The effect of gluten on skin and hair: a systematic review

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Abstract

Non-celiac gluten sensitivity is often clinically indistinguishable from celiac disease, and patients show improvement or resolution of their symptoms with a gluten-free diet. In contrast to celiac disease, the effects of gluten on the skin and hair in the context of non-celiac gluten sensitivity are not as clear. This review aims to describe the impact of gluten on the skin and hair in patients with non-celiac gluten sensitivity and those without a definitive celiac disease diagnosis. A literature search was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) reporting guidelines for systematic reviews. Forty-two publications met inclusion criteria with five studies describing the skin manifestations of non-celiac gluten sensitivity. Trials identifying the impact of a gluten-free diet on skin disease, as well as dermatologic conditions and their associations with antigliadin antibodies were also identified. Dermatologic manifestations in patients with non-celiac gluten sensitivity vary and may be non-specific. It may be appropriate for some of these patients with skin manifestations to trial a gluten-free diet. Dermatologic conditions that may respond positively to a gluten-free diet include psoriasis, atopic dermatitis, vitiligo, and palmoplantar pustulosis, while linear IgA disease does not appear to improve with this dietary change.

Keywords: diet, gluten, hair, non-celiac gluten sensitivity, skin

Introduction

The increasingly popular global market for gluten-free foods is projected to be valued at 8.1 billion U.S. dollars by the end of 2023 [1], and growing evidence supports the notion that dietary modifications may play a valuable role in the treatment of skin conditions [2].

A gluten-free (GF) diet is not only embraced by individuals with celiac disease (CD) or wheat allergy (WA), but also an expanding number of patients without these diagnoses [3,4]. Non-celiac gluten sensitivity (NCGS) describes such individuals who have had CD and wheat allergy definitely ruled out. Patients with NCGS have intestinal and extraintestinal manifestations soon after gluten ingestion, relief of symptoms with a GF diet, negative CD serology (anti-tissue transglutaminase and anti-endomysial antibodies), normal intestinal biopsy, and negative skin prick or serum IgE testing on a gluten-containing diet [3,5,6], (**Figure 1**). There are no specific diagnostic criteria for NCGS. Some authors suggest use of antigliadin antibodies (AGAs), particularly of the IgG subtype, to aid in the diagnosis [3], while others assert it is too non-specific [7]. A 2015 consensus highlighted that diagnosis should include assessment of clinical response to a GF diet, as well as worsening symptoms with either a single-blind or double-blind placebo-controlled gluten challenge [8].

While dermatitis herpetiformis (DH) is a well-known manifestation of CD, the effects of gluten on the skin and hair in the context of NCGS are not as clear. This

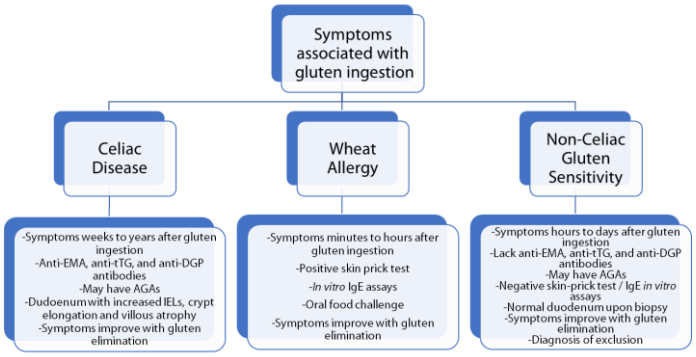

Figure 1. *Disease entities related to the ingestion of gluten [3].*

AGAs, antigliadin antibodies; DGP, deamidated gliadin peptide; EMA, endomysial antibodies; IELs, intraepithelial lymphocytes; IgE, immunoglobulin E; tTG, tissue transglutaminase antibodies.

systematic review aims to review the effect of gluten on the skin and hair in NCGS patients and those without a definitive CD diagnosis.

Methods

A primary literature search was conducted in September 2019 using the databases PubMed/MEDLINE and Web of Science with the following search terms: "((((hair) OR hair[MeSH Terms])) OR ((skin) OR skin[MeSH Terms])) AND gluten" in PubMed and "TOPIC: (skin OR hair) AND TOPIC: (gluten)" in Web of Science according to the PRISMA reporting guidelines for systematic reviews [9]. All available studies prior to September 2019 were considered for inclusion. Bibliographies of the articles were also searched to identify additional studies for inclusion. The inclusion criteria for this article were: 1) relevant human studies on gluten and its association with changes in skin or hair; 2) articles relating gluten exposure to skin and hair disease; and 3) studies relating AGAs to skin or hair given its prior association with NCGS and lack of specificity for CD. Exclusion criteria were studies written in non-English languages, review articles, correspondence articles, non-human studies, articles discussing gluten and skin and hair disease only in the context of CD, DH, or wheat allergy. No randomized controlled trials were available. Studies included were graded using the Oxford Center for Evidence-Based Medicine 2011 Levels of Evidence [9].

