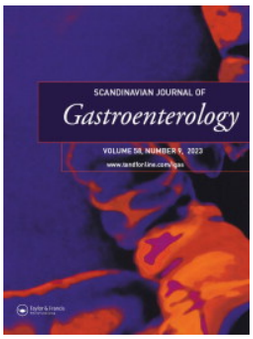

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ORIGINAL ARTICLE

Patient-reported burden of skin disorders in coeliac disease

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ABSTRACT

Objectives: The current knowledge on the associations between coeliac disease and different skin diseases is contradictory and the patient's perspective on the burden of these is lacking. This study aimed to investigate patient-reported frequency, severity and quality of life effects of skin disorders in coeliac disease patients compared to controls and moreover to study the impacts of gluten-free diet on these skin diseases.

Materials and methods: A study questionnaire designed for the purposes of this study and a validated Dermatology Life Quality Index (DLQI) questionnaire were posted to 600 adult members of the Finnish Coeliac Society and 1173 matched controls. Responses from 327 coeliac disease patients and 382 non-coeliac controls were compared.

Results: Coeliac disease patients were shown to be at no increased risk of atopic dermatitis, acne, rosacea, psoriasis, alopecia areata, vitiligo or chronic urticaria. The severity of these skin diseases did not differ between study groups, but the risk for at least moderate effects on quality of life caused by dermatological diseases was increased among those with coeliac disease. Positive response from gluten-free diet was most commonly experienced by coeliac disease patients with atopic dermatitis.

Conclusions: Even though the risk for skin diseases was shown not to be increased among coeliac disease patients, there is still an increased burden related to experienced skin symptoms among these patients, which non-dermatologists treating coeliac disease patients should acknowledge.

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Introduction

Coeliac disease is an autoimmune disorder triggered by dietary gluten intake in genetically predisposed individuals, causing villous atrophy in the small bowel and autoantibody response to tissue transglutaminase (TG2) [1]. The classic symptoms of coeliac disease are gastrointestinal, but extremely heterogenous extraintestinal symptoms have become increasingly more common [2]. Dermatitis herpetiformis (DH) is an itchy, blistering skin disease and the most common and well-characterized extraintestinal manifestation of coeliac disease [3,4], currently affecting approximately 13% of coeliac disease patients [5,6].

Coeliac disease may also be virtually asymptomatic, and therefore at-risk groups, such as first-degree relatives of patients and those affected with diseases associated with coeliac disease, are screened [1]. Type 1 diabetes mellitus and thyroid diseases are autoimmune diseases strongly linked to coeliac disease [7,8]. In addition to these systemic autoimmune disorders, coeliac disease has less convincingly been associated with autoimmune skin diseases such as alopecia areata and vitiligo [9,10]. Studies have moreover linked coeliac disease to several other skin diseases such as psoriasis, atopic dermatitis, chronic urticaria and acne [11–15]. However, the current data are contradictory as other studies have reported no association between coeliac disease and, for example, alopecia areata, chronic urticaria and vitiligo [16–18].

The treatment for all phenotypes of coeliac disease is a lifelong gluten free diet (GFD), resulting in mucosal healing and normalizing antibody levels, as well as resolution of clinical symptoms [1,3]. Additionally, strict dietary adherence decreases the risk of coeliac disease complications, most importantly the risk of lymphoma development [19]. The impact of GFD on the associated diseases is less certain. As regards skin disorders linked to coeliac disease, the role of GFD is particularly inconclusive and only scarcely studied, but there are studies reporting positive effects of GFD on psoriasis and alopecia areata [20–24] while in other studies no such positive effect could be demonstrated [25–27].

In addition to current knowledge on the linkage of coeliac disease and different skin diseases being insufficient and somewhat conflicting, there is an obvious lack of studies addressing the patient perspective on skin diseases in association with coeliac disease. Hence, this questionnaire study aimed to investigate patient-reported frequency, severity and

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quality of life effects of skin diseases in patients with coeliac disease and in controls. We moreover aimed to study the impacts of GFD on these skin diseases as experienced by coeliac disease patients.

Materials and methods

Patients and study protocol

The study patients were collected in co-operation with the Finnish Coeliac Society, a national patient organization providing information and advice for its members, amounting to over 21,000. After diagnosis, approximately 70% of all patients with coeliac disease in Finland join the Finnish Coeliac Society, and also individuals without coeliac disease, for example family members of coeliac disease patients, may join the society.

