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ORIGINAL ARTICLE

Prevalence of Celiac Disease in Adult Patients with Iron Deficiency Anemia

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ABSTRACT

Background and Aim: Celiac disease is a gastrointestinal condition that is chronic and mediated by an immunological reaction to gluten present in different grains such as wheat, barley, and rye. Studies document that the incidence of celiac disease within the Pakistani population to be 29.3% and is highly prevalent among the younger age groups. Iron deficiency anemia is a major cause of anemia around the world, especially in developing countries such as Pakistan. Anemia has been acknowledged to be one of the major manifestations of celiac disease worldwide. This study will aim to assess the incidence and burden of celiac disease among the known anemic adult population of due to iron deficiency in tertiary care hospitals of Khyber Pakhtoonkhaw.

Methodology: A cross-section study was conducted in the department of Gastroenterology Bacha Khan Medical Complex, Swabi and Northwest General Hospital & Research Centre Hayatabad, Peshawar during the period of six months from May 2021 to October 2021. Participants were recruited after assessment of criteria. All recruited participants were anemic and underwent extensive serological assessment for screening of celiac disease. For confirmation of celiac disease duodenal biopsies were performed at five different levels.

Results: 5.4% of the participants (n= 108) were found to have positive results for screening of IgA tTG. 38% of these participants (n= 41) showed IgA tTG ranging between 20 – 79 who were found negative for IgA EMA. These participants were kept on a gluten-free diet for the following 6 months and were scheduled on a recall assessment after 6 months and then 1 year of diet. On follow up duodenal biopsies were performed for these participants and the outcomes were classified as Marsh 0. These participants comprising 38% of IgA tTG screening were discarded from the possible suspect of celiac disease.The remaining 62% (n= 67) population of positive IgA tTG screening test, comprising 3.35% of the entire recruited population had values for IgA tTG of greater than 100 and showed positive results in serology reports of IgA EMA. All 67 participants who tested positive underwent duodenal endoscopy on five sites for a definite diagnosis of celiac disease and were found to be celiac disease positive

Conclusion: The study concludes that the prevalence of the celiac disease among the anemic population is high, and anemia can be considered an extra gastric manifestation of celiac disease. Majority of identified participants were female and shows a predilection for female susceptibility.

Keywords: Iron deficiency, Celiac disease, Prevalence, Correlation.

INTRODUCTION

Celiac disease is a gastrointestinal condition that is chronic and mediated by an immunological reaction to gluten present in different grains such as wheat, barley, and rye [1], and [2]. The transmission of the disease has been documented to be genetic [3], [4]. Genetic studies of celiac disease transmission show a major role of Histocompatibility leukocyte antigens (HLA) genes, predominantly that of HLA-DQ2 and HLA-DQ8 [5], [6]. Genetic predisposition is documented to be a 95% cause of celiac disease etiology [7]. Celiac disease has been a cause of enteropathy in all countries. The prevalence of celiac disease has been widely studied within the population of Pakistan. Studies document that the incidence of celiac disease within the Pakistani population to be 29.3% and is highly prevalent among the younger age groups [8]. Due to the inaccessibility of the population to the health care system in light of poor health resources within the country, this figure remains an understatement for the actual prevalence of disease within the population that remains undiagnosed. The treatment of celiac disease is mainly done by eliminating gluten from the diet of people and enforcing a gluten-free diet which is not the complete cure of the disease but is associated with remission of gluten antibodies [9].

Iron deficiency anemia is a major cause of anemia around the world, especially in developing countries such as Pakistan and it has been appreciated that iron-deficiency anemia has a prevalence of almost up to 50% of young adults in Pakistan [10]. Anemia has been acknowledged to be one of the major manifestations of celiac disease worldwide [11]. The correlation between iron deficiency anemia and celiac disease has been largely studied throughout the world. However, due to poor health resources within the country, this relationship has largely been neglected by the population of Pakistan. This study will aim to assess the incidence and burden of celiac disease among the known anemic population of Khyber Pakhtoonkhaw due to iron deficiency in tertiary care hospitals.

METHODOLOGY

Study design: A cross-sectional study was conducted in the department of Gastroenterology Bacha Khan Medical Complex, Swabi and Northwest General Hospital & Research Centre Hayatabad, Peshawar, during the period of six months from May 2021 to October 2021. The study was conducted after taking ethical approval from relevant authorities.

