

## Association between celiac disease and vitiligo: A review of the literature

Jing-Zhan Zhang, Dilinuer Abudoureyimu, Man Wang, Shi-Rong Yu, Xiao-Jing Kang

**ORCID number:** Jing-Zhan Zhang 0000-0002-2813-4962; Dilinuer Abudoureyimu 0000-0002-8058-141X; Man Wang 0000-0003-2726-7218; Shi-Rong Yu 0000-0002-0884-9987; Xiao-Jing Kang 0000-0002-6683-0707.

**Author contributions:** Zhang JZ designed the study and drafted the article; Abudoureyimu D, Wang M, Yu SR and Kang XJ revised the article critically for important intellectual content; all the authors approved the version to be published.

**Conflict-of-interest statement:** All authors declare no conflicts-of-interest related to this article.

**Supported by** National Natural Science Foundation of China, No. 81760563.

**Country/Territory of origin:** China

**Specialty type:** Medicine, research and experimental

**Provenance and peer review:** Invited article; Externally peer reviewed.

**Peer-review report's scientific quality classification**

Grade A (Excellent): A  
Grade B (Very good): 0  
Grade C (Good): C  
Grade D (Fair): 0

**Jing-Zhan Zhang, Dilinuer Abudoureyimu, Shi-Rong Yu, Xiao-Jing Kang,** Department of Dermatology, People's Hospital of Xinjiang Uygur Autonomous Region, Xinjiang Key Laboratory of Dermatology Research, Urumqi 830001, Xinjiang Uygur Autonomous Region, China

**Man Wang,** Department of Gastroenterology, People's Hospital of Xinjiang Uygur Autonomous Region, Urumqi 830001, Xinjiang Uygur Autonomous Region, China

**Corresponding author:** Xiao-Jing Kang, MD, PhD, Chairman, Chief Doctor, Professor, Department of Dermatology, People's Hospital of Xinjiang Uygur Autonomous Region, Xinjiang Key Laboratory of Dermatology Research, NO. 91 Tianchi Road, Tianshan District, Urumqi 830001, Xinjiang Uygur Autonomous Region, China. [drkxj@sina.com](mailto:drkxj@sina.com)

### Abstract

Celiac disease (CD) is an autoimmune intestinal disease caused by the intake of gluten-containing cereals and their products by individuals with genetic susceptibility genes. Vitiligo is a commonly acquired depigmentation of the skin; its clinical manifestation are skin patches caused by localized or generalized melanin deficiency. Both diseases have similar global incidence rates (approximately 1%) and are associated to similar diseases, including autoimmune bullous disease, inflammatory bowel disease, autoimmune thyroiditis, autoimmune gastritis, and type 1 diabetes. The relationship between CD and vitiligo has been reported in several studies, but their conclusions are inconsistent. Further, it has also been reported that a gluten-free diet (GFD) can improve the symptoms of immune-related skin diseases such as vitiligo. In this mini-review, we summarize and review the literature on the relationship between CD and vitiligo, assess the therapeutic significance of GFD for patients with vitiligo, and explore their possible physiopathology. We are hopeful that the information summarized here will assist physicians who treat patients with CD or vitiligo, thereby improving the prognosis.

**Key Words:** Celiac disease; Gluten-free diet; Vitiligo; Dermatitis herpetiformis

©The Author(s) 2021. Published by Baishideng Publishing Group Inc. All rights reserved.

Grade E (Poor): 0

**Open-Access:** This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

**Received:** May 2, 2021**Peer-review started:** May 2, 2021**First decision:** June 12, 2021**Revised:** June 25, 2021**Accepted:** October 20, 2021**Article in press:** October 20, 2021**Published online:** December 6, 2021**P-Reviewer:** Sideris N, Wierzbicka A**S-Editor:** Fan JR**L-Editor:** A**P-Editor:** Fan JR

**Core Tip:** Both celiac disease (CD) and vitiligo are autoimmune-related diseases, and their global incidence rates are similar (approximately 1%). This article reviews recent studies on the relationship between CD and vitiligo, and gluten-free diet (GFD) and vitiligo and explores their possible pathogenesis. An analysis based on existing evidence supports the association between CD and vitiligo. Patients with vitiligo and positive serum gluten markers, or with CD, may benefit from a GFD; it could be a valid option depending on the patient's preference. We hope this review will be useful for future treatment.

**Citation:** Zhang JZ, Abudoureyimu D, Wang M, Yu SR, Kang XJ. Association between celiac disease and vitiligo: A review of the literature. *World J Clin Cases* 2021; 9(34): 10430-10437

**URL:** <https://www.wjgnet.com/2307-8960/full/v9/i34/10430.htm>

**DOI:** <https://dx.doi.org/10.12998/wjcc.v9.i34.10430>

## INTRODUCTION

Celiac disease (CD) is an autoimmune intestinal disease caused by the intake of gluten-protein containing cereals and its products by individuals with genetic susceptibility genes. The disease can lead to intestinal mucosal damage, mainly manifested as abdominal pain, diarrhea, and other gastrointestinal symptoms. It can also lead to extraintestinal symptoms caused by secondary malnutrition and is associated with an increase in mortality[1]. The global prevalence of CD is approximately 1.4%, and it is gradually increasing[2]. The detection of anti-tissue transglutaminase immunoglobulin A (anti-tTG IgA), anti-endomysial antibody (EMA), and anti-gliadin antibody plays an important role in the diagnosis of CD[3-5]. Anti-tTG IgA is considered the first choice for the serological examination of CD. However, duodenal mucosal biopsy remains the gold standard for the diagnosis of CD[6].

