed and additional information were collected through parental interview. The diagnosis of CD was made according to ESPGHAN criteria. SARS-CoV-2 infection was diagnosed based on pre-vaccination positive serum antibodies or nasopharyngeal swabs. Z test and chi-square were used for statistical analysis.

Results: The overall number of paediatric diagnosis of CD did not differ between the two years pre-pandemic and pandemic periods (177 and 172 cases) in the three Italian participating centres. Clinical presentation of CD was also similar throughout the study periods. SARS-CoV-2 infection has been documented in 10.6% of children but only in 5.8% of these occurred before CD diagnosis.

Conclusion: Different to what reported for other autoimmune diseases, the incidence and presenting symptoms of CD in our paediatric population did not change during the COVID-19 pandemic compared to the previous 2 years.

KEYWORDS
anti-transglutaminase, autoimmunity, celiac disease, children, COVID-19, gluten, pandemic, SARS-CoV-2

Abbreviations: CD, celiac disease; COVID-19, Coronavirus Disease 19; EMA, anti-endomysial antibodies; HLA, Human Leukocyte Antigen; SARS-CoV-2, Severe Acute Respiratory Syndrome Coronavirus 2; tTG, anti-transglutaminase antibodies; T1D, Type 1 Diabetes mellitus.

1 | INTRODUCTION

The effect of Coronavirus Disease-19 (COVID-19) pandemic on the onset of celiac disease (CD) in children is still unclear due to limited and conflicting data.[1,2] CD is a chronic immune-mediated disease related to gluten in subjects with genetic predisposition.[3] As it is well known, CD is characterised by the presence of enteropathy manifesting with gastrointestinal and/or extraintestinal symptoms (classical and non-classical ones) specific serum antibodies (anti-tissue transglutaminase, tTG, and anti-endomysial antibodies, EMA) and human leukocyte antigen (HLA)-DQ2 and/or HLA-DQ8 haplotype.[3,4] In some patients CD is asymptomatic and associated to other autoimmune disorders, particularly Type 1 Diabetes mellitus (T1D). Current prevalence of CD is estimated 0.5%–1% of the global population[5] with a significant increase in the last decades, particularly in some countries like Italy,[3,6] where recent school-age screening studies reported a prevalence of 1.65%.[7,8] The pathogenesis of CD still needs to be completely elucidated and infections are one factor that may contribute to its development.[9] Severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2) can invade host cells through the angiotensin-converting enzyme 2 (ACE2)[10,11] which is also expressed on epithelial intestinal cells.[12] By acting via mucosal and systemic mechanisms SARS-CoV-2 infection may trigger local and systemic inflammation and autoimmune responses, as suggested in many studies.[12–14]

An increased incidence and severity of T1D during the COVID-19 pandemic has been widely reported.[15,16] Since CD is an autoimmune disease sharing with T1D the HLA haplotypes, altered gut permeability and mucosal inflammation,[17,18] we aimed to investigate whether the COVID-19 pandemic has increased the number of paediatric CD diagnoses or changed the presenting symptoms in children living in two Italian regions.

2 | MATERIALS AND METHODS

We conducted a multicentre study including three Italian Paediatric Gastroenterology centres (Varese, Como and Catanzaro), two located in the North and the third in the South of Italy. The number of new diagnoses of CD carried out from April 2020 to March 2022 (pandemic period) was compared to the previous 2 years (from April 2018 to March 2020, pre-pandemic period) based on electronic medical records and local registration database. Additional information was collected through parental interview during follow-up visits. The following data were recorded and analysed: gender, age, date of the outpatient visit, date of CD diagnosis, symptoms at diagnosis, eventual comorbidity, results of the CD specific antibodies (tTG, EMA) and of intestinal biopsy, when performed. The total annual number of children referred to the paediatric gastroenterology clinics during the study periods was also retrieved to minimise a possible diagnostic bias due to a general decreased access to our clinic during the lockdown.

In addition, SARS-CoV-2 infection was diagnosed based on pre-vaccination positive serum antibodies or nasopharyngeal swabs.[15]

Key notes

- The impact of Coronavirus Disease 19 (COVID-19) pandemic on celiac disease (CD) in children is still uncertain.
- We did not find an increased frequency or a different clinical presentation of CD in Italian children before and during the pandemic.
- Exploring the effect of COVID-19 infection in a large paediatric population and in a longer period of time will provide a firm conclusion on the possible relation between these two diseases.

