Impact of the COVID-19 Pandemic in Romanian Celiac Disease Patients by E-Survey

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Received XX; Revised XXXX; Accepted XXXX

Abstract Background: The coronavirus disease 2019 (COVID-19) pandemic has immeasurably struck healthcare systems worldwide, generating disruptions in the care of chronic disease patients. We herein aimed to assess the impact of the COVID-19 pandemic on celiac disease (CD) patients. Materials and Methods: An online questionnaire with 46 cascade questions was designed and distributed through the social media channel of the Romanian CD patient association. Results: Altogether, 113 respondents accessed the questionnaire, of whom 95 adult CD patients with complete responses were included in the analysis. The median age of the surveyed participants was 44 years, with the majority (86.3%) being female. Despite concerns, the availability of gluten-free products was reported as being unchanged compared to before the pandemic by 3 out of 4 respondents. Also, our survey did not reveal significant changes regarding adherence to gluten-free diet during the pandemic, as assessed by Biagi score. However, 25.3% of respondents reported feelings of anxiety and 29.5% of depression, but only 3.2% benefited from psychological or psychiatric support. About one quarter of participants postponed their medical checkups due to fear of getting infected. One fifth of respondents declared having been infected with the novel coronavirus, but only 10% of them were hospitalized. One third of respondents had already gotten the COVID-19 vaccine and reported only minor side effects. Also, over half (57.9%) of survey participants declared they had not received enough information during the pandemic. Conclusions: Among our study respondents, availability and adherence to gluten-free diet was not markedly changed during the pandemic, but they were significantly impacted by the lack of CD-specific information about SARS-CoV2 infection and vaccination.

Keywords: celiac disease, pandemic, COVID-19, gluten-free diet, vaccination

Cite This Article: Vasile Daniel Balaban, Alina Dima, Catalin Augustin Dima, Alina Popp, Ciprian Jurcut, and Mariana Jinga, “Impact of the COVID-19 Pandemic in Romanian Celiac Disease Patients by E-Survey.” International Journal of Celiac Disease, vol. 10, no. x (2022): XX-XX. doi: xxxxxxxx.

1. Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) disease (COVID-19) pandemic, as declared by WHO on March 11th 2020 [1], has put unprecedented pressure on healthcare systems worldwide, creating gaps in care for both acute and chronic patients. Especially in limited resource countries, the burden of the pandemic overwhelmed the already fragile medical systems, both at infrastructure and human resource level. While medical emergencies have been prioritized even in the peak months of the pandemic, care of patients with chronic diseases has suffered significant disruptions due to COVID-19 [2,3]. In fact, chronic diseases account for significant resources in healthcare systems, and the relocation of some of these resources to COVID-19 has created discontinuities in the provision of chronic patients’ medical care, including those suffering from digestive diseases [4,5].

Celiac disease (CD) is one of the most frequent chronic digestive diseases, affecting about 1 in 100 individuals, but remains severely underdiagnosed [6,7]. CD is a systemic immune-mediated disease triggered by gluten ingestion in genetically susceptible individuals [8,9]. Unlike other chronic digestive diseases, CD is distinguished by the fact that, on the one hand, it does not require frequent medical visits for routine prescriptions or follow-up exams if the course of the disease is uneventful. On the other hand, CD management is dietary, so access to gluten-free products is essential for controlling the gluten-driven autoimmune cascade in these individuals. Moreover, the novel coronavirus SARS-CoV-2 is known to enter human cells using the Angiotensin Converting Enzyme 2 (ACE2) receptor, which is highly expressed in
enterocytes too [10]. As CD affects mainly the small bowel, the SARS-CoV2 interaction with the diseased intestinal mucosa of CD patients seems highly relevant to getting in-depth insight on gastrointestinal involvement in COVID-19.

For patients with chronic diseases, the most important obstacles during the pandemic were the limitation of access to medical services, the designation of their usual healthcare provider as a COVID-19 unit, and the avoidance of medical institutions due to fear of getting infected [11]. For CD patients, a potential major concern was that of reduced access to gluten-free foods and restaurants. Given the particularities of CD, we hypothesize a lower impact of the pandemic on CD itself concerning the limited interaction with the healthcare system, but a significant impact concerning access to gluten-free diet, in the setting of the lockdown measures. With a gluten-free diet being the only treatment for CD, social restriction and home isolation measures generated significant changes in the lifestyle s of CD individuals by interfering with eating-out habits, provisioning of gluten-free products, and at-home preparation of food. In this setting, CD patients were challenged to adapt their habits in order to maintain strict adherence to the gluten-free diet. Along with the impact on diet, COVID-19 related restrictions have also generated CD diagnostic and therapeutic delays, which may sometimes be life-threatening, such as the celiac crisis [12,13].

With this research, we aimed to assess the impact of the pandemic in Romanian CD patients, both on a personal and medical level, using an online survey.

2. Materials and Methods

2.1. Study Design and Participants

An online questionnaire was designed by the study authors according to the Checklist for Reporting Results of Internet E-Surveys (CHERRIES) [14], and distributed through the social media channel of the Romanian CD patient association. Inclusion criteria for participants were: (1) having a diagnosis of CD, (2) understanding all aspects of the survey and consenting to participate, (3) being ≥ 18 years old at the time of completing the questionnaire. Pediatric CD individuals were excluded for the purpose of this study.

The survey consisted of 46 cascade questions, assessing the demographic profile of respondents, diagnostic features, the impact of restrictions on personal and professional life, as well as experience with COVID-19 infection and vaccination, when applicable – available as Supplementary File 1. Several filter questions were designed throughout the survey, with skip logic if the item in question was not applicable to the respondent – specifically those regarding the COVID-19 infection (Q29 was set as skip logic for Q30-39) and COVID-19 vaccination (Q40 and Q42 were skip logic questions for Q43-46). All questions were marked as mandatory and required at least one valid response. The first eleven questions (Q1-Q11) surveyed the demographic profile of respondents, referring to age, gender, socio-economic status, and details about the CD diagnosis (type of medical unit and physician who set the diagnosis, diagnostic workup, and gluten-free diet recommendation – as presented in Table 1). Q12-Q15 and Q24-Q28 addressed the impact of COVID-19 on personal and professional levels, as well as on access to healthcare services (See Table 2). Questions 16-23 assessed the adherence to the gluten-free diet (presented in Table 3), before and during the pandemic, and were adapted after the Biagi score [15]. Question 29 asked whether respondents had been infected with SARS-CoV2, and Q30-39, which asked for details about the clinical course of the infection, were available only for participants who declared having had COVID-19 (see Table 4). The last block of questions was designed to look at respondents’ experience with COVID-19 vaccination, whether they had been vaccinated or not, the reason for not being vaccinated, and adverse reactions due to vaccination, Q40-46 (see Table 5).

