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A COMPARATIVE STUDY ON THE CELIAC DISEASE AMONG CHILDREN AT SHEIKH ZAYED HOSPITAL RAHIM YAR KHAN

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Abstract:

Objective: *To find out the clinical features as well as associated investigation of laboratory testing of the patients suffering from celiac disease and the comparison of the Classical Celiac Disease with the Non-Diarrheal Celiac Disease.*

Methodology*: This retrospective research work was carried out at* Sheikh Zayed Hospital Rahim Yar Khan *from January 2016 to December 2019. The patients which were included in this study was from 1 to 15 years of age from both genders with the confirmed diagnosis of the Celiac Disease according to revised Espghan standard. We considered the samples of biopsy with Grade-2 or higher on MMC (Modified Marsh Classification) as consistent with the celiac disease. The categorization of the patients of celiac disease was carried out into classical celiac disease with chronic diarrhea and non-diarrheal celiac disease with atypical celiac and we recorded the clinical aspects and associated investigation of the laboratory testing of the patients.*

Results: *In this study 66 patients who fulfilled the criteria of this study were the participants of this research, we labeled 59.09% (n: 39) patients as classical celiac disease and 40.91% (n: 27) patients as non-diarrheal celiac disease. Marsh grading, 3a and higher were marked more in classical celiac disease patients in comparison with the patients having non-diarrheal celiac disease. Average titer for the TTG (Tissue Transglutaminase Antibodies) was much high in the patients of classical celiac disease group as compared to the patients of non-diarrheal celiac disease group. Abdominal distension was the most common presentation in the patient of classical celiac disease whereas in the patients of non-diarrheal celiac disease, most common feature was recurring abdominal pain (62.90%). Rate of occurrence of failure to thrive is much higher in the patients of classical celiac disease as 82.05% but the patients present were short stature were more frequent in the group of non-diarrheal celiac disease (33.30%). There was presence of refractory anemia in 66.60% patients with non-diarrheal celiac disease and 41.10% patients in the group of classical celiac disease. In the 74.30% classical celiac disease patients, there was deficiency of Vitamin-D while in 85.0% patients of non-diarrheal celiac disease group, there was deficiency of Vitamin-D (P= 0.030).*

Conclusion: *Non-diarrheal celiac disease is common in our community. Recurring pain in abdomen cavity, thrive failure or patients having short stature and anemia are noticeable features in the patients of non-diarrheal celiac disease group while abdominal distension, recurring pain in abdomen cavity and failure to thrive were important features in the patients of classical celiac disease group. Histopathology of high grade and elevated antibodies titer are classical celiac disease's hallmark. There was not much difference in the deficiency of Vitamin-D in both groups.*

KEYWORDS: *Classical Celiac Disease, Non-Diarrheal Celiac Disease, Anemia, Histopathology, Abdomen, Thrive, Recurring, Antibodies.*

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INTRODUCTION:

Celiac Disease is enduring intolerance to the gluten because of chronic systemic auto-immune procedure in the genetically susceptible persons causing injury to the mucosa of the small intestine [1]. The rate of incidence of the celiac disease is approximately 1.0% in the whole world with a range of male to female ratio from 1:2 to 1:3 [2]. All the patients suffering from celiac disease normally present with the chronic diarrhea, distension in abdomen cavity, pain in abdomen, anorexia and vomiting [3]. There is division of celiac disease according to clinical symptoms and initial presentations into classical or diarrheal celiac disease and non-diarrheal celiac disease. Classical celiac disease or classical celiac disease in addition with chronic diarrhea is present with chief complaints along with some associated symptoms. In the non-presence of typical diarrheal appearance, majority of patients suffering from celiac disease are ignored and non-diarrheal celiac disease remains an unidentified entity in our areas [4].

There is much variation in the presentation of the non-diarrheal celiac disease short stature, failure to thrive, rickets, nausea, refractory anemia, vomiting and recurring oral ulcers [5-9]. Identification of these particular features in the initial stages of the disease and examining promptly with upper gastrointestinal endoscopy, serology and biopsy will help timely diagnosis and in time application of diet free from gluten. This leads to the improvement in the Quality of Life of these children and reduces the danger of these complication as well as malignancies in future [10]. In comparison with the presentation, examinations conducted in laboratory and co-morbid conditions of both classical celiac disease and non-diarrheal celiac disease will facilitate us to comprehend the various spectrum of celiac disease. The rationale of this research work was to determine the clinical and laboratory parameter detected in our region.