The diagnosis of CD was made in all patients by positive antibodies and/or intestinal biopsies, according to the ESPGHAN guidelines.[19,20] Despite the introduction of possible lower antibodies cut-off (>7.5 × normal values) for the diagnosis of CD in children during the pandemic period, these ad interim SIGENP criteria[21] were not used in our patients. Clinical presentation at diagnosis was also analysed according to the Oslo criteria, as for classical, non-classical or asymptomatic CD.[22]

2.1 | Statistical analysis

All data were recorded in an excel file and descriptive statistic, as median and mean for continuous variables and number and percentage for categorical variables, was used to provide information about the included population. Chi-square and *Z* tests were applied for the comparison of the rate of clinical manifestations and incidence of celiac diagnosis occurring in the pre-pandemic and pandemic periods. A p-value <0.05 was considered as statistic significant.

3 | RESULTS

Our cohort of children with a new diagnosis of CD included 349 subjects (121 males, 35%; median age 4.3 years; mean age ± SD 6.1 ± 4.2 years). Overall, the number of new diagnoses of CD in the three participating centres was 177 in the pre-pandemic period (70 in Varese, 59 in Catanzaro and 48 in Como) and 172 in the pandemic period (67 in Varese, 67 in Catanzaro and 38 in Como) (Figure 1), with a negative trend of 2.8% in the latter, despite 1.2% decrease of total number of annual visits during the pandemic. When considering the total number of first visits to the paediatric gastroenterology clinics, the rate of new diagnosis of CD was 7.4% and 6.7%, respectively, in the pre- and pandemic periods, without a statistic significant difference. In addition, there was no significant difference in the rate of diagnosis of CD between the North and South participating centres comparing the pre-pandemic and pandemic periods (118 vs. 59 diagnosis and 105 vs. 67 diagnosis) ($p = 0.27$). Surprisingly, the number

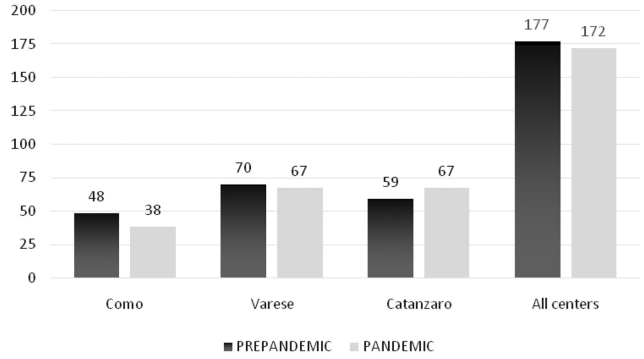

FIGURE 1 The total number of CD diagnoses before and during the pandemic distributed in the three participating centres.

TABLE 1 Comparison of different presentations of CD diagnosed in the pre-pandemic and pandemic periods.

Period	Pre-pandemic	Pandemic
Classical CD	290 (290.05) [0.00]	294 (293.95) [0.00]
Non-classical CD	57 (59.60) [0.11]	63 (60.40) [0.11]
Asymptomatic	24 (21.36) [0.33]	19 (21.64) [0.32]

of endoscopies performed to diagnose CD slightly increased in the pandemic compared to the previous 2 years (29 vs. 22; $p=0.24$).

No significant difference was noted in sex (68/177 vs. 53/172 males) and age (median 4.5 vs. 3.3 years; mean ± SD 6.2 ± 3.8 years vs. 5.9 ± 4.6 years) between the two study periods. Clinical presentation at diagnosis was analysed according to the Olso criteria[22] and showed no significant difference between the two study periods ($p=0.65$), as summarised in Table 1.

In our population, the three more common classical presentations of CD were: abdominal pain referred by 122 children (35% of total presenting symptoms), exactly by 61 children in both study periods ($p=0.77$); diarrhoea reported in 85 children (24.4%; 48 vs. 37 cases; $p=0.22$) and failure to thrive in 76 children (21.8%; 36 vs. 40 cases; $p=0.50$). The three more frequent non-classical manifestations were: headache overall reported by 26 children (7.5% of total presenting symptoms), exactly by 13 children in both study periods ($p=0.94$); sleep disorders noted in 22 children (6.3%; 7 vs. 15 cases; $p=0.07$) and irritability in 18 children (5.2%; 7 vs. 11 cases; $p=0.30$). It is worth to note that the only significant difference between the two study periods was found for joint pain reported by 14 children (4% of total presenting symptoms): 11 cases in the pre-pandemic 2 years and 3 cases during the pandemic ($p=0.03$). Overall, 43 children (12.3%) were asymptomatic (24 vs. 19 children in the two study periods; $p=0.48$) and were screened for CD because of family history or comorbidity or detection of iron deficiency. The complete list of symptoms and signs at CD diagnosis and the comparison between the pre-pandemic and pandemic periods are reported in Table S1. T1D was present in only three children of the pre-pandemic group and in two children of the pandemic group.