Results

A total of 180 articles were reviewed in their entirety; 42 articles met the inclusion/exclusion criteria (**Figure 2**). Three main themes were identified relating gluten to skin and hair: dermatologic manifestations in patients with NCGS, response to dietary gluten exclusion or inclusion, and dermatologic manifestations and AGAs.

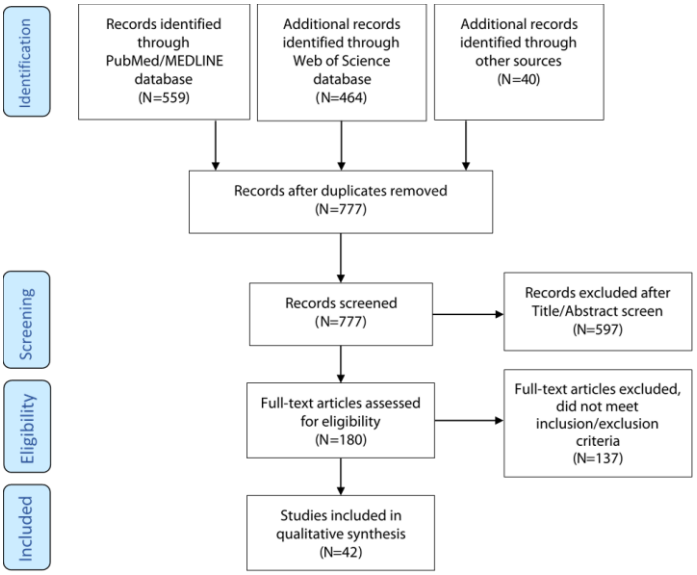

Figure 2. *Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) flow diagram for the literature review of gluten and its association with skin and hair.*

Dermatologic manifestations in patients with non-celiac gluten sensitivity

Five studies were identified that explicitly described skin manifestations in patients with NCGS (**Table 1**). Across the five studies, a range of specific and non-specific skin findings were described. There was limited evidence for papular-vesicular lesions, urticaria-angioedema, generalized pruritus, and psoriasis-like lesions as presenting features of NCGS [10,11]. The most commonly described manifestation was a non-specific dermatitis, eczema, and/or rash, seen across four studies [3,6,11,12].

In a cohort study of 17 NCGS patients with cutaneous manifestations, skin findings included erythematous, excoriated, papular-vesicular, pruritic lesions resembling subacute eczema and dermatitis herpetiformis, as well as hyperkeratotic lesions resembling psoriasis [10]. The distribution mimicked

Table 1. *Dermatologic manifestations in patients with non-celiac gluten sensitivity.*

Study	Study Design (Evidence Level)	Subjects (N)	Patient Description	Skin Findings
Bonciolini et al. [10]	Cohort Study (II)	17	NCGS with skin manifestations improved by GFD; excluded WA and CD; used gluten elimination followed by DBPC food challenge to diagnose NCGS	Erythematous, excoriated, papular-vesicular itchy lesions similar to subacute eczema or DH likely represented early manifestations Hyperkeratotic scaly lesions overlying erythematous infiltrative lesions resembling psoriasis likely represented later lesions secondary to frequent excoriation Proclivity for the extensor surfaces such as the elbows (94%) and knees (59%) Lesions disappeared 1 month after GFD A specific histological pattern was not identified, though lesions appeared to have a lymphocytic infiltrate and spongiosis in earlier lesions, and hyperkeratosis and a mixed infiltrate in lesions present for a longer duration. Histologically lesions resembled eczema, DH, and psoriasis On direct immunofluorescence, 82% of patients had C3 deposition along the dermoepidermal junction in a granular or micro-granular pattern
Volta et al. [6]	Cohort Study (II)	486	Patients with NCGS diagnosed after exclusion of CD and WA	18% of patients had an associated dermatitis and 29% had an associated skin rash Symptoms occurred in 95% of NCGS patients every time or often after gluten ingestion, most commonly within 6 hours of ingestion 25% IgG AGA positive
Volta et al. [12]	Cohort Study (II)	78	Patients with NCGS in Italy	33% of patients had eczema or skin rash IgG AGA was present in 56.4% of patients
Faina et al. [11]	Cross-Sectional (IV)	339	Patients with NCGS in Italy	65.6% had cutaneous manifestations: Eczematous dermatitis (45%) – atopic dermatitis, chronic hand eczema, psoriasiform-dermatitis, and generalized eczematous dermatitis Urticaria-angioedema (36.4%) Generalized itching (10%) Psoriasiform lesions (9%)
Sapone et al. [3]	Cross-Sectional (IV)	347	Patients with NCGS at the Center for Celiac Research, University of Maryland	40% experienced symptoms of eczema and/or rash