In this study, questionnaires (see in more detail below) were sent to 600 members of the Finnish Coeliac Society who were at least 18 years old and had joined the society 1.5–3.5 years earlier. Patient recruitment of the same type has been used in our previous studies [28]. This above mentioned timeframe for joining the society was chosen to increase the likelihood that the individuals would be able to recall whether they had been diagnosed with skin diseases before or after coeliac disease and could also estimate the effect of GFD on their skin symptoms. For each society member, two controls matched for age (±2 years), sex and place of residence were selected from the Finnish Digital and Population Data Services Agency, which maintains the Population Information System containing personal data about Finnish citizens and foreign citizens in Finland on a permanent or temporary basis.

The questionnaires were posted to the Finnish Coeliac Society members in April 2019 and to the controls in May 2019. As not all society members could be matched, the final number of questionnaires posted to controls was 1173. A reminder was sent to non-respondents 2 weeks later. Of those responding, all subjects under 18 years of age were excluded. Also, those without a reliable coeliac disease or DH diagnosis were excluded from the coeliac disease study group, and those diagnosed with coeliac disease or DH from the non-coeliac control group (see in more detail below). The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the regional Ethics Committee of Tampere University Hospital (R18180). All study participants gave their written informed consent.

Questionnaires

Two questionnaires were posted to the study subjects, a study questionnaire designed for the purposes of this study by coeliac disease/DH specialized dermatologists and a validated Dermatology Life Quality Index (DLQI) questionnaire [29]. The study questionnaire posted to Coeliac Society members contained questions confirming coeliac disease or DH diagnosis similarly as in previous studies [28,30]; there were questions whether the person had been diagnosed with coeliac disease, DH, or neither, about the year of coeliac disease/DH diagnosis and clinical symptoms at the time of the diagnosis. The questionnaire posted to controls likewise included a question whether they had been diagnosed with coeliac disease, DH or neither. Also, in both questionnaires there were open-ended questions and questions with multiple response options about sociodemographic and life-style characteristics, long-term illnesses and medications used. Height and weight were also elicited and body mass index (BMI) was calculated from these. The questionnaires included individual questions about the year of diagnosis, severity and treatment of allergies, psoriasis, atopic dermatitis, chronic urticaria, acne, rosacea, alopecia areata and vitiligo. The severity of each disease was evaluated by the respondents as mild, moderate or severe and the treatment for each disease was elicited through open-ended questions. Presence of other possible skin diseases was also enquired as well as skin diseases in family members. The questionnaire posted to the members of the Finnish Coeliac Society included additional questions about their current adherence to GFD. Dietary adherence was estimated as strict, lapses less than once a month, lapses one to five times a month, lapses once a week or more often, or no adherence at all. Additionally, the effect of GFD on allergies and skin diseases was elicited from those diagnosed before coeliac disease/DH with response options: complete recovery, partial response, no impact at all, or deteriorating.

The DLQI questionnaire was used to evaluate the quality of life associated with dermatological diseases. It has ten items and six different sections concerning: symptoms and feelings, daily activities, leisure, work and school, personal relationships and treatment unit. Each question is scored on a four-point Likert scale (0–3), total score ranging 0–30. Higher score indicates worse quality of life. More specifically, scores of 0 – 1 are interpreted as no effect on patient's life, 2–5 small effect, 6–10 moderate effect, 11–20 very large effect and 21–30 extremely large effect on patient's life [29].

Statistical analysis

Quantitative data were expressed as numbers of subjects and percentages, or as medians and ranges. To assess statistical differences between patients with coeliac disease and non-coeliac controls, chi-square, Fisher's exact and Mann–Whitney U tests were used. DH and all other coeliac disease phenotypes were also separately compared to non-coeliac controls. When different treatment modalities for skin diseases were compared between study groups, only the most commonly reported skin diseases, atopic dermatitis and acne, were analyzed further, and in these analyses, the different treatments were categorized as: no treatment, topical treatment, phototherapy and systemic treatment. Moreover, coeliac disease patients reporting alleviation of skin disease during GFD were compared to those reporting no alleviation only in the skin disease group where GFD response was most evident.

A p value less than 0.05 was considered statistically significant. Odds ratios (ORs) and 95% confidence intervals (CI) were calculated using binary logistic regression analysis.

In the logistic regression for 'any skin disease', diagnosis of psoriasis, atopic dermatitis, chronic urticaria, acne, rosacea, alopecia areata, vitiligo, as well as other skin diseases listed separately were all included. All statistical analyses were conducted using SPSS version 28 (IBM, Armonk, NY: IBM Corp.).

