Original Article
DOI: https://doi.org/10.70749/ijbr.v3i2.1828

INDUS JOURNAL OF BIOSCIENCE RESEARCH
https://ijbr.com.pk
ISSN: 2960-2793/ 2960-2807

Different Clinical Presentations of Celiac Disease in Children

Iqra Naheed[1], Rashid Nawaz[1], Hina Umbreen[1], Uzma Yasmeen[1]

[1]Department of Pediatrics, DHQ Hospital, Faisalabad, Punjab, Pakistan.

ARTICLE INFO

Keywords

Celiac Disease, Clinical Presentation, Gastrointestinal Symptoms.

Corresponding Author: Iqra Naheed
Department of Pediatrics, DHQ Hospital, Faisalabad, Punjab, Pakistan.
Email: qranaheed9@gmail.com

Declaration

Authors' Contribution: All authors equally contributed to the study and approved the final manuscript.
Conflict of Interest: No conflict of interest.
Funding: No funding received by the authors.

Article History

Received: 19-11-2024, Revised: 24-01-2025
Accepted: 12-02-2025, Published: 28-02-2025

ABSTRACT

Objective: To determine the frequency of different clinical presentations in children having celiac disease. **Study design:** Cross sectional validation study. **Settings:** Department of Pediatrics, DHQ Hospital, Faisalabad. **Study duration:** April 21, 2024 to October 20, 2024. **Materials and Procedures:** This study included both male and female patients with celiac disease whose ages ranged from 1 to 14 years: Exclusion criteria were giardiasis, immunodeficiency, growth hormone deficit, IBD, abdominal TB, infective gastroenteritis, cystic fibrosis, primary malnutrition, and chronic kidney disease. The pathologist reported that a blood sample was sent to the hospital's pathology laboratory to estimate the ferritin level. With a dermatologist's opinion, dermatitis herpartiformis was evaluated. The patient or parent was asked about their stool history. The following conditions were evaluated: failure to thrive, dermatitis herpetiformis, iron deficiency anemia, and chronic diarrhea. **Results:** Following clinical presentations were common among children with celiac disease: iron deficiency anemia in 39 (43.33%), failure to thrive in 29 (32.22%), dermatitis herpetiformis in 22 (24.44%), short stature in 24 (26.67%), and chronic diarrhea in 43 (47.78%) patients. **Conclusion:** In this study, diarrhea, iron deficiency anemia, and failure to thrive were the most prevalent symptoms that children with celiac disease presented with.

INTRODUCTION

In genetically predisposed individuals, gluten and related prolamines can cause celiac disease (CD), an immune-mediated systemic condition that damages the mucosa of the small intestine. Around 1% of people worldwide have CD, and women are more likely to have it than men. Regretfully, epidemiological research demonstrating the true frequency of CD in Pakistani society is lacking. [1] It is unknown how common CD is in Pakistan. The estimated undiagnosed prevalence in Pakistan, however, is 36 per 10,000 people.[2] First and second-degree relatives of the afflicted persons have a greater likelihood of developing CD.[3]

The interaction of environmental and genetic variables causes CD. Nearly 80% CD patients have either HLA-DQ2 or HLA-DQ8. After entering the small intestinal submucosa, the gliadin peptide binds to HLA peptides on antigen-presenting cells, causing helper T cells to become activated and intraepithelial cells to proliferate. This results in crypt hyperplasia, villous atrophy, and the development of CD-related antibodies.[4] Nutrient malabsorption results from damage to the small intestine's proximal mucosa.[5] In the past, children who presented with gastrointestinal symptoms and underdevelopment were labeled with CD. A practical first-line diagnostic test was made possible by the identification of tissue transglutaminase as an immunological target, and the expansion of screening led to the identification of numerous additional CD presentations unrelated to the digestive system.[6]

Its clinical presentation is incredibly diverse. If a disease is identified in a kid during the first two years of life, gastrointestinal symptoms are typical; but, as the illness progresses into later years, extra-intestinal manifestations that impact nearly every organ system have come to light.[7] Abdominal distension, chronic diarrhea, and failure to thrive are the hallmarks of the classic type, but they are just the first signs of the disease's full burden. The non-

classical variety usually manifests as small stature, refractory anemia, unexplained rickets, vomiting, recurrent abdominal pain, recurrent oral ulcers, constipation, and failure to thrive.[1]

