OPEN ACCESS

Original Article

# High Prevalence of Celiac Disease among Pediatric Population; A Cross Sectional Survey

**Muhammad Asim[1], Hassan Riaz[2]**

[1]University Institute of Medical Laboratory Sciences, University of Lahore

[2]Fatima Memorial Medical College, Lahore.

**Author`s Contribution**

[MA, MI,] Conception and design, Collection and assembly of data, [HR]Analysis and interpretation of the data, Statistical expertise,[MI]Final approval and guarantor of the article

**Article Info.**

Received: Jan 27, 2022
Acceptance: April 07, 2022

*Conflict of Interest: None*

*Funding Sources: None*

**Address of Correspondence**

Hassan Riaz
Fatima Memorial Medical College, Lahore

DOI: 10.53389/RJAHS.2022010106

A B S T R A C T

Background: Celiac disease (CD) is a multifactorial, complex disease caused by a complex interaction of genetic, immunological, and environmental factors.

Objective: The current study was designed to evaluate the incidence rate of this disease among paediatric population of both genders in Lahore region.

Methodology: A total of 1000 celiac disease suspected pediatric patients of both genders i.e., male and female were enrolled in present study. Antibodies against tissue transglutaminase (anti-tTG) IgG and IgA were detected by using ELISA method.

Results: Eight hundred twenty-two (822) of 1000 suspected patients of celiac disease (82.1%) showed negative transglutaminase TGA (IgA, IgG) levels and 178 patients (17.8%) showed positive TGA (IgA, IgG) levels. Total 565 patients (56.6%) were males while 434 patients (43.4%) were females. Out of 822 patients having negative TGA (IgA, IgG) 476 (57.97%) were males and 345 (42,02%) were females. Out of 178 patients of celiac disease 99 (55.61%) were males and 79 (44.38%) were females. TGA levels were found to be more positive in males as compared to females.

Conclusion: This study reports the high prevalence and incidence rate of celiac disease in the pediatric population of Lahore with 17.8% positive patients and reports approximately every 18 out of 100 children are suffering from this disease. The incidence rate of the disease was found to be alarmingly high (1 in every 6 children) in the Lahore region. Further studies are warranted to explore the associated risk factors.

Key Words: Celiac disease, Pediatric population, tissue transglutaminase, ELISA, Lahore.

## Introduction

Celiac disease (CD) is an autoimmune disease caused by a complex interplay of genetic, immunological, and environmental factors. The disease is often chronic and results in degeneration of intestinal mucosa. Cereals with high level of gluten (i.e., wheat, rye, and barley) are found to be lethal for patients with this disease.[1] European countries presents the highest incidence rate of the disease (1% to 0.3%).[2] A study conducted in North America reported the incidence rate from 0.5% to 1% of population, and majority of patients were asymptomatic.[3] Recent studies performed in Asian and North African countries also revealed high incidence rate (i.e. Egypt: 0.53%, Iran: 0.88%, India: 0.70%, Libya: 0.79%, Tunisia: 0.6%, and Turkey: 0.60%).[4] This high incidence rate may be attributed to the advancements in diagnostic methods.[5] Malabsorption was found to be the most representing symptom in Turkish population, whereas, American population expressed atypical symptoms (i.e., fatigue, abdominal pain, and bloating).[6] Although the incidence of major depressive and stress related disorders such as dysthymia ranges from 10% to 80%, CD is the most common cause of such problems in adults and children.[7]

CD patients are sensitive to gliadin (gluten protein) which is a prolamin found in wheat. These storage proteins are rich in proline and glutamine amino acids and are not digested by major proteolytic enzymes

present in the gut (proteases and peptidases).[8] There are different variants of prolamins found in different cereals grains i.e. hordein in barley, zein in corn, gliadin in wheat, secalin in rye, and avenin in oats. Intestinal cells are stimulated by α-gliadin part, disrupt tight junctions and allow larger peptides to enter the circulation.[9,10]

CD being a multifactorial disease is caused by combination of environmental factors and genetic predisposition. There are seven HLA-DQ variants (DQ2,4-9) which are susceptible to this disease. The most crucial and inheritable genetic factors are HLA-DQ2 and HLA-DQ8. Receptors of the mentioned genetic variants binds gliadin peptides more tightly and cause increased risk of acquiring CD. HLA-DQ2 and DQ8 are found to be the main predisposing variants but only 4% people with this variant were found to develop disease after taking gluten diet.[11,12] As most of the people with CD are asymptomatic, it can complicate to cause type I diabetes, anemia, multiple sclerosis, osteoporosis, dermatitis, intestinal cancer, reproductive problems, and neuronal conditions. [3]

