Epidemiology of Celiac Disease in The Children Presenting at The Tertiary Care Hospital of Pakistan

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ABSTRACT

***Objective*:** To determine the epidemiology of coeliac disease in the children presenting at the tertiary care hospital.
***Study Design*:** Cross-sectional study.
***Place and Duration of Study*:** Department of Paediatrics, Pak Emirates Military Hospital, Rawalpindi Pakistan, from Apr 2015 to Jul 2016.
***Methodology*:** Ninety-five consecutive children presenting with the suspicion of celiac disease were included in this study after taking written informed consent. A pre-designed proforma was used to record the patient's demographic details and the presenting complaints, laboratory, endoscopic and histological findings.
***Results*:** The mean age of the patients was 6.48 ± 3.20 years and the majority 53 (55.8%) of the children, were aged between 5 to 10 years. Failure to thrive was the most frequent presenting complaint and was recorded in 53 (55.8%) children, followed by pallor (54.7%), chronic diarrhoea (34.7%), short stature (29.5%), pain abdomen (28.4%) and recurrent vomiting (6.3%). The patients' haemoglobin ranged from 5.3 g/dl to 12.8 g/dl with a mean of 8.81±1.24 g/dl. The serum Anti-tTG level ranged from 8.0 U/ml to 759.0 U/ml with a mean of 298.75 ± 225.51 U/ml. Upon endoscopy, atrophic mucosa was revealed in 60 (63.2%) children, while 24 (25.3%) children had normal mucosa. Partial villous atrophy was the most frequent histological diagnosis (37.9%). Normal duodenal mucosa was reported in 4 (4.2%) children, while 21 (22.1%) children had mild non-specific duodenitis. Frequency of pallor (p=0.025), anaemia (p=0.017) and complete villous atrophy on histology (p=0.004) were significantly higher in patients with higher anti-tTG levels.
***Conclusion*:** Celiac disease has a diverse presentation for age, gender and clinical and biochemical markers.

Keywords: Anti-tTG, Anemia, Celiac disease, Failure to thrive.

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NTRODUCTION

Coeliac disease is an autoimmune disorder characterized by chronic enteropathy, triggered by the ingestion of food containing gluten.[1] There is genetic predisposition evident from a study, which showed that 75% of both the twins suffered celiac disease.[2] It is frequently associated with autoimmune disorders like autoimmune thyroid disease, insulin-dependent diabetes mellitus, Sjögren's syndrome and Addison's disease.[3,4] The presentation of celiac disease can be classical or atypical. The child presents with gastrointestinal symptoms in its classical form, such as chronic diarrhoea, recurrent abdominal pain, abdominal distension, constipation, failure to thrive, and weight loss. While in atypical form, gastrointestinal symptoms may be less prominent or absent and the child may present with anaemia, coagulopathy and osteopenia.[3-5] The current gold standard investigation for celiac disease is the endoscopic biopsy of small bowel.[6,7] Serological tests are preferred for screening and biopsy, while invasive treatment is performed to confirm the diagnosis when in doubt.[6,7,8] However, serological testing is expensive and cannot be performed routinely.[9] Therefore, a strong index of suspicion is required to identify a suspect who is then investigated further to reach the final diagnosis. It, in turn, requires knowledge of common presenting features of celiac disease.

Celiac disease is one of the most common chronic gastrointestinal disorders. The disease occurs in about 1% of the population. However, around 90% of these individuals remain undiagnosed.[10] The purpose of the current study was to do an epidemiological analysis of children presenting with the suspicion of celiac disease at a tertiary care hospital so that the common age group, gender and clinical presentation are known, which would enable the identification of high-risk patients in future practice followed by a proper diagnostic workup. It would, in turn, enable timely diagnosis and anti-

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cipated management, decreasing the morbidity and mortality associated with celiac disease.

METHODOLOGY

This Cross-sectional study was conducted at Department of Paediatrics, Pak Emirates Military Hospital, Rawalpindi, from April 2015 to July 2016.

Inclusion Criteria: Children of either gender, aged between 2 months to 14 years presented with persistent diarrhoea, abdominal pain, vomiting, abdominal distension, constipation, failure to thrive (FTT), idiopathic short stature, unexplained anaemia or iron-deficient anaemia unresponsive to treatment and lassitude/ weakness were included in this study.

Exclusion Criteria: Children with inflammatory bowel disease, abdominal tuberculosis, cystic fibrosis, and other established causes of FTT and short stature were excluded from the study.

