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EVALUATING IRON STATUS IN PATIENTS WITH GLUTEN-SENSITIVE ENTEROPATHY: A STUDY AT A TERTIARY CARE HOSPITAL

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Abstract

Gluten-sensitive enteropathy, or celiac disease (CD), is an autoimmune disorder affecting the small intestine, characterized by inflammation and malabsorption in response to gluten ingestion. The global prevalence of CD is estimated at 1.4% of the world's population, with a comparable rate of 1.3% in Pakistan. This study aimed to investigate the relationship between CD and iron deficiency anemia (IDA) in patients aged 2-15 years, focusing on the nutritional adequacy of their gluten-free diets and exploring how dietary habits relate to patients' physical, socioeconomic, and biochemical characteristics. The cross-sectional study was conducted at a tertiary care hospital in Faisalabad, Pakistan, involving 100 CD patients (66 females, 34 males) diagnosed with associated IDA. Anthropometric measurements, medical history, biochemical parameters, and dietary assessments were performed. Results showed that 44% of patients were aged 0-5 years, with a higher prevalence in females. Low hemoglobin levels were observed in 81% of patients, indicating severe or partial IDA. Biochemical analysis revealed low ferritin levels in 99% of patients and elevated transferrin in 98%. Dietary assessment found that 66% of patients adhered to a gluten-free diet, with varying consumption patterns of different food groups. The study highlighted the complex relationship between CD, IDA, and nutritional status, emphasizing the importance of dietary modifications in managing CD and related complications. These findings provide valuable insights for enhancing CD management strategies and addressing associated nutritional deficits, particularly IDA, in young patients.

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Keywords: Celiac Disease, Iron Deficiency, Gluten Free Diet, Autoimmune Disorder, Gluten Free Diet, Gluten Sensitive Enteropathy, Dietary Intervention.

1. INTRODUCTION

Gluten-sensitive enteropathy, commonly referred to as celiac disease (CD), is an autoimmune disorder primarily affecting the small intestine. This condition is characterized by inflammation, malabsorption, distention, and bloating in response to gluten ingestion (Mohammed et al., 2022). Gluten, a protein found in various cereals and cereal-based products, triggers an immune response in individuals with CD, leading to an inability to properly digest this protein (Mazzola et al., 2024). The global prevalence of CD is estimated at 1.4% of the world's population, highlighting the significant impact of this condition on public health (WHO 2022). In Pakistan, the average prevalence rate is reported to be 1.3% of the total population, indicating a comparable burden of disease in this region (Pakistan Health Survey 2021).

Several risk factors have been identified for the development of CD, including gluten intolerance, lifestyle choices, early weaning practices, dietary factors such as monotonous diets, and genetic predisposition (Turner and Schwartz, 2022). The World Health Organization recommends introducing complementary foods after six months of age; however, early weaning with gluten-containing products may compromise digestion due to the immaturity of the infant's digestive system (WHO, 2020). The clinical presentation of CD often mimics common gastrointestinal disorders, with symptoms including diarrhea, vomiting, abdominal distention, bone disease, and anemia (Thompson and Lee, 2021). Persistent diarrhea, characterized by watery stools and severe abdominal pain, is frequently observed in CD patients. Additionally, bone disease and low hemoglobin levels are common manifestations, likely due to compromised nutrient absorption resulting from small intestinal damage (Babonji et al., 2021). Micronutrient deficiencies are prevalent among CD patients, with zinc, calcium, and iron deficiencies being particularly common. Studies indicate that approximately 11% of individuals with CD experience iron deficiency anemia (IDA) on a regular basis (Wilson and Taylor, 2020). The impaired absorption of iron in CD is attributed to the disruption of the small intestinal villi and microvilli caused by gluten ingestion and the subsequent immune response (Fig. 1) (Montoro-Huguet et al., 2021).