Abbreviations: AGA, antigliadin antibodies; CD, celiac disease; DH, dermatitis herpetiformis; DBPC, double-blind placebo-controlled challenge; GFD, gluten free diet; NCGS, non-celiac gluten sensitivity; WA, wheat allergy.

that of dermatitis herpetiformis and psoriasis, with a proclivity for the extensor surfaces, and lesions histologically resembled eczema, dermatitis herpetiformis, and psoriasis [10]. A total of three patients were AGA-positive, though the subtype was not specified [10]. On average, skin manifestations resolved with one month of a GF diet [10].

In survey-based study of 486 NCGS patients, skin manifestations included associated dermatitis in 18% of patients and unspecified skin rash in 29% of patients [6]. Antigliadin-IgG antibodies were present in 25% of patients tested [6]. In these patients, CD and wheat allergy were ruled out with serologic, IgE, and/or skin prick testing [6]. Importantly, however, the patients did not undergo a double-blind

placebo-controlled gluten challenge [6]. In a similar NCGS study with 78 patients, 33% reported symptoms of eczema and skin rash while on a gluten-containing diet [12]. Antigliadin-IgG antibodies were present in 56% of patients [12]. Celiac disease and wheat allergy were excluded by CD serologic tests, IgE and skin prick tests, and small intestinal biopsies, all while on a gluten-containing diet [12].

In another study involving 339 NCGS patients, 65.6% experienced cutaneous manifestations including eczematous dermatitis (45%), urticaria-angioedema (36.4%), generalized itching (10%), and psoriasiform lesions (9%) [11]. It was not specified how the diagnosis of NCGS was made in these patients [11]. In a cross-sectional study involving 347 individuals at the Center for Celiac Research, 40% of the patients who met criteria for NCGS with negative CD testing experienced symptoms of an unspecified eczema and/or rash [3].

Dermatologic conditions and their responses to gluten exclusion or inclusion

The evidence for clinical improvement in cutaneous conditions is limited. Two studies described the response of psoriasis to a GF diet. In the first study encompassing 1,206 patients, 53% of individuals experienced improvement in their skin disease [13], while in the second study with 39 patients, 73% of AGA-positive patients experienced improvement [14]. One atopic dermatitis study with 5,202 children was identified in which early gluten exposure decreased the risk of eczema until age ten [15]. Though studies describing the response of vitiligo to a GF diet are limited, vitiligo appeared to favorably respond to a GF diet in a single case study [16]. Linear IgA disease (LAD) did not appear to improve with a GF diet, though the evidence was limited as only one case series with six patients was identified [17]. In a cohort study examining the effect of a GF diet on pustulosis palmoplantaris, three AGA-positive patients had improvement in their skin disease with a GF diet [18]. In a single study, skin pruritus appeared to be more common in patients without a clear CD diagnosis as compared to those with CD while on a GF diet [19].

Psoriasis

In a National Psoriasis Foundation survey study, 53% of 1,206 respondents reported clearance or improvement of psoriasis with a GF diet (**Table 2**), [13]. Whether or not patients had CD or NCGS was not specified. In a prospective, nonrandomized, controlled study of 39 psoriasis patients, after a 3-month GF diet, 73% of AGA-positive patients had a decrease in Psoriasis Area and Severity Index (PASI), 24% had a decrease in treatment regimen, and 0% had an increase in treatment regimen [14]. In contrast, AGA-negative patients did not have PASI improvements or treatment regimen decreases, while 33% had increases in treatment regimen. Notably, two AGA-positive patients were EMA-IgA positive and 15 had duodenal intraepithelial lymphocytes [14]. However, 16 patients with AGA-positivity whose skin improved on a GF diet had normal pre-GF diet duodenal biopsies [14].

Not only are there clinically apparent changes in psoriasis lesions with a GF diet, but there may be accompanying histologic changes. After a 3-month GF diet in 31 AGA-positive individuals, there was a decline in CD4+ lymphocytes in psoriasis-affected epidermis (P=0.027), [20]. Notably, two patients had EMA-IgA positivity and two had partial villous atrophy [20], suggesting undiagnosed CD.

