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Prevalence of skin disorders and associated factors among patients with celiac disease: a cross-sectional study

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Abstract

Background Although celiac disease (CD) commonly presents with gastrointestinal symptoms, extraintestinal manifestations, particularly cutaneous disorders, are increasingly recognized. Despite this association, data on the prevalence and associated factors of skin involvement in CD remain limited. We determined the prevalence and related predictors of skin disorders in patients with CD.

Methods This cross-sectional study evaluated patients registered in the National Celiac Registry in Tehran, Iran, who had clinically, serologically and histopathologically confirmed CD. Demographic variables, CD staging, clinical symptoms, comorbidities and family history of related conditions were collected. Statistical analysis was performed using SPSS version 25.0.

Results Among 4357 CD patients, 18.2 percent exhibited skin disorders. The cohort consisted of 65.7 percent males, and the sex distribution did not differ significantly between patients with and without skin disorders. Individuals with skin disorders were slightly older (29±17 vs. 27±17 years). Eczema was the most common skin disorder (3.73%), followed by dermatitis herpetiformis (3.46%), and psoriasis (0.71%), contrasting with previous studies in which dermatitis herpetiformis predominated. Multivariate logistic regression identified constipation, mouth rash, iron deficiency anemia, thalassemia, osteoarthritis, Sjögren's disease, and family history of skin disorders as independent predictors of skin disorders. Type 1 diabetes mellitus was a protective factor.

Conclusion Considering the increased likelihood of skin disorders in CD patients with identified clinical and familial risk factors and the unexpectedly higher prevalence of eczema in this cohort, regular dermatologic evaluation is recommended to facilitate early diagnosis and management of associated skin diseases.

Keywords Celiac disease, skin diseases, skin manifestations, dermatitis herpetiformis, autoimmune diseases

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Introduction

Despite significant advances in the understanding and management of celiac disease (CD) over recent decades, this autoimmune disorder still presents numerous

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diagnostic and therapeutic challenges. CD results from an inappropriate immune response to gluten in genetically predisposed individuals—particularly those carrying the HLA-DQ2 and HLA-DQ8 alleles—and is characterized by chronic inflammation and destruction of the small intestinal mucosa [1]. The global prevalence of CD is estimated at approximately 1-2%, yet a considerable proportion of cases remain undiagnosed because of its highly variable clinical spectrum, especially in individuals lacking classic gastrointestinal (GI) symptoms [1,2]. Over recent decades, its prevalence has shown a rising trend, partly attributable to improved awareness, more sensitive diagnostic techniques, and possibly changes in dietary patterns [3].

Although CD has classically been recognized for its GI, it is now well established that the disease can present with a broad spectrum of extraintestinal features, including neurological, skeletal, hematologic, endocrine, and dermatologic disorders [4,5]. In some cases, these extraintestinal features may constitute the only clinical presentation [4]. Among them, skin disorders represent one of the most frequent and clinically evident [6].

A large study by Lebwohl *et al* demonstrated that CD patients have a significantly higher risk of developing skin disorders compared with healthy controls [7]. Apart from dermatitis herpetiformis (DH)—the most common skin disorder in CD—the prevalence of psoriasis, eczema and urticaria is also higher in CD patients than in the general population [8,9]. Nevertheless, the exact mechanism of the association between CD and these skin disorders remains unclear.

The detection of celiac-specific autoantibodies in certain skin lesions, including DH, and their resolution following adherence to a gluten-free diet provides evidence of an immunological link between the 2 disease groups [10]. Furthermore, skin disorders in CD may co-occur with other autoimmune diseases, such as type 1 diabetes mellitus (T1DM) and thyroid diseases, which are themselves more prevalent in CD [8]. Genetic studies have identified several shared susceptibility loci between CD and dermatologic conditions such as DH and psoriasis [11]. Immunologically, both conditions may share common pathogenic mechanisms—for example, more T cells and T cell-mediated inflammation observed in patients with psoriasis and CD [12,13]. Taken together, these observations suggest a potential pathophysiological relationship between CD and skin disorders, although the precise mechanisms remain to be elucidated.