IgA is monomeric in the plasma but in the secretion it exist in dimeric form. In serum IgA has four-polypeptide chains (two heavy (H) and two light (L) chains), additional polypeptide-J and secretory component which are linked by disulfide bonds. IgA deficiency is reported in 2.3% of CD patients and is responsible for tenfold increased risk of the disease. Moreover, these patients are also more susceptible to acquiring infections and autoimmune diseases.[14] Therefore, assessment of IgA autoantibodies against IgA tissue transglutaminase (tTG-IgA) in serum is the initial step in the diagnosis of CD.[15] Tissue transglutaminase (tTG) alters the gluten peptides to stimulate immune response more effectively.[16]

Imran and co-workers conducted a study on clinical presentation of CD in pediatric population of Lahore but have not reported the prevalence of the disease.[17] In another study high prevalence of the disease was reported in short stature children of Faisalabad region but no such study was conducted in Lahore region.[18].Therefore, the present study was designed to find out the prevalence of CD in pediatric population of Lahore region.

## Methodology

This cross-sectional study was designed to investigate the prevalence of CD in pediatric population of Lahore, Pakistan. The study was approved by ethical review committee of Children's Hospital, Lahore. Celiac disease suspected patients admitted at Children Hospital, Lahore, Pakistan, from May 2019 to August 2020 were recruited with informed consent. A convenience sampling technique was used to enrol 1000 children <18 years of age in the study. Patients belonging to both genders were included. Patients presenting with diarrhea, or any other gastrointestinal disease were excluded from study. 3ml blood sample was collected in plain serum tubes from each enrolled patient, and serum was isolated by centrifugation at 1800 rpm for 2 minutes. Serum samples were stored in sterilized eppendorf tubes at -20°C till further processing.

All serum samples were diluted (1:100) by adding 10 µl serum and 1000ul sample buffer in a polystyrene tube. Samples were mixed thoroughly and vortexed. Detection of anti-tTG-IgG and IgA was performed by commercial kit (orgentec diagnostika GmbH-ELISA). Cutoff value (10U/ml) was used according to the manufacturer's instructions. Negative samples contained optical density (OD) less than cutoff value whereas, positive samples contained OD greater than cutoff value. Detection was performed briefly as, 100 µl of the control sera was taken from positive and negative samples, diluted (1:100), placed into microwells plate and incubated for 30 minutes. After 30 minutes contents were aspirated, and wells were washed three times. After that 100 µl of the conjugate solution was added into all wells and incubated again for 15 minutes and wells were washed. At the end substrate was added and plate was incubated for 15 more mins. The reaction was then ceased by adding 0.5 mole/liter sulfuric acid as stop solution. All the incubations were done at room temperature. ELISA reader was used to read the color development at 450 nm. Obtained data was analyzed by using Microsoft Excel 2007 And SPSS version 21.

## Results

A total of 1000 suspected cases of celiac disease with <18 years of age and belonging to both male

and female genders were enrolled in the study. Frequency of male and female enrolled patients along with their percentage is shown is the Figure 1.

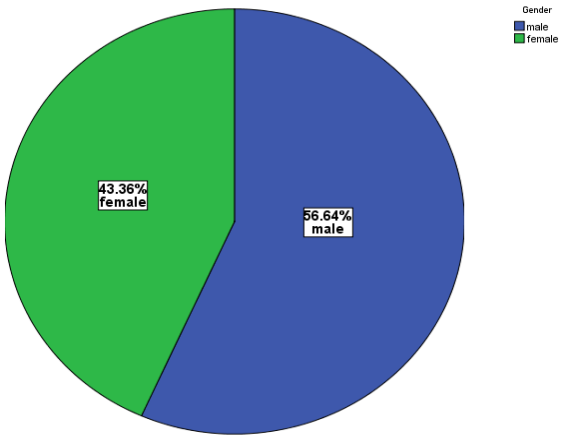


**Figure. 1. Frequency of gender in suspected cases of celiac disease.**

ELISA results revealed 822 patients (82.2%) were negative for TGA (IgA, IgG) levels (cutoff value <10U/ml) whereas, 178 patients (17.8%) were positive for TGA (IgA, IgG) levels (cutoff value >10U/ml). Among TGA (IgA, IgG) negative patients 476 (57.97%) were males and 345 (42.02%) were females. However, among 178 positive patients 99 patients (55.61%) were males and 79 (44.38%) were females. Higher number of male patients were found to be positive for celiac disease as compared to female patients. Frequency and percentages of all enrolled patients is shown in Table 1.