Atopy

In the Generation R study, a population-based prospective cohort study involving 5,202 children, compared to gluten exposure after six months of age, gluten exposure at less than six months decreased eczema risk until age ten (adjusted OR=0.84) [15]. Furthermore, in a cross-sectional study of 169 patients, 51% of individuals with atopic dermatitis who removed gluten from their diet reported skin disease improvement [21]. Whether or not these individuals who reported improvement had concomitant CD or NCGS was not specified [21].

Vitiligo

A single case report highlights the relationship between vitiligo and gluten. A 22-year-old South Indian female, without gastrointestinal symptoms or history of CD, had a 3-year history of recalcitrant acrofacial vitiligo [16]. The patient experienced significant re-pigmentation within the first month of

a GF diet, with peak repigmentation at three months [16]. Long-term follow up was limited [16].

Linear IgA disease

In a case series of six patients with LAD without clear evidence of CD, four of six patients had no significant reduction in drug requirements after adopting a GF diet [17]. Two of six patients had significant decreases in drug requirements, however they did not require a subsequent increase after re-introduction of gluten [17]. Thus, LAD activity did not appear to be affected by a GF diet. Of note, one patient had evidence of CD with subtotal villous atrophy upon repeat intestinal biopsy after resumption of a gluten-containing diet [17].

Pustulosis palmoplantaris

In a cohort study involving 123 patients with pustulosis palmoplantaris, 13 patients with AGAs and/or tissue transglutaminase antibodies adhered to a GF diet for at least six months [18]. Three patients without AGAs and tissue transglutaminase also adhered to a GF diet. One patient with AGA-positivity, tissue transglutaminase-negativity, and normal duodenal mucosa had clearance of their pustulosis palmoplantaris with a GF diet, and subsequent recurrence after a gluten-containing diet [18]. Two patients with AGA-positivity and tissue transglutaminase-negativity with increased intraepithelial lymphocytes on biopsy had clearance of their pustulosis palmoplantaris with a GF diet [18]. The three patients without AGA and tissue transglutaminase antibodies had no change in pustulosis palmoplantaris severity with a GF diet [18].

Skin pruritus

In a retrospective cohort study with 137 patients, patients on a self-treated GF diet without a clear CD diagnosis had an increase in frequency of skin pruritus compared to those with CD (16% versus 9%, P=0.02) [19]. In the self-treated cohort, however, CD was not definitively excluded as multiple individuals were ultimately positive for CD-specific antibodies [19].

Dermatologic conditions and their associations with antigliadin antibodies

A total of 17 studies highlighted a relationship between psoriasis and AGA. Psoriasis patients had higher rates of AGA-IgA positivity compared to controls in approximately half of studies, and higher rates of AGA-IgG positivity compared to controls in two of three studies [22-30]. Linear IgA disease patients had higher rates of AGA-IgA positivity compared to controls in the one study identified [31]. Bullous Pemphigoid (BP) patients had higher rates of AGA-IgG and IgA positivity than controls in one study, [32] and some patients were positive for AGA-IgG and IgA in two cross-sectional studies [33,34]. Similarly, in two cross-sectional studies, some patients with pemphigus vulgaris (PV) were positive for AGA-IgG and IgA [33,34]. Of the two pustulosis palmoplantaris studies identified, in one study some patients were AGA-IgA positive, while in the other study no patients had elevated AGA of either subtype [35,36]. Two case reports linked chronic mucocutaneous candidiasis (CMC) to the presence of AGA [37,38]. One case report was identified describing AGA positivity in a cutaneous hyalinosis patient, and another case report described AGA positivity in a patient with lipodystrophia centrifugalis abdominalis infantilis [39,40].

Psoriasis

In nine of the 17 studies identified examining the relationship between psoriasis and AGAs, more psoriasis patients were AGA-IgA positive compared to controls, though this difference was not statistically significant across all studies (**Table 3**) [22-30,41-48]. In two studies with 116 and 87 patients, respectively, more psoriasis patients were AGA-IgG positive compared to controls (P<0.05 and P=0.073), [23,28], while in one study with 398 patients, controls had higher rates of AGA-IgG positivity (P=0.062), [29]. In contrast, four studies encompassing over 800 patients showed no significant difference between rates of both IgA and IgG AGA positivity in psoriasis patients compared to controls [42,44-46], and in one study with approximately 150 patients there was no significant difference between rates of AGA-IgG positivity between psoriasis patients and controls [24]. In a meta-analysis of 9 studies, psoriasis patients had over twice as high odds of testing positive for AGA-IgA compared to controls (OR=2.36, P=0.015), [48].

