

Frequency of Celiac Disease in Children Presenting with Iron Deficiency Anaemia: A Single Centre Experience from Southern Punjab, Pakistan

Nadeem Iqbal Qaisrani¹, Mubina Ifat², Muhammad Aslam³, Masooma Ifat⁴, Abdul Qudoos Mujahid⁵, Muhammad Khalil Surani⁶, Muhammad Asif⁷, Fatima uz Zahra⁸

¹Consultant Pediatric, Shahbaz Sharif DHQ Hospital Multan, ²PGR Pediatric Neurology Department CHC/ICH, Multan, ³Assistant Professor Pediatric Medicine Pediatric Gastroenterology CHC and ICH Multan, ⁴WMO, BHU Hospital, Muzaffargarh, ⁵Medical Officer Nishtar Burn Center, Multan, ⁶PGR Neonatology Department CHC/ICH, Multan, ⁷Consultant Pediatrician THQ Hospital, Muzaffargarh, ⁸Consultant Pediatrician THQ Hospital, Multan.

Corresponding author: Dr. Nadeem Iqbal Qaisrani, Email: nadeemqaisrani88@gmail.com

ABSTRACT

Background: Celiac disease (CD) is a chronic disease of immune-mediated damage to the small intestine resulting in variable symptoms of malabsorption. Iron deficiency anaemia (IDA) is one such frequent symptom. As these are high percentages for celiac disease in patients presenting with iron deficiency anaemia, the study's main aim was to determine the frequency of celiac disease in children presenting with IDA.

Material and Methods: It was a descriptive cross-sectional study conducted at Children's Hospital & the Institute of Child Health, Multan, for a duration of 6 months from 16th January 2020 to 15th July 2020. A total of 132 patients were enrolled; we included patients from Ages one year to 14 years of both genders, newly diagnosed patients with iron deficiency anaemia who are not taking treatment for this, we studied age, sex, duration of anaemia, the severity of anaemia, we investigated Hb, serum ferritin, anti-tissue transglutaminase antibodies level and endoscopic biopsy done.

Results: We enrolled 132 patients presenting with IDA. Among all 132 patients, CD was found in 23 (17.4%) Mean age of the patients was 7.61±4.21 years. The mean value of the duration of anaemia of the patients was 20.39±6.17 days. 60(45.45%) patients were male, and 72 (54.55%) were female.

Conclusion: The frequency of CD in children with iron deficiency is found to be 17.4%. Therefore, we recommend a Multicenter study at regional and national levels to assess the disease burden and early diagnosis for appropriate and timely management of this vulnerable population.

Keywords:

Iron Anemia Deficiency, Children, Celiac Disease

INTRODUCTION

Celiac disease (CD) or non-tropical sprue is an autoimmune disease characterised by enteropathy due to antibody-mediated damage to the proximal portion of the small bowel resulting in villous atrophy, hypertrophy of crypts and increased intraepithelial lymphocytosis.⁷ Its cause is hypersensitivity to gluten, a protein in wheat, barley, and rye flour. Genetic predisposition to this hypersensitivity plays a significant role in the aetiology of this disease.⁵ CD is associated with HLA DQ2/DQ8. However, environmental and immunologic factors also contribute to its development, with only 4% of the genetically susceptible persons developing the disease manifestations after the introduction of gluten in the diet.⁶ Also, high titers of,

Anti-Endomysial antibodies (Anti-EMA), Anti-Tissue Transglutaminase (Anti-TTG) antibodies) and Anti Deaminated Gliadin (DGP) is found in patients of celiac disease.

Abdominal distension, loss of appetite and chronic diarrhoea are frequently encountered clinical presentations. Subsequent manifestations of CD include malabsorption of nutrients, with disturbance in iron absorption being the most important.¹⁻⁷ However, in children during their growing age, the failure to grow normally with resultant short stature and iron deficiency anaemia are common presentations.¹⁻⁷

Iron deficiency anaemia (IDA) is a public health problem worldwide.⁸ Deficiencies of other nutrients like folic acid and vitamin B12 also predispose to the development of anaemia because of malabsorption associated with CD. However, iron deficiency appears to be clinically more associated in this regard.⁹ Cekin and Co-Authors reported the prevalence of CD in patients presenting with iron deficiency anaemia to be 7.14%.² In the Northern Indian tertiary-care hospital outpatient setting, Celiac disease was associated with

Conflict of Interest: The authors declared no conflict of interest exists.

