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Original article

Prevalence of Malabsorption Leads to Celiac Disease among the Libyan Population: Pathological and Therapeutic Rules

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Abstract
Celiac disease is a chronic autoimmune disorder that primarily impacts the small intestine. It arises from the consumption of gluten in individuals who possess specific genetic markers, namely the HLA-DQ2 or HLA-DQ8 antigens, leading to mucosal inflammation and villous atrophy, which ultimately results in malabsorption. Diagnosis is typically achieved through various diagnostic methods, including a small bowel biopsy. The global prevalence of CD in the general population is approximately 1%, with rates in North Africa ranging from 0.5% to 1%, aligning with global averages. Recent findings indicate that celiac disease is not necessarily less prevalent in certain regions but often goes undiagnosed. The cornerstone of treatment following a confirmed diagnosis is lifelong adherence to a gluten-free diet. This study aims to examine the prevalence of malabsorption associated with celiac disease in the Libyan population, along with its epidemiology, pathogenesis, clinical manifestations, diagnostic approaches, and current therapeutic strategies. Despite an anticipated rise in celiac disease cases in Africa due to enhanced disease awareness and diagnostic advancements, reports of celiac disease in North Africa, particularly Libya, remain scarce. This paper will present documented cases of celiac disease in Libya while summarizing key aspects. Additionally, we will discuss the epidemiology, diagnostic criteria, and treatment protocols for celiac disease in Libya.
Keywords: Celiac Disease, Epidemiology, Pathophysiology, Genetics, Diagnosis.

Introduction

Celiac disease (CD), also known as celiac sprue or gluten sensitivity enteropathy, is a condition affecting the small intestine that arises from an immune response triggered by the consumption of gluten proteins found in foods such as wheat, barley, and rye. This systemic disorder occurs in genetically predisposed individuals. The estimated prevalence of CD in the general population worldwide is approximately 1% [1]. It presents as an autoimmune enteropathy of the small bowel, characterized by the presence of specific circulating autoantibodies and the human leukocyte antigen haplotypes HLA-DQ2 or HLA-DQ8. The intake of gluten proteins leads to immune-mediated inflammation of the mucosa in the proximal small intestine (duodenum and jejunum), resulting in villous atrophy and crypt hyperplasia (Figure), which in turn causes malabsorption and various gastrointestinal symptoms[2-4].

Diagnosis of CD can be achieved through three methods: serological tests, duodenal histology, and genetic testing. Adopting a gluten-free diet can alleviate intestinal damage and symptoms. Unlike other autoimmune disorders, the immunogenic antigens responsible for the immune response in CD have been well identified and characterized[5]. Gluten consists of proteins in wheat that include two primary components: monomeric water-soluble gliadins and multimeric water-insoluble glutenins. These gluten proteins are notably high in proline (15% of their amino acid composition) and glutamine (35% of their amino acid composition), which contributes to their resistance against human proteases in the intestinal lumen[6], leading to the formation of highly immunogenic peptides that can be 30 to 40 amino acids long [7].

CD was initially thought to be confined to Caucasian Europeans; however, it is now found across the globe. In many regions, the prevalence of CD in the general population varies between 0.5% and 2%, with an average prevalence of about 1% [8,9]. CD can develop at any age, starting from childhood after the age of two and extending into the second and third decades of life or beyond, with a higher incidence observed in females [10,11]. The global prevalence of CD is believed to align with the distribution of HLA genotypes that are susceptible to the disease, provided that individuals are exposed to gluten [12].

In celiac disease (CD), gluten serves as the most critical stimulatory agent. After gluten is consumed, its peptides traverse the epithelial barrier and are modified by the enzyme tissue transglutaminase 2 through deamidation. The resulting deaminated gluten peptides have a strong affinity for HLA-DQ2/8 molecules present on antigen-presenting cells, which triggers the activation of gluten-specific CD4+ T cells. These T cells then release pro-inflammatory factors, including interferon, interleukin-2, interleukin-21, and tumor necrosis factor (TNF). This immune reaction leads to inflammation and damage to the gut tissue [13, 14]. In response to gluten consumption, gluten-specific CD4+ T-cells produce IL-2 and other inflammatory mediators, which can manifest as gastrointestinal symptoms like nausea and vomiting [15,16].

