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*Original article*

# Clinical and Biochemical Profile of Libyan Patients with Serology and Biopsy Proven Celiac Disease

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## ABSTRACT

***Background and aims****. Celiac disease is a long-term immune disorder that primarily affects the small intestine. Iron deficiency anemia is the most widely experienced anemia in humans, which is a common extra intestinal manifestation of celiac disease. The aim of the current study is to describe the clinical and biochemical profile of adult Libyan celiac disease patients.* ***Method.*** *This was a case series study conducted by reviewing the medical records of the 100 patients diagnosed as celiac disease and followed in gastro-enterology clinic in Tripoli university hospital during the study period. A relevant data obtained from the records in a preformed case sheet.* ***Result.*** *The total number of celiac disease patients was 100 patients. Of them, 88 patients were females (88%) and 12 patients were males (12%). Patient age during the study were from 15 years to 45 years. Total villous atrophy (type3 lesion) was the commonest histopathological finding (62%) and subtotal villous atrophy in (38%) and none had T-Cell Lymphoma. About 9% of patients were asymptomatic and 91% symptomatic. Gastrointestinal symptoms (diarrhea in 60%, weight loss in 24%, and 17% of patients with abdominal distension), non- gastrointestinal symptoms like skin disorders (dermatitis herpetiformis) were diagnosed in 4 patients 4%. While, neuropsychiatric disorder (depression) was seen in 1 patient 1%, osteopenia in 2 patients 2% (low vitamin D and low serum Ca+2 and Mg+2), 5% of patients had raised AST and ALT, and prolonged PT in 3%.* ***Conclusion****. There was significant correlation between female patients having iron deficiency anemia and/or diarrhea to be celiac disease. Female patients present with iron deficiency anemia and / or diarrhea should be routinely screened for celiac disease by serological tests and then confirmed by endoscopic small bowel biopsies.*

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## INTRODUCTION

Celiac disease characterized by abnormal intestinal mucosa, histologic severity ranges from a mild alteration characterized by increased intraepithelial lymphocytes (type 0 lesion) to flat mucosa with total mucosal atrophy, complete loss of villi, enhanced epithelial apoptosis and crypt hyperplasia (type 3 lesion), and type 4 lesion is a characteristic of T- Cell lymphoma which is the most serious complication of celiac disease [1]. The condition occurs worldwide and it is a common cause of malabsorption with a significant geographic variation in incidence [2]. The frequent intra-familial occurrence and the remarkably close association with the HLA-DQ2 and |or DQ8 gene locus provide the basis of our current understanding of celiac disease, as an immune disorder that is triggered by an environmental agent (the gliadin component of gluten) in genetically predisposed individuals [3,4]. Celiac disease is associated with other auto immune diseases such as type I diabetes mellitus, thyroid disease, and liver disease [5]. Recent studies using serological testes, however suggest that the disease is more common than before maybe because of the availability of serological tests and upper GIT endoscopy for small bowl biopsy [6]. The disease is classified to classic disease, latent disease and potential celiac disease [7].

The clinical manifestation in the disease often presents between the ages of ten and forty [8]. The disease manifestation is either as: subclinical disease (patients with mild or unspecific symptoms) or by gastro intestinal manifestation including diarrhea with bulky, Foul-smelling floating stool due to steatorrhea, Flatulence. These symptoms are paralleled by the consequence of malabsorption such as growth failure in children, weight loss due to excess loss of intestinal cells and |or malabsorption of peroxidase containing food, severe anemia, neurological disorders from deficiencies of vitamins B and Ig

A tissue transglutaminase deposition around vessels predominantly in the cerebellum, osteopenia from deficiency of vitamin D and calcium, and hyposplenism [9].
The presentation is variable depending on the severity and extent of small bowel involvement [10]. Serum autoantibodies: Serologic studies are now used to further confirm the diagnosis of Celiac disease, these [include the ELISA for Ig A antibodies to gliadin and the immunofluorescence test for Ig A antibodies to endomysium, a structure of the smooth muscle connective tissue, the presence of which is virtually pathognomonic for Celiac disease, the target autoantigen contained within the endomysium was identified as tissue transglutaminase which are highly sensitive and specific [11]. The aim of the current study was to describe the clinical and biochemical profile of adult Libyan celiac disease patients.