In 81.3%, 73%, 89.6%, 89.6%, 2 75%4, and 15% of the cases, respectively, chronic diarrhea, iron deficiency anemia, short stature, failure to thrive, osteopenia, and dermatitis herpetaformis were observed.[8]

This study aims to characterize the several forms of celiac disease that affect our people, with an emphasis on dermatitis herpetiformis, iron deficiency anemia, short stature, and failure to thrive. Early sickness detection and timely treatment will help us lower associated morbidities both now and in the future.

MATERIALS AND METHODS

This cross-sectional validation study was carried out by the pediatric department at DHQ hospital in Faisalabad between April 21, 2024 and October 20, 2024. P = 15%8, absolute precision needed = 7.5%, confidence level = 95%, and sample size = 90 were determined using the WHO sample size calculator. This study included both male and female patients with celiac disease whose anti-TTG levels were greater than 100 IU/L and whose ages ranged from 1 to 14 years: Exclusion criteria were giardiasis, immunodeficiency, growth hormone deficit, inflammatory bowel illness, abdominal TB, cystic fibrosis, infective gastroenteritis, primary malnutrition, and chronic kidney disease.

Patients who met the inclusion criteria were enrolled and their parents' informed agreement was obtained after the hospital ethical committee gave its approval. A weight machine and measuring tape were used to determine the patients' height and weight. The pathologist reported that a blood sample was sent to the hospital's pathology laboratory to estimate the ferritin level. With a dermatologist's opinion, dermatitis herpartiformis was evaluated using the operational definition. The patient or parent was asked about their stool history. The following conditions were evaluated: iron deficiency anemia (serum ferritin < 10 ng/ml), failure to thrive (On a growth chart, weight deceleration that crosses two major percentile lines or growth (weight for age) below the third centile), dermatitis herpetiformis (clusters of itchy bumps / blistering skin, especially on elbow, knee, and buttocks that can be obscured by excoriations), and chronic diarrhea (For more than 14 days, the child or parents have reported passing watery or semi-solid stools or having an increased fluidity in stool consistency). I gathered all of the data on the proforma on my own.

The data was analyzed using SPSS V-25. The mean and standard deviation were used to display quantitative data such as age, height, weight, ferritin level, bone mineral density, and length of celiac disease. Frequencies and percentages were used to display qualitative characteristics such as gender, iron deficiency anemia, chronic diarrhea, short stature, failure to thrive, and dermatitis herpetiformis. To adjust for effect modifiers like age and gender, stratification was used. The chi-squared post-stratification test was used. A P-value of less than 0.05 was considered significant.

RESULTS

The study's age range was 1–14 years old, with a mean age of 7.59 ± 2.92 years. According to Table I, the majority of the patients—57, or 63.33%—were between the ages of 7 and 14. With a male to female ratio of 2.2:1, 62 (68.89%) of the 90 patients were men and 28 (31.11%) were women (Figure I). Ferritin level, bone mineral density, height, weight, and length of celiac disease were, respectively, 89.32 ± 12.34 cm, 26.32 ± 8.67 kg, 17.32 ± 9.46 ng/ml, −0.34±0.72, and 4.53 ± 3.61 months.

According to Table II, I discovered that the following clinical presentations were common among children with celiac disease: iron deficiency anemia in 39 (43.33%), failure to thrive in 29 (32.22%), dermatitis herpetiformis in 22 (24.44%), short stature in 24 (26.67%), and chronic diarrhea in 43 (47.78%). Table III and Table IV, respectively, stratify the frequency of various clinical manifestations in children with celiac disease by age and gender.

Table I

Age distribution of patients (n=90).

Age	No. of Patients	%age
1-6 years	33	36.67
7-14 years	57	63.33
Total	90	100.0

Figure I

Distribution of patients according to gender (n=90).