The presentation of CD has evolved, largely due to the enhanced identification of asymptomatic and mild cases facilitated by advancements in serological screening techniques [17]. Historically, CD was primarily diagnosed in infants and young children, who exhibited symptoms of malabsorption and failure to thrive.

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However, more recently, the onset of CD has been observed in individuals aged between 10 and 40 years, often manifesting with milder gastrointestinal or non-gastrointestinal symptoms [18]. The clinical manifestations of CD are diverse and can affect multiple organ systems. Symptoms are generally categorized into intestinal and extra-intestinal, with variations depending on the patient's age [19]. Common gastrointestinal symptoms include nausea, vomiting, chronic diarrhea or constipation, abdominal pain or bloating, and, in children, failure to thrive, while adults may experience weight loss. Extra-intestinal symptoms encompass headaches, fatigue, osteoporosis, arthritis, myalgia, and central nervous system-specific issues such as seizures and psychiatric disorders [20]. Dermatitis herpetiformis is a frequently observed extra-intestinal skin condition [21], characterized by clusters of intensely itchy blisters, primarily located on the elbows, knees, back, and buttocks [22]. In female patients, irregular menstrual cycles and early menopause are also noted [21].

The diagnosis of CD relies on a strong clinical suspicion, serological tests, and small bowel biopsies. A widely used screening method for CD involves detecting an immunoglobulin, an anti-tissue transglutaminase-2 antibody (IgA TG2Ab), while the patient is on a regular diet. Endoscopic small bowel biopsies are regarded as the definitive method for diagnosing CD [23]. The American College of Gastroenterology (ACG) in 2023 continues to advocate for esophagogastroduodenoscopy (EGD) accompanied by multiple duodenal biopsies to confirm the diagnosis in both children and adults [24]. To rule out CD, negative results for HLA-DQ2 or DQ8 are essential. In adults, the presence of TG2Ab along with changes in duodenal histopathology typically confirms the diagnosis of CD [25].

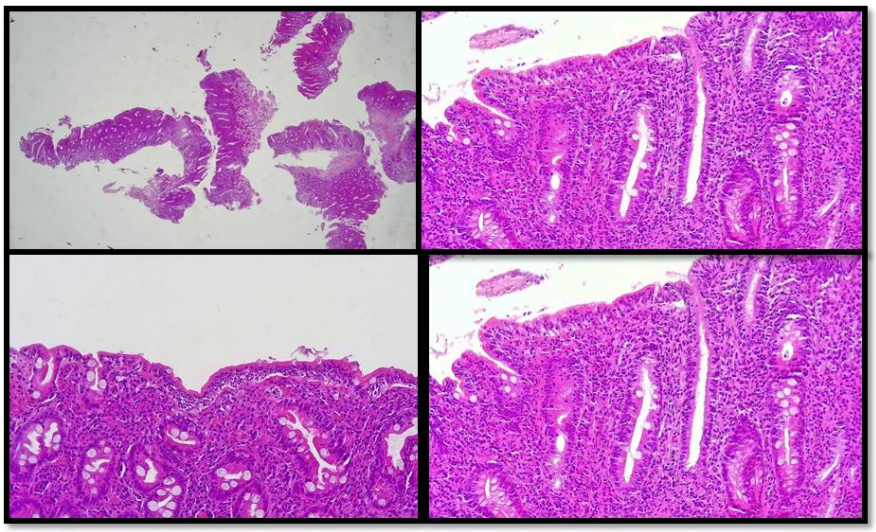

Figure 1. Total villous atrophy with increased intraepithelial lymphocytes

Methodology

Study design

This study employed a retrospective descriptive approach to examine patient data obtained from the Sara Salam Center located in Tripoli, Libya.

