Celiac Disease Investigation with Marsh Classification in Paediatric Population

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ABSTRACT

Objective: To determine the celiac disease using Marsh classification in the paediatric population at the Pak Emirates Military Hospital.

Study Design: Cross-sectional study.

Place and Duration of Study: Department of Paediatrics, Pak Emirates Military Hospital Rawalpindi Pakistan, from Aug 2020 to Mar 2021.

Methodology: Patients of either gender aged 1 to 14 years with three or more clinical features of celiac disease such as chronic diarrhoea, any degree of malnutrition, short stature, abdominal distension, anaemia, and clubbing at the time of admission, were included in this study.

Results: There were 97 patients in this study. Among them, 61 (62.9%) were males, and 36 (37.1%) were females. There were 56 (57.7%) patients who were histology positive and 41 (42.3%) patients who were histology negative. There were 37 (38.1%) patients in Marsh III a, 15 (15.5%) were in Marsh III b, and 4 (4.1%) patients were in the Marsh III c category. Gender distribution showed that 33 (58.9%) males were positive compared to 23 (41.1%) females. Even though the frequency was higher among males, the difference was not statistically significant (*p*-value=0.23).

Conclusion: Celiac disease is a possible reason for anaemia among patients with iron deficiency anaemia of unknown origin. Therefore, the histopathological diagnosis should be completed when celiac disease is suspected.

Keywords: Celiac disease, Histopathology, Marsh classification.

INTRODUCTION

Celiac disease is an autoimmune, multi-system illness caused by interaction among environmental and genetic issues. The significant features of the disease are malabsorption and villous atrophy that occur in the intestinal system when a person ingests food which contains gluten.[1] To obtain a confirmed identification of celiac disease, a biopsy of the small intestine is often documented to be the preferred method of diagnosis. Celiac disease has been noted to have a varied presentation.[2-3] Subsequently, the celiac disease diagnosis could be missed or delayed.[4] This is an issue particularly for the developing world, as the resources are already scarce. Literature shows that conducting an endoscopic small bowel biopsy has rendered celiac disease detection simpler.[5] Hence, it has been the "gold standard". The confirmed diagnosis of celiac disease is based on the small intestine's biopsy showing an increased proportion of crypt hyperplasia.[6] The gravity of these injuries ranges from the III Marsh stage to above and has essentially been deliberated to be suggestive of celiac disease.[7] However, a biopsy may not always be feasible in developing countries. Therefore, physicians have relied on serological tests to diagnose celiac disease in such a scenario.

Celiac disease has been noted among Asians in Pakistan, India and Iran.[8-9] Literature shows that celiac disease prevalence has been altered over previous decades, and this is attributed primarily to highly sensitive serologic tests. Nevertheless, the problem is that there is insufficient research conducted in this area; the investigative value of the clinical utility and the endoscopic markers is rather unclear. Presently, about 3 out of 4 celiac disease patients stay undiagnosed. This is primarily because the physicians do not identify the atypical presentations, there is a scarcity of extensive screening among the high-risk people, and there may be wrong labelling as irritable bowel syndrome. There is a need for a higher diagnosis rate to prevent celiac disease complications, for example, anaemia or cancer.[8-10]

Several studies have found the varying frequency of diagnosed cases of celiac disease on histopathology markers. However, there have been limited studies conducted over the last five years to study histopatho-

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logy results, as there is a dearth of local data in Pakistani context.

METHODOLOGY

This cross-sectional study was conducted at the Department of Pediatrics, Pak Emirates Military Hospital Rawalpindi Pakistan, from August 2020 to March 2021, after approval from the Institute Ethical Committee (ERC approval certificate number: A/28/ EC/ 31/9/20). The sample size was calculated using WHO calculator by taking the prevalence of celiac disease 71.6%, using histopathology.[11] With a margin of error of 9% and the noted confidence level of 95% was selected. The sample thus estimated was 97. Sampling was done using a non-probability convenient sampling technique.

Inclusion Criteria: Patients of either gender aged between 1 to 14 years who presented at Pak Emirates Military Hospital Rawalpindi with three or more clinical features of celiac disease such as chronic diarrhoea, any degree of malnutrition, short stature, abdominal distension, anaemia, and clubbing at time of admission, were included in the study.