MATERIAL AND METHODS:

This research work carried out at Sheikh Zayed Hospital Rahim Yar Khan from January 2016 to December 2019. In this research work, children suffering from celiac disease of both genders from 1 to 15 years of age got recruitment. All these patients were fulfilling the criteria prescribed by Espghan [11]. All these children were on the gluten diet with increased ATT (Anti-Tissue Transglutaminase) titer (>18.0 IU/L) went through upper gastro-intestinal endoscopy and biopsies of duodenal. The utilization of the MMC (Modified Marsh Classification) was carried out for the grading of the histopathology of specimens of biopsy. We considered the specimens of biopsy with Grade-2 or higher as consistent with the celiac disease diagnosis. Chronic Diarrhea was elaborated as the passage of semisolid or watery stools or high stool liquidity inconsistency as stated by the child for higher than fourteen days. All the patients were not present with the chronic diarrhea were labeled as patients of non-diarrheal celiac disease. Therefore, the classification of the patients carried out into classical celiac disease and non-diarrheal celiac disease groups. We documented the clinical features and associated examinations of laboratory.

The patients of both groups started on diet free from gluten and supplements of micronutrient and we documented the improvement of symptoms in these patients after 3 months of using this diet free from gluten. Various indicators of the improvement include stool with less liquid, weight improvement, and increase in the level of hemoglobin of ≥2.0 g/dl in the patients of both groups. We also measured the short stature and failure to thrive with standard measures. All the patients who were giving no response to three months of diet modification were labeled as suffering from refractory anemia. We also identified the presence of rickets in the patients. We noted the findings of examinations about level of hemoglobin, level of Vitamin-D, Transaminases and serum albumin. We also reviewed the charts of the patients to identify the presence of co-morbid conditions as thyroiditis, Diabetes Mellitus, Down's syndrome and epilepsy in the both groups of the celiac disease patients. The analysis of all the continuous variables was carried out with the utilization of the T-test. Chi square test was in use for the analysis of all proportions. SPSS V.20 was in use for the statistical analysis of all collected information.

RESULTS:

In this study 66 patients who fulfilled the criteria of this study were the participants of this research,, out of these patients 59.09% (n: 39) patients were present with the classical presentation of celiac disease present with chronic diarrhea and labeled as classical celiac disease and 40.91% (n: 27) patients were present with the atypical presentation without availability of chronic diarrhea and labeled as Non-Diarrheal Celiac Disease. The ratio of females to male was 4:1. The range of the age of the patients in this research work was from sixteen months to one hundred and seventy-five months. The patients of non-diarrheal celiac disease group were present with the symptoms later in their lives in comparison with the patients of classical celiac disease group. There was extended duration of the symptoms in the patient's non-diarrheal celiac disease with average age at the time diagnosis as 7.32±1.67 years as compared with the group of classical celiac disease where average age at the time of diagnosis was 5.21±1.34 years. Table-1 displays the presentation of characteristics of demography of the patients of both classical celiac disease and non-diarrheal celiac disease groups.

Table-I: Demographic Feature of Celiac Patients

	Classical (n=39) 59.09%	Atypical (n=27) 40.91%	Total (n=66)
Mean age at onset of symptoms (years)	3.53±1.26	4.24±1.74	3.88±1.38
Mean age at diagnosis (years)	5.21±1.34	7.32±1.67	6.25±1.56
Male	22(56.41%)	17(62.96 %)	39 (59.09%)
Female	17(43.58%)	10 (37.03%)	27(40.91%)
Male: Female Ratio (M: F)	1.29	1.7	1.44
Family History	3 (7.69%)	1 (3.70%)	4 (6.06%)
Consanguinity	14 (35.89%)	13(48.14%)	27 (40.90%)
Mean weight (Kg)	15.23±1.89	18.15±1.67	15.93±1.78
Mean Height (cm)	102.12±1.37	112.40±1.56	105.02±1.43

Marsh grading 3a and above were highly marked in the patients of classical celiac disease as compared to the patients of non-diarrheal celiac disease as presented in Figure-1.