2.2. Instrument

The survey was introduced on a dedicated platform (SurveyMonkey®) and a collector link was generated to be distributed online. Based on the IP address registered, only one response from the same device was allowed. Response editing was available until the survey was completed. All respondents voluntarily filled out the survey during a one-month period (March 21st – April 21st, 2021). The timing of data collection was set after one year of the pandemic and overlapped with the third wave of COVID-19 infections in Romania, along with a steady increase in vaccination rates in the second round of the vaccination schedule, which included chronic disease patients and individuals aged over 65. Social restriction and evening lockdown measures were in force during the time-period of the survey, according to the State of Alert on the Romanian territory [16,17]. Upon accessing the survey link, an introduction was available for respondents, stating the premises, terms of participation, and goals of the research. Only fully completed questionnaire reports meeting inclusion and exclusion criteria were included in the final analysis – Figure 1.

2.3. Ethics

As stated in the introductory section, participation in the survey was voluntary and filling out the survey implied the respondents’ consent to be included in this research. Ethics approval was granted by the local Ethics Committee (No 5752/2021).

2.4. Data Analysis

Descriptive statistics were used for reporting the data gathered through the questionnaire. Statistics were done using Microsoft Excel 16.35 and SPSS Statistics 25 software Armonk, NY, USA. Continuous variables are expressed as median (range) and categorical variables are expressed as count and percentage.
### Table 1. Demographic profile of the study participants included (n=95)

| Questions 1-11 (%) | Gender          |
|--------------------|-----------------|
| Q1 Male            | 13 (13.7%)      |
| Female             | 82 (86.3%)      |
| Q2 Age, years (median, range) | 44 (19-69) |
| Q3 Disease duration, years (median, range) | 5 (0-47) |
| Q4 Introduction of the GFD | At diagnosis 79 (83.2%) |
|                     | Before diagnosis 7 (7.4%) |
|                     | Some weeks-months after diagnosis 7 (7.4%) |
|                     | Not yet started, still in the course of getting diagnosed 2 (2.1%) |
| Q5 Setting where diagnosis was done | Public Clinic/Outpatient/Hospital 61 (64.2%) |
|                     | Private Clinic/Outpatient/Hospital 32 (33.7%) |
|                     | General practitioners’ office 2 (2.1%) |
| Q6 Physician who set the diagnosis | Gastroenterologist 81 (85.3%) |
|                     | Internal medicine specialist 8 (8.4%) |
|                     | General practitioner 1 (1.1%) |
|                     | Other (dermatologist, nutritionist, pediatrician) 5 (5.3%) |
| CD diagnosis – tests used * | Serology 69 (72.6%) |
|                     | Genetic testing (HLA) 9 (9.5%) |
| Q7 Endoscopy without biopsy | 9 (9.5%) |
| Endoscopy with biopsies | 76 (80%) |
| Other (videocapsule, stool analysis) | 5 (5.3%) |
| Don’t remember | 1 (1.1%) |
| Disease activity at the last medical visit | Stationary 19 (20%) |
|                     | Remission 24 (25.3%) |
| Q8 Improved | 30 (31.6%) |
| Never went to the doctor after diagnosis | 17 (17.9%) |
| Don’t know | 3 (3.2%) |
| Other (pending test results) | 2 (2.1%) |
| Marital status | Single 24 (25.3%) |
| Q9 Married | 60 (63.2%) |
| Divorced | 8 (8.4%) |
| Widowed | 3 (3.2%) |
| Living conditions * | Single 16 (16.8%) |
|                     | With husband/wife 58 (61.1%) |
|                     | With kids 48 (50.5%) |
|                     | With parents 14 (14.7%) |
|                     | Something else (with partner, friends) 6 (6.3%) |
| Monthly income * | Salary 75 (78.9%) |
| Q11 Pension | 13 (13.7%) |
| Income from other family members | 16 (16.8%) |
| Something else | 3 (3.2%) |

* Multiple answers. Abbreviations: Q – question, CD – celiac disease, GFD – gluten-free diet.

### Table 2. Impact of COVID-19 on respondents’ personal and professional life

| Questions 12-15 and 24-28 (%) | Q12 Change in monthly income during pandemic |
|--------------------------------|--------------------------------------------|
|                                | Unchanged 71 (74.7%)                       |
|                                | Lower monthly income 14 (14.7%)            |
|                                | Higher monthly income 5 (5.3%)             |
|                                | I lost my monthly income 2 (2.1%)          |
|                                | Something else 3 (3.2%)                    |
| Q13 Changes in workplace activity during pandemic | Unchanged 50 (52.6%) |
|                                | Same employer, but at-home work 19 (20%)   |
|                                | Same employer, less working days and lower salary 4 (4.2%) |
|                                | Lost my job and got another one 1 (1.1%)   |
|                                | Lost my job and couldn't get another one 2 (2.1%) |
|                                | Other responses 19 (20%)                   |
| Q15 to get out less frequent | A single family member went shopping, to limit risk of infection 48 (50.5%) |
|                                | Emotional status during pandemic * 35 (36.8%) |
|                                | More sad/depressed 24 (25.3%)              |
|                                | More nervous/angry 28 (29.5%)              |
|                                | Alternating feelings of anxiety/depression 16 (16.8%) |
|                                | Benefited of psychological/psychiatric support 3 (3.2%) |
|                                | More relaxed/calm 6 (6.3%)                 |
| Q25 Less available | 70 (73.7%) |
|                                | Don’t know 6 (6.3%)                       |
|                                | Access to medical services during pandemic GP only 15 (15.8%) |
|                                | GP and private clinics only 23 (24.2%)     |
|                                | Admitted in a public hospital 9 (9.5%)     |
|                                | Did hot have access to public hospital services 2 (2.1%) |
|                                | Postponed medical visits due to fear of getting infected 24 (25.3%) |
|                                | Did not need healthcare during pandemic 22 (23.2%) |
|                                | Was there enough information available for CD patients during pandemic? 28 (29.5%) |
| Q27 Yes | 18 (18.9%) |
| No | 55 (57.9%) |
| Don’t know/don’t answer | 22 (23.2%) |
| Q29 Sources of information about COVID-19 in CD individuals * | GP 11 (11.6%) |
|                                | Specialist physician 12 (12.6%)            |
|                                | Online support groups 49 (51.6%)           |
|                                | Patients’ association 23 (24.2%)           |
|                                | Did not have access to information 26 (27.4%) |
|                                | Other 10 (10.5%)                          |