Study population and sampling

The analysis focused on the records of 128 consecutive patients who underwent upper gastrointestinal endoscopy accompanied by duodenal biopsies between January 1, 2023, and December 31, 2023. Patients were generally referred for evaluation due to symptoms indicative of malabsorption, chronic diarrhea, unexplained anemia, or a clinical suspicion of CD. Records lacking complete demographic or critical histological information were excluded from the study.

Data collection

Data were gathered from patient medical files, endoscopy documentation, and histopathology reports utilizing a standardized data collection form. The variables collected encompassed: Demographics: Age (classified into specific groups: 1-20, 21-40, 41-60, 61-80, 81-100 years) and gender (Male/Female) (Figure 2).

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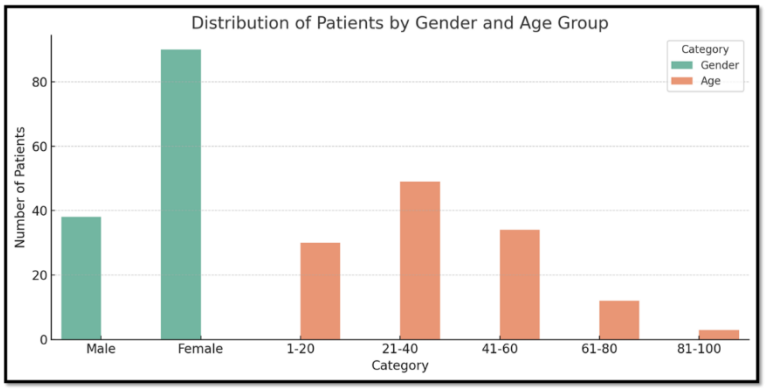

Figure 2. Demographics of participants

Clinical diagnosis

Anemia has been diagnosed based on the existing medical documentation.

Final diagnosis

The diagnosis of Celiac Disease has been confirmed, presumably through a synthesis of clinical evaluations, serological data (if conducted), and histological analysis, adhering to established guidelines such as those from ESPGHAN and ACG.

Histopathological Observations

The results of the duodenal biopsy were categorized into the following groups: a) Marsh classification (IIIA, IIIB, IIIC) for patients with a diagnosis of Celiac Disease. b) Detection of Subtotal Villous Atrophy (SVA). c) Presence of non-specific histological features that align with Celiac Disease (HFCCD). d) No Significant Abnormalities (NSA) observed.

Data analysis

The data was summarized using descriptive statistics. Frequencies and percentages were computed for categorical variables, including gender, age groups, diagnoses, and histological findings. The analysis was conducted utilizing SPSS version V20.

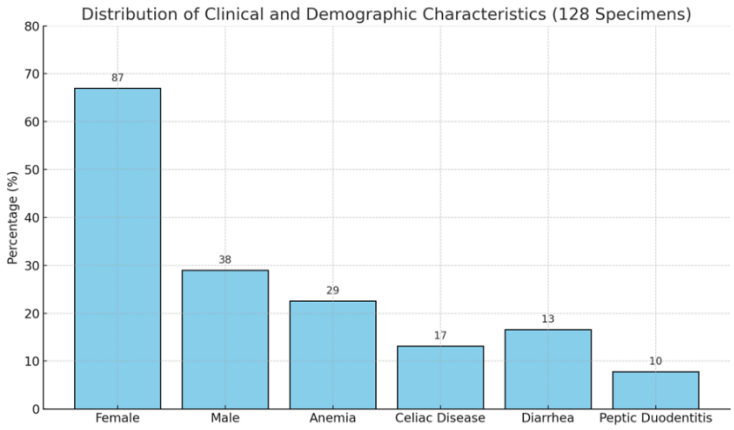

Figure 3. Demographic and diagnostic characteristics of patients

Discussion

This study offers insights into the demographic and diagnostic characteristics of 128 patients who received upper GI endoscopy and biopsy at a healthcare facility in Libya. The findings highlight a considerable female majority in the overall patient population, particularly among those identified with CD. Furthermore, there is a pronounced peak prevalence in the young to middle-aged adult demographic, alongside significant rates of anemia and histologically confirmed cases of CD. Regarding of demographic profile (Figure 3).