Citation: Qaisrani NI, Ifat M, Aslam M, Ifat M, Mujahid AQ, Surani MK, Asif M, Zahra F. Frequency of Celiac Disease in Children Presenting with Iron Deficiency Anaemia: A Single Centre Experience from Southern Punjab, Pakistan. J Fatima Jinnah Med Univ. 2023; 17(1):33-36.

DOI: <https://doi.org/10.37018/LBEC4340>

4% of children presenting with moderate-to-severe anemia recent study.¹²

Most of the Pakistani population suffers from IDA especially pregnant women, nursing mothers and children. CD disease often goes undiagnosed when presented as IDA because local data on its prevalence and aetiology needs to be more comprehensive in Pakistan. A complete workup to find the cause, especially for CD, could be improved. Failure of oral iron supplementations in settings of IDA should raise the suspicion of CD.³ This study aims to determine the frequency of CD in children presenting with iron deficiency anaemia in one of the tertiary care referral centres in the Southern Punjab region of Pakistan.

PATIENTS AND METHODS

This cross-sectional observational study was conducted at the Department of Pediatric Gastroenterology Children's Hospital & the Institute of Child Health, Multan, for six months from 16th January 2020 to 15th July 2020. It aimed to determine the frequency of CD in children presenting with IDA. Permission from the institution's ethical review board was obtained, and a sample size of 132 was calculated, keeping a 95% confidence interval and a 5 % margin of error with an expected prevalence of 21.3%. Celiac disease was diagnosed as either having Anti-TTG IgA levels greater than 90 u/ml or IgA levels between 18 to 90 u/ml with endoscopic duodenal biopsy showing histological features suggestive of CD (intraepithelial lymphocytes >30/100 enterocytes-duodenum, hyperplastic crypts positive in histopathology, partial or total villous atrophy). At the same time, IDA was declared for patients having haemoglobin < 9mg /dl and a ferritin level of <15ug/L. Pediatric patients of age range from 1 year to 14 years from both gender who were newly diagnosed with IDA and had not taken any treatment were included in this study. Patients with a history of recurrent bleeding, a gluten-free diet, and chronic liver or kidney disease were excluded from the study. In addition, all the anaemic patients with congenital malformations (malrotation of the gut, Down's syndrome, etc.) diagnosed based on dysmorphic features on physical examination were also excluded.

Anaemic children were examined in haematology OPD, and those children who fulfilled the criteria were recruited for the study. After explaining the risks and benefits, written informed consent was taken from the parents/guardians. IDA was diagnosed and was further assessed for its severity as mild (Hb, 8-9mg/dl), moderate (Hb 7-8mg/dl), and severe (Hb <7mg/dl).

Then serum sample for anti-tissue transglutaminase IgA level was sent. If this level was less than 90u/ml or between 18-90u/ml, then an endoscopic duodenal biopsy for histological evidence was sent, and a diagnosis of CD was confirmed.

Parameters studied included demographic details, duration of anaemia by history, body weight, the severity of anaemia, Hb, serum ferritin, anti-TTG IgA level, biopsy result and presence of celiac disease. Data were entered in a pre-designed Performa. Outcome variables included the presence of CD and IDA. Data was entered in SPSS version 23.0. Mean and standard deviation was calculated for the quantitative variables like age, body weight and duration of anaemia. In contrast, frequencies and percentages were determined for qualitative variables like outcome variables (frequency of celiac disease) and gender.

Effect modifier like age, sex, duration of anaemia and severity of anaemia was controlled by stratification to see the effects of these on outcomes variable. The chi-square test determined and analysed the relationship between anti-tissue transglutaminase (anti-TG) IgA level >90u/ml and the severity of anaemia. A P-value of less than 0.05 was taken as significant.