* Multiple answers. Abbreviations: Q – question, COVID-19 - the coronavirus disease 2019, CD – celiac disease, GFD – gluten-free diet, GP - General practitioner.
Table 3. Adherence to the GFD, before and during the pandemic

| Questions 16-23 (%) | Yes, a normal portion (%) | Yes, more frequent (%) | No (%) | As compared to before the pandemic, did you eat gluten voluntarily during the pandemic? | Yes, the same amount (%) | Yes, more frequent (%) | No (%) |
|---------------------|--------------------------|------------------------|--------|---------------------------------------------------------------------------------|--------------------------|------------------------|--------|
| Before the pandemic - did you eat gluten voluntarily? | 7 (7.4%) | 1 (1.1%) | 83 (87.4%) | Yes, to the same extent | 7 (7.4%) | 2 (2.1%) | 3 (3.2%) |
| Q16 Just a taste, rarely | 4 (4.2%) | 1 (1.1%) | 3 (3.2%) | No, before I used to eat gluten, but now I’m strictly avoiding gluten | 75 (78.9%) | No, I did not eat gluten neither before, nor during the pandemic |
| Q17 Yes, less frequent | 8 (8.4%) | 10 (10.5%) | Before the pandemic - When you ate out, did you tell the person who was cooking about your disease? | Yes, to the same extent | 77 (81.1%) | No, I was not checking the labels neither before, nor during the pandemic |
| Q18 Yes | 84 (88.4%) | 7 (7.4%) | No | No, before I used to tell the cooking staff, but during pandemic I did not | 1 (1.1%) | No, I was not telling the cooking staff about my disease neither before, nor during the pandemic |
| Q19 Yes, more frequent | 3 (3.2%) | 2 (2.1%) | Before the pandemic – Did you check the labels of packaged food? | Yes, to the same extent | 85 (89.5%) | No, before I used to check the labels, but during pandemic I did not |
| Q20 Yes, less frequent | 4 (4.2%) | 2 (2.1%) | No | No, I was not checking the labels neither before, nor during the pandemic | 1 (1.1%) | Before the pandemic – Did you only eat packaged food guaranteed by the Coeliac Association/crossed grain symbol? |
| Q21 Yes | 64 (67.4%) | 2 (2.1%) | No | As compared to before the pandemic, did you only eat packaged food guaranteed by the Coeliac Association/crossed grain symbol during the pandemic? | Yes, as before the pandemic, I eat only certified products | 64 (67.4%) | No, before the pandemic I used to eat non-certified products, but now I eat only certified products |
| Q22 Yes | 64 (67.4%) | 4 (4.2%) | Yes | Yes, as before the pandemic, I eat only certified products, but now I eat non-certified products also | Yes, before the pandemic, I eat non-certified products 23 (24.2%) |
| Q23 Yes, a normal portion | 7 (7.4%) | 4 (4.2%) | Yes | No, as before the pandemic, I eat non-certified products 23 (24.2%) |

Abbreviations: Q – question, COVID19 - the coronavirus disease 2019, CD – celiac disease.

Table 4. COVID-19 infection among study participants

| Questions Q29-Q39 (%) | COVID-19 diagnosis (%) | No (%) | Month of diagnosis (%) | Feb-June 2020 (%) | July-December 2020 (%) | January-April 2021 (%) | Exposure and setting for getting infected with COVID-19 (%) | Workplace (%) |
|-----------------------|------------------------|--------|------------------------|-------------------|------------------------|------------------------|----------------------------------|-------------|
| Q29 Yes | 20 (21.1%) | 75 (78.9%) | No | 1 (5%) | 14 (70%) | 5 (25%) | 3 (15%) |
| Q30 Yes, more frequent | 3 (3.2%) | 4 (20%) | As compared to before the pandemic, did you only eat packaged food? | Yes | 6 (30%) | 11 (55%) | 1 (5%) | 9 (45%) |
| Q31 Yes, less frequent | 2 (15.4%) | 8 (40%) | No, before I used to eat gluten, but now I'm strictly avoiding gluten | Yes, less frequent | 13 (65%) | 13 (65%) | 2 (10%) | 3 (15%) |
| Q32 Yes, more frequent | 10 (10.5%) | 40 (20%) | No, before I used to tell the cooking staff, but during pandemic I did not | Yes, to the same extent | 3 (15%) | 3 (15%) | 3 (15%) | 4 (20%) |
| Q33 Yes, less frequent | 1 (1.1%) | 2 (10%) | No, I was not checking the labels neither before, nor during the pandemic | No, I was not telling the cooking staff about my disease neither before, nor during the pandemic | 9 (45%) | 9 (45%) | 2 (10%) | 2 (10%) |
| Q34 Yes, a normal portion | 7 (7.7%) | 4 (20%) | Before the pandemic – When you ate out, did you tell the person who was cooking about your disease? | Yes, to the same extent | 69 (78.9%) | 69 (78.9%) | 69 (78.9%) | 2 (10%) |
| Q35 Yes, less frequent | 1 (5%) | 1 (5%) | No | No, before I used to check the labels, but during pandemic I did not | 1 (5%) | No, I was not checking the labels neither before, nor during the pandemic | 3 (15%) | 2 (10%) |
| Q36 Yes, more frequent | 13 (65%) | 7 (35%) | No | No, before I used to tell the cooking staff, but during pandemic I did not | 1 (5%) | No, before I used to check the labels, but during pandemic I did not | 3 (15%) | 2 (10%) |
| Q37 Yes, less frequent | 13 (65%) | 7 (35%) | No, before I used to tell the cooking staff, but during pandemic I did not | No, I was not checking the labels neither before, nor during the pandemic | 1 (5%) | No, before I used to check the labels, but during pandemic I did not | 3 (15%) | 2 (10%) |
| Q38 Yes, a normal portion | 7 (7.7%) | 4 (20%) | Before the pandemic – Did you only eat packaged food guaranteed by the Coeliac Association/crossed grain symbol? | Yes, as before the pandemic, I eat only certified products | 69 (78.9%) | 69 (78.9%) | 69 (78.9%) | 2 (10%) |
| Q39 Yes, less frequent | 1 (5%) | 1 (5%) | No | No, before I used to check the labels, but during pandemic I did not | 1 (5%) | No, before I used to check the labels, but during pandemic I did not | 3 (15%) | 2 (10%) |

