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Prevalence of celiac disease in Libyan patients with iron deficiency anemia (Tripoli University hospital 2011-2020)

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Abstract:

Background: Celiac disease is a long-term immune disorder that primarily affects the small intestine due to a permanent sensitivity to gluten in genetically susceptible people .Iron deficiency anemia is the most widely experienced in humans .Iron deficiency anemia additionally is a common extra intestinal manifestation of celiac disease.
Aim: Todetermine the prevalence of celiac disease in patients with iron deficiency anemia.
Method: in this case series study 533 patients with diagnosis of iron deficiency anemia of obscure origin were included in the study, all patients were subjected to full history of gastrointestinal symptoms of celiac disease, complete blood picture, serum iron, serum ferritin, patients were also screened by serological tests include anti-gliadin and anti-endomysial antibodies, upper gastrointestinal endoscopy was done and a histologic finding for celiac disease were investigated in biopsy specimen taken from the second part of duodenum, the diagnosis was confirmed by both histopathological and serological tests.

Result: Thepresent study showed that the total number of celiac disease patients was 100 patients about 19% of cases with iron deficiency anemia were ultimately diagnosed as cases of celiac disease while 388 patients 73% were non –celiac disease and 45 patients 8% were diagnosed according to duodenal biopsy as potential celiac disease (where there was positive serology and normal histopathology),88 patients were females (88%) and 12 patients were males (12%).Patient age during the studywere 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,9% of patients were asymptomatic and 91% symptomatic.

Conclusion: There is significant correlation between iron deficiency anemia and celiac disease and all patients especially females with iron deficiency anemia of obscure origin should be screened for celiac disease by serological and histopathological tests.

Recommendations: patients present with iron deficiency anemia of obscure origin should be routinely screened for celiac disease by serological tests and then confirmed byendoscopic 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), type 4 lesion is characteristic of T Cell lymphoma [(1)].

The condition occursworldwide and it is a common cause of malabsorption with asignificant geographic variation in incidence [(2)].The frequent intra-familial occurrence and the remarkably close association with the HLA-DQ2 and ǀor DQ8 gene locus provide the basis of our current understanding of celiac disease[(3)] as an immune disorder that is triggered by an environmental agent (the gliadin component of gluten) in genetically predisposed individuals[(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 iseither 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 ǀor 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 studiesare 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)].

Patient and methods:

During the study period from 2011 to 2020 the patients referred to the gastroenterology department in Tripoli university hospital (endoscopy unit) were 533 patientswith a diagnosis of iron deficiency anemia of obscure originwith different presentations and from different departments and outpatient clinics(from indoor and outdoor the hospital) , all patients were subjected to full history of gastrointestinal symptoms, complete blood picture, serum iron, serum ferritin, upper gastrointestinal endoscopy was done and histological finding of celiac

disease were investigated in biopsy specimen taken from the second part of duodenum of all patients, also these patients were screened by serological tests which include anti-gliadin and anti-endomysial antibodies (immunoglobulin A and immunoglobulin G) and the diagnosis was confirmed by both histopathological and serological tests. The medical records of these patients reviewed and the relevant data for the purpose of this study obtained and the predesigned case sheet completed, the collected data analyzed using statistical program (SPSS) version 16, andDescriptive statistics were used as mean, SD, and percentage. Chi square test was used to find the significance of difference between categorical variables, a p value less than 0.05 considered significant.

Result:

During the study period from 2011 to 2020 for 533 patients with iron deficiency anemia of obscure origin the total number of Celiac disease patients was 100 patientsabout 19%of cases, and 388 patients which represent 73% were non-celiac (with deferent diagnosis as esophagitis, gastritis, duodenitis, peptic ulcer disease, and cancer), and 45 patients 8% were diagnosed according to duodenal biopsy as potential celiac disease (were there was positive serology and normal histopathological study). 88 patients were females (88%) and 12 patients males (12%).

Patient age during the studyranged from 15 years to 45 years (mean patient age 30 years),9% of the patients were asymptomatic and 91% were symptomatic, for those symptomatic patients they presents with symptoms and signs of anemia like malaise and general fatiquablity(hemoglobin less than 10gm/dl) andserum iron and serum ferritin was low for all patients ..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, subtotal villous atrophy was noted in 38% subjects. None of them had T-cell lymphoma. the chi square test was applied to test if there is any relation between anemia in female patient with Hb less than 10gm/dl and celiac disease, the ($p= 0.019$) so there is significant correlation between female patients having anemia with hemoglobin less than 10gm/dl and celiac disease. Other studies including some references in this article discuss the prevalence of celiac disease in patients with iron deficiency anemia of obscure origin have the same result [13,17], so our study is a confirmation of the finding.