Whether or not patients with AGA positivity also met criteria for CD was not highlighted in most studies.

Linear IgA disease
In one case control study with 97 patients, adults with LAD had higher IgA and similar IgG AGA titers compared to controls (P<0.05) [31].

Bullous pemphigoid and pemphigus vulgaris
Three studies examined the occurrence of AGA in BP and PV. In a case control study involving 89 patients comparing BP and PV patients to healthy controls, those with BP had higher IgG and IgA AGA titers than controls (both P<0.001), [32]. In a cross-sectional study with 112 patients, 34% and 37% of PV patients were IgG and IgA AGA positive, respectively [33]. Similarly, 35% and 33% of BP patients were IgG and IgA AGA positive, respectively [33]. In another cross sectional study with 105 patients, 78% of PV and 75% of BP patients were positive for AGA-IgG by ELISA, while 56% of PV and 31% of BP patients were positive for AGA-IgG by immunofluorescence [34]. No patients were positive for AGA-IgA [34]. Whether or not patients had CD was not elucidated in the three studies.

Pustulosis palmoplantaris
In a cross-sectional study of 59 pustulosis palmoplantaris patients, five patients reported a personal history of gluten intolerance [35]. Additionally, of the 39 patients who had blood samples evaluated, 10 were AGA-IgA positive. Two of these ten patients had a history of villous atrophy on intestinal biopsy [35], evidence of concomitant CD. In contrast, in another cross-sectional study of 62 pustulosis palmoplantaris patients, no patients had elevated AGA titers [36].

Chronic mucocutaneous candidiasis
Two case reports have linked CMC to the presence of AGAs. In one report, a 4-year-old male with CMC and symptoms of CD was found to have elevated AGA-IgG without DGP or tTG antibodies [37]. Despite a lack of laboratory or histologic findings suggestive of CD, a double-blind placebo-controlled gluten challenge was not performed. Another case of CMC associated with AGA-positivity has also been reported in a 13-year-old male, though this patient lacked symptoms of gluten sensitivity [38].

Cutaneous hyalinosis
A 75-year-old female with cutaneous hyalinosis was found to have elevated IgG and IgM antigluten antibodies, though she lacked symptoms of gluten sensitivity [39].

Lipodystrophia centrifugalis abdominalis infantilis
A 3-year-old female with lipodystrophia centrifugalis abdominalis infantilis without CD was positive for AGA-IgG in the setting of partial IgA deficiency [40]. She had no evidence of malabsorption and was negative for IgA AGA-IgA, EMA, and HLA haplotype associations typical for CD [40].

Alopecia areata
In a case control study, one alopecia areata patient was positive for CD antibodies, though the subtype was not specified [49]. There was no significant difference in AGA levels between cases and controls [49].

Discussion

The aim of this systematic review was to investigate the effect of gluten on the skin and hair in patients with NCGS and those without a definitive CD diagnosis. Three main themes were identified relating gluten to skin and hair: articles detailing the dermatologic manifestations in patients with NCGS, articles describing dermatologic conditions and their response to dietary gluten exclusion or inclusion, and articles relating dermatologic manifestations to antigliadin antibodies.

The dermatologic manifestations in patients with NCGS are often non-specific. The primary and secondary morphologies vary, ranging from erythematous, excoriated, papulovesicular lesions to hyperkeratotic scaly lesions [10]. An eczematous and/or non-specific dermatitis may be a more common skin manifestation of NCGS, though urticaria-angioedema, skin pruritus, and psoriasiform lesions are also seen (**Figure 3**), [6,10-12].

Dermatologic conditions which have been found to respond positively to a GF diet include psoriasis [13,14,50], atopic dermatitis [21], vitiligo [16], and pustulosis palmoplantaris [18], while LAD does not