The primary management strategy for CD involves adherence to a gluten-free diet (GFD), often in conjunction with addressing nutritional deficiencies such as IDA through iron replacement therapy, typically in the form of oral supplements like ferrous sulfate (Martin and Green, 2021). However, maintaining a strict GFD presents challenges, particularly in developing countries where wheat-based products are dietary staples. The nutritional composition of gluten-free foods (GFFs) often fails to meet WHO and Food and Agriculture Organization (FAO) recommendations, with many products being low in protein content (Johnson et al., 2022). The present study aimed to investigate the relationship between CD and IDA in patients aged 2-15 years, focusing on the nutritional adequacy of their gluten-free diets. By analyzing dietary habits, food preferences, and

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compliance with gluten-free regimens, the study explored how these factors relate to patients' physical, socioeconomic, and biochemical characteristics. These interrelated goals will generate valuable insights to enhance CD management strategies and address associated nutritional deficits, particularly IDA, in this young patient population.

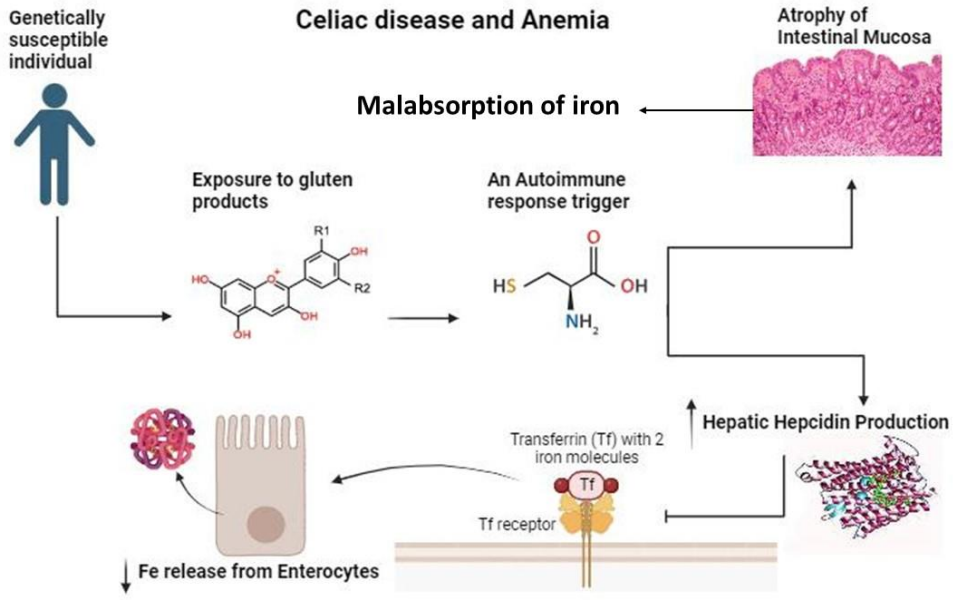

Fig 1: This diagram illustrates pathophysiological pathway associating celiac disease to iron deficiency anemia. On the left side is a healthy small intestine, where normal muscles absorb iron well. The right side is damaged intestinal mucosa in celiac disease, with thin mucosa and inflammation that impair iron absorption

2. MATERIALS AND METHODS

2.1 Data collection

The study was completely randomized cross-sectional survey conducted in Children Hospital & Institute of Child Health Faisalabad. The hospital is known as the tertiary hospital of Faisalabad and covers patients from 8 districts of Punjab. So, a variety of patients had gluten-sensitive enteropathy in the outdoor patient department (OPD) and gastroenterology ward of the hospital.

2.2 Sampling

The study subjects were admitted patients in the gastroenterology ward of the hospital, patients in (out-patient department) OPD and awareness camps for gluten-sensitive enteropathy and iron deficiency anemia were organized to encourage the patient count in the hospital. A total of 142 patients were enrolled who were assessed either they meet the standard criteria or not. The inclusion criteria for subjects include the age limit of 2-15

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years along with celiac disease and associated IDA. The Celiac disease confirmation in selected patients was done through intestinal biopsy reports. The subjects with diarrhea, abdominal distention and other chronic diseases were excluded from the survey. After screening, 100 subjects were finalized to undergo designed survey including 66 females and 34 males.

2.3 Questionnaire development

A standardized questionnaire was developed according to the method of Salih et al. (2021) that consisted of demographic information and other medical history of patients. A food frequency questionnaire was also used to investigate the diet history of the patients. The food groups included in FFQ were cereals, lentils, meat and meat products, dairy and dairy products, fruits, vegetables, sugar, fats and oil. After finalizing the questionnaire from experts, a refined form of the questionnaire was used for collection of data. The questionnaire is attached below.