Table 1: Hematological profile of celiac disease patients (Tripoli University hospital 2011-2020)

type	No. (%)
Hemoglobin	< 10gm/dl
Serum Iron	< 8µmol/l
Serum Ferritin	< 30µg/l

Table 2: Relation between iron deficiency anemia and celiac disease (Tripoli University hospital 2011-2020)

Character	No. (%)
Iron deficiency anemia	533 (100%)
Celiac disease	100(19%)
Non-celiac disease	388 (73%)
Potential celiac disease	45 (8%)

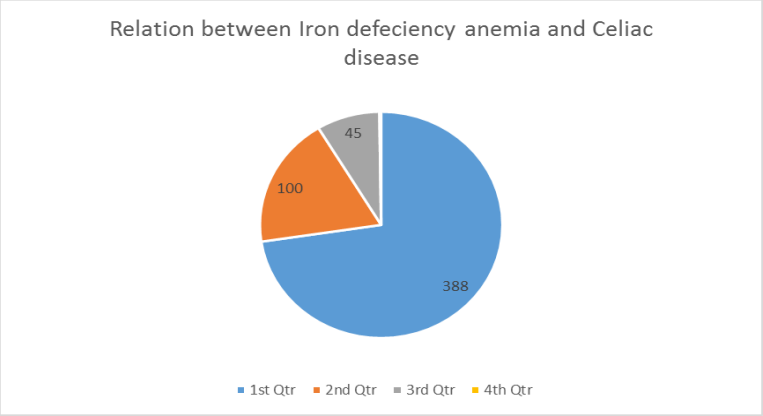
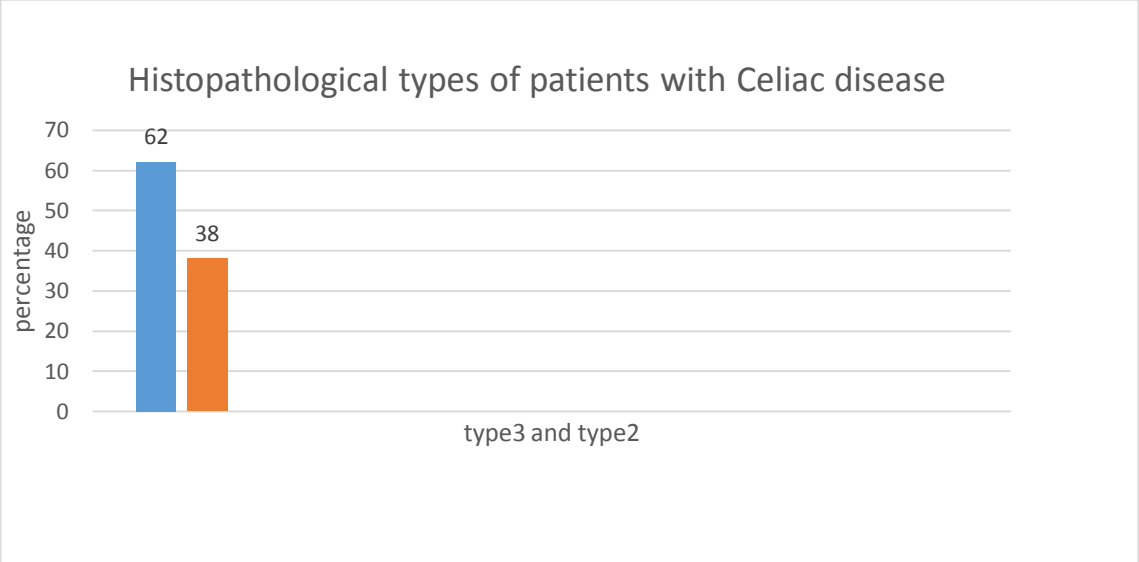


Table 3: Histopathologicalfeatures of patients with Celiac disease (Tripoli University hospital 2011-2020)

Character	No. (%)
Total villous atrophy (type 3 lesion)	**62 (62%)**
Subtotal villous atrophy (type 2 lesion)	**38 (38%)**



Discussion:

During the study period from 2011 to 2020 the patients number were 533 and all of them have iron deficiency anemia of obscure origin referred to the gastroenterology department 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) , 100 patients 19% ultimately diagnosed as cases of celiac disease and 388 73% of these patients were non-celiac disease and 45 patients 8% were diagnosed as potential celiac disease.

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].

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].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]

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].

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

Conclusion:

There is significant correlation between female patients having iron deficiencyanemia to be celiac disease.

Recommendations:

Female patients presentwith iron deficiency anemia of obscure origin 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, and is not part of a thesis project.

Conflict of Interest

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

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