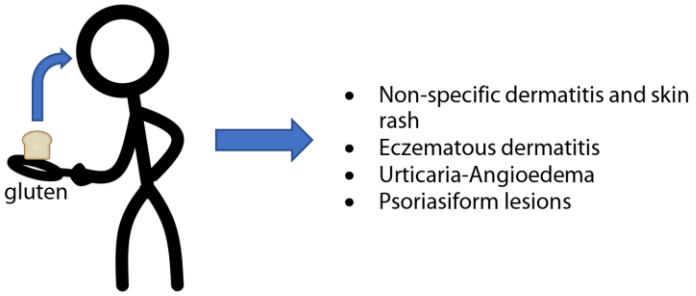

Figure 3. *Dermatologic manifestations related to non-celiac gluten sensitivity.*

appear to improve [16]. The data is mixed as to whether AGA positivity is required for psoriasis patients to benefit from a GF diet. One study found benefit of a GF diet in half of psoriasis patients, without mention of AGA status [13], while another study found benefit only in patients who were AGA-positive [14]. In a set of dietary recommendations by the National Psoriasis Foundation based on a systematic review of 55 studies evaluating a GF diet in 4,534 psoriasis patients, a three-month trial of a GF diet is weakly recommended for psoriasis patients with positive serologic markers for gluten sensitivity, even in the absence of CD [50]. However, universal screening for serologic markers in psoriasis patients without gastrointestinal symptoms or without a first-degree relative with CD is not recommended due to the high rate of false positive results [50]. In atopic dermatitis, there is evidence that a GF diet may improve symptoms [21], and early gluten exposure in children under the age of six months may decrease the risk of childhood eczema under age 10 [15]. The evidence supporting improvement of vitiligo with a GF diet in patients without CD is limited to a single case report identified describing repigmentation after treatment with a GF diet [16]. The vitiligo patient denied any gastrointestinal symptoms, which may be suggestive of absence of NCGS [16]. Linear IgA disease did not appear to improve with a GF diet in a case series with six patients [17]. In the only study identified on the utility of a GF diet in pustulosis palmoplantaris, there is some evidence of benefit in patients with AGA positivity and without a clear diagnosis of CD, but not in those patients without AGA positivity [18]. A limitation to many of these studies was that they did not specify if patients who improved on a GF diet also met criteria for CD or NCGS.

Some studies have found AGAs to be elevated in psoriasis patients, while other studies did not have this association [22-30,41-46]. Other conditions associated with AGA positivity include LAD [31], BP and PV [32-34], pustulosis palmoplantaris [35], CMC [37,38], cutaneous hyalinosis [39], and lipodystrophia centrifugalis abdominalis infantilis [40]. The clinical significance of this association is unclear as AGAs are non-specific for the diagnosis of either NCGS or CD, and can be found in either disease as well as in healthy individuals. Additionally, whether or not patients were on a GF diet or gluten-containing diet during measurement of the AGA was not standardized. Furthermore, some patients with dermatologic disease and AGA positivity had objective findings suggestive of CD, and in several cases CD was not ruled out. Whether AGAs were a marker for patients with NCGS in these studies is unclear, as patients often lacked a clear diagnosis of NCGS or CD. More studies are needed to elucidate a sensitive and specific marker for NCGS.

There are several limitations of this systematic review. No objective laboratory biomarkers are specific for NCGS and the diagnosis is based on exclusion criteria. Additionally, double-blind placebo-controlled food challenge tests, the gold standard for diagnosis, were rarely performed across studies. Symptom resolution reported by patients after a GF diet was also often based on subjective, and not objective findings, and symptoms related to gluten ingestion were not assessed in all studies. Furthermore, serologic tests were not always performed and in many studies it is unclear whether the patients truly had NCGS, or undiagnosed CD or wheat allergy. Lastly, the placebo/nocebo effect may also be responsible for the clinical response to a GF diet [51].

Conclusion

Patients often inquire about dietary advice for supplemental treatment of their skin conditions, and dermatologists have the opportunity to play a role in advising patients on these highly sought-after lifestyle modifications. It may be appropriate for some patients with NCGS and skin manifestations to trial a GF diet, though more high-quality studies are

needed to elucidate this benefit in patients who have had CD and wheat allergy definitively excluded.

Potential conflicts of interest

The authors declare no conflicts of interest.

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Table 2. *Dermatologic conditions and their responses to dietary gluten exclusion or gluten inclusion.*

