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Original Article

Inferring Association of Celiac Disease and Helicobacter Pylori Infection in Children from Rawalpindi, Pakistan: a Single-Center Experience

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ABSTRACT

Objective: To assess the relationship between Helicobacter pylori infection and gluten-sensitive enteropathy, commonly known as Celiac disease in children.
Study Design: Cross-sectional study.
Place and Duration of Study: Combined Military Hospital, Rawalpindi Pakistan, from Aug 2020 to Feb 2021.
Methodology: A total of 94 participants in the age range of 3–13 years were randomly distributed in Group–A (Coeliac Disease Patients) and n Group–B (Non-Coeliac Disease Patients). Frequency of Helicobacter pylori in children with Celiac disease versus non-celiac disease correlated. Tissue transglutaminase (tTG) IgA antibody assay (tTG levels >18 U/mL) and Helicobacter pylori prevalence were recorded.
Results: In Group A and Group B the mean age was 6.43±2.48 (3-13years) and 5.5±1.6 (6–9 years) respectively, with the male preponderance of 54(57.4%) compared to 40(42.6%) in females. Celiac disease patients with Helicobacter pylori infection were only 8(14.3%), with 4(7.1%) being males and 4(7.1%) being females. Level of tissue transglutaminase (tTG) IgA antibody was less than 10 in controls.
Conclusion: In conclusion, Helicobacter pylori infection was recorded to be lower in pediatric patients who presented with celiac disease hence proved to have an inversely proportional relationship.

Keywords: Celiac disease, Hemoglobin, Helicobacter pylori.

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INTRODUCTION

Infection by Helicobacter pylori is commonplace among children where infection may be acquired due to poor socioeconomic status.[1] It is a very important and well-studied microorganism of the upper gastrointestinal tract which can manifest as a wide variety of disorders. The most route of helicobacter infection is either oral to oral or fecal to oral route. This microorganism causes many diseases with a causal association between Helicobacter pylori, and peptic ulcer disease gastric adenocarcinoma, gastric non-Hodgkin lymphoma, and gastric mucosa-associated lymphoid tissue lymphoma (MALToma).[2,3]

Since Helicobacter pylori, is also associated with gastric anomalies, its association with Celiac disease has been previously studied by scientists in various population groups around the globe. Helicobacter pylori infection may affect inflammatory and immune responses in the small intestine and therefore lead to the development of gluten-related enteropathy in genetically susceptible individuals. Celiac disease is a gluten-related enteropathy, which can be characterized as an autoimmune inflammatory disease. In genetically predisposed people, it may be precipitated by the gluten (a component of wheat protein) intake.[4,5] Celiac disease has been linked with gastric histology and function abnormalities. Several studies quoted up to 93% association between Helicobacter pylori, and celiac disease.[6] Most of these Helicobacter pylori, positive patients had histological abnormalities but no significant association could be inferred.[7]

Patients having Marsh IIIa grade Celiac disease had increased Helicobacter pylori, positivity, with risk factors being gastritis, hemoglobin, and absence of scalloping.[8] With increasing time, information and knowledge of Celiac disease are improving. An inverse relation was predicted by between Celiac disease and Helicobacter pylori presence in both adults and children, with Helicobacter pylori, prevalence 4.4% in patients with Celiac disease (4.4%) compared to those without the Celiac disease (~9%).[9]

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It has been previously implicated for two decades ago that HP infection may impact the incident and progression of Celiac disease in the small intestine via amendment of inflammatory as well as immune responses.[10]

The rationale of the study was to evaluate the correlation of this microorganism's presence with Celiac disease and related factors in the pediatric population in this study.

METHODOLOGY

This cross-sectional study was conducted at Combined Military Hospital, Rawalpindi after approval of the ethical review board (ERB Number - A/28/EC/318/2020) over seven months from August 2020 to Feb 2021.

The minimum sample size calculated for the study was 22 where the prevalence of celiac disease was 1.4% with a 95% confidence level and 5% margin of error as reported by Singh *et al*.[11] With non-probability consecutive sampling a total of 94 participants were randomly distributed in two uniform groups having n=56 in Group–A (Celiac Disease Patients) and n=38 Group–B (Non-Celiac Disease Patients) considered as cases and controls respectively.

Inclsuion Criteria: The screening population for this study consisted of children of either sex who were referred to our institute for suspected celiac disease.

Exclusion Criteria: Nil

The written informed consent was obtained from parents/guardians, and approval was taken from children ≥7 years of age. Other factors like age, chronic diarrhea, hemoglobin, tissue transglutaminase (tTG) IgA antibody assay, and Helicobacter pylori prevalence were recorded. The tissue transglutaminase (tTG) IgA antibody presence is correlated with gluten-sensitive enteropathies e.g. celiac disease as well as dermatitis herpetiformis. Concentrations >18 U/mL usually link with celiac disease outcomes (from the duodenal biopsies), hence tTG levels >18 U/mL were considered positive.

Data was entered and analyzed by data management software IBM SPSS (version 23.0). The descriptive statistics for the categorical variable were presented as frequency and percentage while the mean and standard deviation was reported for continuous variables. The categorical groups were compared by using the Chi-square test. A significance value of ≤0.05 was considered statistically significant.

RESULTS

A total of 94 participants enrolled in the study, Group B (Controls), the mean age was 5.5±1.6 with a range of six to nine years. In Group A (Cases) the mean age was 6.43±2.48 range of three to thirteen nine years. The gender-wise distribution of Group A was 32(57.1%) male and 24(42.9%) females. Whereas in Group B was 16(42.9%) male and 22(57.1%) females.

