PREVALENCE OF CELIAC DISEASE AMONG PATIENTS WITH IRON DEFICIENCY ANEMIA: PERSONAL EXPERIENCE AND REVIEW OF LITERATURE

Abbas Ali Mansoor [1] & Sarkis K. Strak [2]

ABSTRACT

Background: Iron Deficiency Anemia (IDA) is one of the most common presenting features of Celiac Disease (CD).

Objective: The aim of this study is to find the prevalence of CD among patients with otherwise unexplained IDA and review the literatures.

Setting: Al-Faiha & the Basrah Teaching Hospitals in Basrah for the period from May to December 2004.

Methods: This was a cross sectional study of patients with IDA. Gastroduodenoscopy was performed to determine the cause of anemia. Four biopsies were taken from the second part of duodenum. Small intestinal histologic features were interpreted according to the revised Marsh criteria. Total number of patients was 47, 28 males and 19 females, with a mean age of 26.9±13.3 years.

Results: Twenty of 47 patients (42%) had biopsy result consistent with CD. All CD patients were at age of 28 year and below, except one who was 45 year of age. Out of 20 CD patients, 16 were having Marsh grade IIIB and 4 with Marsh grade IIIC. Fourteen were males and 6 were females

Conclusion: All patients with other wise unexplained IDA should have upper gastrointestinal endoscopy with at least four biopsies from the duodenum to exclude CD.

Key words: Celiac Disease (CD), Iron Deficiency Anemia (IDA), duodenal biopsy

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INTRODUCTION

Celiac Disease (CD) is an immune-mediated enteropathy triggered by the ingestion of gluten-containing grains (including wheat, rye, and barley) in genetically susceptible persons.[1] Adult and adolescent patients with CD may present with symptoms in almost any hospital department.[2]

Iron Deficiency Anemia (IDA) is one of the most common presenting features of CD.[3] IDA is also common at the diagnosis in patients with CD.[4] Iron deficiency with or without anemia, typically refractory to oral iron supplementation, can be the only presenting sign of CD, [5] although as many as one half of anemic patients with untreated CD have iron deficiency.[6-10]

In 2000, The British Society of Gastroenterology proposed that all adult male patients and postmenopausal female patients, without overt blood loss or any other obvious cause of IDA, should undergo upper gastrointestinal endoscopy, including duodenal biopsy, and colonoscopy or barium enema, with or without flexible sigmoidoscopy.[11]

Screening for CD in patients with common symptoms of irritable bowel syndrome, IDA, unexplained arthritis, and even chronic elevations of aminotransferases is becoming the accepted standard of practice.[11-13]

The potential advantages of screening for asymptomatic CD include a reduction in risk for

1. Dr. Abbas Ali Mansour MD
2. Dr. Sarkis K. Strak FRCP
1-2: Department of Medicine,
Basrah College of Medicine,
Basrah, IRAQ

Correspondence:

Dr. Abbas Ali Mansour
Hattin Post Office Box: 142,
Basrah-42002 IRAQ
E-mail: aambaam@yahoo.com

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enteropathy-associated T-cell lymphoma, a reversal of unrecognized nutritional deficiency states, resolution of mild or ignored intestinal symptoms, avoidance of other auto-immune disorders, and an improvement in general well-being.[14] Proximal intestinal biopsies remain the gold standard for diagnosing patients with suspected CD.[15] The characteristic histological features of proximal small bowel villous atrophy (either total or subtotal) with associated crypt hyperplasia and intraepithelial lymphocytosis are the hallmark of diagnosing CD. Many gastroenterologists do not take a follow-up biopsy specimen and the cost-effectiveness of this approach has not been demonstrated. Most clinicians also do not undertake formal gluten challenge to show the resultant deterioration of the small intestinal villous architecture. However, gluten challenge should be performed if there is any doubt concerning the correct diagnosis.[2]

The aim of this study was to find the prevalence of celiac disease among patients with otherwise unexplained IDA and reviewing the literatures.

PATIENTS AND METHODS

This was a cross sectional study of patients with IDA carried in Al-Faiha and the Basrah Teaching Hospitals in Basrah for the period from May to December 2004. IDA was defined as hemoglobin < 12 g/dl, with hypochromic microcytic morphology, normal hemoglobin electrophoresis, and depleted marrow iron stores (done for 40 patients).