Abbreviations: Q – question, COVID19 - the coronavirus disease 2019.
Table 5. Experience with COVID-19 vaccination among study respondents

| Questions Q40-Q46 | (%)       |
|-------------------|-----------|
| Q40 Did you get vaccinated against COVID-19? |            |
| Yes               | 34 (35.8%)|
| No                | 61 (64.2%)|
| Q41 Reasons for not being COVID-19 vaccinated * |            |
| Not assured I can get the vaccine, as I'm suffering from CD | 24 (39.3%) |
| Did not manage to get an appointment, but I intend to get vaccinated | 19 (31.1%) |
| Q42 Partial or full vaccination |            |
| Both doses        | 20 (58.8%)|
| First dose only, scheduled for the second | 14 (41.2%) |
| Q43 Side effects after first dose of COVID-19 vaccine * |            |
| Not applicable, did not have any side effects | 7 |
| Pain at the injection site | 15 |
| Swelling at the injection site | 1 |
| Neck/axillary lymphadenopathy | 1 |
| Fatigue | 1 |
| Q44 Additional side effects after the 2nd dose of COVID-19 vaccine * |            |
| None, neither after first nor after second dose | 7 |
| Same side effects as after first dose | 4 |
| Same side effects as after first dose, but more severe | 1 |
| Additional side effects compared to first dose | 8 |
| Q45 Onset of side effects after the second dose of COVID-19 vaccine |            |
| 4-8 hours | 4 |
| 8-12 hours | 4 |
| Day after | 4 |
| 2-3 days after | 1 |

* Multiple answers., Abbreviations: Q – question, COVID19 - the coronavirus disease 2019, CD – celiac disease.

Figure 1. Flow-chart for recruitment of respondents
3. Results

Altogether, 113 responses were gathered during the one-month study period, of which 102 were complete responses. Furthermore, 7 respondents were excluded as being self-diagnosed with CD, and the remaining 95 were included in the final analysis. The median age of respondents was 44 (range 19-69), with 86.3% of the female gender (see Table 1).

80% of patients were biopsy-proven CD, and the diagnosis was set by the gastroenterologist in 85.3% of cases. Most of the respondents (64.2%) were diagnosed in a public medical institution, while the remaining received their diagnosis in a private medical unit or at their general practitioner’s office. Regarding disease activity, over half (56.9%) of interviewed patients were either improved or in remission at the time of the survey.

At a professional level, half of the respondents (52.6%) reported unchanged activity at their workplace, and three out of four participants (74.7%) did not have a change in their revenue related to COVID-19. However, 3.2% of respondents had an early retirement during the pandemic, but none reported higher levels of anxiety or depression (Table 2).

Regarding adherence to the gluten-free diet, as assessed by Biagi questionnaire, there were insignificant changes in gluten consumption, eating-out behavior, or food-packaging check during the pandemic, as compared to the period before the pandemic – 87.4% participants reported strict adherence to gluten-free diet before COVID-19 while 78.9% continued strict exclusion of gluten during the pandemic (Table 3). Similar results were seen when asking patients if they were telling the cooking personnel about their disease when eating out: an affirmative answer was reported by 88.4% of participants for the period before and by 81.1% during the pandemic. Subjects taking part in the survey were carefully checking the labels of packaged food both before and during the pandemic, with a frequency of 95.8% and 89.5%, respectively. A lower rate of positive responses was registered when inquiring participants if they only ate packaged foods certified with the crossed grain symbol, with 67.4% of patients having declared so both before and during the pandemic time.

Regarding the impact on a personal level, 28/95 (29.5%) and 24/95 (25.3%) CD patients reported being either more anxious or depressed, while a minority of them (3.2%) required psychological or psychiatric support during the pandemic. Among respondents who reported higher levels of anxiety, the vast majority (96.4%) were female CD patients.

With regard to the accessibility of gluten-free foods, 73.7% of the survey participants considered that dietary products were available to the same extent as before the pandemic. On the other hand, access to healthcare services was somehow limited, with one fourth of respondents (24.2%) having declared they could only be seen by their general practitioner and in private medical clinics, and another fourth (25.3%) postponing their medical checkups due to fear of getting infected (see Table 2). Among those who reported postponing of medical visits, higher anxiety was declared by one out of three respondents.

Over half of survey participants (57.9%) were not satisfied with the information available for CD individuals during the COVID-19 pandemic, regarding specific implications for their digestive disease, risks associated with SARS-CoV2 infection, and COVID-19 vaccination. Of note, over two thirds of CD respondents who experienced COVID-19 (14/20) were among them. Most of the respondents were getting informed by means of online support groups (51.6%) or patients’ associations (24.2%) (Table 2).

About one in five (21.1%) subjects reported having COVID-19, but only two out of twenty (10%) needed hospitalization. The median age of SARS-CoV2 infected CD respondents was 36 years, lower than that of noninfected study participants. Also, the proportion of males was higher among infected than non-infected respondents (25% vs 10.7%). 85% of participants who declared having COVID-19 were on a gluten-free diet for more than two years. None of the hospitalized patients required supplemental oxygen. With all non-severe COVID-19, no rescue therapies were reported.

COVID-19-related symptoms usually lasted less than one week (40%), except for anosmia and ageusia, which lasted for more than two weeks in 45% and 30% of respondents, respectively (Table 4).

About one third of respondents (35.8%) declared having been vaccinated with at least one dose of the available vaccines. There was significant uncertainty with regard to interactions between vaccination and CD-autoimmunity, with as much as 39.3% of study participants not getting vaccinated because they were not assured that CD patients could have the vaccine. Among vaccinated subjects, the most frequent side effect was pain at the injection site in 44.1%, followed by headache and chills in 11.8% (Table 5).

