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Asthma Atopic Dermatitis, and Allergic Rhinitis in Pediatric Celiac Disease: A Case-control Study

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ABSTRACT

Celiac disease is a gluten-induced immune-mediated enteropathy. Recent studies suggest an increasing association between celiac disease and atopic conditions such as asthma, atopic dermatitis, and allergic rhinitis, although the underlying mechanisms are not fully understood.

In this matched case-control study, the prevalence of asthma, atopic dermatitis, and allergic rhinitis was evaluated among 173 children with celiac disease and 173 age- and sex-matched healthy controls in Zahedan, Iran, in 2023. The diagnosis of celiac disease was based on European Society for Paediatric Gastroenterology, Hepatology and Nutrition guidelines. Allergic conditions were assessed using the International Study of Asthma and Allergies in Childhood questionnaire and confirmed through clinical evaluation.

Children with celiac disease had a significantly higher prevalence of asthma (12.1% versus 5.8%; odds ratio, 2.25; 95% confidence interval, 1.15 to 4.05) and allergic rhinitis (29.5% versus 14.5%; odds ratio, 2.47; 95% confidence interval, 1.4 to 4.26) compared to controls. There was no significant difference in the prevalence of atopic dermatitis between the two groups (12.1% versus 9.2%; odds ratio, 1.35).

These results indicate that children with celiac disease are at increased risk for certain respiratory allergic diseases, particularly asthma and allergic rhinitis. This highlights the need for integrated care between gastroenterology and allergy specialists. Further research is needed to clarify the shared immunological pathways involved.

Keywords: Allergic; Asthma; Atopic; Celiac disease; Child; Dermatitis; Rhinitis

INTRODUCTION

Celiac disease (CD) is a genetically mediated autoimmune disorder characterized by an immune response to gluten, resulting in unintended damage to the small intestine. Gluten, a protein present in wheat,

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barley, and rye, elicits an immune-mediated attack on the intestinal villi—finger-like projections critical for nutrient absorption. This immune-driven destruction impairs the absorptive function of the small intestine, leading to malabsorption and subsequent clinical complications.[1]

A pivotal advancement in understanding celiac disease was the identification of tissue transglutaminase as its primary autoantigen, firmly establishing its classification as an autoimmune condition.[2] Despite significant research progress, no definitive cure exists for celiac disease. Current management relies on strict adherence to a gluten-free diet, requiring the elimination of gluten-containing grains such as wheat, barley, and rye. This dietary intervention is crucial to preventing immune activation and subsequent intestinal injury.[3,4]

Globally, celiac disease affects approximately 70 million individuals, representing roughly 1% of the population across all age groups.[5] In recent years, a marked increase in both incidence and prevalence has been observed, particularly in Asian regions, with higher rates reported in the Middle East and Mediterranean areas.[6]

The association between celiac disease and pulmonary or allergic conditions was first documented in 1970 by Hood et al.[7] Subsequent research has further elucidated this relationship, uncovering potential mechanistic links. Additionally, allergic disorders in these patients may coexist with autoimmune conditions, likely stemming from a combination of genetic susceptibility and environmental triggers.[8]

The co-occurrence of allergic diseases—such as asthma, allergic rhinitis, and atopic dermatitis—with celiac disease has significant clinical implications. This comorbidity not only exacerbates the social and lifestyle burden on patients but also increases psychological distress, escalates healthcare costs, and substantially diminishes quality of life.[9-11]

Asthma remains one of the most prevalent chronic allergic diseases worldwide, with a notable rise in global prevalence over the past 25 years. Recent epidemiological data indicate asthma prevalence rates of approximately 6% in Asian children and 8% in adolescents, with slight variations between sexes (8% in boys vs. 9% in girls).[12]

Atopic dermatitis, particularly in moderate to severe cases, is associated with significant cutaneous inflammation and imposes a considerable economic and psychosocial burden. U.S.-based studies report healthcare-diagnosed eczema prevalence rates ranging from 11% to 13%, with substantial regional variability.[9-18] These findings are consistent with global epidemiological trends.[13]

Allergic rhinitis is another common allergic disorder, with widely varying prevalence rates across different populations. Globally, estimates range between 0.8% and 14.9% in children aged 6–7 years and between 1.4% and 39.7% in adolescents aged 13–14 years.[14]

Several systematic reviews and cross-sectional studies suggest no significant association between asthma, allergic rhinitis, or atopic dermatitis and celiac disease.[7] However, existing research on the relationship between these conditions remains inconsistent, with conflicting findings reported in the literature. Given the high prevalence of both allergic and autoimmune diseases in central and eastern Iran, further comprehensive studies are warranted to establish definitive conclusions.[1,12-14]

In light of these knowledge gaps, the present study was designed to investigate potential associations between asthma, allergic rhinitis, and atopic dermatitis with celiac disease. The findings may contribute to more precise clinical management strategies, heightened awareness of overlapping symptomatology in celiac patients, and ultimately, a reduction in the economic, psychological, and social burdens faced by affected individuals.