Results

Coeliac disease patients and non-coeliac controls

Among members of the Finnish Coeliac Society, the response rate was 60% (359 out of 600 responded). Altogether 32 patients were excluded: five for being under 18 years of age, 26 for not having coeliac disease or DH or with unreliable diagnosis, and one had died. Thus, the coeliac disease study group consisted of 327 patients, of whom 22 were diagnosed with DH. Of the controls, 33% (389 out of 1173) responded. Five were excluded for having coeliac disease, one for having DH, and one for not confirming no diagnosis of coeliac disease or DH. Finally, the non-coeliac control group consisted of 382 subjects. Due to the lower response rate among controls, all statistical analyses comparing coeliac disease and non-coeliac control groups were performed without matching.

The gender or age of the study groups did not differ statistically significantly, as 77% of the coeliac disease and 79% of the non-coeliac controls were females and the respective median ages at the time of the study were 55 and 57 (Table 1). At the time of study, there were no differences in the other background data either, except among coeliac disease patients use of over-the-counter medications was more common than among non-coeliac controls (p = 0.001) and non-coeliac controls were more commonly current smokers (p = 0.037).

Median age at coeliac disease diagnosis among coeliac disease patients was 48 (range 1–82) years, and in 45% of the patients, coeliac disease was suspected due to gastrointestinal symptoms. In 6% the patients' skin symptoms were the reason to suspect coeliac disease, and 9% of those with other primary symptoms reported having also suffered from some type of skin symptoms at diagnosis. Other extraintestinal symptoms were the main reason for coeliac disease suspicion in 26% of the patients and 12% were diagnosed due to screening of at-risk groups. At the time of the study, 99% of the coeliac disease patients reported following GFD and the median duration was three (range 1–48) years. Dietary adherence was strict in 81% of the patients with data available (257 out of 317); 16% reported having lapses in their diet less than once per month, 2% lapses in the diet at least one to five times a month, 1% lapses at least once a week and one patient (0.3%) reported eating normal gluten-containing diet.

Skin disorders in coeliac disease patients and non-coeliac controls

In both study groups, 35% of the patients had a diagnosis of a skin disease, atopic dermatitis being the most common disease reported by both study groups, followed by acne (Table 2). Compared to non-coeliac controls, patients with coeliac disease were not at increased risk for any skin disease, atopic dermatitis, acne, rosacea, psoriasis, alopecia areata, vitiligo or chronic urticaria. Nor were any differences detected in the prevalence of these skin diseases between the study groups when females and males and age groups ≤50 and >50 years of age (data not shown) were analyzed separately. When DH and all other coeliac disease phenotypes were compared separately to non-coeliac controls, DH patients were shown to have increased risks for rosacea and alopecia areata, but other significant differences were not detected (Supplementary Table 1).

Median age at the time of atopic dermatitis diagnosis was 7 years in patients with coeliac disease and 8 years in non-coeliac controls (p = 0.519), the corresponding ages of acne diagnosis being 17 and 15 (p = 0.186), of rosacea 47 and 44 (p = 0.635), of psoriasis 55 and 24 (p = 0.115), of alopecia areata 34 and 17 (p = 0.201) and of vitiligo 26 and 17 years (p = 0.630). Regarding severity of each skin disease, no statistically significant differences were detected between coeliac disease and non-coeliac controls (Supplementary Table 2). Further, when treatment options for atopic

Table 1. Demographic and background data on coeliac disease patients and non-coeliac controls at the time of the study.

	CD patients n = 327[a]		Non-CD controls n = 382		
	n	%	n	%	p Value
Age, median (range)	55	18–86	57	19–84	0.064
Females	252	77	303	79	0.468
Diabetes[b]	26	8	26	7	0.560
Thyroid disease	53	16	45	12	0.089
Cerebrovascular disease	12	4	8	2	0.207
Coronary heart disease	10	3	6	2	0.184
Hypercholesterolemia	57	17	76	20	0.402
Cancer[c]	25	8	32	8	0.730
Number of long-term illnesses, median (range)	1	0–9	1	0–9	0.145
Number of prescription medication used, median (range)	1	0–20	1	0–13	0.229
Number of over-the-counter medications used, median (range)	1	0–10	0	0–13	0.001
Current smoker	23	7	44	12	0.037
BMI, median (range), kg/m^2	25	18–43	26	17–64	0.228
Family history of skin diseases	121	37	123	32	0.153

CD: coeliac disease; BMI: body mass index.
[a]Including 22 patients diagnosed with dermatitis herpetiformis.
[b]Diabetes type I and II.
[c]Including all cancer types reported by the patient, also skin cancers.

Table 2. Odds Ratios and 95% confidence intervals for reported skin diseases in coeliac disease patients compared to non-coeliac controls and skin disease frequencies reported in previous studies.