During the pandemic period, the diagnosis of COVID-19 was made in 10.6% (37/349) children; only in one case it was based on pre-vaccination positive SARS-CoV-2 serum antibodies. In 10/172 (5.8%) children COVID-19 was documented before the diagnosis of CD. However, we could not assess the exact prevalence of SARS-CoV-2 infection in our population or a different rate between the North and South of Italy. Indeed, many data were missing and most children were not properly investigated because of lack of diagnostic tests or parental refusal or limited access to the hospital, particularly during the first year of the pandemic.

4 | DISCUSSION

Our study is the first paediatric multicentre study providing data about the incidence and clinical characteristics of CD diagnosed during COVID-19 pandemic. Two recent reports showed conflicting results on the incidence of CD in children during the pandemic and did not detail the clinical manifestations.[1,2,23] In our Italian paediatric population frequency and presenting symptoms of CD were similar to the previous 2 years. Despite the lockdown, the total number of children referred to our paediatric clinics and of endoscopies performed to diagnose CD did not change significantly between the 2 years study periods. However, we could not exclude a possible change in diagnostic delay due to restrictions during the pandemic. Since recording of the time of symptom onset was inaccurate and incomplete, we could not analyse these data.

CD is a multifactorial autoimmune disease which afflicts 0.5%–1.6% of world population with raising number of diagnosis in the last decade.[5,8] Several factors may contribute to its pathogenesis in genetic predisposed individuals carrying the haplotype HLA DQ2 and/or DQ8.[23–25] In particular, viral infections has long been considered as a trigger of autoimmunity[1] acting through molecular mimicry, bystander and epitope spreading, inflammation and abnormal intestinal permeability.[12] SARS-CoV-2 infection has a wide clinical spectrum, including gastrointestinal symptoms and severe inflammatory syndrome possibly driven by zonulin-dependent loss of gut mucosal barrier.[12,26–28] There is a recent emerging evidence on the possible role of SARS-CoV-2 in triggering different inflammatory and autoimmune disorders.[12,26,28–30]

A dramatic increased incidence and severity of presentation of T1D have been reported simultaneously or immediately after SARS-CoV-2 infection.[31,32] Relationship between T1D and respiratory infections had already been pointed out in the so-called TEDDY study, in which it was demonstrated that the number of respiratory infections in children in a 9-month period was linked to consequent onset of autoimmunity against pancreatic islet cells in the following 3 months.[33]

In the North of Italy, a net increase in the incidence of T1D up to 77% was detected compared to the year preceding the pandemic.[15] An action of the virus on intestinal permeability is conceivable as for the development of autoimmune disease: the gut represents a favourable place for SARS-CoV-2 replication and for immune activation due to the expression of target molecules ACE2 and TMPRSS2 on ciliate cells and on brush border of enterocytes.[34] The frequent

intestinal involvement and viral persistence is well documentable by faecal excretion of SARS-CoV-2 in more than half of infected individuals and by its finding in intestinal biopsies 4 months after infection in adults.[26] Mucosal inflammation and altered permeability and zonulin occurred in CD, allowing the passage of a large amount of antigens into the bloodstream.[34,35]