4. Discussion

The novel coronavirus and its associated disease COVID-19 have undoubtedly kept the headlines for the beginning of the twenty-twenties decade. Medical professionals, patients and healthcare policymakers altogether had to deal with rapidly evolving changes in providing medical services [18].

As a chronic digestive disease with special dietary needs, CD was in the spotlight during the pandemic. The main issues for CD patients were availability and adherence to a gluten-free diet, as well as uncertainties regarding an elevated risk of infection and worse outcomes with COVID-19.

Among the factors that might influence the impact of COVID-19 in CD individuals, disease activity and adherence to a gluten-free diet have been assessed in several papers focusing on the consequences of the pandemic in CD. Falcomer et al. [19] have shown that the quality of life of Brazilian CD patients was mostly impacted by gastrointestinal aspects, independently of gender, age, marital status, and SARS-CoV2 infection, but was correlated with adhesion to the gluten-free diet. Others have looked at the impact of lockdown measures on diet and revealed improved adherence, particularly in patients with worse disease control, in whom home isolation provided an opportunity to avoid contamination and encouraged at-home cooking using naturally...
gluten-free foods [20]. An increase in home food preparation was also reported by Bascuñán et al. [21], among 331 individuals following a gluten-free diet, but over half of the respondents in this study admitted having consumed gluten-containing foods also, without any differences seen between those who were on the diet because of medical reasons (CD, non-celiac gluten sensitivity or wheat allergy) or those who were following it as a trendy healthy diet, and independently of diet duration [21].

Due to reports of increased risk of infections in CD, a major concern for contacting SARS-CoV-2 and developing severe COVID-19 emerged among CD patients during pandemic. Indeed, CD has been previously reported to be associated with an increased risk of respiratory infections and viral illness [22-28] and increased mortality attributed to respiratory disease [27,29]. This has been hypothesized to be due to functional hyposplenism and defective immunity in CD [30-33]. Immune dysregulation has been reported in COVID-19 and this may trigger the development of associated autoimmune phenomena, which have been associated with poor prognosis [34].

However, according to available reports, there is no data to support an increased risk of COVID-19 in CD patients [35-39]. In fact, currently available data has shown that the risk of contracting COVID-19 is not higher in CD patients [35-37]. Moreover, a population-based study from Sweden has shown that CD is not associated with severe COVID-19 (hospitalization for COVID-19, admission to an ICU unit, and/or death attributed to COVID-19) compared to controls [36]. Among our SARS-CoV2 infected study participants, only non-severe disease was reported. Resolution of symptoms which occurred at diagnosis was seen in 4 out of 10 COVID-19 CD patients within the first week, but some of these symptoms or later-occurring ones, considered COVID-19 related, were declared to last more than two weeks by 65% of infected respondents. Anosmia and ageusia were reported as persistent symptoms beyond the acute phase, but neurological manifestations may also be related to extraintestinal autoimmune phenomena in CD individuals [40,41].

Despite evidence showing the odds of contracting COVID-19 in CD patients is similar to that of the general population, individuals suffering from CD still perceive they are at higher risk [42]. This can be associated with higher levels of pandemic-related anxiety and could be due to insufficient communication of reliable data about their illness during the pandemic. In our survey, over half of respondents (57.9%) considered there was not enough information available for celiac individuals during pandemic and over one fourth (29.5%) reported higher anxiety due to the pandemic. This can contribute to increased pandemic-related stress and generate detrimental consequences for mental health, which in turn has been reported to be associated with decreased immunity [43]. Of note, in the survey by Zhen et al. [42], members of CD’s associations were less likely to perceive detrimental consequences for mental health, which in turn has been reported to be associated with decreased immunity [43]. Of note, in the survey by Zhen et al. [42], members of CD’s associations were less likely to perceive detrimental consequences for mental health, which in turn has been reported to be associated with decreased immunity [43]. Of note, in the survey by Zhen et al. [42], members of CD’s associations were less likely to perceive detrimental consequences for mental health, which in turn has been reported to be associated with decreased immunity [43]. Of note, in the survey by Zhen et al. [42], members of CD’s associations were less likely to perceive detrimental consequences for mental health, which in turn has been reported to be associated with decreased immunity [43]. Of note, in the survey by Zhen et al. [42], members of CD’s associations were less likely to perceive detrimental consequences for mental health, which in turn has been reported to be associated with decreased immunity [43]. Of note, in the survey by Zhen et al. [42], members of CD’s associations were less likely to perceive detrimental consequences for mental health, which in turn has been reported to be associated with decreased immunity [43]. Of note, in the survey by Zhen et al. [42], members of CD’s associations were less likely to perceive detrimental consequences for mental health, which in turn has been reported to be associated with decreased immunity [43]. Of note, in the survey by Zhen et al. [42], members of CD’s associations were less likely to perceive detrimental consequences for mental health, which in turn has been reported to be associated with decreased immunity [43]. Of note, in the survey by Zhen et al. [42], members of CD’s associations were less likely to perceive detrimental consequences for mental health, which in turn has been reported to be associated with decreased immunity [43]. Of note, in the survey by Zhen et al. [42], members of CD’s associations were less likely to perceive detrimental consequences for mental health, which in turn has been reported to be associated with decreased immunity [43]. Of note, in the survey by Zhen et al. [42], members of CD’s associations were less likely to perceive detrimental consequences for mental health, which in turn has been reported to be associated with decreased immunity [43]. Of note, in the survey by Zhen et al. [42], members of CD’s associations were less likely to perceive detrimental consequences for mental health, which in turn has been reported to be associated with decreased immunity [43]. Of note, in the survey by Zhen et al. [42], members of CD’s associations were less likely to perceive detrimental consequences for mental health, which in turn has been reported to be associated with decreased immunity [43]. Of note, in the survey by Zhen et al. [42], members of CD’s associations were less likely to perceive detrimental consequences for mental health, which in turn has been reported to be associated with decreased immunity [43]. Of note, in the survey by Zhen et al. [42], members of CD’s associations were less likely to perceive detrimental consequences for mental health, which in turn has been reported to be associated with decreased immunity [43].
and checking of labels of packaged food during the pandemic, as compared to the period before the pandemic. Lockdowns and social restriction measures imposed by authorities during the pandemic have undoubtedly created disruptions in healthcare access for a significant proportion of patients suffering from chronic diseases, CD included. A significant proportion of our study respondents declared limited access to medical services during the pandemic, some being able to reach their GP only, others seeking care in private clinics also, and an alarmingly high rate of 25.3% reporting postponing of medical visits due to fear of contracting SARS-CoV2. There are several studies showing that reduced access to healthcare during the pandemic was successfully substituted by the use of telemedicine for CD patients [44,51,52,53]. In fact, CD patients declared themselves satisfied with remote consultations and even explicitly asked for them [44]. This could represent an opportunity to set new approaches for follow-up of CD patients, which has been reported to be far from satisfactory due to low adherence [54,55].