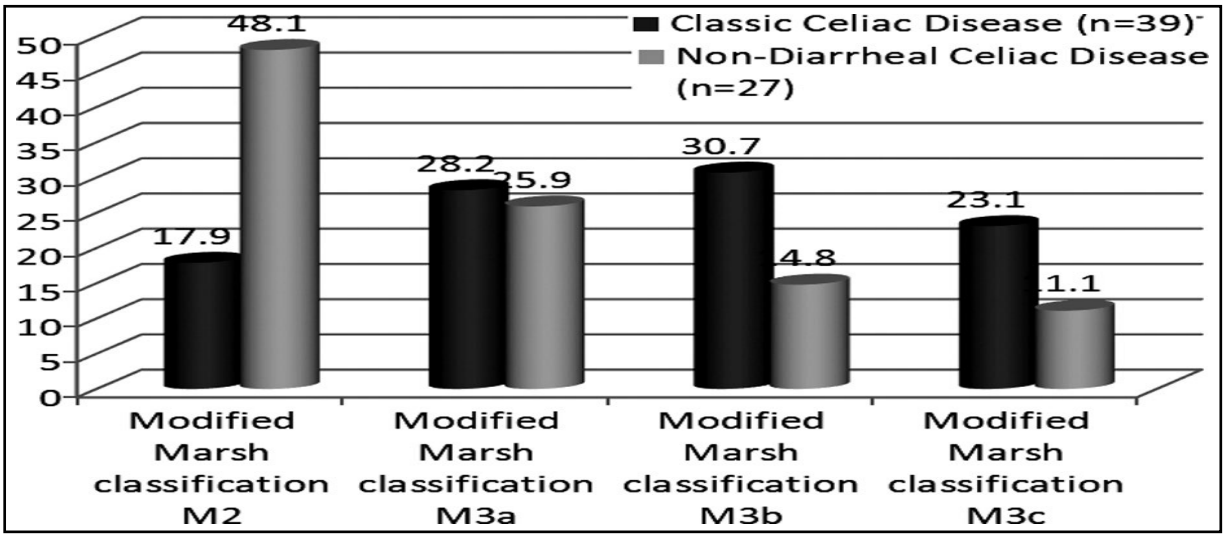

Fig: 1

In classical celiac disease, most frequent clinical presentations were distension of abdomen cavity in 61.50% (n: 24) patients and recurring pain in abdomen in 53.80% (n: 21) patients. In the patients of non-diarrheal celiac disease group, most common clinical presentation were recurring pain in abdomen in 62.90% (n: 17) and vomiting in 48.10% (n: 13) followed by distension in abdomen in 44.40% (n: 12), recurring oral ulcers in 40.70% (n: 11) and constipation in 22.20% (n: 6) patients. The rate of occurrence of failure to thrive is much high in the patients of classical celiac disease groups but this occurrence was much common in the patients of non-diarrheal celiac disease group having short stature. Figure-2 displays the various clinical presentations of the patients of both groups.

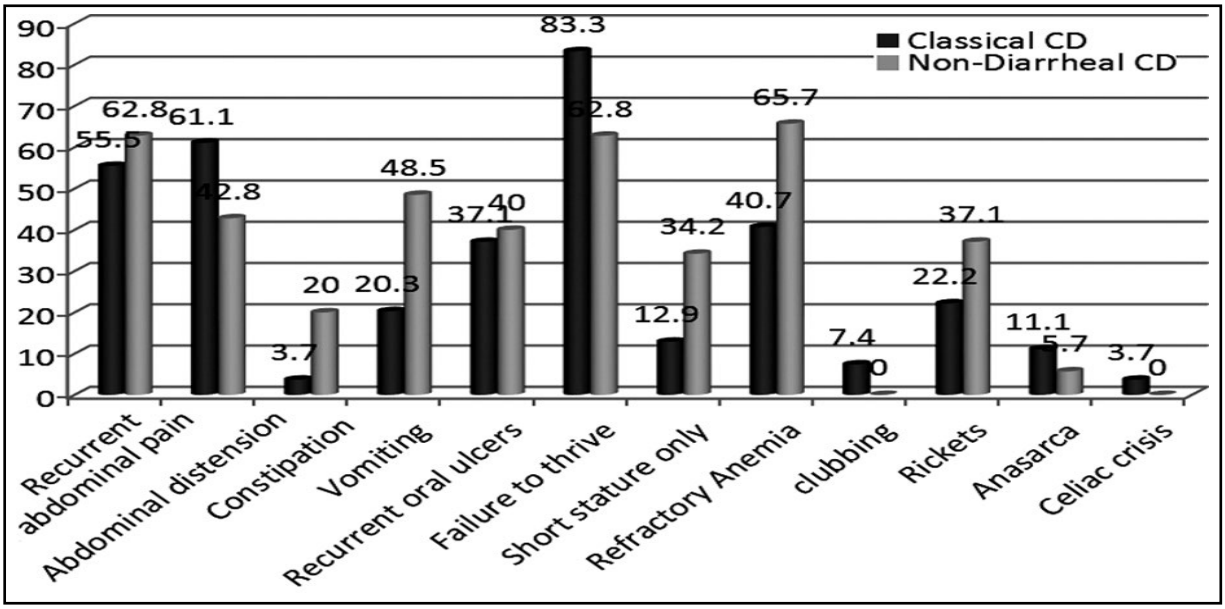

Fig: 2

Average titer for the TTG (Tissue Transglutaminase Antibodies) were much high in the patients of classical celiac disease group as compared to the patients of the non-diarrheal celiac disease group (P=0.040). There was deficiency of Vitamin-D in the patients of both groups, with 74.30% (n: 29) patients were present in the group of classical celiac disease with deficiency of Vitamin-D and 85.20% (n: 23) patients in the non-diarrheal celiac disease group were present with deficiency of Vitamin-D (P=0.03). Investigations conducted in laboratory and their comparisons between the patients of both groups are present in Table-2.