Vitiligo is a commonly acquired depigmentation of the skin that clinically manifests as skin patch caused by localized or generalized melanin deficiency[7]. It is considered an autoimmune disease, although its pathogenesis is not clear and is affected by multiple factors, including autoimmunity, oxidative stress, and genetic susceptibility [8,9]. The incidence rate of vitiligo worldwide is 0.5%–2.0% [10].

Many studies have confirmed that CD and vitiligo are associated with a variety of autoimmune diseases, including autoimmune bullous disease, inflammatory bowel disease, autoimmune thyroiditis, autoimmune gastritis, and type 1 diabetes[11-17]. The relationship between CD and some immune-related skin diseases has been studied and confirmed, but its relationship with vitiligo is controversial. For example, some studies have shown that the incidence of vitiligo in patients with CD is higher than that in patients without CD[18,19]. However, the study by Volta *et al*[20] did not find any correlation between these two immune diseases[20]. Further, a gluten-free diet (GFD) has been reported to improve the symptoms of patients with immune-related skin diseases, such as dermatitis herpetiformis (DH), psoriasis, and vitiligo, who are seropositive for CD-related autoantibodies[21-23]. The purpose of this mini-review was to explore the relationship between CD and vitiligo, assess the therapeutic significance of GFD for patients with vitiligo, and investigate the underlying mechanisms.

## LITERATURE ANALYSIS

We reviewed the literature on the role of CD and gluten in vitiligo. We searched the PubMed, Ovid, Web of Science and Cochrane databases for published articles from their inception to February 2021. The search terms used were "celiac disease" or "gluten-free diet" and "vitiligo." We first screened the titles and abstracts to select potential studies and, then, performed a full-text review. We also reviewed the references in the selected articles to identify any other relevant studies. We included cohort studies, cross-sectional studies, case-control studies, reviews, and case reports that studied the relationship between vitiligo and CD. The duplicates were then removed. If the article lacked clinical relevance or the full text was not available, it was

excluded. There was no restriction based on language.

## CLINICAL CHARACTERISTICS

### **Study characteristics**

After a literature search, 878 studies were included, of which 102 duplicates were excluded. The titles and abstracts of 776 studies were screened. After reviewing the selected articles and their references, 15 eligible studies were included. Four studies examined the relationship between vitiligo and the incidence of CD (Table 1), and seven studies reported a relationship between CD and incidence of vitiligo (Table 2). In four studies, the relationship between GFD and vitiligo was studied (Table 3).

### **Vitiligo and the incidence of CD**

Four studies, including two case-control and two cross-sectional studies, investigated the incidence of CD in patients with vitiligo. One cross-sectional study investigated the incidence of CD in 176 patients with vitiligo; five (2.8%) of these patients were diagnosed with CD[24]. Further, in a case-control study, Seyhan *et al*[25] assessed serum anti-endomysial IgA antibody in 61 patients with vitiligo (21 children) and 60 controls. Eleven patients with vitiligo and one control were positive, and among these seropositive patients, five were younger than 18 years of age. The seroprevalence rates for children and adults were 23.8% and 15%, respectively. Seropositive patients underwent endoscopic duodenal biopsy of the upper gastrointestinal tract, and the prevalence of CD confirmed by biopsy was 3.2%[25]. The second case-control study by Shahmoradi *et al*[16] assessed EMA and anti-tTG IgA in 64 patients with vitiligo and 64 controls; each group included 41 (64.1%) women and 23 (35.9%) men. Among the patients with vitiligo, autoantibody tests were positive in two (3.1%) women. No one in the control group has positive results for autoantibodies[16]. However, the other cross-sectional study investigated the incidence of CD in 198 patients with vitiligo and found no positive CD serology in any of the participants[20].

### **CD and incidence of vitiligo**

The incidence of vitiligo among CD patients was examined in six cross-sectional studies and one population-based cohort study. Ertekin *et al*[18] reported on 140 children with CD, of whom 3 (2.1%) had vitiligo[18], while Lancaster-Smith *et al*[26] found that 1 (1.8%) out of 57 patients with CD had vitiligo[26]. Further, Seyhan *et al*[19] studied 55 cases of children and adolescents with CD and found that 45 children (81.8%) had gastrointestinal symptoms; 5 of them were subsequently diagnosed with vitiligo, with an incidence rate of 9.1%[19]. A Swedish population-based cohort study, in which each CD patient was matched with five control patients, demonstrated that among 43300 patients with CD, 106 cases (0.2%) were affected by vitiligo. Moreover, in a population of 198532 patients, vitiligo was diagnosed in 261 cases (0.1%), and the incidence of vitiligo was statistically significant[27]. In a study in Italy, 1 of 82 patients with CD had vitiligo (incidence rate of 1.2%)[28]; another report including 1010 patients with CD in Spain found that only 4 children (0.4%) had vitiligo[29]. However, surprisingly, Reunala *et al*[30] did not report the onset of vitiligo in 383 patients with CD who received GFD[30]. GFD may reduce the risk of vitiligo.