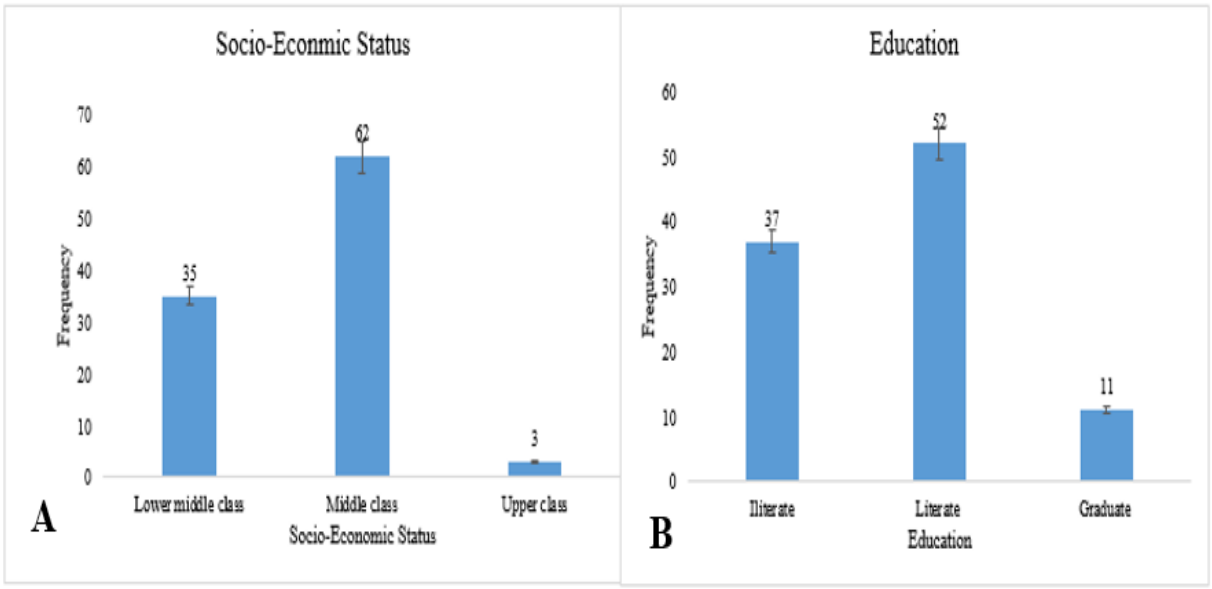

Fig 2: (A) Bar graph represents the distribution of socio-economic status levels on the incidence of gluten sensitive enteropathy in children including three sub categories of lower middle class, middle class and upper class (B) Potential impact of education on the disease status with respect to illiterate, literate and graduated patients diagnosed with gluten sensitive enteropathy among 100 patients

2.4 Statistical Analysis

The information gathered was examined by using IBM SPSS 26.0. The significance of numerous independent variables was shown by a Pearson-Chi Square Test score of less than 0.05 (Montgomery, 2017).

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3. RESULTS

3.1 Demographic data

The demographic data of patients diagnosed with CD and IDA were investigated (Fig. 2) to get insights into lifestyle patterns and their impact on daily life. This study observed that individuals with lower educational attainment were more susceptible to the disease and associated complications, primarily due to reduced awareness and knowledge. Socioeconomic status (SES) is another crucial factor in determining lifestyle patterns and understanding patient demographics. Lower socioeconomic status often correlates with reduced educational attainment and limited access to GFD and other disease management strategies

3.2 Anthropometric Information

The anthropometric measurements revealed that 44 patients were aged 0-5 years, representing the most typical group. In contrast, the lowest frequency was observed in the 10-11 age group, with 16 patients (Fig. 3). This age distribution indicates a higher incidence of lifetime diagnosis in the study population. The study examined gender distribution among 100 patients diagnosed with celiac disease (CD) and iron deficiency anemia (IDA). Results revealed a predominance of female patients (n=66) compared to male patients (n=34), indicating a higher prevalence of CD and IDA in females within this cohort. Body Mass Index (BMI) distribution revealed that 27 patients had low BMI, 65 had normal BMI, 4 were overweight, and 4 were obese. Height-for-age analysis showed that 62 patients had low height for their age. Weight-for-age assessment indicated that 31 patients had low weight according to the percentile chart, while 9 patients were up to the 85th percentile. Statistical analysis revealed a significant relationship between weight and height (p≤0.00), as well as between age and height (p≤0.01).