**Table 1: Frequency and percentages of CD suspected patients enrolled in the study**

| Characteristic | N | Percentage (%) |
|---|---|---|
| Enrolled Patients | 1000 | 100% |
| TGA (IgG/IgA) Positive | 178 | 17.8% |
| Male | 99 | 55.61% |
| Female | 79 | 44.38% |
| TGA (IgG/IgA) Negative | 822 | 82.2% |
| Male | 466 | 57.90% |
| Female | 356 | 42.09% |
| Levels of Positive Patients | | |
| IgG level >10U/ml | 115 | 64.60% |
| IgG level >20 U/ml | 63 | 35.39% |
| IgA level >10U/ml | 78 | 43.82% |
| IgA level >20U/ml | 100 | 56.17% |

Mean values of IgG and IgA in TGA positive patients is shown as bar graph in Figure 2. As figure 2 shows there is a statistically significant difference in serum IgA and IgG levels ($p<0.05$). Serum IgA levels are significantly high as compared to serum IgG levels in positive patients. Prevalence of the disease was calculated to be 18 in 100 children and 1 in every 6 children.

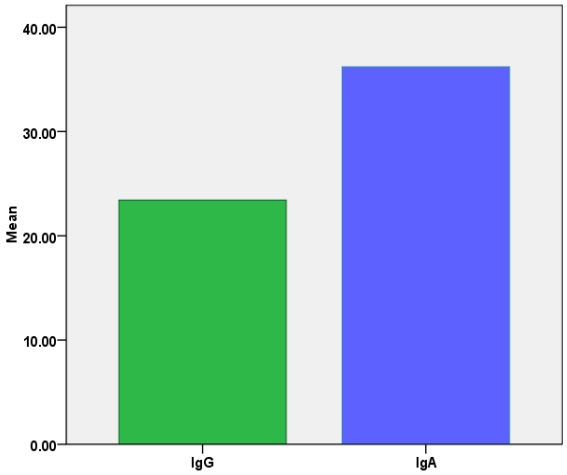


**Figure 2. Mean value of IgG and IgA in TGA positive patients of CD**

## Discussion

CD is a complex trait, multifactorial, autoimmune disorder which affects genetically predisposed population of all age groups. It is stimulated by environmental factors (i.e., gluten and related prolamins), and the autoantigen (tissue transglutaminase). Tissue transglutaminase (tTG) plays a role as an autoantigen in this disease. Antibodies level against tTG are measured by ELISA assay. Present study was designed to determine the prevalence of CD in pediatric population of Lahore. Study reports high prevalence of CD in pediatric male population as compared to females and males were found to be more prone to the disease as compared to females. Similar study was previously carried out by Marine and co-workers and reported five times higher incidence rate of CD in childhood as compared to adults. They reported the prevalence of CD in children as 1:71 which is quite high as compared to adults 1:357.[19]

High frequency of CD in children was also explored by Abu Zekry and colleagues who conducted a study to assess the frequency and incidence of CD in Egyptian children. They investigated a total number of 1500 general pediatric population between 7-18 years of age. The enrolled patients were screened by using anti-tTG antibody, total IgA, IgG, and small bowel biopsy methods. They concluded that most of the patient's sera

showed positive results to both the IgA, anti-tTG and the IgA anti-endomysium test as compared to IgG-anti-tTG and reported the prevalence of CD as 1:187 in children. [20]

Our study reports the higher levels of serum IgA as compared to serum IgG and 56% of CD positive patients had IgA levels >20U/ml whereas, only 35% patients had IgG levels >20U/ml. Hill and Holmes, in 2008 conducted a study on 1554 adults and reported the use of anti-transglutaminase antibody levels as positive predictive marker for diagnosis of CD. They stated that serum IgA IgG levels above the cutoff value of 30U/ml nullify the use of biopsy methods. The study eliminates the confirmation of disease by invasive biopsy methods leading to quick diagnosis of the disease for better treatment options.[21]

## Conclusion

This study concludes that the frequency of CD in pediatric population of Lahore is 17.8% and approximately every 18 children out of 100 are having this condition. The prevalence of CD reported in Lahore region is alarmingly high and warrant further studies on the disease to examine the associated risk factors.