Although CD and its skin disorders appear relatively common in Middle Eastern populations, including Iran, systematic research on their prevalence, clinical patterns, and associated factors remains limited [14]. Inconsistent findings across available studies highlight the need for well-designed, large-scale investigations. Clarifying the relationship between CD and skin disorders, and identifying demographic, clinical, and histopathological predictors, could facilitate earlier diagnosis, improve disease monitoring, and optimize patient management. Accordingly, this study aims to determine the prevalence of skin disorders in patients with CD and explore factors influencing their occurrence.

Patients and methods

Study setting and population

This cross-sectional study was conducted to evaluate the prevalence of skin disorders among CD patients and to compare the demographic, clinical, and histopathological characteristics of patients with and without skin disorders. Patients were recruited from the Celiac Registry Center at Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran, between 2019 and 2022. The diagnosis of CD was confirmed by an experienced gastroenterologist, based on clinical evaluation, serological testing and compatible intestinal histopathology.

Inclusion criteria were: (1) confirmed diagnosis of CD with Marsh stage ≥2 based on small intestinal biopsy; (2) positive anti-tissue transglutaminase (tTG) IgA or IgG test results;

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(3) only adult patients (age≥18 years); and (4) willingness to participate in the study. Exclusion criteria were: (1) Marsh stage <2; (2) negative anti-tTG test results; (3) diagnosis of inflammatory bowel disease; (4) refusal to participate; and (5) incomplete demographic or clinical data.

CD diagnosis protocol

The diagnostic protocol involved a combination of clinical evaluation, serological testing, and histopathological assessment. Serum anti-tTG IgA and IgG antibodies were measured using the ELISA method in patients with suspected clinical manifestations. Patients with positive anti-tTG test results underwent upper GI endoscopy and small intestinal biopsy performed by an expert gastroenterologist. Four to 6 biopsy samples were collected from the small intestine and examined by experienced pathologists. The severity of villous atrophy was classified according to the Marsh system, ranging from Marsh 0 (normal villi) to Marsh IIIc (total villous atrophy). Patients with positive anti-tTG test results and Marsh stage ≥2 were diagnosed with CD.

Definition of skin disorders

Skin disorders were defined as dermatological conditions either directly associated with CD (e.g., DH) or observed in patients who had CD without an alternative documented underlying systemic cause. Skin disorders were recorded as part of routine clinical care rather than through systematic dermatologic screening.

Diagnosis was made by board-certified dermatologists based on clinical examination, with histopathological confirmation obtained only in cases where the clinical presentation was atypical or when a CD-specific diagnosis, such as DH, was suspected, in accordance with standard dermatologic practice.

Given the registry-based and retrospective nature of the study, detailed information regarding treatments specific to the skin disorder (e.g., topical corticosteroids or dapsone) was not consistently available and therefore was not included in the analysis.

Additionally, although efforts were made to ensure diagnostic accuracy, the possibility of misclassification, particularly among non-CD-specific inflammatory dermatoses such as eczema, cannot be completely excluded and was considered in the interpretation of results.

Data collection

Demographic data (age, sex), clinical features (GI, cutaneous, oro-dental, hematologic, and neurologic symptoms), comorbidities, and family history (FH) of related disorders were obtained through structured interviews conducted by trained interviewers. Marsh classification results were extracted from pathology reports, and comorbidity data were obtained from medical records. All data were recorded in an electronic registry database and subsequently analyzed retrospectively.

The primary objective was to determine the prevalence of cutaneous disorders among CD patients. The secondary objective was to examine the association between demographic, clinical, and histopathological variables, and the occurrence of skin disorders.

Ethical issues

The study protocol was approved by the Ethics Committee of Tehran University of Medical Sciences (Ethics code:416/642/12) and was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants prior to enrolment.

Statistical analysis

Statistical analysis was performed using SPSS software version 25.0 for Windows. Proportions were compared using the chi-square test and Fisher's exact test, as appropriate. Descriptive statistics were presented as frequencies, percentages, means, and standard deviations (SD). Multivariate logistic regression was performed to evaluate the association between patient age, sex, clinical symptoms, underlying comorbidities; and FH of associated disorders and skin disorders. A P-value of less than 0.05 was considered statistically significant.