With regard to vaccination, CD has been reported to be associated with low responsiveness to hepatitis virus B vaccination [56,57]. Among our study respondents, there was significant uncertainty regarding the COVID-19 vaccine among CD patients, with 39.3% reporting being unsure if CD individuals could get vaccinated. Vaccine hesitancy among our participants might be a consequence of the reduced availability of information about COVID-19 vaccination among this patient group. As a chronic disease, CD was eligible for vaccination in the second round according to the Romanian COVID-19 vaccination schedule, which was underway during the time of data collection. An Italian study looking at vaccination willingness among 103 CD patients revealed that 25.2% of respondents were hesitant and 4.8% were refusing the COVID-19 vaccine, the main reason being fear of adverse effects (68.2%); factors associated with vaccine willingness were positive attitude to vaccination in general, adherence to the gluten-free diet, and perception of good knowledge about COVID-19 and its vaccines [58]. Vaccination hesitancy among CD respondents in our study was higher compared to surveyed physicians or autoimmune disease patients during a similar time period of the pandemic [59,60]. Data on immune response to COVID-19 infection has shown that CD patients exhibit an anti-SARS-CoV-2 Ig positivity and profile similar to non-celiac controls, except for anti-nucleocapsid IgA, probably due to the associated IgA hypogammaglobulinemia [61]. A study including a small cohort of CD individuals did not show an increased risk of disease flaring after COVID-19 vaccination [62]. Also, only mild side effects were reported by our study respondents. Further data on vaccinated CD patients will shed light on this topic.

Our survey intended to capture the self-perceived burden of COVID-19 on Romanian CD patients, one year after being declared pandemic, in a time-frame with increasing number of infections (277 new cases per million people on March 21st 2021, more than double compared to the incidence one month previously), despite social restriction and lockdown measures (COVID-19 stringency index – 63.89 out of 100, which is the strictest) and despite a good progression of the vaccination campaign (14.56% vaccinated with at least one dose on April 21st, 2021) [63,64].

The current web-based research has some limitations. The first is represented by the low number of respondents, which is a risk in survey-based research – up to ten times lower response rates have been reported in online surveys compared to face-to-face direct collection of data [65]. However, there is wide age distribution among the study respondents, which reflect active members in CD communities. Also, the use of a convenience sample is also a potential source of bias, but internet dissemination of the survey in online patient groups was the most accessible way to reach individuals during pandemic. Considering the large female predominance of respondents, we acknowledge that there may be some gender-specific effects in self-reported items such as emotional swings during pandemic or vaccination side-effects. We also acknowledge the limit in using an unvalidated questionnaire, however its development was based on a thorough literature search conducted by the study authors in generating the survey items, design of straightforward questions and adapting of previously validated scales such as Biagi score. Not least, our research does not provide a comparison with the general population or other disease patient groups. However, data resulted from this survey adds to the currently available international experiences on COVID-19 and CD, which are each particular by specific culinary behavior and by extent of COVID-19 impact on local healthcare systems.

5. Conclusion

In a survey which assessed perceptions of CD individuals during the COVID-19 crisis, no significant impact was seen concerning availability and adherence to gluten-free diet. However a large proportion of CD patients reported feelings of anxiety and depression, amid growing concerns about COVID-19 and a lack of CD-specific information during the pandemic. Significant vaccine hesitancy was also seen among CD patients, mostly due to the low availability of information about COVID-19 vaccination among this patient group. Better awareness is needed for CD patients and online channels of patient groups or associations, along with implementation of virtual communication platforms, seem appropriate for conveying COVID-19-related messages.

Author Contributions

All authors discussed the research idea and agreed on the manuscript structure and content. All authors contributed to the manuscript writing. All authors approved the last draft and the manuscript submission.

Funding

No specific grant from any public agency, commercial or not-for-profit sectors was received for the presented research.
Conflicts of Interest

None of the authors has any interests that would constitute a conflict of interest with the current article.

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Supplementary File

RO-Celiac-COVID: A questionnaire-based study on the impact of the COVID-19 pandemic on Romanian patients with celiac disease

Dear patient,

You are in medical records with celiac disease (gluten enteropathy). As you well know, the COVID-19 pandemic has put unprecedented pressure on global health systems. Patients with chronic digestive diseases also suffered in the context of the COVID-19 pandemic, due to limited healthcare access and allocation of significant resources (human, material, infrastructure) for SARS-CoV2 infected patients. This questionnaire is intended for all patients diagnosed with celiac disease and is conducted by a multidisciplinary team of doctors from UMF Carol Davila. We invite you to take part in this questionnaire that evaluates the impact of the COVID-19 pandemic on patients with celiac disease. By participating in this research, you bring a benefit to the entire celiac community, by helping to determine the current problems and needs of patients with celiac disease in the context of the COVID-19 pandemic. Your participation is voluntary and implies your agreement to use the answers to conduct an analysis of the consequences of the COVID-19 pandemic among celiac disease individuals. The questionnaire takes about 5-10 minutes to complete. Data collected through this
questionnaire will be processed completely anonymously. You can refuse to participate in this questionnaire or withdraw your participation at any time before completing the survey. Results will be presented in the form of a research paper that will be available online. For further questions or details, please contact physician.survey.covid19@gmail.com. Thanks for taking the time to complete this questionnaire!

Q1. What is your gender?
   • Male
   • Female

Q2. What is your age?

Q3. What year were you diagnosed with celiac disease?