Dermatologic Condition	Study	Study Design (Evidence Level)	Subjects (N)	Patient Description	Skin Findings / Skin Response
Psoriasis	Afifi et al. [13]	Cross-Sectional (IV)	1206	Psoriasis patients in the U.S. participating in a National Psoriasis Foundation survey	53% of respondents reported full clearance or improvement of psoriasis after GFD
	Michaëlsson et al. [14]	Prospective, nonrandomized, controlled (IIb)	39	Psoriasis patients, some with AGA positivity (n=33) and some with AGA negativity (n=6)	AGA positive patients: PASI improved from 5.5 to 3.6 after GFD (P<0.001); 24% of patients decreased their psoriasis treatment during GFD and 0% increased treatment; 60% of patients increased their psoriasis treatment during gluten-containing diet AGA negative patients: PASI worsened from 8.9 to 10.2 (P=0.47); 0% of patients decreased their psoriasis treatment during GFD and 33% increased treatment; 0% of patients increased their psoriasis treatment during gluten-containing diet
	Michaëlsson et al. [20]	Prospective, nonrandomized, controlled (IIb)	37	Patients with Psoriasis, n=31 who are AGA positive and n=6 who are AGA negative	AGA positive patients: significant reduction in CD4+ T lymphocytes in psoriasis-affected epidermis (P=0.027), tTG expression in psoriasis-affected dermis (P=0.0079), and Ki67+ cells in psoriasis-affected (P=0.0079) and normal (P=0.04) dermis after GFD
Atopic Dermatitis	Elbert et al. [15]	Population-based Prospective Cohort Study (II)	5202	Children in the Generation R Study	Risk of eczema in children introduced to gluten at age 6 months or younger was less than in children introduced over the age of 6 months (aOR=0.84)
	Nosrati et al. [21]	Cross-Sectional (IV)	169	Patients with Atopic Dermatitis	Improvement in skin was reported when removing gluten in 51.4% of patients Gluten was reported as a dietary trigger for AD symptoms in 18.3% of patients GFD was one of the three most successful diets for improving AD (along with dairy free and paleo diets) Gluten was avoided in 49% of patients
Vitiligo	Khandalavala et al. [16]	Case Report (V)	1	22-year-old female of South Indian ethnicity with a 3-year history of acrofacial vitiligo	Repigmentation after GFD

Linear IgA Disease	Leonard et al. [17]	Case Series (IV)	6	Patients with Linear IgA disease	4/6 patients had no significant alteration in drug requirements with GFD 2/6 patients had decrease in drug requirement with GFD but no increase after gluten reintroduction
Pustulosis Palmoplantaris	Michaëlsson et al. [18]	Cohort Study (II)	123	Patients with Palmoplantar Pustulosis, some of whom had IgA AGA and/or tTG	1 patient AGA positive, tTG negative, normal biopsy: clearance of PPP with GFD 2 patients AGA positive, tTG negative, increased IEL: clearance of PPP with GFD 3 patients AGA and tTG negative, normal biopsy or increased IEL: no change in PPP with GFD
Skin Pruritus	Coburn et al. [19]	Cohort Study (II)	137	Patients on ST-GFD prior to CD testing; Patients on physician-recommended GFD without clear evidence of CD; Patients with clear evidence of CD were excluded from the ST-GFD group	Compared to CD patients, ST-GFD patients more frequently had itchy skin (16% vs 9%; P=0.02)

Abbreviations: AGA, antigliadin antibodies; CD, celiac disease; GFD, gluten free diet; IEL, intraepithelial lymphocytes; PASI, psoriasis area severity index; PPP, palmoplantar pustulosis; ST-GFD, self-treated gluten free diet; tTG, tissue transglutaminase.

Table 3. *Dermatologic conditions and their associations with antigliadin antibodies.*