The level was less than 10 in controls and considered a constant. In cases, values were categorized as below 100 (as the least value was 67) or above 100. Among males 3(5.3%) and females 3(5.3%) showed a count of less than 100 U/ml, while 21(37.5%) females and 29(51.7%) males showed values above 100. 17(18.4%) children in controls and 34(36%) children in cases did not have diarrhea, compared to13(23.2%) having diarrhea in cases and 9(23.6%) having in controls. Distribution of gender between two groups and the overall prevalence of Helicobacter pylori infection demonstrated in (Table–I). 8(14.3%) had Helicobacter pylori infection (*p*-value<0.001) as elucidated in (Table–II). Hemoglobin levels distribution between groups is elaborated in (Table-III).

Table–I: Association of Celiac Disease and Helicobacter Pylori Infection

		Celiac Disease		*p*-value
		No	Yes	
Helicobacter Pylori	No	0	48(85.7%)	<0.001*
	Yes	38(100%)	8(14.3%)	

**Statistically significant p-value*

Table-II: Association of Gender with Celiac Disease and Helicobacter Pylori Infection

		Gender		*p*-value
		Female	Male	
Helicobacter Pylori	No	20(51.3%)	28(50.9%)	1.00
	Yes	19(48.7%)	27(49.1%)	
Celiac Disease	No	15(38.5%)	23(41.8%)	0.83
	Yes	24(61.5%)	32(58.2%)	

Table-III: Hemoglobin Levels Distribution between Groups

Hemoglobin Levels	Group A n(%)	Group n(%)
≥ 12 g/dl	3(5.3%)	8(21.0%)
≥ 11 g/dl	4(7.1%)	23(60.5%)
≥ 10 g/dl	13(23.2%)	-
≥9 g/dl	36(64.2%)	-

DISCUSSION

This study deciphered significant association of celiac disease by elucidation that the prevalence of Helicobacter pylori infection is not a predominant etiological factor in causing the disease as only 8(14.3%) participants among cases represented

evidence of infection. In correspondence with a preceding study conducted by Luzza *et al*., 1999, this study demonstrates that the Helicobacter pylori prevalence in Celiac disease smitten children is lower than in control subjects.[12]

Recently, Amlashi *et al*., conducted a meta-analysis to find an association between Celiac disease and Helicobacter pylori infection. A weak but statistically significant negative association was found between the both, which tallies with our results.[13]

Comparing findings with pediatric cohorts from various countries, several interesting insights were gained related to the relation between the Helicobacter infection and Celiac disease. Only 1.3% of the pediatric population of the United States manifested Helicobacter pylori-positive Celiac disease as quoted by Lebwohl *et al*.[14] Polish cohort depicted 5.4% evaluated by Jozefczuk *et al*.,[15] compared to our 14% pediatric population. In Celiac disease patients of Italy, the overall rate of Helicobacter pylori prevalence in Celiac disease cases was lower than controls but compared to our cohort, the rate of Helicobacter pylori prevalence was ~4% higher. This is important to consider for Helicobacter pylori correlation to Celiac disease since the general prevalence of Helicobacter pylori is lower in developed nations compared to developing nations. In Indian Celiac disease manifesting pediatric patients, Narang *et al*., could not decipher any significant differences regarding gender but hemoglobin was found a significant predictor for Celiac disease in the pediatric population. In our study, males were significantly found to have a higher rate of Celiac disease compared to females. This brings to mind the notion of whether most female patients are being brought to the hospital or not, thus the male preponderance observed in this study could be a result of selection bias. This is something, which could be explored further, in future studies. As for hemoglobin, Celiac disease cases had lower Hemoglobin but results were statistically non-significant. They also reported higher Helicobacter pylori prevalence in patients without Celiac disease which was similar to our results as all non- Celiac disease patients were Helicobacter pylori positive. Diarrhea was prevalent in Celiac disease patients unlike our study, where no statistically significant results could be inferred.[16]

Aydogu *et al*., reported 66% Helicobacter pylori-positive Turkish female pediatric Celiac disease patients. 80% of the cohort had chronic diarrhea in Celiac disease patients from Turkey.[17] Maxim *et al*., reported 32% Helicobacter pylori-positive Romanian Celiac disease females compared to our study showing just 20%.[18]

58.5% from another cohort in Turkey in the study of Bayrak *et al*., although results were statistically non-significant. Results for Hemoglobin for the Turkish cohorts were also not significant, similar to our study. Stark contrast was observed for tTG IgA positivity in Celiac disease patients in the Turkish cohort, with 100% positivity in Celiac disease patients (statistically significant) compared to complete absence in Celiac disease negative pediatric patients. Although our results showed a similar trend they were statistically non-significant.[19]

This study significantly emphasized the need to explore the etiology of celiac disease as there could be numerous etiological, genetic and environmental factors that are required to unravel to achieve better care and treatment standards for the fragile one of the communities.

LIMITATIONS OF STUDY

An increased number of relevant clinic pathologic features influencing the condition should also be accounted for in addition to molecular and genomic analysis, to add weight to observational studies. These could help clear the association between Celiac disease and Helicobacter pylori further.

CONCLUSION

In conclusion, Helicobacter pylori infection was recorded to be lower in pediatric patients who presented with celiac disease hence proved to have an inversely proportional relationship.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

MG & FI: Study design, drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

HR & JB: Data acquisition, data analysis, approval of the final version to be published.

AA & MWB: Critical review, concept, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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