Participant inclusion and exclusion criteria: The study recruited participants who presented to hematology departed with complaints or diagnosis of Iron deficiency anemia. Diagnosis of iron deficiency anemia was made if hemoglobin levels were found to be less than 13 g/dL in men and less than 12 g/dL in females. Other diagnostic values were mean corpuscular volume lesser than 80 femtoliters and serum ferritin levels of less than 30 ng/mL. Other inclusion criteria included participants being older than 16 years and having previously did not undergo any diagnostic measure for celiac disease. Participants who presented with dark stools, bloody vomit, hematochezia, spontaneous hemoptysis, persistent epistaxis, and previously diagnosed with celiac disease. Other comorbidities which may influence the diagnosis such as the history of malignancy, and chronic diseases of the kidney, liver, and heart were excluded from the study. A further set of exclusion criteria for females included menstruation periods longer than 7 days, current pregnancy, or previous abdominal surgery.

All the participants received verbal as well as written details of a clinical study. A written consent form was signed by participants aging older than 18 years. Consent forms were signed by parents or legal guardians of participants younger than 18 years. Failure to give consent for the study resulted in the termination of participants from the recruited sample size.

Diagnosis of celiac disease: Confirming the diagnosis of celiac disease among participants was done by inflammatory markers and duodenal biopsy. Participants were evaluated for IgA, IgA tTG, and IgA EMA. Positive inflammatory markers were an indicator of performing a duodenal biopsy for confirmation of celiac disease. The immunoassay test for IgA was performed within a private laboratory at the personal expense of the participants. IgA-tTG was considered the first screening diagnostic measure and was done within a hospital setting using an enzyme-linked immunosorbent assay (ELISA). Participants with positive IgA and IgA tTG were subjected to confirmation by assessing the indirect immunofluorescence test of IgA EMA. This assessment was conducted within the hospital and was assessed by an independent pathologist.

Participants who were found to have positive results of serum immunoglobulin tests were then found eligible for duodenal biopsy. IgA tTG and IgA EMA are considered to have over 95% sensitivity and specificity for the diagnosis of celiac disease, this study used duodenal biopsy as a definitive measure for diagnosis of celiac disease. Duodenal biopsies were performed using an endoscopic system and at least 5 biopsies were performed with at least 4 biopsies being taken from post bulbar area for diagnosis of celiac disease under direct vision. Biopsies of various anatomical sites were labeled as such to avoid false-positive reports by a pathologist.

Management of Participants: Participants who presented with IgA tTG levels ranging between 20 – 89 were put on a gluten-free diet and were kept on follow-up of six months followed by 1 year, after which participants were re-evaluated for serology tests. If found persistently positive, the participants were subjected to another biopsy evaluation.

RESULTS

A total number of 3436 participants were interviewed for the recruitment of the study. After assessing the participants regarding inclusion and exclusion criteria and achieving written consent, a total number of 2000 participants were made part of the study sample. The gender breakdown of participants showed an 11.5% prevalence of males (n= 230) whereas females predominated the study population comprising 88.5% (n= 1770). The mean age of participants was 42 years ± 18.3 years.

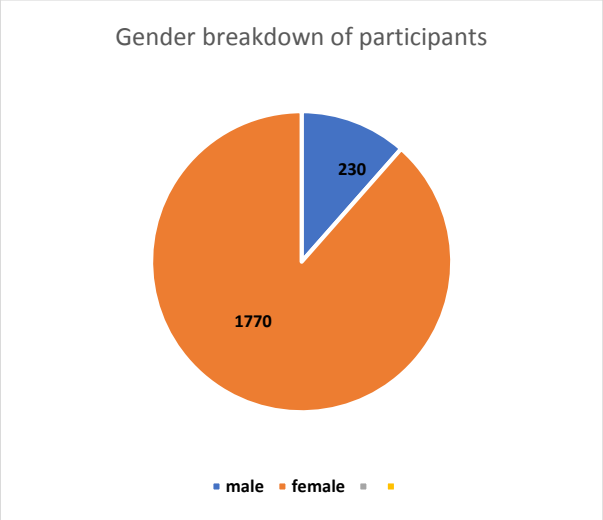

Figure-1 Gender distribution

Outcomes of immunologic tests and duodenal biopsy: The reports for serum IgA levels were within normal ranges, however, 5.8% of the participants (n= 108) were found to have positive results for screening of IgA tTG. 38% of these participants (n= 41) showed IgA tTG ranging between 20 – 79 who were found negative for IgA EMA. These participants were kept on a gluten-free diet for the following 6 months and were scheduled on a recall assessment after 6 months and then 1 year of diet. On follow up duodenal biopsies were performed for these participants and the outcomes were classified as Marsh 0. These participants comprising 38% of IgA tTG screening were discarded from the possible suspect of celiac disease.