Dermatologic Condition	Study	Study Design (Evidence Level)	Subjects (N)	Patient Description	AGA Associations
Psoriasis	Nagui et al. [22]	Case Control (III)	82	Patients with PsO and controls	34% PsO AGA-IgA positive vs 2% controls
	Singh et al. [23]	Case Control (III)	116	Patients with PsO and controls	Elevated IgA AGA and IgG AGA in PsO vs controls (both P<0.05)
	Damasiewicz-Bodzek and Wielkoszynski [24]	Case Control (III)	142-152	Patients with PsO and controls	Elevated IgA AGA in PsO vs controls (P<0.05) No significant difference between IgG AGA in PsO vs controls
	Ojetti et al. [25]	Case Control (III)	182	Patients with PsO and controls	Elevated IgA AGA in PsO vs controls (P<0.05)
	Lindqvist et al. [26]	Case series (IV)	114	Patients with PsA with skin lesions	Higher IgA AGA in PsA vs controls (P<0.0005)
	Michaëlsson et al. [27]	Case Control (III)	401	Patients with PsO in Sweden and controls	Elevated IgA AGA in males only vs controls (P=0.03)
	Akbulut et al. [28]	Case Control (III)	87	Patients with PsO and controls	Higher IgA AGA in PsO vs controls (P=0.039) Higher IgG AGA in PsO vs controls (P=0.073)
	Votrubova et al. [29]	Case Control (III)	398	Czech patients with PsO and controls	IgA AGA levels higher in PsO vs controls (P=0.039) IgG AGA levels lower in PsO vs controls (P=0.062)
	Woo et al. [41]	Cross-Sectional (IV)	130	Patients with Psoriasis in Ireland	5 patients IgG AGA+, 11 patients IgA AGA+ 3 patients had CD
	Juzlova et al. [42]	Case Control (III)	189	Patients with plaque PsO	IgA and IgG AGA in PsO vs controls not statistically different
	Khan et al. [43]	Cross-Sectional (IV)	80	Patients with PsO over age 15	No patients found with IgA or IgG AGA
	Sultan et al. [44]	Case Control (III)	240	Native Kashmiri patients with PsO	IgA and IgG AGA in PsO vs controls not statistically different
	Kia et al. [45]	Case Control (III)	300	Patients with PsO, PsA, and controls	IgA and IgG AGA in PsO vs controls not statistically different
	Kalayciyan and Kotogyan [30]	Case Control (III)	164	Patients with PsO, CD, and controls in Turkey	IgA AGA in higher in PsO (17%) vs controls (10%) but not statistically different
	Cardinali et al. [46]	Case Control (III)	78	Patients with PsO and controls	IgA and IgG AGA in PsO vs controls not statistically different
	De Vos et al. [47]	Case series (V)	76	Patients with PsO in the Netherlands	No PsO patients with IgA AGA
	Bhatia et al. [48]	Meta-analysis (Ia)	N/A	Studies examining the co-occurrence of PsO and CD Ab	Higher odds of testing positive for IgA AGA in patients with PsO vs controls (OR=2.36, P=0.015)
Linear IgA disease	Ciclitira et al. [31]	Case Control (III)	97	Patients with LAD, untreated CD, CD, DH, and controls	IgG AGA titers similar in children and adults with LAD vs controls IgA AGA titers higher in children with LAD vs controls though not statistically significant IgA AGA titers higher in adults with LAD vs controls (P<0.05)

Bullous Pemphigoid and Pemphigus Vulgaris	Kieffer et al. [32]	Case Control (III)	89	Patients with BP, PV and healthy controls	IgG AGA titers higher in BP vs controls (P<0.001) and BP vs PV (P<0.001) IgA AGA titers higher in BP vs controls (P<0.001) and BP vs PV (P<0.05)
	Kumar et al. [33]	Cross-Sectional (IV)	112	Patients with PV and BP	PV: 34% IgG AGA and 37% IgA AGA BP: 35% IgG AGA and 33% IgA AGA
	Kumar et al. [34]	Cross-Sectional (IV)	105	Patients with PV and BP	PV: 78% IgG AGA by ELISA; 56% IgG AGA by Immunofluorescence BP: 75% IgG AGA by ELISA; 31% IgG AGA by Immunofluorescence No patients IgA AGA positive by ELISA
Pustulosis palmoplantaris	Eriksson et al. [35]	Cross-Sectional (IV)	59	Patients with PPP in Sweden	5 of 59 patients had associated gluten sensitivity (not specified if gluten intolerance was CD) 10 of 39 patients had IgA AGA
	Weiseneel et al. [36]	Cross-Sectional (IV)	62	Patients with PPP and PsO in Germany	PPP: 0% AGA positive PsO: 3% AGA positive
Chronic mucocutaneous candidiasis	Brinkert et al. [37]	Case Report (V)	1	4-year-old male with CMC	Positive IgG AGA; negative IgA AGA, DGP, and tTG. Duodenum without villous atrophy
	Garcia et al. [38]	Case Report (V)	1	13-year-old male with CMC	AGA positive
Cutaneous hyalinosis	Maury et al. [39]	Case Report (V)	1	75-year-old female with massive cutaneous hyalinosis	IgG and IgM antigluten antibodies
Lipodystrophia centrifugalis abdominalis infantilis	Muller et al. [40]	Case Report (V)	1	4-year-old girl with Lipodystrophia Centrifugalis Abdominalis Infantilis	AGA positive
Alopecia areata	Mokhtari et al. [50]	Case Control (III)	70	Patients with AA and controls in Iran	1 AA patient with CD antibodies (subtype not specified); No difference in CD antibodies between AA cases vs controls (P=0.31)

AA, alopecia, areata; AGA, antigliadin antibodies; BP, bullous pemphigoid; CD, celiac disease; DH, dermatitis herpetiformis; LAD, linear IgA disease; NCGS, non-celiac gluten sensitivity; PsA, psoriatic arthritis; PsO, psoriasis; PV, pemphigus vulgaris; tTG, tissue transglutaminase.