Results

Demographic and baseline characteristics

A total of 4357 CD patients met the inclusion criteria and were enrolled (Fig. 1); 65.7% were male, 81.8% had no skin disorders, whereas 18.2% reported skin presentations. The proportion of male participants did not differ significantly between patients with and without skin disorders (65.9% vs. 68.7%). There was no statistically significant difference in sex distribution between the 2 study groups (P=0.29). The mean age of patients with skin disorders was slightly higher compared to those without (29±17 vs. 27±17 years, P<0.001). Regarding disease severity, intestinal biopsy findings based on the Marsh classification revealed 36.5% Marsh IIIa, 34.2% Marsh IIIb, and 29.2% Marsh IIIc, with no statistically significant difference between the 2 groups. Detailed baseline characteristics are summarized in Table 1.

Prevalence of skin disorders

Overall, 18.2% of CD patients reported skin disorders. Although subgroup analyses were not included in the tables,

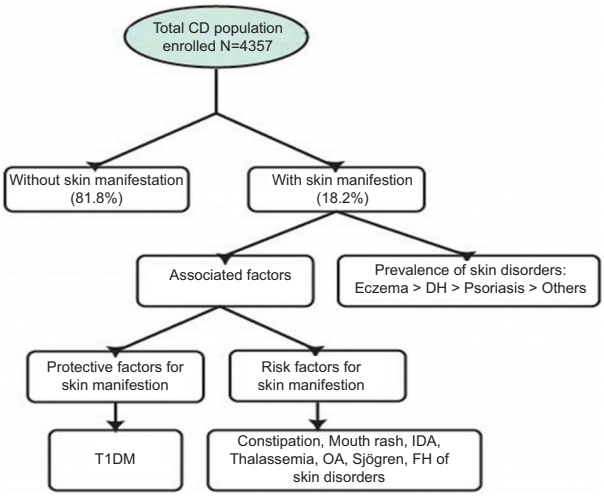


Figure 1 Flowchart of the study design and analytical pathway, created by the authors
CD, celiac disease; DH, dermatitis herpetiformis; T1DM, type 1 diabetes mellitus; IDA, iron deficiency anemia; OA, osteoarthritis; FH, family history

Table 1 Demographic and histopathological characteristics of patients with and without skin disorders

Variables	Patients without skin disorders (n=3564)	Patients with skin disorders (n=793)	P-value
Sex, n (%)			
Male	2347 (67.89)	515 (65.94)	0.293
Age at diagnosis, year (mean±SD)	27±17	29±17	0.001
Marsh classification, n (%)			0.819
Marsh IIIa	1306 (36.64)	286 (36.07)	
Marsh IIIb	1212 (34.01)	279 (35.18)	
Marsh IIIc	1046 (29.35)	228 (28.75)	

SD, standard deviation

qualitative assessment indicated that eczema and DH were the most frequently observed skin disorders, followed by occasional cases of psoriasis and other nonspecific skin lesions. This pattern underscores the heterogeneity of cutaneous involvement in CD.

GI manifestations

The most common GI symptom was abdominal pain (60.6%), followed by flatulence (50.9%), anorexia (38.7%), diarrhea (33.7%), reflux (31.4%), constipation (30.7%), nausea (26.6%), and vomiting (14.3%). The prevalence of these GI symptoms was significantly higher among patients with skin disorders compared with those without (P<0.05 for all comparisons). Detailed data are presented in Table 2.

Extraintestinal manifestations

Celiac patients with skin disorders had a significantly higher prevalence of mouth rash (30.9% *vs.* 21.4%, respectively; P<0.001), mouth ulcers (11.8% vs. 6.3%, respectively; P<0.001), and swollen tongue (4.2% vs. 1.6%; P=0.001). The prevalence of non-migraine headaches was significantly higher among celiac patients with cutaneous disorders than in patients without skin disorders (31.8% *vs.* 21.5%; P<0.001). The prevalence of both types of anemia was significantly higher among celiac patients with skin disorders (62.9% *vs.* 55.2%; P=0.001 for iron deficiency anemia [IDA] and 10.8% *vs.* 7.5%; P=0.023 for thalassemia) (Table 2).

Associated disorders

Compared with patients without skin disorders, those with cutaneous involvement showed a significantly higher prevalence of osteoarthritis (3.4% vs. 1.1%, P=0.001) and Sjögren's disease (0.8% vs. 0.2%, P<0.001). In contrast, T1DM was significantly more common among patients without skin disorders (14.4% vs. 6.9%, P<0.001). The prevalence of other associated disorders did not differ significantly between groups (P>0.05) (Table 3).