RESULTS

One Hundred thirty-two enrolled IDA patients, the mean age of the patients was 7.61±4.21 years (range 1-14 years). The mean weight of the patients was 26.37±11.93 kg in table 1. A total of 60(45.45%) patients were male, and 72 (54.55%) were females in table#3.

Table 1:

	Minimum	Maximum	Mean	SD
Age	1	14	7.61	4.21
Weight	8	20	26.37	11.93

Table 2: Relationship of the stratified variable with Celiac Disease.

Variable	Celiac Disease		p-Value
	Yes	No	
>7 years (68)	13	55	0.597
Age ≤ 7 years	10	54	
Male (60)	11	49	0.802
Gender Female(72)	12	60	
>20days (68)	10	58	0.396
Duration of the Disease ≤ 20 days (64)	13	51	
Mild(33)	3	30	0.04
Severity of Anemia Moderate (58)	8	50	
Severe (41)	12	29	0.000
Yes (18)	18	0	
Ig A levels greater than 90u/ml No (114)	5	109	

Severe anaemia was found in 41 (31.06%) patients, moderate anaemia was found in 58 (43.94%) patients, and mild anaemia was found in 33 (25%) patients. In our study, the mean value of the duration of anaemia of the patients was 20.39 ± 6.17 days with a minimum and maximum duration of 10 & 30 days, respectively. The frequency distribution of gender, the severity of anaemia, and anti-tissue transglutaminase IgA level. The CD was found in 23 (17.42%) (Table 2)

The stratified results for age, gender and duration of disease revealed no statistical significance with CD (p -value >0.05). However, the severity of anaemia and IgA levels greater than 90u/ml were associated with CD with a significant p -value of 0.04 and 0.000, respectively. The descriptive details of stratified variables and their relationship with CD are well depicted in Table 5.

DISCUSSION

CD is a chronic immune-mediated disease that manifests itself after exposure to gluten in genetically predisposed individuals. The symptoms range from asymptomatic to gastrointestinal disturbance to atypical symptoms of malabsorption like IDA. Due to this reason, the diagnosis of CD is often missed when presented with atypical symptoms. Therefore, this study aimed to find the prevalence of CD and hence the burden of disease in children of IDA.

This study found CD in 17.42% (23) of children presenting with IDA. This percentage depicts higher proportion and undiagnosed pool of CD. In a study by Shafat Khatoon, Aijaz Ahmed, Shazia Yousaf, the prevalence of celiac disease in iron deficiency anaemia is 11%.¹ In another study by Çekin AH, Çekin Y, Sezer C, the prevalence of celiac disease in iron deficiency anaemia is 7.14%.² This pool needs further timely referral. A study from India reported higher percentages of up to 37% of CD in IDA children.¹⁰ Whereas contrasting results of lower percentages of CD in a study by Çekin AH, Çekin Y, Sezer C, the prevalence of celiac disease is 7.14% more than current studies, have been reported in India. A study from Iran reported 10.4% (42) CD in 402 enrolled patients of IDA.¹³ So, the literature varies in the prevalence of CD in patients of IDA.

A recent meta-analysis of the association of celiac disease with IDA was made from 18 studies. It included 2998 patients (adults and children). The diagnosis of CD made by different tools like serology and biopsy were both considered separately. The analysis reported a cumulative percentage of 4.8% of CD in patients presented as IDA.¹¹ This is in contrast to the current

study but this involved population from the West. Asian population varies in disease burden greater than Europe. Further increased burden of IDA and less disease screening or diagnosis due to limited resources could be the possible cause of these different results in Pakistan. Larger multicenter screening studies at the national level are required to find out more precise prevalence and association of IDA with CD.

In this study, all patients having anti-TG IgA levels greater than 90u/ml were found to have CD, whereas only five out of 114 patients had the CD with IgA levels less than 90. This data proves anti-TG IgA levels are sensitive and specific in diagnosing CD. This fact has been confirmed by several other studies as well.⁴

Forty-one patients with severe anaemia and the severity were found to be significantly associated ($p=0.04$) with CD. The degree of anaemia in the patient is also related to CD since it involves destroying the small intestine's absorbing villi. This observation is consistent with another recent study conducted in Pakistan.¹

There are a few limitations to our study. It was a single-centre study with a limited sample size and was biased to a specific area of the country. A large multicenter study involving different regions of Pakistan is recommended considering the massive burden of IDA in the country.