	CD patients $n = 327$	%	Non-CD controls $n = 382$	%	OR	95% CI	Previously reported frequencies %
Any skin disease[a]	113	35	132	35	1.0	0.7–1.4	43 [31]
Atopic dermatitis	45	14	49	13	1.1	0.7–1.7	25–30 [32]
Acne	27	8	34	9	0.9	0.5–1.6	9 [33]
Rosacea	17	5	18	5	1.1	0.6–2.2	5.5 [34]
Psoriasis	13	4	11	3	1.4	0.6–3.2	1.5–3.9 [31,35]
Alopecia areata	7	2	5	1	1.6	0.5–5.2	5.1 [31]
Vitiligo	7	2	7	2	1.2	0.4–3.4	0.5–2 [36]
Chronic urticaria	5	2	12	3	0.5	0.2–1.4	1.0 [31]

CD: coeliac disease; OR: odds ratio; CI: confidence interval.
[a]Including skin diseases listed in the table and all others reported by the study patients.

Table 3. Changes in the severity of skin disease after initiation of gluten-free diet in coeliac disease patients[a].

	Number of CD patients	Improvement[b]	
		n	%
Atopic dermatitis	41	23	56
Acne	23	8	35
Rosacea	12	6	50
Psoriasis	11	3	27
Alopecia areata	7	3	43
Vitiligo	6	0	0
Chronic urticaria	5	2	40

CD: coeliac disease.
[a]Including only patients diagnosed with skin diseases before coeliac disease diagnosis.
[b]Patients reporting partial or complete response in skin symptoms during gluten-free diet.

dermatitis and acne, two of the most commonly reported skin diseases, were compared between the study groups, no statistically significant differences were detected ($p = 0.069$ and $p = 0.588$, respectively). For any skin disease, use of topical corticosteroids or emollients likewise did not differ between the groups as in both groups 6% used topical corticosteroids and 47% emollients at the time of the study.

Risk for any allergy was not shown to be increased among coeliac disease patients compared to non-coeliac controls (OR 1.0, 95% CI 0.7–1.4). In both study groups, allergies were diagnosed in 31% of the patients ($p = 0.972$), the most common allergy in both groups being pollen allergy, reported by 67% of patients with coeliac disease and 56% of non-coeliac controls ($p = 0.095$). Contact allergy was reported in 14% and 18% in the respective groups ($p = 0.447$).

Out of 709 coeliac and non-coeliac respondents, 659 completed the DLQI questionnaire, 79% being females. Altogether, 9% (25 out of 275) of the patients with coeliac disease had a DLQI score ≥6 indicating at least moderate effect on life quality compared to 5% (19 out of 362) of the non-coeliac controls ($p = 0.004$). When patients with DH were analyzed separately from the patients with other coeliac disease phenotypes, DLQI score ≥6 was found in 23% (5 out of 22) of the patients with DH. Among all coeliac disease patients, the likelihood of having DLQI score ≥6 was increased (OR 2.03, 95% CI 1.12–3.68), but when DH and other phenotypes of coeliac disease were analyzed separately, DLQI score ≥6 was statistically significantly more likely to be increased among DH patients (OR 5.31, 95% CI 1.77–15.93) and borderline increase was detected among patients with other coeliac disease phenotypes (OR 1.81, 95% CI 0.97–3.35).

Effects of gluten-free diet in skin diseases in coeliac disease patients

When the effect of GFD on skin diseases was analyzed among coeliac disease patients diagnosed with a skin disease prior to coeliac disease, 56% of those with atopic dermatitis reported alleviation of their skin symptoms due to the diet (Table 3). When these patients were compared to patients experiencing no positive effect of GFD on atopic dermatitis, they reported suffering from some type of skin symptoms at the time of coeliac disease diagnosis more often ($p = 0.051$), but no other differences were detected in the demographic or background data. In addition, 50% of the patients with rosacea and 43% of those with alopecia areata reported alleviation of skin symptoms after initiation of GFD, but among those with vitiligo none reported benefitting from the diet.

Discussion

This study investigating patient-reported prevalence and severity of skin diseases did not find increased risk for atopic dermatitis, acne, rosacea, psoriasis, alopecia areata, vitiligo, chronic urticaria or any skin disease among patients with coeliac disease. Moreover, from the patient perspective, the severity of all of these skin diseases was found not to differ between coeliac disease patients and non-coeliac controls. Surprisingly, quality of life effects of dermatological diseases were more notable among patients with coeliac disease, and the effect was related especially, but not solely, to DH, a cutaneous phenotype of coeliac disease.