Exclusion Criteria: Patients who had asthma, type 1 diabetes, abdominal tuberculosis, congenital heart anomalies, colorectal neoplasia, inflammatory bowel disease, cystic fibrosis, children already on a wheat-free diet, history of premature birth and patients who had short height were excluded from the study.

Marsh-Oberhuber grading and histopathology showing (Marsh III) were taken as diagnostic of celiac disease. Informed consent was noted from all parents after we had fully disclosed the risk profile and benefits of the study. Data were collected, a unique identifier was assigned to each patient, and strict confidentiality was maintained throughout the study. Strict ICH good clinical practice guidelines were followed. This study was HIPAA compliant. A brief history of demographic information was taken.

Statistical Package for Social Sciences (SPSS) version 27.0 was used for the data analysis. Mean and standard deviation were estimated for continuous covariates. Frequency and percentages were analyzed for gender, and celiac disease was confirmed on histopathology (Positive/Negative). The chi-square test observed the disparity among the strata of patients. The p-value of ≤0.05 was considered signi-ficant.
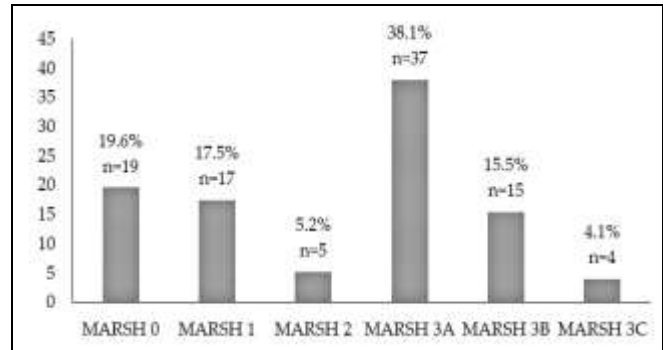
RESULTS

There were 97 patients in this study. Among them, 61 (62.9%) were males, and 36 (37.1%) were females. Patients were divided into two categories: 1 to 7 years of age and 8 to 14 years of age. There were 72 (74.2%) patients who fit the younger age strata of 1 to 7 years and 25 (25.8%) patients between 8 to 14 years of age. In addition, there were 56 (57.7%) patients who were histology positive and 41 (42.3%) patients who were histology negative (Table-I).

Table-I: Characteristics of the Study Sample (n=97)

Characteristics	n (%)
Age Groups	
1-7 years	72 (74.2)
8 – 14 years	25 (25.8)
Gender	
Male	61 (62.9)
Female	36 (37.1)
Histopathology	
Positive	56 (57.7)
Negative	41 (42.3)

There were 19 (19.6%) patients who belonged to Marsh-0, 17 (17.5%) patients were in Marsh-I, 5 (5.2%) patients were in the Marsh-II category, 37 (38.1%) patients were in Marsh-IIIa, 15 (15.5%) were in Marsh-IIIb, and 4 (4.1%) patients were in Marsh-IIIc category (Figure).

Figure: The Distribution of Marsh Category (n=97)

There was no significant difference between the age groups and their histopathology results (p-value = 0.51). The frequency of positive cases on histopathology showed that 42 (58.3%) cases were between 1 to 7 years of age, whereas 14 (38.8%) positive patients were 8 to 14 years of age. Looking at the gender distribution, we noted that 33 (58.9%) males were positive compared to 23 (41.1%) females. Even though the frequency was higher among males, the difference was not statistically significant (p-value = 0.23) (Table-II).

DISCUSSION

There were 57.73% positive cases of celiac disease based on the histopathology results and 41 negative

cases. The frequency of celiac disease was higher among males and younger patients (1 to 7 years of age). This brings to mind whether most female patients are being brought to the hospital or not. Thus the male preponderance observed in this study could result from selection bias. This is something which could be explored further in future studies. Celiac disease (celiac disease) is an enteropathy that is immune-mediated and caused by eating grains containing gluten, such as rye, barley and wheat, in genetically susceptible people.