### **GFD and vitiligo**

Only a few cases of GFD and vitiligo have been reported in the literature. Our literature review identified two case reports describing the recoloring of vitiligo lesions after the onset of a GFD. One case reported a 9-year-old child with both CD and vitiligo who developed extensive repigmentation after following a GFD for 1 year [21]. The second report describes a 22-year-old female patient with vitiligo, who received a 2-year treatment including dapsone with no significant response but began to recover after 1 mo of GFD[31]. These cases suggest that elimination of gluten in the early stages of disease may have the potential to encourage and improve the disease.

Additionally, there are some reports on the coexistence of DH and vitiligo. Two case reports describe this relationship; in both, the DH lesions were significantly improved after the patients began a GFD; however, the vitiligo lesions remained unchanged or further aggravated. One report described a 53-year-old woman with vitiligo and DH. The patient began a GFD, and DH was completely relieved after 5 mo, but vitiligo did not subside and further increased[32]; she did not undergo a CD-related examination. The second case report described a 21-year-old patient with vitiligo and DH who was

**Table 1 Summary of studies reporting prevalence of celiac disease in vitiligo**

Ref.	Country	Study design	Setting	Vitiligo, n (%)	CD prevalence (V + CD)	Vitiligo diagnosis	CD diagnosis
Shahmoradi <i>et al</i> [16], 2013	Iran	Case-control study	Hospital	64	3.1% (n = 2)	Medical records	Serology
Volta <i>et al</i> [20], 1997	Italy	Cross-sectional study	Hospital	198	0	NA	Serology and histology
Henker and Hartmann[24], 2019	Germany	Cross-sectional study	Hospital	176	2.8% (n = 5)	Medical records	Serology and histology
Seyhan <i>et al</i> [25], 2011	Turkey	Case-control study	Hospital	61	3.2% (n = 2)	NA	Serology and histology

CD: Celiac disease; NA: Not applicable.

**Table 2 Summary of studies reporting prevalence of vitiligo in celiac disease**

Ref.	Country	Study design	Setting	CD, n (%)	Vitiligo prevalence (V + CD)	Vitiligo diagnosis	Celiac disease diagnosis
Reunala <i>et al</i> [30], 1997	Finland	Cross-sectional study	Hospital	383	0	Medical records	Histology
Ertekin <i>et al</i> [18], 2009	Turkey	Cross-sectional study	Hospital	140	2.1% (n = 3)	Medical records	Serology and histology
Lancaster-Smith <i>et al</i> [26], 1974	United Kingdom	Cross-sectional study	Hospital	57	1.8% (n = 1)	Medical records	Serology and histology
Seyhan <i>et al</i> [19], 2007	Turkey	Cross-sectional study	Hospital	55	9.1% (n = 5)	Medical records	Serology and histology
Lebwohl <i>et al</i> [27], 2020	Sweden	Population-Based cohort study	Database	43300	0.24% (n = 106)	Medical records	Histology
Catassi <i>et al</i> [28], 1996	Italy	Cross-sectional study	School	82	1.2% (n = 1)	questionnaire survey	Serology and histology
Polanco[29], 2008	Spain	Cross-sectional study	Hospital	1010	0.4% (n = 4)	Medical records	Serology and histology

CD: Celiac disease; V: Vitiligo.

**Table 3 Summary of the effect of gluten-free diet on vitiligo**

Ref.	Country	Evidence type	Celiac disease diagnosis	Accompanied diseases	Measure of improvement	Time to dermatologic improvement
Rodríguez-García <i>et al</i> [21], 2011	Spain	Case report	Diagnosis, method not described	None	Repigmentation of skin lesions	1 yr, continuous improvement for 3 yr
Khandalavala <i>et al</i> [31], 2014	United States	Case report	Serology and histology not done	None	Repigmentation of skin lesions	1 mo, continuous improvement for 3 mo
Amato <i>et al</i> [32], 2000	Italy	Case report	Serology	Dermatitis herpetiform	No response	NA
Karabudak <i>et al</i> [33], 2007	Turkey	Case report	Histology	Dermatitis herpetiform	No response	NA

NA: Not applicable

diagnosed with CD after gastrointestinal endoscopy. He was prescribed strict GFD and topical steroids, after which DH significantly improved, although his vitiligo remained unchanged[33].

### Discussion of CD

CD is a chronic autoimmune disease caused by improper absorption of wheat gluten and related cereal peptides by the small intestine, and this causes the human body to lose its ability to absorb nutrients through the villi. The disease may affect patients of any age, with a peak in early childhood and the 4<sup>th</sup> and 5<sup>th</sup> decade[34]. The gastrointestinal symptoms of CD include abdominal distension, abdominal pain, chronic diarrhea, steatosis, anorexia, weight loss, and nutritional deficiency. Further, an increasing number of related diseases and parenteral manifestations have been reported[35]. Vitiligo is also associated with a variety of gastrointestinal comorbidities, including autoimmune liver disease, autoimmune atrophic gastritis, inflammatory bowel disease, and intestinal flora dysfunction[13,36-38]. Furthermore, the incidence of some autoimmune diseases (pernicious anemia, inflammatory bowel disease, systemic lupus erythematosus, Addison's disease, and autoimmune thyroid disease) in patients with vitiligo is significantly increased[39]. These associations indicate that vitiligo has a common genetic etiology with other autoimmune diseases. Studies have found that patients with multiple autoimmune syndromes may have CD and/or vitiligo. In addition to well-defined polygenic syndromes, there may be a positive correlation between CD and vitiligo[40].