In large, register-based studies coeliac disease patients have previously been shown to be at 1.6–1.7-fold risk for psoriasis [12,14,15], at three-fold risk for atopic dermatitis [37] and at 1.5–1.9 increased risk for any kind of urticaria as well as for chronic urticaria [12,15]. Associations between coeliac disease and alopecia areata and vitiligo have mostly been established in studies with limited numbers of patients or studies lacking controls [16,18,38]. Overall, the existing evidence on associations between coeliac disease and skin diseases has been based on highly heterogenous study cohorts

or registers without diagnosis verification. Moreover, some associations have been based on studies demonstrating higher prevalence of coeliac disease among patients with specific skin diseases [39–42] and the diagnosis of coeliac disease has not been biopsy proven in all studies, at times even relying on non-specific antigliadin antibodies [16,24,43]. Moreover, as DH rash is not always easy to recognize, it may be that in some cohorts there are individuals with skin symptoms related to DH but misdiagnosed, for example, as atopic dermatitis. In Finland the prevalence of DH is the highest thus far reported [5], thereby decreasing the possibility of undiagnosed DH in our study cohort, which could at least partly explain the detected lack of increased risk for other skin diseases among patients with coeliac disease. We additionally emphasize that some earlier studies corroborate our current results showing that coeliac disease is not associated, for example, with chronic urticaria, vitiligo, alopecia areata or allergies [16–18,37].

In this study, the prevalence of skin diseases in coeliac disease patients and controls did not differ even when females and males were analyzed separately. Likewise, differences were not detected when analyses were performed in age groups ≤50 and >50 years of age. There is a previous study reporting that only females with chronic urticaria are at increased risk for coeliac disease [39], while another study has demonstrated an increased risk for coeliac diseases in females, but not males, with rosacea [40]. However, the effects of age or gender on the prevalence of different skin diseases in patients with coeliac disease have so far been scarcely studied. In this study, DH and all other phenotypes of coeliac disease were also analyzed separately in terms of skin disease frequencies, since DH patients could be more aware of their skin symptoms and are treated by dermatologists more likely diagnosing also other skin diseases. The risks for rosacea and alopecia areata were shown to be increased among those with DH, but for those with other coeliac disease phenotypes, risks remained unchanged. However, due to low number of DH patients in the study, the results concerning DH subgroup remain unreliable. This issue nevertheless warrants further investigation, since disease associations between DH and coeliac disease patients have been shown to differ [44], and the risk of bullous pemphigoid, for example, has been shown to be 22-fold in DH and only two-fold in coeliac disease [45].

The median age when skin diseases where diagnosed did not differ statistically significantly between patients with coeliac disease and non-coeliac controls. However, psoriasis in particular was diagnosed at an older age among coeliac disease patients, but the number of patients was undoubtedly too low for this analysis. This issue, as the severity of skin diseases between coeliac disease patients and non-coeliac controls should be further investigated as evidence is largely lacking. However, in this study, patient-reported severity of skin diseases was shown to be comparable between coeliac disease patients and non-coeliac controls in all skin diseases investigated. Likewise, the treatment modalities used for the respective skin diseases did not differ significantly between the groups, thereby supporting the finding of similar skin disease severities. Somewhat surprisingly, coeliac disease patients were found to be at increased risk of experiencing at least a moderate effect on their dermatological quality of life. The risk was increased especially among patients with DH, and most likely largely explained by the patient inclusion criteria and somewhat short duration of GFD as the skin symptoms of DH are known to often resolve relatively slowly [46], and as in our earlier study quality of life of long-term treated DH patients was shown not to differ from controls [47]. Nonetheless, even coeliac disease patients seemed to be at increased risk of their skin disease impairing their quality of life at least moderately. This implies that patients with coeliac disease experience more skin-related problems than non-coeliac controls, but this study could not find the reason for this.

In this study, GFD seemed to particularly alleviate symptoms of atopic dermatitis in patients with coeliac disease, especially in those reporting some type of skin symptoms before coeliac disease diagnosis. The possibility therefore undoubtedly exists that these symptoms were indeed coeliac-related skin symptoms, such as DH, in sporadic cases, but most likely does not offer an explanation for the majority of these patients. For other skin diseases the impact of GFD was not quite as evident or was even totally absent. This dietary impact has been studied in particular in psoriasis and alopecia areata, but the results have been inconsistent and population sizes rather limited [23,25,27,48]. Consequently, more research is needed on the effects of GFD in skin diseases occurring in patients with coeliac disease, and, given the results of this study, particularly focusing on atopic dermatitis.