Table-II: Distribution of Age and Gender According to Histo-Pathology Results (n=97)

Characteristics	Histopathology Positive n (%)	Histopathology Negative n (%)	*p*-value
Age Group			
1 – 7 years	42 (75.0)	30 (73.2)	0.51
8 – 14 years	14 (25.0)	11 (26.8)	
Gender			
Male	33 (58.9)	28 (68.3)	0.23
Females	23 (41.1)	13 (31.7)	
Total	56 (100)	41 (100)	

Iron deficiency anaemia might be the initial presentation of celiac disease.[12,13] Mansoor *et al.* conducted a study in which 20 of 47 patients (42%) had biopsy results consistent with celiac disease. The proportion found in our study was slightly higher than Mansoor *et al.* study.[14] Ackerman *et al.* found that patients with celiac disease were younger, had lower mean haemoglobin levels, and had much more incidents of lengthier periods of anaemia and diarrhoea as compared to those who did not have celiac disease.[15] Another study by Grisolano *et al.*[16] found only 8.7% with celiac disease. This study found no significant disparity when the scientists studied reports of incidents of diarrhoea, weight loss, abdominal pain, vomiting, nausea, aspirin or menopausal status or NSAID use, along with the status of celiac disease.[16] This brings to attention the need to know how diverse the celiac disease presentation could be. The physicians must remember to check for celiac disease as a differential diagnosis. This is further corroborated by the study conducted by Cekin *et al.*[17] found that it was noted that histopathologic findings were associated with celiac disease among 6 out of 84 subjects (7.14%). However, that study showed that after 180 days of a gluten-free diet, the patient's average levels of haemoglobin improved from 10.3±0.64 to 12.97±1.48 g/dl (*p* value=0.002).[17] The treatment for celiac disease can yield beneficial results if the disease is caught in

time.[18] Ucerdag *et al.* showed that 6 subjects (7.8%) and 1 control (0.8%) had histopathologic outcomes of celiac disease (*p* value=0.02). 19 Rabbani *et al.*[20] reported an equal gender (Male: Female) distribution (52% vs 48%) in children who had presented at Children Hospital & Institute of Child Health, Multan, Pakistan. The distribution in our study showed that 61 (62.9%) were males and 36 (37.1%) were females. Similarly, Dutta *et al.*[21] (59.8%) and Emami *et al.*[22] (62%) also described male predominance among Indian and Irani patients. In contrast, Jamro *et al.*[23] conveyed a female predominance (71.4%) among children in Pakistani. Moreover, Lodhi *et al.*[13] noted a high prevalence (71.58%) of positive cases of celiac disease among patients presenting with suspected cases of celiac disease. There was a paper by Hashmi *et al.*[24] found a comparable prevalence was noted to be at 63.33% among youngsters who had presented at the Benazir Bhutto Hospital, Rawalpindi.

Our study showed that 37 (38.1%) patients were in Marsh IIIa, 15 (15.5%) were in Marsh IIIc, and 4 (4.1%) patients were in the Marsh IIIc category. The new knowledge thus created by our study demonstrates that many patients in our setting are in the Marsh IIIa classification. Therefore, underlining the significance of histopathological diagnosis when celiac disease is suspected. Lodhi *et al.*[13] had found that Marsh IIIb (atrophy of the partial villous) had been the utmost common histological identification (37.9%), which Marsh IIIc then tails (26.3%) and Marsh IIIa (atrophy of the focal villous=7.4%). Dutta *et al.*[21] described that MARSH IIIc was the most recurrent finding (38.39%), which was followed by Marsh IIIb (33.34%) and then usual mucosa (22.22%) among the celiac disease patients in India. Jamro *et al.*[23] researched that Marsh II (64.3%) and MARSH III (35.7%) were the most frequently observed histological diagnosis among subjects presenting at the Shaheed Mohtrama Benazir Bhutto Hospital. Emami *et al.*[22] had narrated that Marsh IIIb and Marsh IIIa were the common histological discoveries noted among 38% of subjects in the Irani population sample tailed by Marsh IIIc (24%).

CONCLUSION

The developing world faces tremendous health care challenges. This makes it crucial for clinicians to deliberate celiac disease as a probable reason for anaemia among patients with iron deficiency anaemia of incomprehensible origin. In addition, histopathological diagnosis needs to be completed when celiac disease is suspected. Resource-scarce settings are crucial and could be an imperative tool in treating such patients.

Conflict of Interest: None.

Author's Contribution

MG: Data collection, data analysis, results and discussion of literature, FI: Data analysis, data interpretation, discussion of liteature and reviwe, SZK: Review of article, results and correction, JB: Data analysis and results review, ST: Discussion and review of article, MWB: Review of article, discussion and correction.

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