Patients were excluded if they had other significant gastrointestinal diseases like history of surgery or history of frank blood loss during the past three months. Background data were collected from all patients, and gastroduodenoscopy was performed to determine the cause of anemia. Four biopsies were taken from the second part of duodenum. Small intestinal histologic features were interpreted according to the revised Marsh criteria[16-19]. This scoring system comprises a spectrum of consecutive mucosal abnormalities that can be seen in gluten- sensitive enteropathy. Marsh 0 is described as normal mucosal architecture, without significant intraepithelial lymphocytic infiltration. Marsh I (lymphocytic enteritis) is normal mucosal architecture with a marked infiltration of villous epithelium by lymphocytes; marked is defined as more than 30 lymphocytes per 100 enterocytes. Marsh-II (lymphocytic enteritis with crypt hyperplasia) consists of intraepithelial lymphocytosis and elongation and branching of crypts in which there is an increased proliferation of epithelial cells. Marsh-III comprises intraepithelial lymphocytosis, crypt hyperplasia, and villous atrophy. There are three distinct stages of villous atrophy.[18, 19] In Marsh IIIA, partial villous atrophy, the villi are blunt and shortened. Arbitrarily, samples classified as partial villous atrophy if the villus-crypt ratio was less than 1:1. In Marsh IIIB, subtotal villous atrophy, villi are clearly atrophic, but still recognizable, and in Marsh IIIC, total villous atrophy, villi are rudimentary or absent, and the mucosa resemble colonic mucosa. Although characteristic histological features of proximal small bowel villous atrophy (either total or subtotal) with associated crypt hyperplasia and intraepithelial lymphocytosis are the hallmark of diagnosing CD, [15] only Marsh IIIB and C, were considered as having CD and started gluten free diet.

Total number of patients was 47, 28 males and 19 females with mean age of 26.9±13.3 years.

RESULTS

Twenty (42%) patients had biopsy result consistent with CD (Table-I). All CD patients were younger than 28 year, except one patient who was 45 year of age. Out of 20 CD patients, 16 had Marsh grade IIIB and 4 with Marsh grade IIIC. Fourteen were males and 6 were females. Thirteen male had Marsh grade III B while one male had grade IIIC changes. Three females each had Marsh grade IIIB and grade IIIC changes.

DISCUSSION

Celiac Disease may be a surprisingly frequent cause of IDA, which requires duodenal biopsy to confirm the diagnosis. The finding of endoscopic lesions such as esophagitis and gastri-

Table-I: Histological findings in the studied patients.

	No.	*%*
Normal	6	12.8
Duodenitis	5	10.7
Marsh grade I	0	0.0
Marsh grade II	0	0.0
Marsh grade IIIA	16	34.0
Marsh grade IIIB*	16	34.0
Marsh grade IIIC*	4	8.5
Total	47	100

* Celiac patients

tis,that may otherwise explain IDA should not preclude small bowel biopsy and thus delay the discovery of CD[8, 20, 21]. Accordingly some recommended screening for CD in patients with unexplained IDA even when there is local cause for bleeding in the gut.[22]

CD is not an uncommon cause of IDA in patients >65 years and in children below the age of 12 years.[23,24] In this study, only one patient with CD was 45 years of age.

To increase the diagnostic yield of CD we have obtained 4 biopsies from the second part of the duodenum, since histological changes can be patchy[15]. However some patients with CD had biopsies which are not consistent with CD, the so-called potential CD. These patients might show immunologic abnormalities characteristic for the disorder (e.g., positive IgA or IgG to endomysium, and IgA or IgG tissue transglutaminase antibodies, now recognized as the offending endogenous antigen in CD)[25], a "celiac intestinal antibody pattern," and increased intraepithelial lymphocytes .[26] The reason why both IgA and IgG antibodies are used in the diagnosis of CD, is that those people are at least five times more frequently IgA deficient than healthy control subjects, and appropriate screening for CD requires measurement of endomyseal or tissue transglutaminase antibodies and IgA.[27]Unfortunately these autoantibodies were not available at the time of this study was conducted to aid the diagnosis in those patients with negative histology.

The prevalence of CD in this study was 42% compared to other studies (Table-II). The differences between studies may be due to various factors, including age, disease prevalence in the country of origin, and referral bias, [8-24] together with different diagnostic tools used for the diagnosis. For instances in some centers the presence of a few inflammatory cells in an otherwise normal epithelium is sufficient to make the diagnosis in a seropositive patient.[17, 19, 28]

Table-II: Prevalence of CD among patients with IDA (literature review)

	Total study sample	*%of CD*
[8]Ackerman et al Jerusalem	93	11.8
[22]Karnam et al USA	105	2.8
[21]Grisolano et al	103	8.7
[29]Patterson et al Northern Ireland	44	7
[30]Howard et al	258	4.7
[23]Mandal et al UK	504	1.8
[5]Carroccio et al	85	6
[24]Karyda et al Greek	70	20
[7]Bampton et al	79	0.0
[5]Carroccio et al	85	6
[31]Kepczyk et al	70	5.7
[32]Yates et al UK	263	2.2
[33]Al-Hilli et al Baghdad	60	31.7
[34]Hashim et al Basrah	25	88
This study (Basrah)	47	42

Whilst the classic presentation of CD with diarrhoea and malabsorption has become relatively rare (prevalence from 1 in 2000 to 1 in 10 000 in the west), atypical, oligosymptomatic, or even asymptomatic manifestations (with patients having villous flattening of various degrees) are frequent, with an estimated prevalence of 1 in 200 in Europe and the USA, making CD one of the most common inherited disorders. Untreated patients with oligosymptomatic like IDA or asymptomatic CD are of concern, since they might have an increased risk of disease exacerbation later, secondary autoimmune disorders, and gastrointestinal or haematological cancers.[1, 2]

In conclusion, all patients with other wise unexplained IDA should have endoscopy with

at least four biopsies from the duodenum to exclude CD.

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