FH of associated disorders

The prevalence of a positive FH of rheumatoid arthritis (6.5% vs. 3.3%; P=0.002), skin disorders (10.3% vs. 1.8%; P<0.001), and Sjögren's disease (0.8% vs. 0.2%; P<0.001) was significantly higher among celiac patients with skin disorders than among those without. No statistically significant differences were observed between the study groups regarding a positive FH of liver diseases, Down syndrome, Hashimoto's thyroiditis, thalassemia, or Turner syndrome (P>0.05) (Table 3).

Association between cutaneous and GI manifestations

Among the 4357 patients with CD, GI symptoms were reported in 3616 individuals (83.0%), while 623 patients (17.0%) were asymptomatic with respect to GI involvement. Notably, among the 793 patients presenting with skin disorders, 48 (6.1%) did not exhibit any GI symptoms. Statistical analysis demonstrated a significant association between the presence of GI symptoms and skin disorders (P<0.001). These findings suggest that although skin lesions in CD are frequently accompanied by GI complaints, a subset of patients may present exclusively with dermatologic findings in the absence of GI symptoms.

Table 2 Gastrointestinal and extraintestinal manifestations of patients with and without skin disorders

Variables	Patients without skin disorders (n=3564)	Patients with skin disorders (n=793)	P-value
Gastrointestinal manifestations, n (%)	2087 (66.34)	555 (71.06)	0.012
Abdominal pain	1703 (55.96)	518 (67.36)	<0.001
Flatulence	1306 (43.52)	382 (50.33)	0.001
Anorexia	1118 (36.97)	352 (46.19)	<0.001
Diarrhea	1048 (35.45)	322 (43.22)	<0.001
Reflux	1010 (33.61)	329 (43.23)	<0.001
Constipation	884 (29.42)	274 (36.01)	<0.001
Nausea	477 (16.17)	148 (19.58)	0.026
Vomiting			
Orodental manifestations, n (%)			
Mouth rash	377 (21.44)	163 (30.99)	<0.001
Colorless teeth	160 (9.69)	35 (7.48)	0.144
Mouth ulcer	103 (6.35)	57 (11.80)	<0.001
Swollen tongue	25 (1.60)	20 (4.26)	0.001
Neurological manifestations, n (%)			
Non-migraine headache	225 (21.55)	98 (31.82)	<0.001
migraine headache	218 (20.62)	79 (25.82)	0.053
Hematological manifestations, n (%)			
IDA	1208 (55.26)	381 (62.98)	0.001
Thalassemia	120 (7.57)	51 (10.87)	0.023

DH, dermatitis herpetiformis; IDA, iron deficiency anemia; N, number

Table 3 Prevalence of associated disorders and family history of associated diseases in patients with and without skin disorders

Variables	Patients without skin disorders (n=3564)	Patients with skin disorders (n=793)	P-value
Associated disorders, n (%)			
Hypothyroidism	368 (19.91)	125 (22.85)	0.135
Hyperthyroidism	49 (2.90)	19 (3.81)	0.305
Type 1 DM	265 (14.48)	36 (6.99)	<0.001
Type 2 DM	29 (1.72)	15 (3.01)	0.073
RA	52 (3.34)	31 (6.57)	0.599
Growth impairment	51 (3.60)	14 (3.45)	0.143
OA	17 (1.11)	15 (3.41)	0.001
Down syndrome	20 (2.42)	10 (4.48)	0.565
AI hepatitis	12 (0.87)	2 (0.50)	0.456
Turner syndrome	10 (0.67)	2 (0.45)	0.732
Sjögren's disease	3 (0.20)	4 (0.88)	<0.001
Infertility	2 (0.13)	1 (0.22)	0.883
Family history of associated disorders, n (%)			
CD	268 (16.37)	96 (20.17)	0.054
Hypothyroidism	359 (21.29)	124 (24.90)	0.088
Hyperthyroidism	83 (5.32)	21 (4.56)	0.514
Type 1 DM	131 (8.29)	50 (10.68)	0.109
Type 2 DM	197 (12.24)	66 (13.75)	0.380
RA	52 (3.34)	31 (6.57)	0.002
Skin disorders	16 (1.86)	24 (10.39)	<0.001
Liver disorders	20 (2.42)	10 (4.48)	0.102
Down syndrome	10 (0.67)	2 (0.45)	0.599
Hashimoto's thyroiditis	6 (0.40)	2 (0.44)	0.896
Sjögren's disease	3 (0.20)	4 (0.88)	0.033
Thalassemia	6 (0.40)	0 (0.00)	0.178
Turner syndrome	2 (0.13)	1 (0.22)	0.673