Q4. Since when did you start a gluten-free diet? (please choose only one answer)
   • At diagnosis
   • Before diagnosis
   • Some weeks-months after diagnosis
   • Not yet started, still in the course of getting diagnosed
   • Don’t know/don’t remember

Q5. Where did you get the diagnosis of celiac disease? (please choose only one answer)
   • Public Clinic/Outpatient/Hospital
   • Private Clinic/Outpatient/Hospital
   • General practitioners’ office

Q6. Who diagnosed celiac disease: (please choose only one answer)
   • Gastroenterologist
   • Internal medicine specialist
   • General practitioner
   • Self-diagnosed
   • Other (please mention)

Q7. When I was diagnosed with celiac disease, the following tests were performed: (several answers can be checked/completed)
   • Serology (anti-tissue transglutaminase, anti-endomisium, anti-deamidated gliadin peptides)
   • Genetic testing (HLA)
   • Endoscopy without biopsy
   • Endoscopy with biopsies
   • Don’t know/Don’t remember
   • Other (please mention)

Q8. At present, after the last medical visit, the evolution of celiac disease was, according to the discussion with the doctor and the laboratory workup: (please choose only one answer)
   • Stationary
   • Remission
   • Improved
   • Never went to the doctor after diagnosis
   • Don’t know
   • Other (please mention)

Q9. What is your marital status? (please choose only one answer)
   • Single
   • Married
   • Divorced
   • Widowed
Q10. Living conditions: (several answers can be checked/completed)
• Single
• With husband/wife
• With kids
• With parents
• Something else (please mention)

Q11. Where does your monthly income come from?
• Salary
• Pension
• Income from other family members
• Something else (please mention)

Q12. How has your monthly income changed during the COVID-19 pandemic? (please choose only one answer)
Unchanged
• Lower monthly income
• Higher monthly income
• I lost my monthly income
• Something else (please mention)

Q13. How has the COVID-19 pandemic affected your workplace? (please choose only one answer)
• My professional activity was not influenced
• I continued to work for the same employer, but from home
• I continued to work for the same employer, but with mandatory days off and a lower salary
• I involuntarily lost my job and got another job
• I involuntarily lost my job and failed to get another one
• I voluntarily left my job and got another job
• I left my job voluntarily and did not get another job so far
• Not applicable (pupil/student/retired)
• Other (please mention):

Q14. To what extent did you comply with the instructions imposed by the authorities regarding home isolation? (please choose only one answer)
• I strictly adhered to the isolation measures at home
• I tried to follow the isolation instructions (I left the house only for good reasons)
• I tried to respect the most important measures, I left the house for less founded reasons also
• I tried to get out of the house as much as possible during periods of isolation, usually for reasons not considered by the authorities as grounded

Q15. How did you proceed with your daily shopping during the pandemic / isolation period at home? (several answers can be checked/completed)
• I went shopping as often as possible so that I could leave the house motivated
• When we went shopping, we bought products that would last for several days, in order to get out of the house as rarely as possible.
• We usually designated a single family member to go shopping to limit the risk of COVID-19 infection.
• I usually went shopping with another family member

Q16. Before the pandemic - did you eat gluten voluntarily?
• Yes, a normal portion
• Just a taste, rarely
• Just a taste, often
• No

Q17. As compared to before the pandemic, did you eat gluten voluntarily during the pandemic?
• Yes, the same amount
• Yes, more frequent
• Yes, less frequent
• No, before I used to eat gluten, but now I’m strictly avoiding gluten
• No, I did not eat gluten neither before, nor during the pandemic
Q18. Before the pandemic - When you ate out, did you tell the person who was cooking about your disease?
• Yes
• No

Q19. As compared to before the pandemic, when you ate out, did you tell the person who was cooking about your disease during the pandemic?
• Yes, to the same extent
• Yes, more frequent
• Yes, less frequent
• No, before I used to tell the cooking staff, but during pandemic I did not
• No, I was not telling the cooking staff about my disease neither before, nor during the pandemic

Q20. Before the pandemic – Did you check the labels of packaged food?
• Yes
• No

Q21. As compared to before the pandemic, did you check the labels of packaged food during the pandemic?
• Yes, to the same extent
• Yes, more frequent
• Yes, less frequent
• No, before I used to check the labels, but during pandemic I did not
• No, I was not checking the labels neither before, nor during the pandemic

Q22. Before the pandemic – Did you only eat packaged food guaranteed by the Coeliac Association/crossed grain symbol?
• Yes
• No

Q23. As compared to before the pandemic, did you only eat packaged food guaranteed by the Coeliac Association/crossed grain symbol during the pandemic?
• Yes, as before the pandemic, I eat only certified products
• Yes, before the pandemic I used to eat non-certified products, but now I eat only certified products
• No, before the pandemic I ate only certified products, but now I eat non-certified products also
• No, as before the pandemic, I eat non-certified products

Q24. How has the period of the pandemic affected you emotionally? (several answers can be checked/completed)
• I did not notice any changes in my emotional state
• I was sadder, more depressed during this period
• I was more agitated, anxious during this period
• I had alternate periods of depression and anxiety
• I needed psychological or psychiatric medical help for anxiety or depression
• I did not need the intervention of a psychologist or psychiatrist
• I was more relaxed, calmer
• I was more rested

Q25. How do you assess the availability of gluten-free products during the COVID-19 pandemic?
• The products were available to the same extent as before the pandemic
• The products were less available during the COVID-19 pandemic
• The products were more frequently available during the COVID-19 pandemic
• I don't know / can't appreciate

Q26. Did you have access to health services during the COVID-19 pandemic? (please choose only one answer)
• Yes, only at the family doctor
• Yes, only at the family doctor and private medical clinics
• Yes, I benefited from hospitalization in a state hospital
• I needed medical care, but I did not have access to the services offered by public hospitals
• I postponed medical consultations for fear of COVID-19 infection
• I did not need medical services during the pandemic
Q27. Do you consider that there was sufficient information available for patients with celiac disease during the COVID-19 pandemic? (please choose only one answer)
   • Yes
   • No
   • Don’t know/don’t answer

Q28. Where did you get information about the particularities of the new coronavirus infection in people with celiac disease? (several possible answers)
   • General practitioner
   • Specialist physician
   • Online support groups
   • Patients’ association
   • Did not have access to information
   • Other (please mention)

Q29. Have you been diagnosed with COVID-19 infection?
   • Yes
   • No

   These questions are only for patients with celiac disease who have had COVID-19

Q30. What month were you diagnosed with COVID-19 infection?
   • February 2020
   • March 2020
   • April 2020
   • May 2020
   • June 2020
   • July 2020
   • August 2020
   • September 2020
   • October 2020
   • November 2020
   • December 2020
   • January 2021
   • February 2021
   • March 2021
   • April 2021