MATERIALS AND METHODS

This case-control study was conducted in 2023 on pediatric patients with confirmed celiac disease, diagnosed by a pediatric gastroenterologist based on comprehensive clinical, laboratory, and histopathological criteria. Participants were recruited from the Gastroenterology Clinic at Ali Asghar Hospital in Zahedan. Exclusion criteria included children without a gastroenterologist-confirmed celiac disease diagnosis or whose parents declined to provide consent.

The study group was compared to a control group of healthy children, matched by age and sex, who were [admitted/referred] to the hospital on the same day., with no history of celiac disease or associated autoimmune disorders. The study protocol was approved by the Research and Technology Vice-Chancellor and the Ethics Committee of Zahedan University of Medical Sciences (Ethical Approval Code: IR.ZAUMS.REC.1401.317).

All participants underwent specialist-confirmed celiac disease diagnosis using established diagnostic criteria, with study variables collected through a researcher-developed checklist. Allergic diseases were assessed through initial screening with the International Study of Asthma and Allergies in Childhood questionnaire, containing 8 asthma items, 6 allergic rhinitis items, and 7 atopic dermatitis items.[15] All cases underwent clinical evaluation by an asthma and allergy specialist, with asthma diagnosis confirmed by the Asthma Predictive Index plus clinical symptoms in children under 6 years[16] and spirometry in those aged 6 years or older. Allergic rhinitis cases were confirmed by skin prick testing, while suspected atopic dermatitis cases received dermatologist evaluation.

Data were coded and analyzed using SPSS version 22. Point estimates and 95% confidence intervals (CI) were calculated to determine the prevalence of asthma, atopic dermatitis, and allergic rhinitis. The Chi-square test or Fisher's exact test was used to compare condition frequencies between celiac disease and control groups, testing independence. Odds ratios (OR) with 95% CIs were reported to quantify associations. A p value <0.05 was considered statistically significant in all analyses.

RESULTS

This cross-sectional study evaluated 346 pediatric patients (2-15 years old, mean age 8.6±2.8 years) referred to the Children's Clinic at Ali Asghar Hospital, Zahedan. The cohort comprised 173 children with biopsy-confirmed celiac disease and 173 age- and sex-matched controls. All participants underwent standardized assessment for asthma, allergic rhinitis, and atopic dermatitis by board-certified allergists. Demographic characteristics were comparable between groups, with no significant differences in age (p=0.32) or sex distribution (p=0.20) (Table 1).

Key Findings

1. Asthma Prevalence

Children with celiac disease demonstrated significantly higher asthma prevalence compared to controls (12.1% vs 5.8%; p=0.038). The celiac disease group had 2.25-fold increased odds of asthma (OR=2.25, 95% CI:1.03-4.9) (Table 2).

2. Atopic Dermatitis

While atopic dermatitis prevalence was numerically higher in celiac patients (12.1% vs 9.2%), this difference lacked statistical significance (p=0.38; OR=1.35, 95% CI:0.68-2.6) (Table 3).

3. Allergic Rhinitis

A robust association emerged for allergic rhinitis, with celiac patients showing both significantly higher prevalence (29.5% vs 14.5%; p=0.001) and 2.47-fold increased odds (95% CI:1.4-4.26) compared to controls (Table 4).

Gender Stratification

Analysis by sex revealed non-significant trends: boys showed higher asthma (10.8% vs 8.1%) and allergic rhinitis (24.3% vs 20.9%) rates, while girls had greater atopic dermatitis prevalence (11.1% vs 9.9%) (all p>0.30) (Table 5).

Table 1. Baseline characteristics of study participants

Variable	Celiac disease group (N=173)	Control group (N=173)	*p*
Female sex, No. (%)	112 (64.7)	123 (71.1)	0.20
Age, mean ± SD, y	8.79 ± 2.84	8.49 ± 2.82	0.32

Table 2. Asthma prevalence in study groups

Study group	Asthma present, No. (%)	Asthma absent, No. (%)	Total, No. (%)	*p*
Celiac Disease	21 (12.1)	152 (87.9)	173 (100)	0.038
Control	10 (5.8)	163 (94.2)	173 (100)	
Total	31 (9.0)	315 (91.0)	346 (100)	

Table 3. Frequency distribution of atopic dermatitis in children with celiac disease and controls

Study group	Atopic dermatitis present, No. (%)	Atopic dermatitis absent, No. (%)	Total, No. (%)	*p*
Celiac Disease	21 (12.1)	152 (87.9)	173 (100)	0.38
Control	16 (9.2)	157 (90.8)	173 (100)	
Total	37 (10.7)	309 (89.3)	346 (100)	