Ninety-five (95) consecutive children were recruited in the study after taking written informed consent from parents or legal guardian of the patient. Complete blood examination was done, along with serum anti-tTG levels. These patients underwent endoscopic biopsy of the duodenal mucosa. At least four biopsy specimens were taken from the first and second part of the duodenum and one sample was taken from the duodenal bulb. The histopathological reports were evaluated on modified Marsh classification for celiac disease. A pre-designed proforma was used to record the patient's demographic details and the presenting complaints, laboratory, endoscopic and histological findings. A single consultant paediatrician finally assessed all the patients and all the labs and histological reporting were acquired from the same laboratory to eliminate bias.

Statistical Package for Social Sciences (SPSS) version 23.0 and MS Excel 2016 software were used for the data analysis. Mean ± SD were calculated for continuous variables. Frequency and percentage were calculated for categorical variables. The chi-square test was used to find out the association. The *p*-value of ≤0.05 was considered significant.

RESULTS

A total of 95 children were included in the study. The mean age of the patients was 6.48 ± 3.20 years ranging from 7 months to 14 years. The majority 53 (55.8%), of the children were aged between 5-10 years, followed by 34 (35.8%) children aged under five years and 8 (8.4%) children aged between 10-14 years. There were 47 (49.5%) male and 48 (50.5%) female children. Failure to thrive was the most frequent presenting complaint recorded in 53 (55.8%) children. Other complaints that the patients presented with were shown in Table-I.

Table-I: Presenting Complaints of the patients

Presenting Complaints	n (%)
Failure to Thrive	53 (55.8%)
Pallor	52 (54.7%)
Chronic Diarrhea	33 (34.7%)
Short Stature	28 (29.5%)
Pain Abdomen	27 (28.4%)
Recurrent Vomiting	6 (6.3%)
Constipation	3 (3.2%)
Abdominal Distention	2 (2.1%)
Hematemesis	1 (1.1%)
Retrosternal Pain	1 (1.1%)

Haemoglobin of the patients ranged from 5.3 g/dl to 12.8 g/dl with the mean value of 8.81 ± 1.24 g/dl. Using a cut-off value of 8.0 g/dl, 31 (32.6%) children were anaemic. The serum Anti-tTG level ranged from 8.0 U/ml to 759.0 U/ml with the mean of 298.75 ± 225.51 U/ml (Table-II).

Table-II: Laboratory Findings of the patients.

Laboratory Findings	n (%) (n=95)
Hemoglobin(g/dl) Mean ± SD	8.81 ± 1.24
Anemia (<8g/dl)	31 (32.6%)
Anti-tTG (U/ml) Mean ± SD	298.75 ± 225.51

Upon endoscopy, atrophic mucosa was revealed in 60 (63.2%) paients while 24 (25.3%) had normal mucosa. Gastritis/duodenitis was found in 10 (10.4%) children, while one patient had oesophagal candidiasis (Table-III).

Table-III: Endoscopic findings of the patients.

Endoscopic Findings	n (%)
Normal Mucosa	24 (25.3%)
Atrophic Mucosa	60 (63.2%)
Gastritis/ Duodenitis	10 (10.4%)
Esophageal Candidiasis	1 (1.1%)

The histopathological findings on duodenal biopsy were shown in the Table-IV.

Table-IV: Histological findings on duodenal biopsy.

Histological Findings	n (%)
Unremarkable Duodenal Mucosa	4 (4.2%)
Focal villous atrophy Marsh III a	7 (7.4%)
Partial villous atrophy Marsh III b	36 (37.9%)
Complete villous atrophy Marsh III c	25 (26.3%)
Mild Non-specific Duodenitis	21 (22.1%)
Giardiasis	2 (2.1%)

The frequency of pallor (p=0.025), anaemia (p= 0.017) and complete villous atrophy on histology (p= 0.004) were significantly higher in patients with higher anti-tTG levels, as shown in the Table-V.

Table-V: Association of pallor, anaemia and complete villous atrophy on histology with anti-tTG levels.