## METHODS

### *Study design and setting*

During the study period from 2011 to 2020, about 533 patients with symptoms and signs of iron deficiency anemia of obscure origin referred to the gastroenterology department (endoscopy unit) in Tripoli university hospital as suspected celiac disease patients with different presentations and from different departments and outpatient clinics (from indoor and outdoor the hospital) were included in the current study. All of them were subjected to full history of gastro-intestinal symptoms of celiac disease like diarrhea, weight loss, abdominal distension, dermatitis herpetiformis and depression. Consent form of all participants were obtained.

### *Data collection procedure*

Clinical examination and investigations were collected, such as; complete blood picture, serum ferritin, serum iron, liver function test, prothrombin time, vitamin D level, serum Ca+2 and Mg+2, patients. Serological tests include anti-gliadin and anti-endomysial antibodies (Ig A, IgG) were also screened, and all patients did an upper GIT endoscopy and histological finding for celiac disease were investigated using biopsy specimen taken from the second part of duodenum. The diagnosis was confirmed by both histopathological and serological tests.

### *Statistical analysis*

Medical records obtained from the included participants were reviewed and the relevant data for the purpose of this study were obtained in predesigned case sheet. The collected data analyzed using statistical package for the social sciences (SPSS Inc.Released2007.SPSSfor Windows, Version 16.0, Chicago, SPSS Inc.)), and descriptive statistics were used as mean, SD, and percentage. Chi square test was used to find the significance of difference between categorical variables, and p value less than 0.05 were considered significant.

## RESULTS

During the study period from (2011 to 2020), a total of 100 patients (19%) of cases with iron deficiency anemia of obscure origin were diagnosed as cases of celiac disease by both serological and histopathological tests. While, 388 patients (73%) were non-celiac disease, and 45 patients (8%) were diagnosed according to duodenal biopsy as potential celiac disease (were there positive serology and intact villous architecture according to marsh classification). There were 88 female patients (88%) and 12 patients were males (12%). Patient age during the study ranged from 15 years to 45 years (mean patient age 30 years), 9% of the patients were asymptomatic and 91% were symptomatic (Table 1).

***Table 1. Clinical features of Libyan patients with Celiac disease (Tripoli University hospital 2011-2020)***

| Character | No. (%) |
|---|---|
| **Asymptomatic** | 9 (9%) |
| **Anemia** | 100 (100%) |
| **Diarrhea** | 60 (60%) |
| **Weight loss** | 24 (24%) |
| **Abdominal distension** | 17 (17%) |
| **Dermatitis herpetiformis** | 4 (4%) |
| **Depression** | 1 (1%) |

In table 2, all symptomatic patients present with symptoms and signs of anemia like headache, malaise and general fatigue, gastrointestinal symptoms (diarrhea in 60%, weight loss in 24%, and 17% of patients with abdominal distension). Non-

gastrointestinal symptoms like skin disorders (dermatitis herpetiformis) diagnosed in 4 patients, and neuropsychiatric disorder (depression) in 1 patient. All patients with iron deficiency anemia (Hb less than 10gm/dl) & 3% with low platelets, and 5% of patients had raised AST and ALT, and 3% of patients had prolonged PT. Osteopenia was reported in 2 patients (low vitamin D and low serum Ca+2 and Mg+2).

Flat mucosa with total mucosal atrophy, complete loss of villi, enhanced epithelial apoptosis and crypt hyperplasia (type 3 lesion) was the commonest (62%) histopathological feature in our celiac disease subjects. While, subtotal villous atrophy was noted in 38% subjects, and none of them had T-cell lymphoma. Anemia and diarrhea were more common in females. There was a significant relation between female patients having anemia (Hb less than 10gm/dl) and diarrhea in celiac disease patients, the chi square test was applied to test if there is any relation between diarrhea in female patient with Hb less than 10gm/dl, (p= 0.019). Moreover, there was significant correlation in celiac disease female patients having iron deficiency anemia hemoglobin less than 10gm/dl and diarrhea.