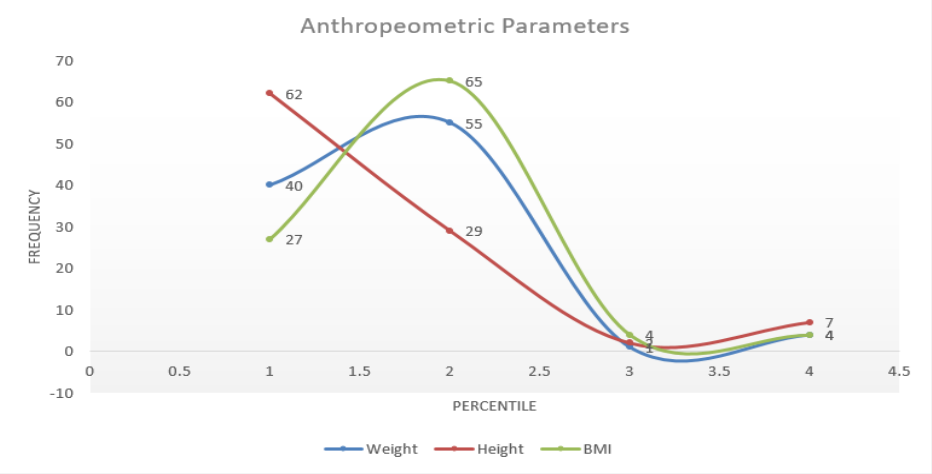

Fig 3: Multivariate analysis of anthropometric parameters in pediatric celiac disease patients. Scatter plot diagram demonstrates the results through different colors (blue= weight, orange= height, grey= body mass index of patients that is the ratio of height and weight)

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3.3 Medical History

Medical history is the most important factor in any diagnosis or survey study. In this study, 83 patients had no family history of CD in past years and 17 patients had a positive family history of the CD. Similarly, Pica is also very common in patients diagnosed with IDA. Pica is a condition in which patients crave for non-food items like chalk, sand, etc. In the present study, 84 patients had anemia and 43 patients with pica. Regarding gluten free diet consumption, 66 patients were taking gluten free diet (Fig. 4).