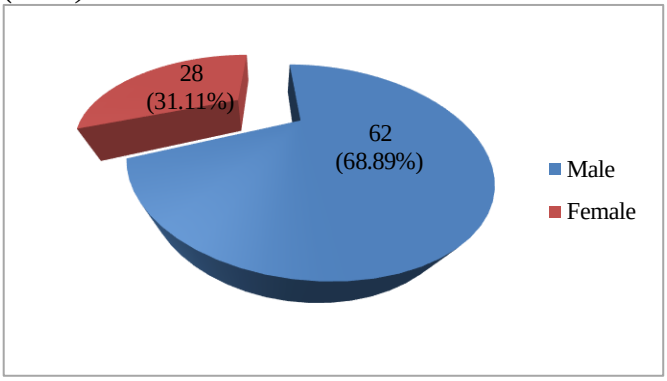

Table II

Frequency of different clinical presentations in children diagnosed with coeliac disease

Clinical presentations	Frequency (%)	
	yes	no
Chronic diarrhoea	43 (47.78%)	47 (52.22%)

Dermatitis herpetiformis	22 (24.44%)	68 (75.56%)
Failure to thrive	29 (32.22%)	61 (67.78%)
Short stature	24 (26.67%)	66 (73.33%)
Iron deficiency anemia	39 (43.33%)	51 (56.67%)

Table III

Stratification of different clinical presentations with respect to age.

Clinical presentations		1-6 years (n=33)	7-14 years (n=57)	P-value
Chronic diarrhoea	Yes	18 (54.55%)	25 (43.86%)	0.328
	No	15 (45.45%)	32 (56.14%)	
Dermatitis herpetiformis	Yes	09 (27.27%)	13 (22.81%)	0.635
	No	24 (72.73%)	44 (77.19%)	
Failure to thrive	Yes	11 (33.33%)	18 (31.58%)	0.864
	No	22 (66.67%)	39 (68.42%)	
Short stature	Yes	11 (33.33%)	13 (22.81%)	0.277
	No	22 (66.67%)	44 (77.19%)	
Iron deficiency anemia	Yes	13 (39.39%)	26 (45.61%)	0.566
	No	20 (60.61%)	31 (54.39%)	

Table IV

Stratification of different clinical presentations with respect to gender.

Clinical presentations		Male (n=62)	Female (n=28)	P-value
Chronic diarrhoea	Yes	36 (58.06%)	07 (25.0%)	0.004
	No	26 (41.94%)	21 (75.0%)	
Dermatitis herpetiformis	Yes	15 (24.19%)	08 (28.57%)	0.659
	No	47 (75.81%)	20 (71.43%)	
Failure to thrive	Yes	23 (37.10%)	06 (21.43%)	0.141
	No	39 (62.90%)	22 (78.57%)	
Short stature	Yes	20 (32.26%)	04 (14.29%)	0.074
	No	42 (67.74%)	24 (85.71%)	
Iron deficiency anemia	Yes	29 (46.77%)	10 (35.71%)	0.327
	No	33 (53.23%)	18 (64.29%)	

DISCUSSION

In recent years, the number of celiac disease diagnoses has continued to rise. According to recent research, 1.65% of Italians were expected to have CeD between 2017 and 2020.[9] The number of annual diagnoses has increased, according to data in the literature[10]; we also noticed a 52% increase in celiac diagnosis from 2011–2015 to 2019–2023. This can be attributed in part to better screening techniques and in part to the rise in actual pathology brought on by dietary and environmental changes. [11] One may also claim that the media's focus on CeD is contributing to a rise in awareness of the condition.[12] Furthermore, in many affluent nations, the typical age of diagnosis has changed from less than two years to six to nine years.[13] Our results, which show an average diagnostic age of seven years, support this trend.