Table 4. Prevalence of allergic rhinitis in children with celiac disease versus controls

Study group	Allergic rhinitis present, No. (%)	Allergic rhinitis absent, No. (%)	Total, No. (%)	*p*
Celiac Disease	51 (29.5)	122 (70.5)	173 (100)	0.001
Control	25 (14.5)	148 (85.5)	173 (100)	
Total	76 (22.0)	270 (78.0)	346 (100)	

Table 5. Gender-specific prevalence of allergic conditions

Condition	Girls (N=235)	Boys (N=111)	*p*
Asthma	19 (8.1)	12 (10.8)	0.32
Atopic dermatitis	26 (11.1)	11 (9.9)	0.44
Allergic rhinitis	49 (20.9)	27 (24.3)	0.37

DISCUSSION

Our study demonstrates a significantly higher prevalence of both asthma (12.1% vs 5.8%; OR=2.5, p=0.038) and allergic rhinitis (29.5% vs 14.5%; OR=2.47, p<0.001) in children with celiac disease compared to healthy controls. These findings align with established literature documenting increased allergic comorbidity in hospitalized pediatric populations[13,15] and corroborate previous reports by Jonas et al[17] and Shokohi et al. In contrast, atopic dermatitis prevalence did not differ significantly between groups (12.1% vs. 9.2%; OR=1.35, p=0.38).[17] The observed 2.5-fold increased asthma risk in our celiac cohort parallels findings by Khuhro et al[19] reinforcing the well-documented association between celiac disease and atopic conditions.

The rising global prevalence of asthma, particularly among pediatric populations with autoimmune disorders as noted by Wandalsen et al[20] underscores the clinical importance of our findings. Several mechanisms may underlie this association:

Nutritional Factors:

60-70% of celiac patients demonstrate vitamin D deficiency.[21]

Impaired calcitriol-mediated T-cell regulation (reduced interleukin-2 suppression).[22]

Zinc deficiency (3× more prevalent in asthmatic children).[23]

Immunological Mechanisms:

Shared non-human leukocyte antigen genetic loci (e.g., HLA-DQ).[24]

Th1/Th2 imbalance despite opposing cytokine profiles.[11]

Gut microbiota alterations from frequent hospitalizations/antibiotic use.[7]

While we observed a non-significant trend toward increased atopic dermatitis in celiac patients (OR=1.35, p=0.38), this contrasts with Shokohi's findings[18] and may reflect regional variation in disease prevalence. The sex-specific patterns (higher respiratory allergies in boys, atopic dermatitis in girls) mirror global

epidemiological trends[5,12,14] and likely represent inherent immunological differences.

Recent meta-analyses, including Rahimian's 2020 Iranian study,[12] support our observations, reporting fourfold higher allergic prevalence in autoimmune populations. However, conflicting data exist - while Yavuzylimaz's Turkish study found no celiac-allergy association,[7] Alwal et al documented 27.8% asthma prevalence in Maltese celiac children with symptomatic improvement post gluten-free diet.[21]

Study Limitations and Future Directions

Although we controlled for major confounders, unmeasured variables (breastfeeding duration, environmental exposures, maternal nutrition knowledge) may influence results. The celiac-allergy relationship, first identified by Hood et al in 1970,[25] requires further investigation regarding:

Precise immunological mechanisms

Impact of gluten-free diet on atopic symptoms

Genetic/environmental interactions

Our findings, consistent with Kero's demonstration of 1.6× increased asthma risk in Swiss celiac children,[26] contribute to growing evidence of autoimmune-atopic overlap. Future studies should employ longitudinal designs to elucidate causal pathways and evaluate targeted screening protocols for atopic conditions in celiac patients.

Children with celiac disease demonstrate an elevated risk of asthma and allergic rhinitis compared to the general pediatric population, potentially mediated by genetic predisposition or environmental factors like nutritional status. This association warrants clinical consideration during patient management, with further research needed to elucidate underlying mechanisms. While prior studies have identified demographic variables influencing atopy risk including gender, age, urbanization, residential area, and parental occupation,[19] these confounders were not addressed in the present study. Future investigations should account for these factors to strengthen causal inferences.

STATEMENT OF ETHICS

The study protocol was approved by the Research and Technology Vice-Chancellor and the Ethics Committee of Zahedan University of Medical Sciences (Ethical Approval Code: IR.ZAUMS.REC.1401.317).

FUNDING

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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DATA AVAILABILITY

The data supporting the findings of this study are available from the corresponding author upon reasonable request to ensure compliance with ethical and privacy considerations. Interested readers may contact the corresponding author by email to request access to the anonymized dataset for academic purposes. Due to patient confidentiality and ethical restrictions, the data are not publicly deposited in a repository.

AI ASSISTANCE DISCLOSURE

This article was written using artificial intelligence tools, Deep Seek and Perplexity

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