There is no published research explaining the pathophysiological relationship between CD and vitiligo; both are T cell-mediated disorders in which gamma-delta T cells, T-helper 1, and T-helper 17 play important roles[41-44]. CD has been found to be highly correlated with interleukin (IL)-2, IL-6, IL-17, and IL-21[45-47] which have been proven to play important roles in the pathogenesis of vitiligo[48,49]. The shared immunogenic mechanisms between the two conditions could explain their association. The incidence rate of autoimmune diseases is increased in patients with prolonged gluten exposure, due to the intestinal barrier dysfunction associated with CD and increased permeability to immunogenic triggers[50]. CD patients exposed to gliadin can show triggering of the CD4 + T cell responses, causing the production of high levels of interferon-gamma; this has been related to the severity of psoriasis[51,52]. A similar mechanism may be involved in the pathogenesis of vitiligo. On the other hand, in vitiligo, nuclear factor-erythroid 2-related factor 2 activation decreased in keratinocytes with impaired phosphoinositide 3-kinase phosphorylation, increasing the susceptibility to reactive oxygen species (ROS), leading to chemically induced apoptosis[53]. Moreover, IL-15 and CD4 + T cytokines (TNF, IL-2, IL-21) increased the phosphorylation of activators of transcription (STAT) 5 and protein kinase b, as well as the transcription of B-cell lymphoma-extra large (BCL-xL) protein. Further, TNF, IL-2, and IL-21 synergistically trigger the proliferation of Lin(-) intraepithelial lymphocytes (IELs) and CD3-CD56 + IELs in duodenal biopsy specimens of refractory CD type II (RCDII), while CD4 + T cytokines are involved in its pathogenesis[54]. Additionally, another possible mechanism linking vitiligo and CD is vitamin D deficiency in CD patients due to intestinal malabsorption[55]. Vitamin D deficiency can make susceptible individuals develop vitiligo[56]. However, this mechanism may not be important as it has been previously reported that patients with vitiligo have significant recoloring after a GFD. Large population-based studies in the future may provide better insight into the role of GFD in vitiligo.

Furthermore, CD is closely related to DH. Sulfasalazine, a commonly used treatment for DH, may induce vitiligo in patients with CD and DH[57] as it can consume glutathione, leading to a large amount of ROS accumulation, resulting in melanocyte damage[58,59]. Further, sulfasalazine is an inhibitor of the thioredoxin pathway[60], and reduced thioredoxin participates in the inhibition of tyrosinase, which is the rate-limiting enzyme in melanin biosynthesis and inhibits melanogenesis [61,62]. Moreover, sulfasalazine may reduce the level of cofactor tetrahydrobiopterin (BH4) by inhibiting the squid reductase that plays a crucial role in melanin production [63]; BH4 can also lead to the production of ROS, leading to the disruption of melanin biosynthesis[64].

---

### CONCLUSION

---

The analysis based on a review of existing evidence supports the association between CD and vitiligo. In the treatment of vitiligo patients, this information is particularly important because the intestinal symptoms are usually non-specific and are often ignored by doctors and patients. Further, patients with vitiligo may benefit from CD screening, while early diagnosis of vitiligo in CD patients may be beneficial because GFD may improve both conditions. However, large-scale, long-term follow-up studies

are needed to further endorse these findings.