Para-meters	Anti-tTG levels				*p*-value
	<200 U/ml n=37	200-400 U/ml n=24	400-600 U/ml n=27	>600 U/ml n=7	
Pallor	14 (37.8%)	15 (62.5%)	20 (74.1%)	3 (42.9%)	0.025*
Anemia	7 (18.9%)	6 (25.0%)	14 (51.9%)	4 (57.1%)	0.017
Complete Villous Atrophy	5 (13.5%)	4 (16.7%)	11 (40.7%)	5 (71.4%)	0.004

DISCUSSION

In the present study, the mean age of the patients was 6.48 ± 3.20 years. Babar *et al*,[11] reported similar mean age of 6.35 ± 2.83 years in paediatric patients presenting at Sheikh Zayed Hospital, Rahim Yar Khan. Jamro *et al*,[12] Rabia *et al*,[13] and Ikram *et al*,[14] reported relatively higher mean age of 7.11 ± 2.8 years, 8 ± 3 years and 8.9 ± 3.7 years, respectively. A much higher mean age of 11 ± 3.6 years has been reported previously by Makharia *et al*,[15] in Indian.

The majority 53 (55.8%) of the children were aged between 5-10 years. A similar higher frequency of this age group among such children has been reported previously by Jamro *et al*, 12 (50.0%). There were 47 (49.5%) male and 48 (50.5%) female children in the study group. Jamro *et al*,[12] reported much higher female predominance with a male to female ratio of 1:2.5. A female predominance has also been reported in another local study by Babar *et al*,[11] (1:1.5). Hussain *et al*,[16] (1.3:1), Rabbani *et al*,[17] (1.1:1) and Makharia *et al*,[15] (1.1:1), on the other hand, reported a male predominance among such children.

Failure to thrive was the most frequent presenting complaint and was recorded in 53 (55.8%) children, followed by pallor (54.7%), chronic diarrhoea (34.7%), short stature (29.5%), pain abdomen (28.4%) and recurrent vomiting (6.3%). A similar frequency of failure to thrive (54%), chronic diarrhoea (52%) and vomiting (8.4%) have been reported previously by Cheema *et al*,[18] among children presenting at the Children's Hospital & the Institute of Child Health, Lahore, Pakistan. They, however, reported a much higher frequency of pallor (82%) and abdominal distension (83%). Hussain *et al*,[16] also reported a similar frequency of failure to thrive (53.8%), but they too reported a much higher frequency of pallor (85.6%), chronic diarrhoea (73.1%) and abdominal distension (73.1%). Alvi *et al*,[19] reported chronic diarrhoea, failure to thrive and anaemia as the commonest clinical features in 82.6%, 89% and 95.6% patients. Aziz *et al*,[20] found chronic diarrhoea, failure to thrive, weight loss and short stature in 69%, 61%, 77% and 32% of patients, respectively. Rabia *et al*,[13] reported common presenting features to be chronic diarrhoea (32%), abdominal pain (17.5%), short stature (22.5%) and failure to thrive (2.5%).

The mean serum Anti-tTG level was 298.75 ± 225.51 U/ml in our study. Upon endoscopy, atrophic mucosa was revealed in 60 (63.2%) children, while 24 (25.3%) children had normal mucosa. Partial villous atrophy (Marsh IIIb) was the most frequent histological diagnosis (37.9%), followed by complete (Marsh IIIc, 26.3%) and focal villous atrophy (Marsh IIIa, 7.4%). Normal duodenal mucosa was reported in 4 (4.2%) children, while 21 (22.1%) children had mild non-specific duodenitis. Dutta *et al*,[21] reported Marsh IIIc being the most frequent finding (38.39%), followed by Marsh IIIb (33.34%) and normal mucosa (22.22%) in Indian patients of celiac disease. Emami *et al*,[22] reported Marsh IIIa and Marsh IIIb being the most frequent histological findings in 38% Irani such patients, followed by Marsh IIIc (24%). Jamro *et al*,[12] reported Marsh II (64.3%) and Marsh III (35.7%) being the most common histological diagnosis in such patients at Shaheed Mohtrama Benazir Bhutto Hospital, Sukkar, Pakistan, while Babar *et al*,[11] reported M3 type in 13 cases (32.5%) and M2 type in 18 cases (45%) at Sheikh Zayed Hospital, Rahim Yar Khan.

In our study, the patients with coeliac disease presented with failure to thrive chronic diarrhoea, unexplained anaemia, short stature and abdominal distension. Keeping in mind the changing trends in the clinical presentation of coeliac disease, proper workup should be done at an early stage in suspected patients to avoid chronic illness and complications associated with celiac disease.

CONCLUSION

Celiac disease has a diverse presentation for age, gender and clinical and biochemical markers.

Conflict of Interest: None.

Authors' Contribution

MAL: Direct contribution, ZS: AA, TM: SH: Intellectual contribution.

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