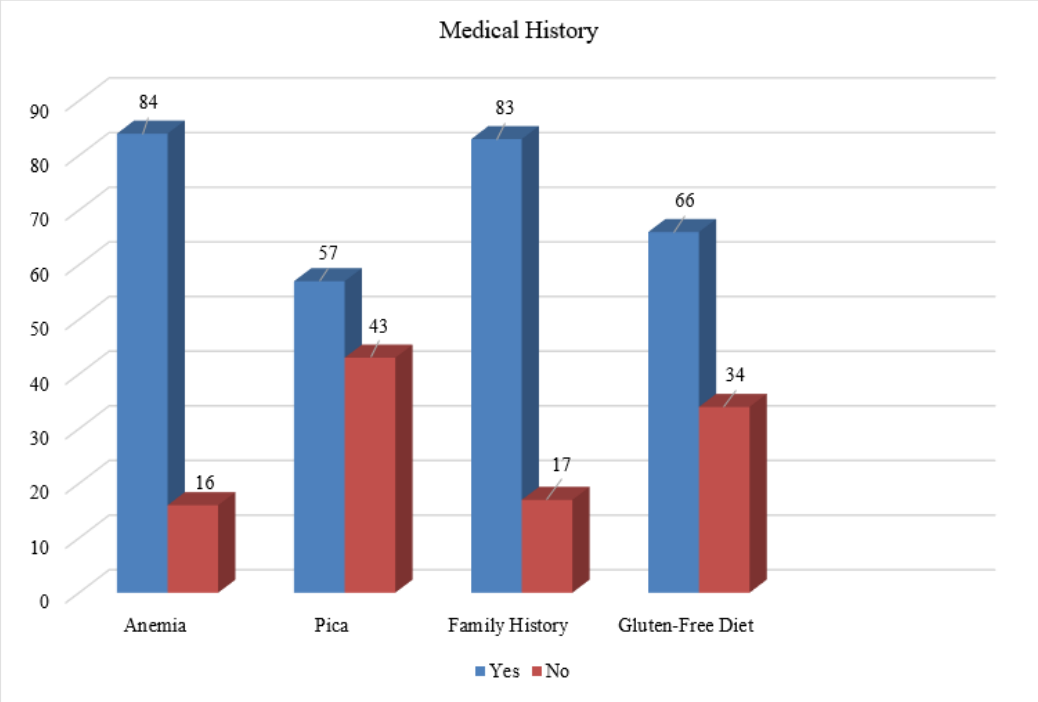

Fig 4: Key aspects of medical history and dietary habits of patients using four bar charts. It shows the proportion of patients with family history of celiac disease, presence of anemia, occurrence of pica, and adherence to a gluten-free diet

3.4 Biochemical parameters

This study observed a prevalence of low hemoglobin (Hb) levels among celiac disease (CD) patients. The investigation revealed that 81% of patients had Hb levels below 10, indicating severe or partial iron deficiency anemia (IDA). Only 17 patients had Hb levels above 10, with merely 2 patients exceeding 12. Furthermore, 84% of patients were anemia-positive, while 16% were anemia-negative (Fig. 5). Ferritin, an iron storage protein, regulates iron levels in the body. In CD and IDA, ferritin levels typically decrease due to elevated transferrin, an iron-binding protein. The study found that 99% of patients had low ferritin levels, indicative of mild or severe anemia, while only 1% had normal levels. Regarding transferrin, 98% of patients exhibited higher levels, with only 2% showing normal levels.

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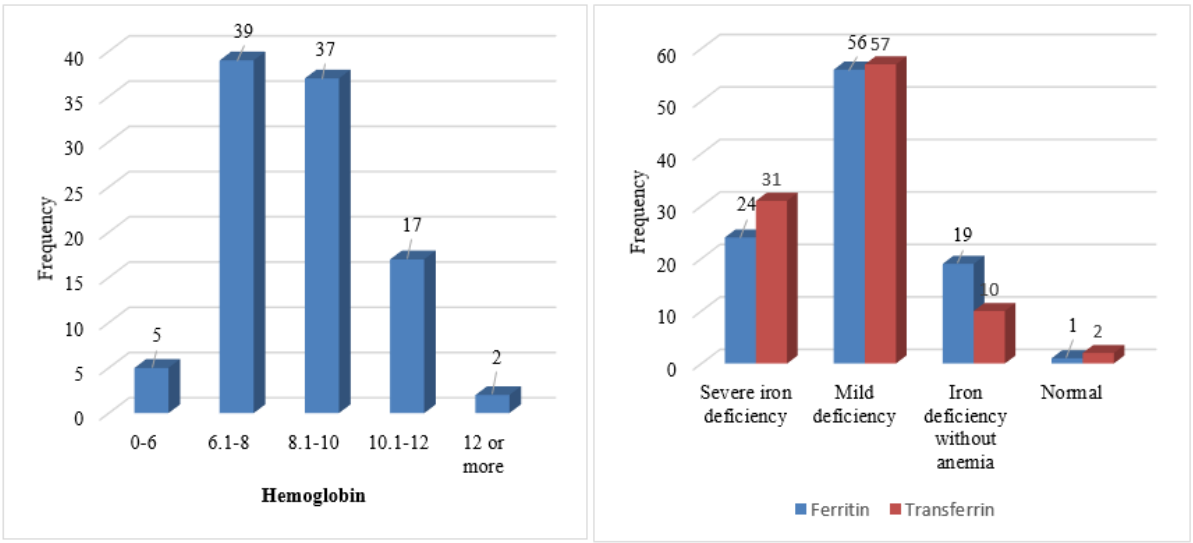

Fig 5: This figure presents hemoglobin levels, serum ferritin levels and transferrin levels in the study population. It highlights the high prevalence of anemia, markedly low ferritin levels suggesting depleted iron stores, and elevated transferrin levels indicative of the body's attempt to compensate for iron deficiency