CONCLUSION

The frequency of CD in patients with iron deficiency was 17.42%. The study may pave the way for the doctor community to keep a high index of suspicion for CD in children with IDA. These findings may also urge them refer the children early to specialist centres for further screening and management

REFERENCES

- 1- Khatoon S, Ahmed A, Yousaf S. Iron Deficiency Anaemia in Pakistan: Celiac Disease an Underlying Cause. *J Ayub Med Coll Abbottabad*. 2018 Jul-Sep;30(3):372-376. PMID: 30465368.
- 2- Çekin AH, Çekin Y, Sezer C. Celiac disease prevalence in patients with iron deficiency anemia. *Turk J Gastroenterol*. 2012;23(5):490-5. PMID: 23161292.
- 3- Talarico V, Giancotti L, Mazza GA, Miniero R, Bertini M. Iron Deficiency Anemia in Celiac Disease. *Nutrients*. 2021 May 17;13(5):1695. doi: 10.3390/nu13051695. PMID: 34067622; PMCID: PMC8156426.
- 4- Setty M, Hormaza L, Guandalini S. Celiac disease: risk assessment, diagnosis, and monitoring. *Mol Diagn Ther*. 2008;12(5):289-98.
- 5- Green PH, Jabri B. Coeliac disease. *Lancet*. 2003 Aug 2;362(9381):383-91.

- 6- Silano M, Agostoni C, Guandalini S. Effect of the timing of gluten introduction on the development of celiac disease. *World J Gastroenterol.* 2010 Apr 28;16(16):1939-42.
- 7- Ludvigsson JF, Leffler DA, Bai JC, Biagi F, Fasano A, Green PH, Hadjivassiliou M, Kaukinen K, Kelly CP, Leonard JN, Lundin KE. The Oslo definitions for coeliac disease and related terms. *Gut.* 2013 Jan 1;62(1):43-52.
- 8- Desalegn A, Mossie A, Gedefaw L. Nutritional iron deficiency anemia: Magnitude and its predictors among school age children, southwest Ethiopia: a community sbased cross-sectional study. *PLoS One.* 2014 Dec 1;9(12):e114059. doi: 10.1371/journal.pone.0114059.
- 9- Smukalla S, Lebwohl B, Mears JG, Leslie LA, Green PH. How often do hematologists consider celiac disease in iron-deficiency anemia? results of a national survey. *Clin Adv Hematol Oncol.* 2014 Feb;12(2):100-5.
- 10- Bansal D, Trehan A, Gupta MK, Varma N, Marwaha RK. Serodiagnosis of celiac disease in children referred for evaluation of anemia: a pediatric hematology unit's experience. *Indian J Pathol Microbiol.* 2011 Oct-Dec;54(4):756-60. doi: 10.4103/0377-4929.91488. PMID: 22234104.
- 11- Mahadev S, Laszkowska M, Sundström J, Björkholm M, Lebwohl B, Green PHR, Ludvigsson JF. Prevalence of Celiac Disease in Patients With Iron Deficiency Anemia-A Systematic Review With Meta-analysis. *Gastroenterology.* 2018 Aug;155(2):374-382.e1. doi: 10.1053/j.gastro.2018.04.016. Epub 2018 22nd April. PMID: 29689265; PMCID: PMC7057414
- 12- Narang M, Natarajan R, Shah D, Puri AS, Manchanda V, Kotru M. Celiac Disease in Children with Moderate-to-Severe Iron-deficiency Anemia. *Indian Pediatr.* 2018 Jan 15;55(1):31-34. PMID: 29396932.
- 13- Baghbanian M, Farahat A, Vahedian HA, Sheyda E, Zare-Khormizi MR. the prevalence of celiac disease in patients with iron-deficiency anemia in center and south area of iran. *Arq Gastroenterol.* 2015 Dec;52(4):278-82. doi: 10.1590/S0004-28032015000400006. PMID: 26840468.