The demographic analysis of the patient cohort revealed a significant female predominance, with women making up 70.3% of the group. This trend is in line with global observations in gastroenterology referrals, which may suggest differences in healthcare-seeking patterns or the prevalence of certain diseases. The age distribution peaked in the 21–40-year (38.3%) and 41–60-year (26.6%) brackets, reflecting the common age range for the onset or diagnosis of various chronic gastrointestinal disorders, such as celiac disease in respect of celiac disease.

A significant observation was the diagnosis of the disease in 20.3% (26 out of 128) of the patients studied. This prevalence in a symptomatic, referred population emphasizes the critical need to consider Celiac

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Disease in patients exhibiting relevant symptoms in Libya. The remarkable female-to-male ratio among Celiac Disease patients (23 females to 3 males, roughly 7.7:1) is substantially higher than the typical global ratio of 2-3:1. This finding necessitates further investigation in the Libyan context, as possible explanations may include increased awareness or reporting of symptoms among females, true biological differences in susceptibility or presentation within this demographic, or specific referral biases related to the study's setting. In case of the histological severity, which was assessed through the available Marsh classifications (N=20, classified cases from a total of 26 celiac disease diagnoses), predominantly indicated Marsh IIIB, accounting for 65% of the classified cases, which signifies marked villous atrophy. This observation may suggest that the patients in this cohort were diagnosed or presented with the disease at a relatively advanced stage, possibly due to delays in diagnosis that are frequently encountered in regions where awareness or access to specific diagnostic tests, such as serology, is limited. The group categorized as having Histological features compatible with celiac disease (N=9) may reflect earlier disease stages (Marsh I-II) or cases where the diagnosis was not definitively established, thus requiring further clinical and serological correlation. The inconsistency between the total number of celiac disease diagnoses (N=26) and the Marsh classified cases (N=20) necessitates clarification, as it may point to incomplete reporting or differing diagnostic approaches. In the context of anaemia and related findings, in the study, anaemia was observed in 16.4% (21 out of 128) of the patients.

While the summary does not specifically address the relationship with celiac disease (CD), it is important to note that anaemia is a recognized extra-intestinal manifestation and a common symptom of CD, often due to the malabsorption of iron, folate, or vitamin B12. This finding emphasizes the necessity of evaluating Libyan patients with unexplained anaemia for possible underlying CD, particularly in cases of iron deficiency anaemia. Additionally, other prevalent factors in Libya, such as nutritional deficiencies unrelated to CD, parasitic infections like hookworm and giardiasis, and haemoglobinopathies, should also be taken into account. The histological feature of Subtotal Villous Atrophy (SVA) was observed in 14.1% of the cases (18 out of 128). This observation is significantly associated with advanced celiac disease (Marsh IIIB/C); however, the precise nature of this relationship and any potential overlap with the confirmed Celiac Disease group (N=26) and the Marsh classified group (N=20) necessitates further clarification from the original data. A significant percentage of patients (35.9%, N=46) exhibited no notable abnormalities in their biopsy results. This underscores the diagnostic difficulties associated with non-specific gastrointestinal symptoms and emphasizes the importance of endoscopy and biopsy in excluding organic pathology, even when the findings are ultimately normal.