3.5 Dietary assessment

Dietary assessment plays a crucial role in nutrition-related research. This study observed that 66 patients adhered to a gluten-free diet (GFD), while 44 patients did not incorporate GFD into their routine. GFD is the primary intervention to improve intestinal health in celiac disease (CD) patients, as gluten triggers small intestine inflammation and reduces iron absorption. The study found that 70 patients never consumed bread, 11 consumed it daily, 13 weekly, and 6 monthly. This distribution indicates patient awareness of gluten in bread and its unsuitability for CD. The study revealed that 64 patients consumed chapati daily, 22 never consumed it post-CD diagnosis, 11 consumed it weekly, and 3 monthly. The study found 49 patients consuming rice daily, 47 weekly, 3 never, and 1 monthly. The study showed 82 patients never consumed porridge, 17 consumed it weekly, and 1 monthly. Milk consumption was high, with 75 patients consuming it daily, 17 weekly, 5 never, and 3 monthly. Regarding vegetables and fruits, 69 patients consumed vegetables weekly and 19 daily. For fruits, 65 patients consumed them daily and 33 weekly. Protein sources varied in consumption patterns. Chicken was consumed weekly by 76 patients, daily by 7, never by 7, and monthly by 10. Mutton and beef consumption was less frequent, with no daily mutton consumers and only 3 daily beef consumers. Egg consumption was higher, with 37 daily and 57 weekly consumers. Lentils, a gluten-free protein source, were consumed weekly by 82 patients, monthly by 7, never by 7, and daily by 4.

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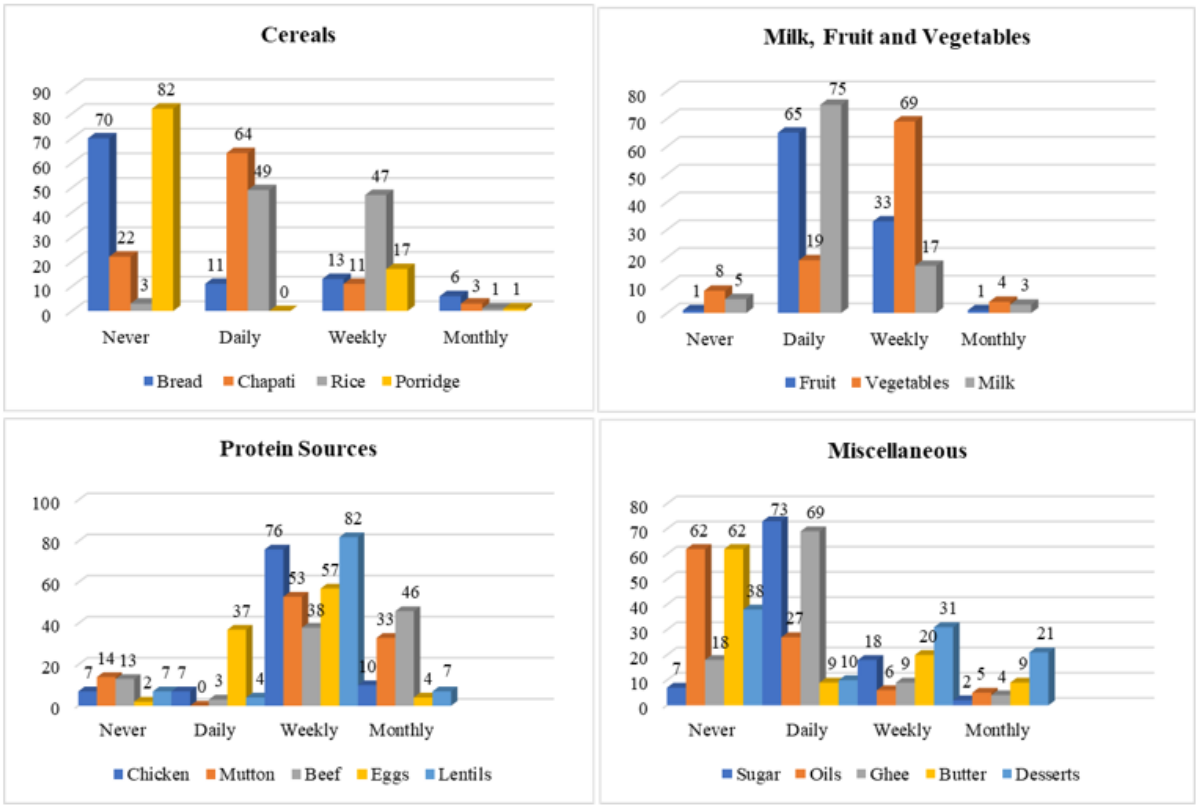