## References


1. Guandalini S. Historical perspective of celiac disease. Frontiers in celiac disease: Karger Publishers.2008;1-11. https://doi.org/10.1159/000128267
2. Mäki M, Mustalahti K, Kokkonen J, Kulmala P, Haapalahti M, et al. Prevalence of celiac disease among children in Finland. New England Journal of Medicine.2003; 348(25): 2517-2524. https://doi.org/10.1056/NEJMoa021687
3. Telega G, Bennet TR, Werlin S. Emerging new clinical patterns in the presentation of celiac disease. Archives of pediatrics & adolescent medicine.2008; 162(2): 164-168. https://doi.org/10.1001/archpediatrics.2007.38
4. Admou B, Essaadouni L, Krati K, Zaher K, Sbihi M, et al. Atypical celiac disease: from recognizing to managing. Gastroenterology research and practice.2012; 2012. https://doi.org/10.1155/2012/637187
5. Rewers M. Epidemiology of celiac disease: what are the prevalence, incidence, and progression of celiac disease? Gastroenterology,2005; 128(4): S47-S51. https://doi.org/10.1053/j.gastro.2005.02.030
6. Palabykoglu M, Botoman VA, Coban S, Ormeci N, Bonner GF, et al. A tale of two cities: typical celiac sprue presenting symptoms are significantly more common in Turkish than in US Patients. Journal of clinical gastroenterology.2008; 42(1): 62-65. https://doi.org/10.1097/01.mcg.0000247998.57828.f7
7. Sevinç E, Çetin FH, Coşkun BD. Psychopathology, quality of life, and related factors in children with celiac disease☆. Jornal de Pediatria. 2017; 93267-273. https://doi.org/10.1016/j.jped.2016.06.012
8. Di Cagno R, De Angelis M, Auricchio S, Greco L, Clarke C, et al. Sourdough bread made from wheat and nontoxic flours and started with selected lactobacilli is tolerated in celiac sprue patients. Applied and environmental microbiology.2004; 70(2): 1088-1096. https://doi.org/10.1128/AEM.70.2.1088-1096.2004
9. Ortiz-Sánchez JP, Cabrera-Chávez F, Calderón de la Barca AM. Maize prolamins could induce a gluten-like cellular immune response in some celiac disease patients. Nutrients.2013; 5(10): 4174-4183. https://doi.org/10.3390/nu5104174
10. Guandalini S. The approach to celiac disease in children. International journal of pediatrics & adolescent medicine.2017; 4(3): 124. https://doi.org/10.1016/j.ijpam.2017.08.002
11. Silano M, Agostoni C, Guandalini S. Effect of the timing of gluten introduction on the development of celiac disease. World journal of gastroenterology: WJG.2010; 16(16): 1939. https://doi.org/10.3748/wjg.v16.i16.1939
12. Holtmeier W, Caspary WF. Celiac disease. Orphanet journal of rare diseases.2006; 1(1): 1-8. https://doi.org/10.1186/1750-1172-1-3
13. Cristofori F, Fontana C, Magistà A, Capriati T, Indrio F, et al. Increased prevalence of celiac disease among pediatric patients with irritable bowel syndrome: a 6-year prospective cohort study. JAMA pediatrics.2014; 168(6): 555-560. https://doi.org/10.1001/jamapediatrics.2013.4984
14. Collin P, Kaukinen K, Välimäki M, Salmi J. Endocrinological disorders and celiac disease. Endocrine reviews, (2002); 23(4): 464-483.https://doi.org/10.1210/er.2001-0035
15. Laass MW, Röber N, Range U, Noß L, Roggenbuck D, et al. Loss and gain of tolerance to pancreatic glycoprotein 2 in celiac disease. PLoS One.2015; 10(6): e0128104. https://doi.org/10.1371/journal.pone.0128104
16. Koning F, Schuppan D, Cerf-Bensussan N, Sollid LM. Pathomechanisms in celiac disease. Best practice & research Clinical gastroenterology.2005; 19(3): 373-387. https://doi.org/10.1016/j.bpg.2005.02.003
17. Imran, Cheema HA, Alvi MA, Rehman MU, Ali M, et al. Spectrum of Clinical Presentation of Celiac Disease in Pediatric Population. Cureus.2021; 13(6): e15582. https://doi.org/10.7759/cureus.15582
18. Masood J, Rehman H, Anjum ZM, Iqbal I, Zafar S, et al. Prevalence of celiac disease in idiopathic short stature children presenting in OPD of children hospital, Faisalabad. Annals of Punjab Medical College.2020; 14(1): 9-12. https://doi.org/10.29054/apmc/2020.706
19. Mariné M, Farre C, Alsina M, Vilar P, Cortijo M, et al. The prevalence of coeliac disease is significantly higher in children compared with adults. Aliment Pharmacol Ther.2011; 33(4): 477-486. https://doi.org/10.1111/j.1365-2036.2010.04543.x
20. Abu-Zekry M, Kryszak D, Diab M, Catassi C, Fasano A. Prevalence of celiac disease in Egyptian children disputes the east-west agriculture-dependent spread of the disease. J Pediatr Gastroenterol Nutr.2008; 47(2): 136-140. https://doi.org/10.1097/MPG.0b013e31815ce5d1
21. Hill PG, Holmes GK. Coeliac disease: a biopsy is not always necessary for diagnosis. Aliment Pharmacol Ther.2008; 27(7): 572-577. https://doi.org/10.1111/j.1365-2036.2008.03609.x