A notable strength of this study is that it investigated skin diseases from the patient perspective; such subjective information cannot be collected from registers. A further strength is that the study was conducted in a country with high clinical prevalence of both DH and coeliac disease an also with good GFD adherence rates [5,49,50]. Additionally, in this study all severities, from mild to severe, of each skin disease could be investigated since the data was not based, for example, on hospital records. On the other hand, all diagnoses as well as the severities of skin diseases and the effects of GFD on them were patient reported and not verified from patient records. However, we highlight that the risk for false diagnosis concerns register-studies as well, as diagnostic codes can be entered in the registers already when the disease is suspected or alternatively, without adequate disease confirmation. Moreover, since this was a questionnaire study, there is a possibility of selection bias, especially among controls with lower response rate. It is conceivable that non-coeliac subjects with diagnosed skin diseases were more likely to respond to the questionnaire study, which may have affected the results of this study. However, we emphasize that the frequencies of various skin diseases in this study were largely congruent with the generally known ones (Table 2) [31–36], thus notable over representation was not detected among controls.

In conclusion, in this patient perspective questionnaire study no association between coeliac disease and studied skin diseases could be established. Considering earlier, large register-based studies demonstrating such connections, more

clinical studies with undisputable diagnoses of both coeliac disease and skin diseases are needed. However, this study showed that coeliac disease patients are at increased risk of their skin disease affecting their quality of life at least moderately, and this seems not to be explained solely by skin symptoms related to DH. Therefore, even though further evidence is needed before coeliac disease patients should be routinely investigated for skin diseases or vice versa, general practitioners and gastroenterologists treating coeliac disease patients should be more aware of the possibility of dermatological concerns and referral to a dermatologist for further examination should be considered.

Disclosure statement

The authors report there are no competing interests to declare.

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Data availability statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to Finnish legislation concerning patient-related data.