## REFERENCES

- 1 **Lebwohl B**, Green PHR, Söderling J, Roelstraete B, Ludvigsson JF. Association Between Celiac Disease and Mortality Risk in a Swedish Population. *JAMA* 2020; **323**: 1277-1285 [PMID: [32259229](#) DOI: [10.1001/jama.2020.1943](#)]
- 2 **Singh P**, Arora A, Strand TA, Leffler DA, Catassi C, Green PH, Kelly CP, Ahuja V, Makharria GK. Global Prevalence of Celiac Disease: Systematic Review and Meta-analysis. *Clin Gastroenterol Hepatol* 2018; **16**: 823-836.e2 [PMID: [29551598](#) DOI: [10.1016/j.cgh.2017.06.037](#)]
- 3 **Sugai E**, Hwang HJ, Vázquez H, Smecuol E, Niveloni S, Mazure R, Mauriño E, Aeschlimann P, Binder W, Aeschlimann D, Bai JC. New serology assays can detect gluten sensitivity among enteropathy patients seronegative for anti-tissue transglutaminase. *Clin Chem* 2010; **56**: 661-665 [PMID: [20022983](#) DOI: [10.1373/clinchem.2009.129668](#)]
- 4 **Giersiepen K**, Leigemann M, Stuhldreher N, Ronfani L, Husby S, Koletzko S, Korponay-Szabó IR; ESPGHAN Working Group on Coeliac Disease Diagnosis. Accuracy of diagnostic antibody tests for coeliac disease in children: summary of an evidence report. *J Pediatr Gastroenterol Nutr* 2012; **54**: 229-241 [PMID: [22266486](#) DOI: [10.1097/MPG.0b013e318216f2e5](#)]
- 5 **Leffler DA**, Schuppan D. Update on serologic testing in celiac disease. *Am J Gastroenterol* 2010; **105**: 2520-2524 [PMID: [21131921](#) DOI: [10.1038/ajg.2010.276](#)]
- 6 **Husby S**, Murray JA, Katzka DA. AGA Clinical Practice Update on Diagnosis and Monitoring of Celiac Disease-Changing Utility of Serology and Histologic Measures: Expert Review. *Gastroenterology* 2019; **156**: 885-889 [PMID: [30578783](#) DOI: [10.1053/j.gastro.2018.12.010](#)]
- 7 **Spritz RA**. The genetics of generalized vitiligo and associated autoimmune diseases. *J Dermatol Sci* 2006; **41**: 3-10 [PMID: [16289692](#) DOI: [10.1016/j.jdermsci.2005.10.001](#)]
- 8 **Rodrigues M**, Ezzedine K, Hamzavi I, Pandya AG, Harris JE; Vitiligo Working Group. New discoveries in the pathogenesis and classification of vitiligo. *J Am Acad Dermatol* 2017; **77**: 1-13 [PMID: [28619550](#) DOI: [10.1016/j.jaad.2016.10.048](#)]
- 9 **Iannella G**, Greco A, Didona D, Didona B, Granata G, Manno A, Pasquariello B, Magliulo G. Vitiligo: Pathogenesis, clinical variants and treatment approaches. *Autoimmun Rev* 2016; **15**: 335-343 [PMID: [26724277](#) DOI: [10.1016/j.autrev.2015.12.006](#)]
- 10 **Ezzedine K**, Eleftheriadou V, Whitton M, van Geel N. Vitiligo. *Lancet* 2015; **386**: 74-84 [PMID: [25596811](#) DOI: [10.1016/S0140-6736\(14\)60763-7](#)]
- 11 **Fan KC**, Yang TH, Huang YC. Vitiligo and thyroid disease: a systematic review and meta-analysis. *Eur J Dermatol* 2018; **28**: 750-763 [PMID: [30698146](#) DOI: [10.1684/ejd.2018.3449](#)]
- 12 **Boniface K**, Seneschal J, Picardo M, Taïeb A. Vitiligo: Focus on Clinical Aspects, Immunopathogenesis, and Therapy. *Clin Rev Allergy Immunol* 2018; **54**: 52-67 [PMID: [28685247](#) DOI: [10.1007/s12016-017-8622-7](#)]
- 13 **Dahir AM**, Thomsen SF. Comorbidities in vitiligo: comprehensive review. *Int J Dermatol* 2018; **57**: 1157-1164 [PMID: [29808541](#) DOI: [10.1111/ijd.14055](#)]
- 14 **Bosca-Watts MM**, Minguez M, Planelles D, Navarro S, Rodriguez A, Santiago J, Tosca J, Mora F. HLA-DQ: Celiac disease vs inflammatory bowel disease. *World J Gastroenterol* 2018; **24**: 96-103 [PMID: [29358886](#) DOI: [10.3748/wjg.v24.i1.96](#)]
- 15 **Näytki A**, Tuusa J, Hervonen K, Kaukinen K, Lindgren O, Huilaja L, Kokkonen N, Salmi T, Tasanen K. Autoantibodies Against the Immunodominant Bullous Pemphigoid Epitopes Are Rare in Patients With Dermatitis Herpetiformis and Coeliac Disease. *Front Immunol* 2020; **11**: 575805 [PMID: [33072118](#) DOI: [10.3389/fimmu.2020.575805](#)]
- 16 **Shahmoradi Z**, Najafian J, Naeini FF, Fahimipour F. Vitiligo and autoantibodies of celiac disease. *Int J Prev Med* 2013; **4**: 200-203 [PMID: [23543680](#)]
- 17 **Rodriguez-Castro KI**, Franceschi M, Miraglia C, Russo M, Nouvenne A, Leandro G, Meschi T, De' Angelis GL, Di Mario F. Autoimmune diseases in autoimmune atrophic gastritis. *Acta Biomed* 2018; **89**: 100-103 [PMID: [30561426](#) DOI: [10.23750/abm.v89i8-S.7919](#)]
- 18 **Ertekin V**, Selimoglu MA, Altinkaynak S. Celiac disease in childhood: evaluation of 140 patients. *Eurasian J Med* 2009; **41**: 154-157 [PMID: [25610093](#)]
- 19 **Seyhan M**, Erdem T, Ertekin V, Selimoğlu MA. The mucocutaneous manifestations associated with celiac disease in childhood and adolescence. *Pediatr Dermatol* 2007; **24**: 28-33 [PMID: [17300645](#) DOI: [10.1111/j.1525-1470.2007.00328.x](#)]
- 20 **Volta U**, Bardazzi F, Zauli D, DeFranceschi L, Tosti A, Molinaro N, Ghetti S, Tetta C, Grassi A, Bianchi FB. Serological screening for coeliac disease in vitiligo and alopecia areata. *Br J Dermatol* 1997; **136**: 801-802 [PMID: [9205530](#) DOI: [10.1111/j.1365-2133.1997.tb03684.x](#)]
- 21 **Rodríguez-García C**, González-Hernández S, Pérez-Robayna N, Guimerá F, Fagundo E, Sánchez R. Repigmentation of vitiligo lesions in a child with celiac disease after a gluten-free diet. *Pediatr Dermatol* 2011; **28**: 209-210 [PMID: [21504457](#) DOI: [10.1111/j.1525-1470.2011.01388.x](#)]
- 22 **Donaldson MR**, Book LS, Leiferman KM, Zone JJ, Neuhausen SL. Strongly positive tissue transglutaminase antibodies are associated with Marsh 3 histopathology in adult and pediatric celiac disease. *J Clin Gastroenterol* 2008; **42**: 256-260 [PMID: [18223500](#) DOI: [10.1097/MCG.0b013e31802e70b1](#)]