Fig 6: Consumption frequency of various food groups among study participants. The y-axis lists food items categorized into cereals, proteins, dairy, fruits, and vegetables, while the x-axis shows consumption frequency. Color intensity corresponds to number of patients in each category. Key patterns include high daily consumption of rice and milk, weekly consumption of meat and vegetables, and low intake of wheat-based products, reflecting dietary adaptations in celiac disease management

4. DISCUSSION

Education and socioeconomic status play significant role in management of celiac disease and the associated complications. The findings of the present study align with Barzegar et al. (2017), who demonstrated that educational interventions can enhance knowledge among CD patients regarding treatment options. Improved patient knowledge may contribute to better health outcomes. Interestingly, this study's results corroborate the findings of Whyte et al. (2014), which indicated higher rates of celiac disease among children from higher socioeconomic groups. While the exact causes remain unclear, factors such as the "hygiene hypothesis" and health-seeking behaviors of higher SES parents may contribute to increased celiac disease diagnoses in this demographic. Conversely, Kondrashova et al. (2008) suggest that lower socioeconomic status and suboptimal hygienic conditions might offer some protection against celiac disease. A

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strong positive correlation exists between education level and socioeconomic status, with the relationship between these factors demonstrating high statistical significance ($p \leq 0.01$).

Patients with CD often face increased developmental issues, cognitive difficulties, and functional challenges for patients and caregivers in the early years of development (Di-Filippo et al., 2013). Young children, especially infants and toddlers, have immature small intestines and developing immune systems. This physiological state may increase their sensitivity to the effects of gluten ingestion, potentially leading to direct effects on the small intestine and potentially greater iron absorption gluten-containing foods (Sahin, 2021). Popp et al. (2019) noted that the effects of gluten intolerance decrease during adolescence. This decrease in severity may be related to the maturation of the small intestine and immune system as individuals age. The frequent lack of diagnosis at 10-11 years of age in the present study seems to support this conclusion, suggesting possible changes in presentation or diagnosis as patients enter adolescence at the beginning.

This gender disparity aligns with previous research, such as the study by Javaed et al. (2017), which reported that females have a 70% higher likelihood of being affected by CD compared to males. This observation is also consistent with earlier findings by Cheng et al. (2010) who reported a direct relationship between patient weight and the severity of anemia and CD. Weight loss is common in CD patients due to frequent diarrhea and irregular eating patterns (Roncoroni et al., 2022). However, the presence of normal or overweight patients in this study corroborates the complex relationship between CD and body composition. The use of BMI and percentiles for anthropometric assessment in this teenage population is consistent with the methodology described by Wang et al. (2020). However, Singh et al. (2016) cautioned against over-reliance on BMI, noting its limitations in accurately representing body composition. The high prevalence of stunting observed in this study supports the findings of Gashu et al. (2015), who identified iron deficiency as a key factor in growth impairment among CD patients. The significant relationships between age, height, and weight underscore the multifaceted impact of CD on physical development.

Medical history of patients indicates the genetic association between families. CD is one of the diseases which are associated with the genetic disorder. In CD, family history is important to diagnose the disease if parents have any condition or are affected by the disease (Akhtar et al., 2021). The study's findings are aligned with Miao et al. (2015), who reported a frequency of 11% of iron-deficient patients with pica symptoms. It has been hypothesized that pica may be causing iron shortage by substituting dietary sources of iron or by preventing iron absorption. However, in another study by Seim et al. (2016), it has been theorized that the chemicals responsible for geophagia do not bind to bioavailable iron and consequently do not decrease iron absorption. Many researchers and clinicians, such as paediatricians and hematologists believe that iron deficiency induces pica. Young et al. (2010), investigated the hypothesis of nutritional deficiency. According to this theory, geophagy takes place to compensate for the deficiency of iron,

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zinc, or calcium, therefore those who have the highest nutritional demands will participate in it most often.