According to this study, the following clinical presentations are common in children with celiac disease: iron deficiency anemia in 39 patients (43.33%), failure to thrive in 29 (32.22%), dermatitis herpetiformis in 22 (24.44%), short stature in 24 (26.67%), and chronic diarrhea in 43 (47.78%). According to a Moroccan survey, growth delay (32.4%) and diarrhea (46%) were the most common reasons for consultations.[14]

When looking at each symptom separately, gastrointestinal problems are the most common. But with time, their prevalence is changing. According to a study done in western New York, the most common symptoms among newly diagnosed celiac patients were constipation and abdominal pain, and these symptoms were more common in older children than in children with classic presentation of CeD.[15] In a US multicentric study, 57% of the participants reported having stomach ache.[16] Less than 45% of patients in Greece presented with malabsorption indicators; vomiting, recurring stomach pain, and constipation were among the most common start symptoms.[17] A recent analysis of the clinical presentation of CeD in children aged 30 years revealed a decrease in diarrhea and an increase in bloating and constipation, according to an Italian study.[18] Our findings support the 47.78% prevalence of gastrointestinal symptoms, such as diarrhea.

6.5% of participants were wasted, 17.2% were underweight, and 14.1% were stunted at the time of diagnosis. It should be noted that in 2020, 10.4% of Lebanon's under-5-year-old population was stunted, compared to 26.2% of the area.[19] Aggarwal et al.'s study shown that individuals with celiac disease in India are not always small in stature.[20] But according to a research conducted in Pakistan, 79% of the population was low in stature, 38% were extremely undernourished, and 8% were severely stunted.[21] 85% of celiac disease patients in a Saudi Arabian research were stunted.[22] The lower rates of underweight and wasted patients in our study could be attributed to Pakistan's Mediterranean diet.

Iron deficiency anemia (IDA) can affect anywhere from 2.3 to 33% of children with celiac disease.[23] Iron deficiency was found in 43.33% of

our cohort's individuals with baseline iron tests. Additionally, the cohort's mean serum vitamin D level fell outside of the desired range. However, studies show that serum vitamin D levels are generally lower in people with untreated celiac disease than in healthy controls without the illness.[24] The low number of participants who had their serum vitamin D levels measured may have contributed to the value of our cohort. Furthermore, when it comes to clinical presentation, it's critical to remember that dermatologic signs like acrodermatitis and pemphigus vulgaris might take on a "strange" and uncommon shape.[24]

Xin et al.'s comprehensive review and meta-analysis demonstrated that the GFD significantly and favorably affects the weight of celiac disease patients.[25] Children in Italy saw slower catch-up growth than their American counterparts, according to a different retrospective study that examined celiac disease patients in the USA and Italy. [26] Due to the lack of gluten-free options and the fact that the Mediterranean diet contains a number of gluten-containing foods, this was connected to the cultural and lifestyle differences, which may also apply to the Lebanese population. There are currently no studies that assess how the gluten-free Mediterranean diet affects children's growth, though this may be a topic for future research.

Our ability to collect precise and comprehensive data was restricted by the cross-sectional design, which also prevented us from having the proper long-term follow-up to assess GFD compliance. Furthermore, the study only contained a small sample size from one Pakistani tertiary medical facility, which could limit its generalizability and result in referral bias.

CONCLUSION

The most common symptoms that children with celiac disease reported in this study were failure to thrive, diarrhea, and iron deficiency anemia. In a country with limited resources like Pakistan, diagnosis and treatment remain challenging because of high cost of procedures and the lack of affordable gluten-free food. Therefore, as demonstrated in this study, choosing less expensive diagnostic measures, such celiac serologies, in certain situations rather than endoscopy may be a viable alternative. Children with celiac disease have poor growth and development, which should improve after GFD is started.