- 23 **Bhatia BK**, Millsop JW, Debbaneh M, Koo J, Linos E, Liao W. Diet and psoriasis, part II: celiac disease and role of a gluten-free diet. *J Am Acad Dermatol* 2014; **71**: 350-358 [PMID: 24780176 DOI: 10.1016/j.jaad.2014.03.017]
- 24 **Henker J**, Hartmann A. [Prevalence of an association between coeliac disease and vitiligo]. *Hautarzt* 2019; **70**: 960-963 [PMID: 31584112 DOI: 10.1007/s00105-019-04482-5]
- 25 **Seyhan M**, Kandi B, Akbulut H, Selimoğlu MA, Karıncaoğlu M. Is celiac disease common in patients with vitiligo? *Turk J Gastroenterol* 2011; **22**: 105-106 [PMID: 21480124 DOI: 10.4318/tjg.2011.0169]
- 26 **Lancaster-Smith MJ**, Perrin J, Swarbrick ET, Wright JT. Coeliac disease and autoimmunity. *Postgrad Med J* 1974; **50**: 45-48 [PMID: 4618907 DOI: 10.1136/pgmj.50.579.45]
- 27 **Lebwohl B**, Söderling J, Roelstraete B, Lebwohl MG, Green PH, Ludvigsson JF. Risk of Skin Disorders in Patients with Celiac Disease: A Population-Based Cohort Study. *J Am Acad Dermatol* 2020; S0190-9622(20)32900 [PMID: 33144153 DOI: 10.1016/j.jaad.2020.10.079]
- 28 **Catassi C**, Fabiani E, Rättsch IM, Coppa GV, Giorgi PL, Pierdomenico R, Alessandrini S, Iwanejko G, Domenici R, Mei E, Miano A, Marani M, Bottaro G, Spina M, Dotti M, Montanelli A, Barbato M, Viola F, Lazzari R, Vallini M, Guariso G, Plebani M, Cataldo F, Traverso G, Ventura A. The coeliac iceberg in Italy. A multicentre antigliadin antibodies screening for coeliac disease in school-age subjects. *Acta Paediatr Suppl* 1996; **412**: 29-35 [PMID: 8783752 DOI: 10.1111/j.1651-2227.1996.tb14244.x]
- 29 **Polanco I**. Celiac disease. *J Pediatr Gastroenterol Nutr* 2008; **47** Suppl 1: S3-S6 [PMID: 18667915 DOI: 10.1097/MPG.0b013e3181818df5]
- 30 **Reunala T**, Collin P. Diseases associated with dermatitis herpetiformis. *Br J Dermatol* 1997; **136**: 315-318 [PMID: 9115907]
- 31 **Khandalavala BN**, Nirmalraj MC. Rapid partial repigmentation of vitiligo in a young female adult with a gluten-free diet. *Case Rep Dermatol* 2014; **6**: 283-287 [PMID: 25685131 DOI: 10.1159/000370303]
- 32 **Amato L**, Gallerani I, Fuligni A, Mei S, Fabbri P. Dermatitis herpetiformis and vitiligo: report of a case and review of the literature. *J Dermatol* 2000; **27**: 462-466 [PMID: 10935345 DOI: 10.1111/j.1346-8138.2000.tb02207.x]
- 33 **Karabudak O**, Dogan B, Yildirim S, Harmanyeri Y, Anadolu-Brasie R. Dermatitis herpetiformis and vitiligo. *J Chin Med Assoc* 2007; **70**: 504-506 [PMID: 18063505 DOI: 10.1016/S1726-4901(08)70049-2]
- 34 **Collin P**, Reunala T. Recognition and management of the cutaneous manifestations of celiac disease: a guide for dermatologists. *Am J Clin Dermatol* 2003; **4**: 13-20 [PMID: 12477369 DOI: 10.2165/00128071-200304010-00002]