Anemia, characterized by iron deficiency and low blood count (Martín-Masot et al., 2019), leads to various clinical issues, including compromised immunity, abnormal growth, shortness of breath, and weakness (Soliman et al., 2019). In CD, anemia frequently occurs due to iron malabsorption caused by damaged villi and microvilli in the small intestine, which are responsible for iron absorption (Jansson-Knodell et al., 2020). These findings align with Baghbanian et al. (2015), who reported that anemia decreases hemoglobin levels, disrupting oxygen transport throughout the body. Low Hb levels in CD patients can result from decreased blood count, iron malabsorption, or insufficient intake of iron-rich foods in the regular diet (Montoro-Huguet et al., 2021). Reduced Hb levels are common among CD patients due to impaired blood production and poor circulation (Roldan et al., 2022).

Low ferritin is common in screen-detected and even asymptomatic CD, particularly in women, and is associated with lower BMI and more severe duodenal mucosal injury rather than symptom severity or quality of life. Despite increases during follow-up, many patients maintained low ferritin levels, necessitating an extended follow-up period to determine data normalization after identifying iron deficiency (Repo et al., 2017). Similarly, elevated transferrin (beta globulin) levels and decreased transferrin iron saturation have been observed in children with CD (Ghadiri et al., 2017). These results are consistent with Haapalahti et al. (2005), who found higher transferrin concentrations in nearly half of the cases, particularly in celiac adults and children with nutritional deficiencies. The study population showed a higher CD ratio in females compared to males. An inverse relationship exists between ferritin and transferrin levels. Patients with lower ferritin levels exhibited higher transferrin levels and vice versa. GFDs often lack sufficient iron content, and prolonged use without iron fortification can lead to iron deficiency. These findings align with Murray et al. (2004), who reported that GFD rapidly and substantially improves gastrointestinal symptoms in CD patients, including atypical symptoms beyond diarrhea, steatorrhea, and weight loss.

Dietary interventions are the most important and influential parameter in the management of celiac disease and its associated iron deficiency anemia. Bread, a common and affordable carbohydrate source, contains gluten, which triggers an immune response in CD patients (Sánchez-León et al., 2021). Guzmán-López et al. (2021) suggested that gluten-free or low-gluten bread could be a better option for CD patients, potentially improving immune response and gastric health. Chapati, a traditional South Asian food, is typically made from wheat containing gluten. For CD patients, rice or corn-based chapati is recommended (Sharma et al., 2020). Patients avoiding chapati showed significant improvements in iron status. Rice, a staple in South Asian countries, is widely cultivated (Bhatt et al., 2021). Its consumption among patients was high due to availability and affordability as a gluten-free option (El-Hadidy et al., 2022). Porridge, a popular global breakfast cereal (Kinyuru et al., 2021), is less common in Pakistan due to limited awareness (Khan et al., 2022). Patients often avoid porridge due to its gluten content or

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lack of awareness about gluten-free alternatives like oats (Pandey et al., 2023; Mehta, 2019). Güngör et al. (2019) noted that human milk consumption in infancy might reduce CD risks and improve digestive health. Aaron and Torsten (2018) clarified that while lactose intolerance may result from CD-damaged intestinal mucosa, lactose exposure does not harm celiac patients' intestines unlike gluten. Brown et al. (2012) suggested that limited plant food intake might contribute to early onset of gastrointestinal symptoms in CD patients, potentially leading to dysbiosis and aberrant immune responses. Sample et al. (2017) proposed oral egg yolk anti-gliadin antibody as a potential gluten-neutralizing therapy.

5. CONCLUSION

Gluten-sensitive enteropathy or celiac disease is an autoimmune disease in 1.4% of the total population of the world and 1.3% of Pakistan. However, still, there is not sufficient awareness of the risk factors and severity of this disease. Celiac disease may lead to further complications, i.e. iron deficiency anemia. The gluten-free diet is the most appropriate strategy for managing celiac disease and its related factors. A diet comprising gluten-free cereals, fresh fruit and vegetables should be consumed regularly as fruit and vegetables are the best sources of micronutrients and red meat and chicken should be taken in fewer amounts. Dietary modification is the only suitable way to live a healthy life with CD.

Conflict of Interest

The Authors declare that there is no conflict of interest

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Ethics Statement

The authors declare that all sources employed in writing **Evaluating Iron Status in Patients with Gluten-Sensitive Enteropathy: A Study at a Tertiary Care Hospital** are duly referenced, and any potential conflicts of interest are disclosed.

Data Availability

Data will be made available on request.

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