References

[1] Lindfors K, Ciacci C, Kurppa K, et al. Coeliac disease. Nat Rev Dis Primers. 2019;5(1):3–3. doi: 10.1038/s41572-018-0054-z.
[2] Leffler DA, Green PH, Fasano A. Extraintestinal manifestations of coeliac disease. Nat Rev Gastroenterol Hepatol. 2015;12(10):561–571. doi: 10.1038/nrgastro.2015.131.
[3] Salmi T, Hervonen K. Current concepts of dermatitis herpetiformis. Acta Derm Venereol. 2020;100(5):adv00056. doi: 10.2340/00015555-3401.
[4] Görög A, Antiga E, Caproni M, et al. S2k guidelines (consensus statement) for diagnosis and therapy of dermatitis herpetiformis initiated by the european academy of dermatology and venereology (EADV). J Eur Acad Dermatol Venereol. 2021;35(6):1251–1277. doi: 10.1111/jdv.17183.
[5] Salmi T, Hervonen K, Kautiainen H, et al. Prevalence and incidence of dermatitis herpetiformis: a 40-year prospective study from Finland. Br J Dermatol. 2011;165(2):354–359. doi: 10.1111/j.1365-2133.2011.10385.x.
[6] West J, Fleming KM, Tata LJ, et al. Incidence and prevalence of celiac disease and dermatitis herpetiformis in the UK over two decades: population-based study. Am J Gastroenterol. 2014;109(5):757–768. doi: 10.1038/ajg.2014.55.
[7] Elfström P, Sundström J, Ludvigsson JF. Systematic review with meta-analysis: associations between coeliac disease and type 1 diabetes. Aliment Pharmacol Ther. 2014;40(10):1123–1132. doi: 10.1111/apt.12973.
[8] Elfström P, Montgomery SM, Kämpe O, et al. Risk of thyroid disease in individuals with celiac disease. J Clin Endocrinol Metab. 2008;93(10):3915–3921. doi: 10.1210/jc.2008-0798.
[9] Caproni M, Bonciolini V, D'Errico A, et al. Celiac disease and dermatologic manifestations: many skin clue to unfold gluten-sensitive enteropathy. Gastroenterol Res Pract. 2012;2012:952753. doi: 10.1155/2012/952753.
[10] Rodrigo L, Beteta-Gorriti V, Alvarez N, et al. Cutaneous and mucosal manifestations associated with celiac disease. Nutrients. 2018;10:800. doi: 10.3390/nu10070800.
[11] Ludvigsson JF, Lindelöf B, Zingone F, et al. Psoriasis in a nationwide cohort study of patients with celiac disease. J Invest Dermatol. 2011;131(10):2010–2016. doi: 10.1038/jid.2011.162.
[12] Ludvigsson JF, Lindelöf B, Rashtak S, et al. Does urticaria risk increase in patients with celiac disease? A large population-based cohort study. Eur J Dermatol. 2013;23(5):681–687. doi: 10.1684/ejd.2013.2158.
[13] Lebwohl B, Sundström A, Jabri B, et al. Isotretinoin use and celiac disease: a population-based cross-sectional study. Am J Clin Dermatol. 2014;15(6):537–542. doi: 10.1007/s40257-014-0090-8.
[14] Egeberg A, Griffiths CEM, Mallbris L, et al. The association between psoriasis and coeliac disease. Br J Dermatol. 2017;177(6):e329–e330. doi: 10.1111/bjd.15684.
[15] Lebwohl B, Söderling J, Roelstraete B, et al. Risk of skin disorders in patients with celiac disease: a population-based cohort study. J Am Acad Dermatol. 2021;85(6):1456–1464. doi: 10.1016/j.jaad.2020.10.079.
[16] Mokhtari F, Panjehpour T, Naeini FF, et al. The frequency distribution of celiac autoantibodies in alopecia areata. Int J Prev Med. 2016;7:109. doi: 10.4103/2008-7802.190607.
[17] Gabrielli M, Candelli M, Cremonini F, et al. Idiopathic chronic urticaria and celiac disease. Dig Dis Sci. 2005;50(9):1702–1704. doi: 10.1007/s10620-005-2919-8.
[18] Volta U, Bardazzi F, Zauli D, et al. Serological screening for coeliac disease in vitiligo and alopecia areata. Br J Dermatol. 1997;136:801–802.
[19] Silano M, Volta U, Vincenzi AD, et al. Effect of a gluten-free diet on the risk of enteropathy-associated T-cell lymphoma in celiac disease. Dig Dis Sci. 2008;53(4):972–976. doi: 10.1007/s10620-007-9952-8.
[20] Barbato M, Viola F, Grillo R, et al. Alopecia and coeliac disease: report of two patients showing response to gluten-free diet. Clin Exp Dermatol. 1998;23(5):236–237.
[21] Naveh Y, Rosenthal E, Ben-Arieh Y, et al. Celiac disease-associated alopecia in childhood. J Pediatr. 1999;134(3):362–364. doi: 10.1016/s0022-3476(99)70466-x.
[22] Fessatou S, Kostaki M, Karpathios T. Coeliac disease and alopecia areata in childhood. J Paediatr Child Health. 2003;39(2):152–154. doi: 10.1046/j.1440-1754.2003.00116.x.
[23] De Bastiani R, Gabrielli M, Lora L, et al. Association between coeliac disease and psoriasis: italian primary care multicentre study. Dermatology. 2015;230(2):156–160. doi: 10.1159/000369615.
[24] Kolchak NA, Tetarnikova MK, Theodoropoulou MS, et al. Prevalence of antigliadin IgA antibodies in psoriasis vulgaris and response of seropositive patients to a gluten-free diet. J Multidiscip Healthc. 2018;11:13–19. doi: 10.2147/JMDH.S122256.
[25] Bhatia BK, Millsop JW, Debbaneh M, et al. Diet and psoriasis, part II: celiac disease and role of a gluten-free diet. J Am Acad Dermatol. 2014;71(2):350–358. doi: 10.1016/j.jaad.2014.03.017.
[26] Bondavalli P, Quadri G, Parodi A, et al. Failure of gluten-free diet in celiac disease-associated alopecia areata. Acta Derm Venereol. 1998;78:319.
[27] Bardella MT, Marino R, Barbareschi M, et al. Alopecia areata and coeliac disease: no effect of a gluten-free diet on hair growth. Dermatology. 2000;200(2):108–110. doi: 10.1159/000018340.
[28] Kurppa K, Lauronen O, Collin P, et al. Factors associated with dietary adherence in celiac disease: a nationwide study. Digestion. 2012;86(4):309–314. doi: 10.1159/000341416.
[29] Finlay AY, Khan GK. Dermatology life quality index (DLQI) - a simple practical measure for routine clinical use. Clin Exp Dermatol. 1994;19(3):210–216. doi: 10.1111/j.1365-2230.1994.tb01167.x.
[30] Paavola S, Lindfors K, Kivelä L, et al. Presence of high-risk HLA genotype is the most important individual risk factor for coealic disease among at-risk relatives. Aliment Pharmacol Ther. 2021;54(6):805–813. doi: 10.1111/apt.16534.
[31] Richard MA, Paul C, Nijsten T, et al. Prevalence of most common skin diseases in Europe: a population-based study. J Eur Acad Dermatol Venereol. 2022;36(7):1088–1096. doi: 10.1111/jdv.18050.