Q31. Where do you think you got COVID-19 from? (several answers can be checked)
   • From work
   • From school / high school / college
   • From a family member who lives with you
   • From a member of the entourage (friends / acquaintances / relatives who do not live with you)
   • From a roommate / apartment / dormitory
   • From the hospital
   • From the family doctor
   • From the means of transport (bus / tram / metro / taxi /uber, etc.)
   • From shopping (supermarkets / markets / neighborhood shops)
   • From the elevator / block staircase
   • I do not know
   • Other (please mention)

Q32. What symptoms did you experience during COVID-19 infection? (several answers can be checked / completed)
I had no symptoms. I tested positive, but I didn't feel bad
   • Fever
   • Shiver
   • Marked fatigue (astenia)
   • Feeling weak
   • Muscle aches (myalgias)
   • Lack of air (dyspnea) at rest
• Lack of air only at exertion
• Dry cough
• Sputum cough
• Sore throat (odynophagia)
• Rhinorrhea
• Diarrhea
• Nausea / vomiting
• Newly installed headache (headache)
• Absence of taste (ageusia)
• Absence of odor (anosmia)
• Other symptoms (please mention)

Q33. How long did the symptoms of COVID-19 infection last? (please choose only one answer)
• I had no symptoms
• Less than a week
• About a week
• About 2 weeks
• Between 2 weeks and a month
• More than a month

Q34. Are there symptoms of COVID-19 that have persisted for more than 2 weeks?
• Yes
• No

Q35. Only if there have been COVID-19 symptoms that have persisted for more than 2 weeks, please mention: (several answers can be checked / completed)
• It does not apply; I did not have symptoms that persisted more than 2 weeks
• Fever
• shiver
• Marked fatigue (asthenia)
• Feeling weak
• Muscle aches (myalgias)
• Lack of air (dyspnea) at rest
• Lack of air only at exertion
• Dry cough
• Sputum cough
• Sore throat (odynophagia)
• Rhinorrhea
• Diarrhea
• Nausea / vomiting
• Newly installed headache (headache)
• Absence of taste (ageusia)
• Absence of odor (anosmia)
• Other symptoms (please mention)

Q36. Have you been hospitalized for COVID-19 infection? (please choose only one answer)
• No, hospitalization was not required
• No, I refused admission
• No, I requested hospitalization, but I was refused
• Yes, I was hospitalized even though I had mild symptoms
• Yes, I was hospitalized with moderate symptoms
• Yes, I was hospitalized in emergency, with severe symptoms
• Initially I refused hospitalization, but then my symptoms got worse and I was later hospitalized

Q37. How many days have you been hospitalized for COVID-19 infection? (please fill in with 0 if you have not been hospitalized)
Q38. During the hospitalization, you benefited from the following: (please choose only one answer)

- It does not apply, I was not hospitalized at all
- Oxygen on the nasal cannulas (small tubes of oxygen inserted in the nostrils)
- Oxygen on the mask
- Hospitalization in the intensive care unit (ICU), for monitoring, without invasive or non-invasive ventilation
- Non-invasive oxygen mask ventilation (CPAP, BPAP ventilation)
- Intubation and mechanical ventilation
- I did not need any of the options mentioned above
- I don't know, I can't specify

Q39. What treatment were you given for COVID-19 infection? (multiple answers can be checked/completed)

- I did not follow any treatment
- Hydroxychloroquine (Plaquenil)
- Lopinavir / Ritonavir (Kaletra)
- Corticosteroids (Dexamethasone, Medrol, Prednisone)
- Tocilizumab (RoActemra)
- Anakinra (Kineret)
- Remdesivir (Veklury)
- Favipiravir
- Convalescent plasma
- Anticoagulant
- Antibiotic
- I don't know the name of the drugs that were given to me
- Other drugs. Please mention:

Next, we want to evaluate your impressions and experience with COVID-19 vaccination.

Q40. Did you get vaccinated against COVID-19?
- Yes
- No

Q41. If you have NOT been vaccinated, please mention the reason (several answers can be checked/completed):
- I have not yet been assured that I can get the vaccine as I suffer from celiac disease
- I haven't been able to get an appointment yet, but I intend to vaccinate
- I didn't understand exactly how to do my scheduling for vaccination
- I believe that the side effects of the vaccine are not known well enough
- I don't think the vaccine works
- I do not believe in the existence of the SARS-CoV2 virus
- I had COVID-19 infection and as such the vaccine would not bring a benefit

Q42. Have you completed the complete vaccination schedule (2 doses) against COVID-19? (please choose a single answer)
- Yes, I received both doses of the vaccine
- No, I only received the first dose and I will get the second dose
- I received the first dose and I refused/will refuse the second dose

Q43. Have you experienced side effects after the first dose of COVID-19 vaccine?
- does not apply, I did not have side effects after the first dose
- pain at the injection site
- swelling at the injection site
- redness at the injection site
- enlarged (swollen) lymph nodes in the lateral area of the neck or in the armpit
- marked fatigue (asthenia)
- headache
- muscle pain (myalgias)
- joint pain (arthralgia)
- chills
- fever
- severe allergic reaction/anaphylactic shock
- mild allergic reactions/rashes
• ringing in the ears (tinnitus)
• dizziness (vertigo)
• others (please mention)

Q44. How did you feel after the second dose of COVID-19 vaccine?
• As usual. I had no side effects at either the first or second dose of the vaccine
• I had the same side effects as after the first dose
• I had the same side effects as after the first dose, but more severe
• I had additional side effects compared to the first dose (will be detailed in the next question)

Q45. If you answered YES to the previous question - you had additional side effects compared to the first dose, please check the correct answers from the list below:
• swelling at the injection site
• redness at the injection site
• enlarged (swollen) lymph nodes in the lateral area of the neck or in the armpit
• marked fatigue (asthenia)
• headache
• muscle pain (myalgias)
• joint pain (arthralgia)
• chills
• fever
• severe allergic reaction / anaphylactic shock
• mild allergic reactions / rashes
• ringing in the ears (tinnitus)
• dizziness (vertigo)
• others (please mention)

Q46. How long did the side effects start after the second dose of the vaccine? (please choose only one answer)
• Immediately, in the first 15 minutes
• Between one hour and 4 hours
• Between 4 hours and 8 hours
• Between 8 hours and 12 hours
• The next day
• In the next 2-3 days

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