***Table 2. Biochemical features of Libyan patient with Celiac disease (Tripoli University hospital 2003-2013)***

| Character | No. (%) |
|---|---|
| **Hb less than 10gm\dl** | 100 (100%) |
| **Low Platelets** | 3 (3%) |
| **Raised AST&ALT** | 5 (5%) |
| **Prolonged PT** | 3 (3%) |
| **Low Vitamin D** | 2 (2%) |
| **Low $Ca^{+2}$** | 2(2%) |
| **Low $mg^{+2}$** | 2(2%) |

## DISCUSSION

During the study period (from 2011 to 2020), a total of 533 patients with iron deficiency anemia of obscure origin referred to the gastroenterology department (endoscopy unit) in Tripoli university hospital as suspected celiac disease patients with different presentations and from different departments and outpatient clinics. These patients present to endoscopy unit with symptoms and signs of anemia as headache, malaise, general fatigue and pallor. All of them underwent upper GIT endoscopy and small bowel biopsy was taken from the second part of duodenum, and serological tests (anti-gliadin and anti-endomysial anti-bodies IgG and IgA) were taken. About 388 patients were non-celiac with different diagnosis such as esophagitis, gastritis, duodenitis, peptic ulcer disease and cancer, 100 patients 19% were ultimately diagnosed as cases of celiac disease and 45 patients 8% were diagnosed according to duodenal biopsy as potential celiac disease (where there was positive serology and intact villous architecture according to march classification).

In this study flat mucosa with total mucosal atrophy, complete loss of villi, enhanced epithelial apoptosis and crypt hyperplasia (type 3 lesion) was the commonest (62%) histopathological feature subtotal villous atrophy was noted in 38% subjects. None of them had T-cell lymphoma. Most of celiac patients have the symptoms and signs of anemia at the time of diagnosis like fatigue, malaise and pallor. Iron is a key micro- nutrient that may be depleted in children and adults with celiac disease. Iron deficiency anemia may also complicate well-defined celiac disease, or actually represent the initial extra-intestinal clinical feature [12].

Similar study result showed that 6 of 84 patients (7.14%) with iron deficiency anemia of obscure origin had serological and histopathological finding correlated with celiac disease, clinician should consider celiac disease as a possible cause of anemia in all patients with iron deficiency anemia of obscure origin even in menstruating women, serologic screening tests should be performed in pre-menopausal women with iron deficiency anemia especially when anemia is refractory to oral iron treatment [13]. About 60 subjects 60% of these celiac patients complaining also from diarrhea. Diarrhea is the most common symptom in untreated celiac disease and is present in 45-85% of all patients, diarrhea caused by celiac disease is due to the maldigestion and malabsorption of nutrients [14]. Diarrhea is the most common distressing symptom among individuals with celiac disease. Two studies have shown that roughly 75 to 80% of individuals with the disease reported experiencing diarrhea [15]. Other gastrointestinal symptoms include weight loss in 24 subjects 24% and abdominal distension in 17 subjects 17%, and non-gastrointestinal symptoms like skin disorders (dermatitis herpetiformis) in 4 subjects 4% and neuropsychiatric disorder (depression) in 1 subject 1%, 2% with osteopenia (low vitamin D and low serum Ca+2 and low serum Mg+2), 5% of celiac disease patients had raised AST and ALT and 3% had prolonged PT.

It is evident in this case series that most patients who seek medical advice and diagnosed to have celiac disease were females 88%. Female are predominantly associated with celiac disease with female to male ratio 3.6:1, efforts have been made to explain this predominance in female gender. Firstly, the female body undergoes menstrual cycle and pregnancy, those usually lead to anemia which can make the signs and symptoms of celiac disease more prominent. Secondly, females usually go to hospital more than males go, and disease are commoner in females than males overall [16]. Approximately, 19% of patients present to endoscopy department with iron deficiency anemia of obscure origin have Celiac disease and 60% of these celiac disease patients complaining of diarrhea.

From these results it is clear that there is relation between female patients having iron deficiency anemia (Hb less than 10gm/dl) and diarrhea in celiac disease, the chi square test was applied to test if there is any relation between diarrhea in female patient with Hb less than 10gm/dl, ($p = 0.019$). So, there is significant correlation between female patients having diarrhea and hemoglobin less than 10gm/dl in celiac disease.

## CONCLUSION

There is significant correlation between female patients having iron deficiency anemia and / or diarrhea to be celiac disease. Female patients present with iron deficiency anemia of obscure origin and / or diarrhea should be routinely screened for Celiac disease by serological tests and then confirmed by endoscopic small bowel biopsies.

### *Disclaimer*

The article has not been previously presented or published.

### *Conflict of Interest*

There are no financial, personal, or professional conflicts of interest to declare.

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