[32] Atopic eczema. Current Care Guidelines. Working group set up by the Finnish Medical Society Duodecim, Finnish Dermatological Society and Finnish Association for General Practice. Helsinki: The Finnish Medical Society Duodecim; 2023. (referred June 24, 2023). Available from: www.kaypahoito.fi

[33] Tan JK, Bhate K. A global perspective on the epidemiology of acne. Br J Dermatol. 2015;172:3–12. doi: 10.1111/bjd.13462.

[34] Gether L, Overgaard LK, Egeberg A, et al. Incidence and prevalence of rosacea: a systematic review and meta-analysis. Br J Dermatol. 2018;179(2):282–289. doi: 10.1111/bjd.16481.

[35] Psoriasis and psoriatic arthritis. Current Care Guidelines. Working group set up by the Finnish Medical Society Duodecim, Finnish Dermatological Society and Finnish Society for Rheumatology. Helsinki: The Finnish Medical Society Duodecim; 2023. (referred June 24, 2023). Available from: www.kaypahoito.fi

[36] Bergqvist C, Ezzedine K. Vitiligo: a review. Dermatology. 2020;236(6):571–592. doi: 10.1159/000506103.

[37] Ciacci C, Cavallaro R, Iovino P, et al. Allergy prevalence in adult celiac disease. J Allergy Clin Immunol. 2004;113(6):1199–1203. doi: 10.1016/j.jaci.2004.03.012.

[38] Shahmoradi Z, Najafian J, Naeini FF, et al. Vitiligo and autoantibodies of celiac disease. Int J Prev Med. 2013;4:200–203.

[39] Confino-Cohen R, Chodick G, Shalev V, et al. Chronic urticaria and autoimmunity: associations found in a large population study. J Allergy Clin Immunol. 2012;129(5):1307–1313. doi: 10.1016/j.jaci.2012.01.043.

[40] Egeberg A, Hansen PR, Gislason GH, et al. Clustering of autoimmune diseases in patients with rosacea. J Am Acad Dermatol. 2016;74(4):667–672.e1. doi: 10.1016/j.jaad.2015.11.004.

[41] Egeberg A, Weinstock LB, Thyssen EP, et al. Rosacea and gastrointestinal disorders: a population-based cohort study. Br J Dermatol. 2017;176(1):100–106. doi: 10.1111/bjd.14930.

[42] Andersen YM, Egeberg A, Gislason GH, et al. Autoimmune diseases in adults with atopic dermatitis. J Am Acad Dermatol. 2017;76(2):274–280.e1. doi: 10.1016/j.jaad.2016.08.047.

[43] Shalom G, Kridin K, Raviv KO, et al. Atopic dermatitis and celiac disease: a cross-sectional study of 116,816 patients. Am J Clin Dermatol. 2020;21(1):133–138. doi: 10.1007/s40257-019-00474-2.

[44] Nurmi R, Pasternack C, Salmi T, et al. The risk of renal comorbidities in celiac disease patients depends on the phenotype of celiac disease. J Intern Med. 2022;292(5):779–787. doi: 10.1111/joim.13532.

[45] Varpuluoma O, Jokelainen J, Försti AK, et al. Dermatitis herpetiformis and celiac disease increase the risk of bullous pemphigoid. J Invest Dermatol. 2019;139(3):600–604. doi: 10.1016/j.jid.2018.10.010.

[46] Pasternack C, Hervonen K, Mansikka E, et al. Persistent skin symptoms after diagnosis and on a long-term gluten-free diet in dermatitis herpetiformis. Acta Derm Venereol. 2021;101(9):adv00555. doi: 10.2340/00015555-3914.

[47] Pasternack C, Kaukinen K, Kurppa K, et al. Quality of life and gastrointestinal symptoms in long-term treated dermatitis herpetiformis patients: a cross-Sectional study in Finland. Am J Clin Dermatol. 2015;16(6):545–552. doi: 10.1007/s40257-015-0149-1.

[48] Ertekin V, Tosun MS, Erdem T. Screening of celiac disease in children with alopecia areata. Indian J Dermatol. 2014;59(3):317. doi: 10.4103/0019-5154.131468.

[49] Virta LJ, Kaukinen K, Collin P. Incidence and prevalence of diagnosed coeliac disease in Finland: results of effective case finding in adults. Scand J Gastroenterol. 2009;44(8):933–938. doi: 10.1080/00365520903030795.

[50] Laurikka P, Salmi T, Collin P, et al. Gastrointestinal symptoms in celiac disease patients on a long-term gluten-free diet. Nutrients. 2016;8:429. doi: 10.3390/nu8070429.