- 35 **Poon E**, Nixon R. Cutaneous spectrum of coeliac disease. *Australas J Dermatol* 2001; **42**: 136-138 [PMID: 11309040 DOI: 10.1046/j.1440-0960.2001.00498.x]
- 36 **Lu CY**, Hsieh MS, Wei KC, Ezmerli M, Kuo CH, Chen W. Gastrointestinal involvement of primary skin diseases. *J Eur Acad Dermatol Venereol* 2020; **34**: 2766-2774 [PMID: 32455473 DOI: 10.1111/jdv.16676]
- 37 **Terzicoli Beretta-Piccoli B**, Invernizzi P, Gershwin ME, Mainetti C. Skin Manifestations Associated with Autoimmune Liver Diseases: a Systematic Review. *Clin Rev Allergy Immunol* 2017; **53**: 394-412 [PMID: 28993983 DOI: 10.1007/s12016-017-8649-9]
- 38 **Ni Q**, Ye Z, Wang Y, Chen J, Zhang W, Ma C, Li K, Liu Y, Liu L, Han Z, Gao T, Jian Z, Li S, Li C. Gut Microbial Dysbiosis and Plasma Metabolic Profile in Individuals With Vitiligo. *Front Microbiol* 2020; **11**: 592248 [PMID: 33381090 DOI: 10.3389/fmicb.2020.592248]
- 39 **Alkhateeb A**, Fain PR, Thody A, Bennett DC, Spritz RA. Epidemiology of vitiligo and associated autoimmune diseases in Caucasian probands and their families. *Pigment Cell Res* 2003; **16**: 208-214 [PMID: 12753387 DOI: 10.1034/j.1600-0749.2003.00032.x]
- 40 **Kahaly GJ**, Frommer L. Autoimmune polyglandular diseases. *Best Pract Res Clin Endocrinol Metab* 2019; **33**: 101344 [PMID: 31606344 DOI: 10.1016/j.beem.2019.101344]
- 41 **Chen J**, Li S, Li C. Mechanisms of melanocyte death in vitiligo. *Med Res Rev* 2021; **41**: 1138-1166 [PMID: 33200838 DOI: 10.1002/med.21754]
- 42 **Zhen Y**, Yao L, Zhong S, Song Y, Cui Y, Li S. Enhanced Th1 and Th17 responses in peripheral blood in active non-segmental vitiligo. *Arch Dermatol Res* 2016; **308**: 703-710 [PMID: 27687555 DOI: 10.1007/s00403-016-1690-3]
- 43 **Behfarjam F**, Mansouri P, Jadali Z. Imbalance of Peripheral Blood T Helper Type 17 Responses in Patients with Vitiligo. *Iran J Allergy Asthma Immunol* 2018; **17**: 171-178 [PMID: 29757590]
- 44 **Bouziat R**, Hinterleitner R, Brown JJ, Stencel-Baerenwald JE, Ikizler M, Mayassi T, Meisel M, Kim SM, Discepolo V, Pruijssers AJ, Ernest JD, Iskarpatyoti JA, Costes LM, Lawrence I, Palanski BA, Varma M, Zurenski MA, Khomandiak S, McAllister N, Aravamudhan P, Boehme KW, Hu F, Samsom JN, Reinecker HC, Kupfer SS, Guandalini S, Semrad CE, Abadie V, Khosla C, Barreiro LB, Xavier RJ, Ng A, Dermody TS, Jabri B. Reovirus infection triggers inflammatory responses to dietary antigens and development of celiac disease. *Science* 2017; **356**: 44-50 [PMID: 28386004 DOI: 10.1126/science.aah5298]
- 45 **Akbulut UE**, Çebi AH, Sağ E, İkbāl M, Çakır M. Interleukin-6 and interleukin-17 gene polymorphism association with celiac disease in children. *Turk J Gastroenterol* 2017; **28**: 471-475 [PMID: 28928101 DOI: 10.5152/tjg.2017.17092]
- 46 **Ecevit ÇÖ**. Interleukin-6 and Interleukin-17 gene polymorphisms and celiac disease susceptibility.