Differently to what reported for T1D[15] we did not find an increased incidence of CD in Italian children living in two regions in the North and South of Italy, during the first 2 years of SARS-CoV-2 pandemic compared to a previous similar period. Overall, in the three participating paediatric centres, the total number of new diagnosis of CD decreased of 2.8% in the pandemic, partially explained by a decrease of 1.2% of total annual visits during that period. The spectrum of clinical presentation of CD is wide and may include weight loss, failure to thrive, chronic diarrhoea, abdominal pain, bloating, vomiting, constipation, iron deficiency anaemia, chronic fatigue, osteoporosis, headache, joint pain, dental enemal defects and other extraintestinal features.[3,4] In our population, the clinical presentation at diagnosis was not significantly different for gastrointestinal and extraintestinal symptoms, before and during pandemic. However, it is interesting to note that the only significant difference between the two study periods was found for joint pain overall reported by 14 children, significantly higher ($p = 0.03$) in the pre-pandemic period than during the pandemic. However, this result should be considered with caution due to the limited number of affected children. Only a few children diagnosed CD presented also T1D with no difference in the two study periods. Data on the impact of SARS-CoV-2 infection and pandemic on CD in children are currently limited and conflicting. Cakir et al. investigated CD percentage in a pre-pandemic and pandemic period in Turkey, reporting an increase of both number of patients per year (from 12.1 to 37.6) and percentage of CD diagnoses (from 2.2% to 10%) in pandemic period.[1] Moreover, in this small population of 47 new cases of CD an increased number of associated T1D was detected strengthenIng the hypothesis about a potential role of SARS-CoV-2 in autoimmune pathogenesis. On the contrary, in a recent Italian study Crocco et al. found a 14.5% decrease of paediatric CD diagnosis in a tertiary centre in Liguria, in the North of Italy during the pandemic compared to the previous 2 years.[2] This change could be attributed to family choices that delayed the screening, or to decreased endoscopic investigations and hospital access during the lockdown, as also considered in another report.[36] Interestingly, Greco et al. suggested that the presence of HLA DQ2 and DQ8 may play as a protective factor against SARS-CoV-2 infection and possible related complications, including the development of autoimmunity.[37]

The main limitations of our study are the limited multicentre recruitment, the retrospective design, the lack of a complete assessment of possible diagnostic delay and of SARS-CoV-2 infections. However, we planned to include two different Italian regions (Lombardia and Calabria) and two close paediatric gastroenterology centres (Varese and Como) to decrease a possible population bias related to monocentre or local recruitment, different severity of SARS-CoV-2 infection or facility to access to the paediatric clinic during the pandemic. In addition, we tried to retrieve all data of patients by using electronic records, patients' database and interview at follow-up visits to compare rate of diagnosis and symptoms of CD and of COVID. Only a limited number of children had a documented SARS-CoV-2 infection before the diagnosis of CD. However, the true incidence of COVID was impossible to calculate because of limited access to the hospital and diagnostic tests, particularly in the first year of the pandemic and the subsequent introduction of vaccination. Nonetheless, the possible causal relation or trigger effect of COVID on CD would be impossible to prove in our patients. Nevertheless, as the impact of SARS-CoV-2 infection may have a delayed effect on intestinal autoimmunity, a prolonged period of study and a larger population are needed to draw a general conclusion on the possible relation between these two conditions.

5 | CONCLUSION

Different to what reported for other autoimmune disorders, the incidence and presenting symptoms of CD in our paediatric Italian population did not change during the COVID-19 pandemic compared to the previous 2 years.

AUTHOR CONTRIBUTIONS

Pietro Guacci: Writing – original draft; investigation; writing – review and editing. **Claudia Ballabio:** Writing – original draft; investigation; writing – review and editing. **Alice Folegatti:** Writing – original draft; investigation; writing – review and editing. **Laura Giancotti:** Investigation. **Alessia Scordo:** Investigation. **Licia Pensabene:** Conceptualization; methodology; data curation; supervision. **Barbara Parma:** Investigation; conceptualization; writing – original draft; writing – review and editing; methodology; data curation; supervision. **Angelo Selicorni:** Conceptualization; investigation; methodology. **Chiara Luini:** Conceptualization; investigation; methodology. **Massimo Agosti:** Conceptualization; project administration; methodology. **Silvia Salvatore:** Conceptualization; investigation; writing – original draft; methodology; validation; writing – review and editing; project administration; data curation; supervision; formal analysis.

FUNDING INFORMATION

This study did not receive any specific funding.

CONFLICT OF INTEREST STATEMENT

None.

ETHICS STATEMENT

This study was performed according to the Helsinki declaration. Exemption from the Hospital Ethical Committee Review was considered since the study was designed as a retrospective observational study conducted during the pandemic with the data properly anonymised and informed consent obtained at the time of original data collection.