AI, autoimmune; CD, celiac disease; DH, dermatitis herpetiformis; DM, diabetes mellitus; N, number; OA, osteoarthritis; RA, rheumatoid arthritis

Multivariate logistic analysis

The multivariate logistic analysis of demographic and clinical characteristics revealed that, among GI manifestations, having constipation was an independent factor for developing skin disorders (odds ratio [OR] 1.62, 95% confidence interval [CI] 1.10-2.38; P=0.01). Regarding oro-dental manifestations, CD patients with mouth rash had a 3.10 times greater likelihood (95%CI 1.80-5.32; P<0.001) of developing skin disorders. IDA (OR 1.54, 95%CI 1.05-2.24; P=0.02) and thalassemia (OR 2.78, 95%CI 1.19-6.50; P=0.01) significantly increased the likelihood of skin disease development. On the other hand, T1DM was identified as a protective factor against development of skin disorders (OR 0.20, 95%CI 0.05-0.81; P=0.02), while osteoarthritis (OA) (OR 6.15, 95%CI 1.15-32.78; P=0.03) and Sjögren's disease (OR 4.82, 95%CI 1.98-11.73; P<0.001) were found to be independent risk factors for developing skin disorders. Regarding the FH of associated disorders, it was found that a positive FH of skin disorders was associated with a 7.99 times greater likelihood (95%CI 2.44-26.13; P<0.001) of developing skin disorders. The results of multivariate logistic analysis are presented in Table 4.

Discussion

Although for many years CD was primarily considered a GI disorder, accumulating evidence suggests an increasing recognition of extraintestinal presentations. A considerable proportion of patients with CD present with extraintestinal manifestations that may precede GI symptoms or, in some cases, represent the sole clinical presentation. Among these, skin disorders are frequently reported. Therefore, improved characterization of dermatologic findings in CD may contribute to earlier recognition and comprehensive clinical assessment. In the present study, 18.2% of CD patients exhibited skin disorders, with eczema being the most commonly reported dermatologic condition, followed by DH and psoriasis. Several clinical variables, including constipation, oral mucosal lesions, IDA, thalassemia, osteoarthritis, Sjögren's disease and a positive FH of skin disorders, were found to be independently associated with skin disorders, whereas T1DM showed an inverse association. However, given the cross-sectional design of the study, these findings should be interpreted strictly as

Table 4 Multivariate logistic analysis of the association between demographic and clinical characteristics and the development of skin disorders

Variables	Odds ratio (95%CI)	P-value
Demographic characteristics		
Gender	0.679 (0.459-1.005)	0.053
Age at diagnosis	0.991 (0.979-1.003)	0.146
Gastrointestinal manifestations		
Abdominal pain	0.752 (0.484-1.169)	0.205
Flatulence	1.042 (0.655-1.657)	0.862
Anorexia	1.173 (0.767-1.794)	0.461
Diarrhea	1.181 (0.796-1.753)	0.408
Reflux	0.934 (0.604-1.443)	0.757
Constipation	1.625 (1.105-2.388)	0.014
Nausea	1.476 (0.920-2.368)	0.107
Vomiting	0.776 (0.434-1.387)	0.392
Oro-dental manifestations		
Mouth rash	3.100 (1.806-5.323)	<0,001
Mouth ulcer	0.831 (0.345-2.002)	0.680
Swollen tongue	2.017 (0.379-10.753)	0.411
Neurological manifestations		
Non-migraine headache	1.521 (0.805-2.874)	0.197
Hematological manifestations		
IDA	1.543 (1.059-2.249)	0.024
Thalassemia	2.784 (1.191-6.509)	0.018
Associated disorders		
Type 1 DM	0.209 (0.054-0.812)	0.024
OA	6.152 (1.155-32.780)	0.033
Sjögren's disease	4.827 (1.986-11.733)	0.001
Family history of associated disorders		
RA	0.636 (0.194-2.078)	0.453
Skin disorders	7.998 (2.447-26.137)	0.001
Sjögren's disease	10.336 (0.389-274.435)	0.163