- Turk J Gastroenterol* 2017; **28**: 432-433 [PMID: 29082885 DOI: 10.5152/tjg.2017.101017]
- 47 **van Heel DA**, Franke L, Hunt KA, Gwilliam R, Zhernakova A, Inouye M, Wapenaar MC, Barnardo MC, Bethel G, Holmes GK, Feighery C, Jewell D, Kelleher D, Kumar P, Travis S, Walters JR, Sanders DS, Howdle P, Swift J, Playford RJ, McLaren WM, Mearin ML, Mulder CJ, McManus R, McGinnis R, Cardon LR, Deloukas P, Wijmenga C. A genome-wide association study for celiac disease identifies risk variants in the region harboring IL2 and IL21. *Nat Genet* 2007; **39**: 827-829 [PMID: 17558408 DOI: 10.1038/ng2058]
- 48 **Sushama S**, Dixit N, Gautam RK, Arora P, Khurana A, Anubhuti A. Cytokine profile (IL-2, IL-6, IL-17, IL-22, and TNF- $\alpha$ ) in vitiligo-New insight into pathogenesis of disease. *J Cosmet Dermatol* 2019; **18**: 337-341 [PMID: 29504235 DOI: 10.1111/jocd.12517]
- 49 **Speeckaert R**, Speeckaert M, De Schepper S, van Geel N. Biomarkers of disease activity in vitiligo: A systematic review. *Autoimmun Rev* 2017; **16**: 937-945 [PMID: 28698094 DOI: 10.1016/j.autrev.2017.07.005]
- 50 **Ventura A**, Magazzù G, Greco L. Duration of exposure to gluten and risk for autoimmune disorders in patients with celiac disease. SIGEP Study Group for Autoimmune Disorders in Celiac Disease. *Gastroenterology* 1999; **117**: 297-303 [PMID: 10419909 DOI: 10.1053/gast.1999.0029900297]
- 51 **Nilsen EM**, Jahnsen FL, Lundin KE, Johansen FE, Fausa O, Sollid LM, Jahnsen J, Scott H, Brandtzaeg P. Gluten induces an intestinal cytokine response strongly dominated by interferon gamma in patients with celiac disease. *Gastroenterology* 1998; **115**: 551-563 [PMID: 9721152 DOI: 10.1016/s0016-5085(98)70134-9]
- 52 **Abdallah MA**, Abdel-Hamid MF, Kotb AM, Mabrouk EA. Serum interferon-gamma is a psoriasis severity and prognostic marker. *Cutis* 2009; **84**: 163-168 [PMID: 19842576]
- 53 **Kim H**, Park CS, Lee AY. Reduced Nrf2 activation in PI3K phosphorylation-impaired vitiliginous keratinocytes increases susceptibility to ROS-generating chemical-induced apoptosis. *Environ Toxicol* 2017; **32**: 2481-2491 [PMID: 28836394 DOI: 10.1002/tox.22461]
- 54 **Kooy-Winkelaar YM**, Bouwer D, Janssen GM, Thompson A, Brugman MH, Schmitz F, de Ru AH, van Gils T, Bouma G, van Rood JJ, van Veelen PA, Mearin ML, Mulder CJ, Koning F, van Bergen J. CD4 T-cell cytokines synergize to induce proliferation of malignant and nonmalignant innate intraepithelial lymphocytes. *Proc Natl Acad Sci U S A* 2017; **114**: E980-E989 [PMID: 28049849 DOI: 10.1073/pnas.1620036114]
- 55 **Abenavoli L**, Proietti I, Leggio L, Ferrulli A, Vonghia L, Capizzi R, Rotoli M, Amerio PL, Gasbarrini G, Addolorato G. Cutaneous manifestations in celiac disease. *World J Gastroenterol* 2006; **12**: 843-852 [PMID: 16521210 DOI: 10.3748/wjg.v12.i6.843]
- 56 **Zhang JZ**, Wang M, Ding Y, Gao F, Feng YY, Yakeya B, Wang P, Wu XJ, Hu FX, Xian J, Kang XJ. Vitamin D receptor gene polymorphism, serum 25-hydroxyvitamin D levels, and risk of vitiligo: A meta-analysis. *Medicine (Baltimore)* 2018; **97**: e11506 [PMID: 30024533 DOI: 10.1097/MD.00000000000011506]
- 57 **Turkowski Y**, Konnikov N. Sulfasalazine-induced generalized vitiligo in a patient with dermatitis herpetiformis and celiac disease. *Dermatol Ther* 2019; **32**: e13007 [PMID: 31237078 DOI: 10.1111/dth.13007]
- 58 **Ma MZ**, Chen G, Wang P, Lu WH, Zhu CF, Song M, Yang J, Wen S, Xu RH, Hu Y, Huang P. Xc-inhibitor sulfasalazine sensitizes colorectal cancer to cisplatin by a GSH-dependent mechanism. *Cancer Lett* 2015; **368**: 88-96 [PMID: 26254540 DOI: 10.1016/j.canlet.2015.07.031]
- 59 **Wang Y**, Li S, Li C. Perspectives of New Advances in the Pathogenesis of Vitiligo: From Oxidative Stress to Autoimmunity. *Med Sci Monit* 2019; **25**: 1017-1023 [PMID: 30723188 DOI: 10.12659/MSM.914898]
- 60 **Harris IS**, Treloar AE, Inoue S, Sasaki M, Gorrini C, Lee KC, Yung KY, Brenner D, Knobbe-Thomsen CB, Cox MA, Elia A, Berger T, Cescon DW, Adeoye A, Brüstle A, Molyneux SD, Mason JM, Li WY, Yamamoto K, Wakeham A, Berman HK, Khokha R, Done SJ, Kavanagh TJ, Lam CW, Mak TW. Glutathione and thioredoxin antioxidant pathways synergize to drive cancer initiation and progression. *Cancer Cell* 2015; **27**: 211-222 [PMID: 25620030 DOI: 10.1016/j.ccell.2014.11.019]
- 61 **Ando H**, Kondoh H, Ichihashi M, Hearing VJ. Approaches to identify inhibitors of melanin biosynthesis via the quality control of tyrosinase. *J Invest Dermatol* 2007; **127**: 751-761 [PMID: 17218941 DOI: 10.1038/sj.jid.5700683]
- 62 **Ito S**, Wakamatsu K, Ozeki H. Chemical analysis of melanins and its application to the study of the regulation of melanogenesis. *Pigment Cell Res* 2000; **13** Suppl 8: 103-109 [PMID: 11041366 DOI: 10.1034/j.1600-0749.13.s8.19.x]
- 63 **Yang S**, Jan YH, Mishin V, Richardson JR, Hossain MM, Heindel ND, Heck DE, Laskin DL, Laskin JD. Sulfa drugs inhibit sepiapterin reduction and chemical redox cycling by sepiapterin reductase. *J Pharmacol Exp Ther* 2015; **352**: 529-540 [PMID: 25550200 DOI: 10.1124/jpet.114.221572]
- 64 **Bailey J**, Shaw A, Fischer R, Ryan BJ, Kessler BM, McCullagh J, Wade-Martins R, Channon KM, Crabtree MJ. A novel role for endothelial tetrahydrobiopterin in mitochondrial redox balance. *Free Radic Biol Med* 2017; **104**: 214-225 [PMID: 28104455 DOI: 10.1016/j.freeradbiomed.2017.01.012]





Published by **Baishideng Publishing Group Inc**  
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA  
**Telephone:** +1-925-3991568  
**E-mail:** [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
**Help Desk:** <https://www.f6publishing.com/helpdesk>  
<https://www.wjgnet.com>