REFERENCES

1. Imran, Cheema, H. A., Alvi, M. A., Rehman, M. U., Ali, M., & Sarwar, H. A. (2021). Spectrum of clinical presentation of celiac disease in pediatric population. *Cureus*, *13*(6). https://doi.org/10.7759/cureus.15582
2. Rasheed, J., Khan, T., Khalid, M., & Zafar, F. (2018). Celiac disease; a medley of clinical features a tertiary care hospital experience. *The Professional Medical Journal*, *25*(05), 669-675. https://doi.org/10.29309/tpmj/2018.25.05.306
3. Siddiqui, K., Rafiq, M., Bhutto, M. A., & Uqaili, A. A. (2021). Red Blood Indices, Platelet Count and Transferrin Levels in Celiac Patients with and Without Type 1 Diabetes Mellitus in Hyderabad, Sindh, Pakistan. *Khyber Medical University Journal*, *13*(1). https://doi.org/10.35845/kmuj.2021.20553
4. Nardecchia, S., Auricchio, R., Discepolo, V., & Troncone, R. (2019). Extra-intestinal manifestations of coeliac disease in children: Clinical features and mechanisms. *Frontiers in Pediatrics*, *7*. https://doi.org/10.3389/fped.2019.00056
5. Rubin, J. E., & Crowe, S. E. (2020). Celiac disease. *Annals of Internal Medicine*, *172*(1), ITC1-ITC16. https://doi.org/10.7326/aitc202001070
6. Therrien, A., Kelly, C. P., & Silvester, J. A. (2019). Celiac disease: extraintestinal manifestations and associated conditions. *Journal of Clinical Gastroenterology*, *54*(1), 8-21. https://doi.org/10.1097/mcg.0000000000001267
7. Javed, F., Sattar, F., Gill, A. A., Lodhi, Y., Iqbal, K., & Nazir, A. (2019). Clinical Spectrum of Celiac Disease in Children: Experience from A Public Hospital in Pakistan. *Annals of Punjab Medical College (APMC)*, *13*(3), 192–196. https://doi.org/10.29054/apmc/2019.145
8. Nurminen, S., Kivelä, L., Huhtala, H., Kaukinen, K., & Kurppa, K. (2018). Extraintestinal manifestations were common in children with coeliac disease and were more prevalent in patients with more severe clinical and histological presentation. *Acta Paediatrica*, *108*(4), 681-687. https://doi.org/10.1111/apa.14324
9. Lionetti, E., Pjetraj, D., Gatti, S., Catassi, G., Bellantoni, A., Boffardi, M., Cananzi, M., Cinquetti, M., Francavilla, R., Malamisura, B., Montuori, M., Zuccotti, G., Cristofori, F., Gaio, P., Passaro, T., Penagini, F., Testa, A.,

Trovato, C. M., & Catassi, C. (2023). Prevalence and detection rate of celiac disease in Italy: Results of a SIGENP multicenter screening in school-age children. *Digestive and Liver Disease*, *55*(5), 608-613. https://doi.org/10.1016/j.dld.2022.12.023