These findings, although based on a small sample, indicate that celiac disease poses a significant health challenge for the population studied in Libya. The potential for delayed diagnosis, as suggested by the predominance of Marsh IIIB, along with the notably high female-to-male ratio, is are critical factors that need to be addressed. Initiatives aimed at raising awareness of celiac disease among the general public and healthcare professionals in Libya could promote earlier diagnosis and better management, potentially reducing the risk of long-term complications. Furthermore, it is vital to provide access to dependable diagnostic resources, including serological screening and expert histopathological analysis. The high incidence of anemia points to the need for comprehensive evaluations beyond simple supplementation, particularly considering celiac disease as a possible underlying cause.

Limitations

The retrospective nature of this study presents certain limitations, including the risk of selection bias and the potential for missing data. With a sample size of 128, which is relatively small and likely sourced from a single center, the findings may not be generalizable to the entire Libyan population. The summary lacks detailed clinical presentations, serological data that align with histological results, and insights into other possible causes of symptoms or histological changes. Furthermore, there is a need for clearer definitions and distinctions among the histological categories (SVA, HFCCD, Marsh). There is a need for extensive, multi-center, prospective studies throughout different regions of Libya to more accurately determine the prevalence and characteristics of Celiac Disease and other pertinent gastrointestinal conditions. These studies should incorporate thorough clinical data, standardized serological assessments (including IgA-tTG and EMA), HLA typing if feasible, and consistent histological reporting. This will facilitate a deeper understanding of the unique female predominance noted in this study. Furthermore, research focusing on the specific causes of anemia in this demographic is also essential.

Conclusion

This study of Libyan patients being assessed for gastrointestinal problems revealed significant occurrences of Celiac Disease and anemia. The notable female predominance and the extent of histological changes observed in Celiac Disease patients point to potential obstacles in awareness and diagnostic approaches in this region. These results emphasize the importance of increased clinical awareness of celiac disease and the need for comprehensive diagnostic evaluations for symptomatic patients in Libya.

Conflict of interest. Nil

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الملخص

الداء البطني هو اضطراب مناعي ذاتي مزمن يُصيب الأمعاء الدقيقة بشكل رئيسي. ينشأ هذا الداء نتيجة تناول الغلوتين لدى الأفراد الذين يحملون علامات وراثية محددة، وهي مستضدات HLA-DQ2 أوHLA-DQ8 ، مما يؤدي إلى التهاب الغشاء المخاطي وضمور الزغابات المعوية، مما يؤدي في النهاية إلى سوء الامتصاص. يُشخَّص هذا الداء عادةً من خلال طرق تشخيصية متنوعة، بما في ذلك خزعة الأمعاء الدقيقة. يبلغ معدل انتشار الداء البطني عالميًا حوالي 1% بين عامة السكان، وتتراوح المعدلات في شمال أفريقيا بين 0.5% و1%، وهو معدل يتماشى مع المتوسطات العالمية. تشير النتائج الحديثة إلى أن الداء البطني ليس بالضرورة أقل انتشارًا في بعض المناطق، ولكنه غالبًا ما لا يُشخَّص. ويُعد الالتزام بنظام غذائي خالٍ من الغلوتين طوال الحياة حجر الزاوية في العلاج بعد التشخيص المؤكد. تهدف هذه الدراسة إلى دراسة معدل انتشار سوء الامتصاص المرتبط بالداء البطني بين السكان الليبيين، بالإضافة إلى علم الأوبئة، وتطور المرض، والمظاهر السريرية، وأساليب التشخيص، واستراتيجيات العلاج الحالية. على الرغم من الارتفاع المتوقع في حالات الإصابة بالداء البطني في أفريقيا نتيجةً لزيادة الوعي بالمرض والتقدم في التشخيص، إلا أن التقارير عن هذا المرض في شمال أفريقيا، وخاصةً ليبيا، لا تزال نادرة. ستعرض هذه الورقة البحثية الحالات الموثقة للداء البطني في ليبيا، مع تلخيص الجوانب الرئيسية. كما ستناقش علم الأوبئة، ومعايير التشخيص، وبروتوكولات العلاج للداء البطني في ليبيا.

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