CI, confidence interval; DM, diabetes mellitus; IDA, iron deficiency anemia; OA, osteoarthritis; RA, rheumatoid arthritis

associations, and no temporal or causal relationships can be inferred. Among CD patients with documented skin disorders, eczema emerged as the most prevalent dermatologic finding. This contrasts with many previous reports in which DH has been described as the most characteristic skin manifestation of CD. For instance, Dev *et al* reported a DH prevalence of 16%, identifying it as the most frequent dermatologic finding in their cohort [15]. Similarly, several other studies have highlighted DH as the classic and most common skin presentation in CD. Niknam *et al* reported a prevalence of skin disorders ranging from 10.9% in children to 27.7% in adults with CD [16], while Salarian *et al* found eczema to be the most common lesion among pediatric and adolescent CD patients, with a prevalence of 18.6%—nearly 5 times higher than that observed in our study [17]. Differences between studies may reflect geographic variability, genetic background, environmental exposures, dietary factors, or differences in diagnostic practices and study design. Furthermore, given the registry-based and clinically documented nature of dermatologic diagnoses, the possibility of misclassification of certain non-specific inflammatory dermatoses, particularly eczema-like conditions, cannot be entirely excluded. Additionally, skin evaluations in this registry were documented during routine clinical assessment and were not necessarily recorded at the exact time of CD diagnosis, which may have influenced prevalence estimates and the temporal interpretation of dermatologic findings.

Constipation and oral mucosal lesions were independently associated with skin disorders in our analysis. Although shared gut–skin axis mechanisms involving microbiome alterations, metabolic signaling, and neuroimmune pathways, have been proposed, the cross-sectional nature of the present study precludes the determination of temporal sequence [18-22]. However, constipation was defined based on clinician-documented patient-reported symptoms recorded in routine clinical evaluations rather than on the standardized Rome criteria, which may have introduced heterogeneity in symptom classification. Similarly, oral mucosal lesions were associated with a higher likelihood of concurrent cutaneous findings**.** Oral mucosal findings were based on clinical descriptions of inflammatory or erythematous mucosal changes, and specific etiologies, including infectious or nutritional causes, were not systematically distinguished within the registry, potentially introducing misclassification bias. Moreover, the higher prevalence of GI and oro-dental symptoms among patients with skin findings may partly reflect increased healthcare utilization or referral bias, as patients with more complex or multisystem presentations may undergo more extensive clinical evaluation.

With respect to hematologic comorbidities, IDA and thalassemia were independently associated with the presence of skin disorders. While iron deficiency and hematologic disorders have been previously linked to alterations in skin integrity and function [23], these associations may not be specific to CD and could reflect underlying systemic conditions that independently contribute to dermatologic findings. Furthermore, studies have indicated that patients with thalassemia may also present with concurrent skin disorders due to several factors, including iron overload, sun exposure, copper deficiency, skin dehydration, inappropriate histamine release, and hemosiderosis [24-27]. Therefore, these findings should not be interpreted as disease-specific dermatologic predictors but rather as clinical associations potentially influenced by underlying systemic factors. We also observed that autoimmune comorbidities influenced the risk profile. Patients with osteoarthritis or Sjögren's syndrome had a markedly higher chance of developing skin disorders, whereas those with T1DM had a surprisingly lower risk. Osteoarthritis was included as a comorbid inflammatory musculoskeletal condition documented in the registry, and is not considered an autoimmune disease. Studies have demonstrated that several autoimmune disorders can co-exist, and having one autoimmune disease may increase the risk of developing others [28-30]. However, the presence of multiple correlated autoimmune and inflammatory variables in the multivariate model, along with wide confidence intervals for several estimates, suggests that these findings should be interpreted cautiously.