The remaining 62% (n= 67) population of positive IgA tTG screening test, comprising 3.35% of the entire recruited population had values for IgA tTG of greater than 100 and showed positive results in serology reports of IgA EMA. All 67 participants who tested positive underwent duodenal endoscopy on five sites for a definite diagnosis of celiac disease. The outcomes of duodenal biopsy are depicted in Table-I:

Table 1: Outcomes of duodenal biopsy

Number of patients	gender	Mean age (years)	IgA tTG	IgA EMA	Biopsy classification (Marsh)
27	Female: 5 Male: 2	Female: 23 ± 12.3 Male: 29 ± 8.3	110.21 – 200	1: 640	III A
6	Female: 21 Male: 5	Female: 28 ± 6.8 years Male: 33.2 ± 1.2	130 – 180	1: 640	III B
34	Female: 17 Male: 3	Female: 26 ± 8 Male: 31 ± 9.4	124 – 164.50	1: 640	III C

Among all the participants who were found positive for celiac disease, the most common symptomatic presentation was that of headache (67.1%) along with abdominal pain (49.5%). Among symptoms specific to GI symptoms, the most common signs were flatulence, postprandial fullness, and abdominal discomfort followed by diarrhea. The majority of diagnosed participants were females with a prevalence of 64%. Patients diagnosed with celiac diseases were similar to normal counterparts in terms of anemic state and weight.

DISCUSSION

The study was conducted in tertiary care hospitals of Khyber Pakhtoonkhaw and the participants of the study were from various economical backgrounds. Therefore, the outcomes of these studies are implacable for the people of Pakistan. Iron deficiency anemia has been a major source of poor health in developing countries and celiac disease has been documented to be a major reason behind the prevalence of iron deficiency anemia in Pakistan [12].

This study showed that among all the recruited participants, 5.8% of the participants (n= 108) were found to have positive results for screening of IgA tTG. 38% of these participants (n= 41) showed IgA tTG ranging between 20 – 79 who were found negative for IgA EMA. These participants were kept on a gluten-free diet for the following 6 months and were scheduled on a recall assessment after 6 months and then 1 year of diet. On follow up duodenal biopsies were performed for these participants and the outcomes were classified as Marsh 0. These participants

comprising 38% of IgA tTG screening were discarded from the possible suspect of celiac disease. The remaining 62% (n= 67) population of positive IgA tTG screening test, comprising 3.35% of the entire recruited population had values for IgA tTG of greater than 100 and showed positive results in serology reports of IgA EMA. All 67 participants who tested positive underwent duodenal endoscopy on five sites for a definite diagnosis of celiac disease. There are many studies conducted which support the findings of this study. Studies that showed celiac disease being prevalent among the anemic population are [13], [14], and [15].

Prevalence of celiac disease among iron deficiency anemia suffering population has been a common finding of the above-mentioned study. A comparison was made in the prevalence of celiac disease among the anemic and non-anemic populations. A study conducted by Harper et al. demonstrated a cohort of anemic and non-anemic groups with a variable prevalence of the celiac disease. the outcomes of the study showed that celiac disease had a prevalence of 12% in the anemic population whereas normal counterparts only showed a prevalence of 5% [16]. Other studies which are in accordance with these outcomes are as follows [17], [18]. These studies are in accordance with the findings of our clinical study however, the incidence of the celiac disease reported in the anemic population in this study is significantly higher than those documented by this clinical research.

The study concludes that the prevalence of the celiac disease among the anemic population is high, and anemia can be considered an extra gastric manifestation of celiac disease. Majority of identified participants were female and shows a predilection for female susceptibility.

CONCLUSION

This study aims to fill the literature gap which existed among the people of Pakistan who were suffering from iron deficiency anemia and concurrent celiac disease prevalence that remained largely unknown in this population. The study will further aim to serve as the basis of newly established research that will allow the practitioner to acknowledge the correlation between the two diseases and to improve diagnosis and management of concurrently presenting two conditions that may lead to major morbidity and mortality.

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