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REFERENCES

1. Cakir M, Guven B, Issi F, Ozkaya E. New-onset celiac disease in children during COVID-19 pandemic. Acta Paediatr. 2022;111(2):383-8. doi:10.1111/apa.16173
2. Crocco M, Calvi A, Canzoneri F, et al. The influence of SARS-CoV-2 pandemic on the diagnosis of celiac disease and clinical practice in pediatric gastroenterology. Nutrients. 2023;15(3):559. doi:10.3390/nu15030559
3. Catassi C, Verdu EF, Bai JC, Lionetti E. Coeliac disease. Lancet. 2022;399(10344):2413-26. doi:10.1016/s0140-6736(22)00794-2
4. Makovicky P, Caja F, Rimarova K, Samasca G, Vannucci L. Celiac disease and gluten-free diet: past, present, and future. Gastroenterol Hepatol Bed Bench. 2020;13(1):1-7.
5. Caio G, Volta U, Sapone A, et al. Celiac disease: a comprehensive current review. BMC Med. 2019;17(1):142. doi:10.1186/s12916-019-1380-z
6. Catassi C, Gatti S, Fasano A. The new epidemiology of celiac disease. J Pediatr Gastroenterol Nutr. 2014;59(Suppl 1):S7-S9. doi:10.1097/01.mpg.0000450393.23156.59
7. Lionetti E, Pjetraj D, Gatti S, et al. Prevalence and detection rate of celiac disease in Italy: results of a SIGENP multicenter screening in school-age children. Dig Liver Dis. 2023;55(5):608-13. doi:10.1016/j.dld.2022.12.023
8. Lionetti E, Fabbrizi A, Catassi C. Prevalence of COVID-19 in Italian children with celiac disease: a cross-sectional study. Clin Gastroenterol Hepatol. 2021;19(5):1075. doi:10.1016/j.cgh.2020.11.035
9. Smatti MK, Cyprian FS, Nasrallah GK, Al Thani AA, Almishal RO, Yassine HM. Viruses and autoimmunity: a review on the potential interaction and molecular mechanisms. Viruses. 2019;11(8):762. doi:10.3390/v11080762
10. Tsang HF, Chan LWC, Cho WCS, et al. An update on COVID-19 pandemic: the epidemiology, pathogenesis, prevention and treatment strategies. Expert Rev Anti-Infect Ther. 2021;19(7):877-88. doi:10.1080/14787210.2021.1863146
11. Kirtipal N, Bharadwaj S, Kang SG. From SARS to SARS-CoV-2, insights on structure, pathogenicity and immunity aspects of pandemic human coronaviruses. Infect Genet Evol Nov. 2020;85:104502. doi:10.1016/j.meegid.2020.104502
12. Trovato CM, Montuori M, Pietropaoli N, Oliva S. COVID-19 and celiac disease: a pathogenetic hypothesis for a celiac outbreak. Int J Clin Pract. 2021;75(9):e14452. doi:10.1111/ijcp.14452
13. Hileman CO, Malakooti SK, Patil N, Singer NG, McComsey GA. New-onset autoimmune disease after COVID-19. Front Immunol. 2024;15:1337406. doi:10.3389/fimmu.2024.1337406
14. Ehrenfeld M, Tincani A, Andreoli L, et al. Covid-19 and autoimmunity. Autoimmun Rev. 2020;19(8):102597. doi:10.1016/j.autrev.2020.102597
15. Denina M, Trada M, Tinti D, et al. Increase in newly diagnosed type 1 diabetes and serological evidence of recent SARS-CoV-2 infection: is there a connection? Front Med (Lausanne). 2022;9:927099. doi:10.3389/fmed.2022.927099
16. McGlacken-Byrne SM, Drew SEV, Turner K, Peters C, Amin R. The SARS-CoV-2 pandemic is associated with increased severity of presentation of childhood onset type 1 diabetes mellitus: a multi-centre study of the first COVID-19 wave. Diabet Med. 2021;38(9):e14640. doi:10.1111/dme.14640
17. Prieto J, Singh KB, Nnadozie MC, et al. New evidence in the pathogenesis of celiac disease and type 1 diabetes mellitus: a systematic review. Cureus. 2021;13(7):e16721. doi:10.7759/cureus.16721
18. Roldán Martín MB, Márquez Romero C, Guerra Vilches E, et al. Celiac disease screening in children and adolescents with type 1 diabetes mellitus: what test should be performed? Endocrinol Diabetes Nutr (Engl ed). 2021;68(3):153-8. doi:10.1016/j.endien.2020.03.011