10. Catassi, C., Verdu, E. F., Bai, J. C., & Lionetti, E. (2022). Coeliac disease. *The Lancet*, *399*(10344), 2413-2426. https://doi.org/10.1016/s0140-6736(22)00794-2
11. Bolia, R., & Thapar, N. (2023). Celiac disease in children: A 2023 update. *Indian Journal of Pediatrics*, *91*(5), 481-489. https://doi.org/10.1007/s12098-023-04659-w
12. Trovato, C. M., Montuori, M., Oliva, S., Cucchiara, S., Cignarelli, A., & Sansone, A. (2020). Assessment of public perceptions and concerns of celiac disease: A Twitter-based sentiment analysis study. *Digestive and Liver Disease*, *52*(4), 464-466. https://doi.org/10.1016/j.dld.2020.02.004
13. Di Biase, A. R., Marasco, G., Ravaioli, F., Colecchia, L., Dajti, E., Lecis, M., Passini, E., Alemanni, L. V., Festi, D., Iughetti, L., & Colecchia, A. (2021). Clinical presentation of celiac disease and diagnosis accuracy in a single-center European pediatric cohort over 10 years. *Nutrients*, *13*(11), 4131. https://doi.org/10.3390/nu13114131
14. Mouslih, A., El Rhazi, K., Bahra, N., Lakhdar Idrissi, M., & Hida, M. (2023). Celiac disease in moroccan children: Diagnostic characteristics and determinants of diagnosis delay. *Cureus*. https://doi.org/10.7759/cureus.50800
15. Khatib, M., Baker, R. D., Ly, E. K., Kozielski, R., & Baker, S. S. (2016). Presenting pattern of pediatric celiac disease. *Journal of Pediatric Gastroenterology and Nutrition*, *62*(1), 60-63. https://doi.org/10.1097/mpg.0000000000000887
16. Krueger, A., Fahey, L., Sun, Q., Regis, S., Khavari, N., Jericho, H., Badalyan, V., Absah, I., Verma, R., Leonard, M. M., Weisbrod, V., Hajjat, T., Lee, D., Shull, M., Silvester, J. A., & Mallon, D. (2024). Clinical presentation and factors associated with gluten exposure in children with celiac disease. *Journal of Pediatric Gastroenterology and Nutrition*, *79*(4), 895-904. https://doi.org/10.1002/jpn3.12321
17. Roma, E., Panayiotou, J., Karantana, H., Constantinidou, C., Siakavellas, S. I., Krini, M., Syriopoulou, V. P., & Bamias, G. (2009). Changing pattern in the clinical presentation of pediatric celiac disease: A 30-Year study. *Digestion*, *80*(3), 185-191. https://doi.org/10.1159/000227275
18. Pedretti, M., Sbravati, F., Allegri, D., Labriola, F., Lombardo, V., Spisni, E., Zarbo, C., & Alvisi, P. (2021). Is the clinical pattern of pediatric celiac disease changing? A thirty-years real-life experience of an Italian center. *Italian Journal of Pediatrics*, *47*(1). https://doi.org/10.1186/s13052-021-01183-5
19. The work of WHO in the Eastern Mediterranean Region-Annual report of the regional director 2019.
20. Aggarwal, N., Dwarakanathan, V., Singh, A., Agarwal, A., Khuttan, A., Ahmed, A., Rajput, M. S., Chauhan, A., Banyal, V., Verma, A. K., Gupta, V., Lodha, R., Ahuja, V., & Makharia, G. K. (2021). Spectrum of height in patients with celiac disease. *Indian Journal of Gastroenterology*, *40*(6), 604-612. https://doi.org/10.1007/s12664-021-01173-9
21. Jabeen, S., Khan, A. U., Ahmed, W., Ahmad, M., Jafri, S. A., Bacha, U., Ali, A., Muzammil, H. S., Alsagaby, S. A., Al Abdulmonem, W., Abdelgawad, M. A., Riaz, M., Mahwish, Nasir, M., Zafar, A., Tufail, T., Imran, M., Anwar Faridi, T., Aslam, M., … Ur-Rehman, H. (2022). Disease specific symptoms indices in patients with celiac disease—A hardly recognised entity. *Frontiers in Nutrition*, *9*. https://doi.org/10.3389/fnut.2022.944449
22. Saadah, O. I. (2021). The impact of a gluten-free diet on the growth pattern of Saudi children with celiac disease. *Journal of the Pakistan Medical Association*, 1-17. https://doi.org/10.47391/jpma.1308
23. Talarico, V., Giancotti, L., Mazza, G. A., Miniero, R., & Bertini, M. (2021). Iron deficiency anemia in celiac disease. *Nutrients*, *13*(5), 1695. https://doi.org/10.3390/nu13051695
24. Lu, C., Zhou, W., He, X., Zhou, X., & Yu, C. (2020). Vitamin D status and vitamin D receptor genotypes in celiac disease: A meta-analysis. *Critical Reviews in Food Science and Nutrition*, *61*(12), 2098-2106. https://doi.org/10.1080/10408398.2020.1772716
25. Xin, C., Imanifard, R., Jarahzadeh, M., Rohani, P., Velu, P., & Sohouli, M. H. (2023).

Impact of gluten-free diet on anthropometric indicators in individuals with and without celiac disease: A systematic review and meta-analysis. *Clinical Therapeutics*, *45*(12), e243-e251. https://doi.org/10.1016/j.clinthera.2023.09.018.

26. Sansotta, N., Guandalini, S., Romano, S., Amirikian, K., Cipolli, M., Tridello, G., Barzaghi, S., & Jericho, H. (2020). The gluten free diet's impact on growth in children with celiac disease in two different countries. *Nutrients*, *12*(6), 1547. https://doi.org/10.3390/nu12061547