While T1DM is generally linked to various skin problems, some studies suggest that strict glycemic control and the

use of antidiabetic agents might reduce this risk, which may partially explain our findings [31-33]. Nevertheless, an unexpected inverse association between T1DM and the likelihood of developing skin disorders was observed in our study. This finding should be interpreted with considerable caution. Potential explanations include residual confounding, differential clinical follow-up, selection bias, or unmeasured factors such as treatment patterns or healthcare access. Given the absence of longitudinal data, no protective relationship can be inferred, and further prospective studies are required to clarify this observation.

In addition, regarding the FH of associated diseases, CD patients with a positive history of skin disorders were at a 7.99-fold higher risk for the development of skin disorders. In line with our results, previous studies also reported that a positive FH of skin disorders can influence the onset, course, and presentation of skin diseases [34-36]. Altogether, it is crucial for clinicians to be aware of the most common skin disorders in patients with CD, especially those with constipation, oral mucosal lesions, IDA, thalassemia, OA, Sjögren's disease and a positive FH of skin diseases, and to regularly assess these patients for the development of any skin presentations, as early diagnosis and treatment of underlying skin disorders may be beneficial in improving CD prognosis and clinical outcomes. Moreover, although no routine screening protocol for the early detection and diagnosis of skin diseases in patients with a FH of cutaneous disorders has been proposed, these individuals could undergo regular clinical examination with the purpose of detecting any cutaneous presentations.

This study has several strengths, including a large cohort of more than 4300 biopsy-confirmed CD patients and evaluation of a wide spectrum of clinical and comorbid variables. Nevertheless, several limitations should be acknowledged. The retrospective cross-sectional design limits causal inference and is subject to potential selection and recall biases. Diagnostic criteria for certain dermatologic conditions were based on clinical registry documentation, and standardized dermatologic assessments or systematic histopathologic confirmation were not uniformly available. Additionally, specific treatment data for dermatologic conditions were not recorded in the registry, limiting assessment of treatment-related confounding. Furthermore, data regarding gluten-free diet initiation, adherence, treatment duration, serologic remission, disease duration, refractory CD status, smoking status, body weight, and concomitant medications were not consistently available, which may have influenced both the GI and dermatologic outcomes. Importantly, the majority of patients included in this registry were newly diagnosed cases of CD at the time of enrolment, and a gluten-free diet had not yet been initiated in most participants. Therefore, the potential modifying effect of dietary treatment on cutaneous manifestations could not be evaluated in the present analysis. Patients with inflammatory bowel disease were excluded to minimize potential confounding from overlapping inflammatory GI conditions; however, future studies including overlapping CD/inflammatory bowel disease populations may provide further insight into dermatologic risk patterns. The inclusion of both pediatric and adult patients may also have contributed to heterogeneity in the clinical presentation.

Despite these limitations, this study provides one of the largest evaluations of dermatologic manifestations among patients with biopsy-confirmed CD in a Middle Eastern cohort. Future prospective multicenter studies with standardized dermatologic evaluation, detailed treatment data, and longitudinal follow-up are needed to clarify temporal relationships and better define the clinical relevance of dermatologic findings in CD.

Taken together, this large cross-sectional cohort of patients with CD, approximately 1 in 5 presented with skin disorders. Several clinical and comorbid variables were independently associated with the presence of dermatologic findings; however, given the cross-sectional design, these relationships should be interpreted as associations rather than causal or predictive factors. Eczema was the most frequently reported dermatologic condition, although potential diagnostic variability and differences in clinical documentation should be considered when interpreting this finding. The observed inverse association with T1DM requires cautious interpretation and further validation in prospective studies. The absence of detailed data regarding gluten-free diet adherence, treatment duration, and dermatologic therapies represents an important limitation. Given that most patients were newly diagnosed and had not yet initiated a gluten-free diet at the time of data collection, the impact of dietary intervention on skin manifestations could not be assessed in this study. Overall, recognition of dermatologic involvement may contribute to a more comprehensive clinical assessment of patients with CD, while future longitudinal research is needed to clarify the mechanisms and temporal relationships of skin disorders and the potential impact of dietary management.

Summary Box

What is already known:

- Celiac disease can be associated with a broad spectrum of extraintestinal manifestations, including skin disorders, but estimates of their frequency and clinical patterns vary across studies.

What the new findings are:

- In this adult Iranian cohort of 4,357 patients with celiac disease, 18.2% had documented skin disorders, with eczema being the most frequently recorded; several clinical and comorbid variables were associated with their presence

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