19. Husby S, Koletzko S, Korponay-Szabó IR, et al. European Society for Pediatric Gastroenterology, hepatology, and nutrition guidelines for the diagnosis of coeliac disease. J Pediatr Gastroenterol Nutr. 2012;54(1):136-60. doi:10.1097/MPG.0b013e31821a23d0
20. Husby S, Koletzko S, Korponay-Szabó I, et al. European society Paediatric gastroenterology, hepatology and nutrition guidelines for diagnosing coeliac disease 2020. J Pediatr Gastroenterol Nutr. 2020;70(1):141-56. doi:10.1097/mpg.0000000000002497
21. Trovato CM, Montuori M, Cucchiara S, Oliva S. ESPGHAN 'biopsy-sparing' guidelines for celiac disease in children with low anti-transglutaminase during COVID-19. Eur J Gastroenterol Hepatol. 2020;32(12):1523-6. doi:10.1097/meg.0000000000001924
22. Ludvigsson JF, Leffler DA, Bai JC, et al. The Oslo definitions for coeliac disease and related terms. Gut. 2013;62(1):43-52. doi:10.1136/gutjnl-2011-301346
23. Lebwohl B, Sanders DS, Green PHR. Coeliac disease. Lancet. 2018;391(10115):70-81. doi:10.1016/s0140-6736(17)31796-8
24. Lindfors K, Ciacci C, Kurppa K, et al. Coeliac disease. Nat Rev Dis Primers. 2019;5(1):3. doi:10.1038/s41572-018-0054-z
25. Troncone R, Discepolo V. Celiac disease and autoimmunity. J Pediatr Gastroenterol Nutr. 2014;59(Suppl 1):S9-s11. doi:10.1097/01.mpg.0000450394.30780.ea
26. Xiao F, Tang M, Zheng X, Liu Y, Li X, Shan H. Evidence for Gastrointestinal Infection of SARS-CoV-2. Gastroenterology. 2020;158(6):1831-1833.e3. doi:10.1053/j.gastro.2020.02.055
27. Monzani A, Lionetti E, Felici E, et al. Adherence to the gluten-free diet during the lockdown for COVID-19 pandemic: a web-based survey of italian subjects with celiac disease. Nutrients. 2020;12(11):3467. doi:10.3390/nu12113467
28. Knight JS, Caricchio R, Casanova JL, et al. The intersection of COVID-19 and autoimmunity. J Clin Invest. 2021;131(24):e154886. doi:10.1172/jci154886
29. Syed U, Subramanian A, Wraith DC, et al. Incidence of immune-mediated inflammatory diseases following COVID-19: a matched cohort study in UK primary care. BMC Med. 2023;21(1):363. doi:10.1186/s12916-023-03049-5
30. Lexner J, Lindroth Y, Sjöberg K. The risk for celiac disease after Covid-19 infection. BMC Gastroenterol. 2023;23(1):174. doi:10.1186/s12876-023-02795-3
31. Liu Y, Sawalha AH, Lu Q. COVID-19 and autoimmune diseases. Curr Opin Rheumatol. 2021;33(2):155-62. doi:10.1097/bor.0000000000000776
32. Kamrath C, Rosenbauer J, Eckert AJ, et al. Incidence of type 1 diabetes in children and adolescents during the COVID-19 pandemic in Germany: results from the DPV registry. Diabetes Care. 2022;45(8):1762-71. doi:10.2337/dc21-0969
33. Lönnrot M, Lynch KF, Elding Larsson H, et al. Respiratory infections are temporally associated with initiation of type 1 diabetes autoimmunity: the TEDDY study. Diabetologia. 2017;60(10):1931-40. doi:10.1007/s00125-017-4365-5
34. Yonker LM, Gilboa T, Ogata AF, et al. Multisystem inflammatory syndrome in children is driven by zonulin-dependent loss of gut mucosal barrier. J Clin Invest. 2021;131(14):e149633. doi:10.1172/jci149633
35. Verdu EF, Schuppan D. Co-factors, microbes, and immunogenetics in celiac disease to guide novel approaches for diagnosis and treatment. Gastroenterology. 2021;161(5):1395-1411.e4. doi:10.1053/j.gastro.2021.08.016
36. Valitutti F, Troncone R, Pisano P, Ciacci C. Where have all the other coeliacs gone in 2020? Road for a 2021 catch-up with

missed diagnoses. Dig Liver Dis. 2021;53(4):504-5. doi:10.1016/j.dld.2021.01.008

37. Greco N, Meacci A, Mora B, Vestri A, Picarelli A. Coeliac disease in the COVID-19 pandemic: does HLA have a protective effect? Ann Med. 2022;54(1):617-21. doi:10.1080/07853890.2022.2039955

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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