Table-II: Laboratory Investigation of Celiac Patients

	Classical (n=39)	Non-diarrheal (n=27)	p-value
Mean Serum TTG IgA (IU/L)	125±54	85±34	0.04
Mean Serum TTG IgG (IU/L)	220±97	148±76	0.01
Vitamin D Deficiency (<30ng/ml)	29 (74.3%)	23(85.2%)	0.03
Mean serum vitamin D level (ng/ml)	15.5±1.7	12.4±1.4	0.05
Iron deficiency Anemia hemoglobin <10gm/dl and serum ferritin< 10ng/ml)	18 (46.1%)	19(70.3%)	0.4
Mean hemoglobin(g/dl)	9.2±1.2	6.9±2.4	0.39
Hyper-transaminases (AST>35U/L, ALT>45U/L)	3(7.6%)	6 (22.2%)	0.14
Mean serum Aspartate aminotransferases (AST) U/L	27.9±1.23	34±1.55	0.3
Mean serum Alanine aminotransferase (ALT) U/L	36±1.02	43±1.32	0.36
Hypoalbuminemia (serum albumin<3gm/dL)	18 (46.1%)	7(25.9%)	0.15
Mean Serum Albumin	2.76±0.97	3.1 ±0.89	0.83

Table-3 shows the frequencies of various linked co-morbid conditions in the patients of both groups.

Table-III: Co-morbid Associated Conditions in Celiac Patients

	Classical (n=39)	Non-diarrheal (n=27)
Down Syndrome	2(5.1%)	1(3.7%)
Insulin depended diabetes mellitus (IDDM)	1(2.5%)	1(3.7%)
Dermatitis herpetiformis	1(2.5%)	0
Autoimmune Thyroiditis	1(2.5%)	1(3.7)
IgA deficiency	2(5.1%)	1(3.7%)
Epilepsy	3(7.6%)	2(7.4%)

DISCUSSION:

This retrospective research work has displayed that non-diarrheal celiac disease is not uncommon in our region. Around 40.0% patients in this research work did not present with chronic diarrhea at diagnosis which is similar with the research work conducted by Kuloglu [12]. It is clearly evident in various research works that patients present with the classical presentation were detected at earlier age as compared to those patients who were present with atypical presentation in the absence of diarrhea [13]. Our research work is favor of those findings. Ouda S stated an Autosomal Recessive inheritance mode with 96.0% patients having the parents present with consanguinity in his research work [14]. In this research work, 40.9% (n: 27) patients were present with parents having consanguinity. Marsh grade 3a and higher was more frequent in the patients of classical celiac disease group as compared to the patients of non-diarrheal celiac disease group. This finding is consistent with various research studies which stated GI symptoms are more frequent in the patients with small intestinal mucosa histopathology of high grade [15]. Bhattacharya M found significant association between the TTG IgA antibodies titers and high grades of the histopathology of small intestines [16,17,18].

In the patients of classical celiac disease group, distension of abdomen was the most common reported complaint [19]. In this research work, recurring pain in abdomen and vomiting were the most dominated features in the patients of non-diarrheal celiac disease group. Letizia stated amazing relation of recurring abdominal pain with celiac disease and discovered that 43.0% patients of celiac disease in their population did not face any symptom other than recurring pain in abdomen cavity [20,21,22]. In this research work, 63.0% patients had recurring pain in abdomen in the group of non-diarrheal celiac disease and 54.0% patients were present with same complaint in the group of classical celiac disease. Although this complaint is commonly reported with celiac disease but recent evidences do not allow screening of these children for celiac disease [23,24]. Aziz S in his research work stated the patients present with failure to thrive were about 61.0% [20]. Different research works recommend the screening for celiac disease in the short stature. One research work conducted in Turkey stated that the rate of occurrence of biopsy proven celiac disease was 15.70% in the children already suffering from epilepsy [25]. In this research work, 3.0% patients were present with Diabetes Mellitus. from various experiences, the incidence of celiac disease was recorded to be 1.0% to 19.0% in the patients suffering from Type-1 Diabetes Mellitus and there is recommendation of the interval screening for other disease in the availability of one disease [26,27].

CONCLUSION:

The presence of non-diarrheal celiac disease is common in our general public. All the patients with absence of chronic diarrhea are present with clinical feature of recurring pain in abdomen cavity, nausea, vomiting and refractory anemia. These features should prompt the professionals to consider and examine for celiac disease. Histopathology of high grade and elevated antibodies titer are the classical celiac disease's hallmark and it has association with the prominent GI symptoms. There was presence of deficiency of Vitamin-D in both groups. Co-morbid complications may appear in the disease course among these children requiring in time follow up in the clinics and screening for co-morbid conditions.

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