**University of Thi – Qar**

 **College of medicine**

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**The prevalence of celiac disease in iron deficiency anemicpatients in Thi \_Qar 2018**

**: A prospective study**

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***Abstract:***

**Background –celiac disease is an immune –mediated enteropathy due to a permanent sensitivity to gluten in genetically susceptible people.Iron deficiency anemia is the most common experienced anemia in humans.IDA additionally is a common extra-intestinal manifestation of celiac disease.**

**Objective: The aim of this study is to find the prevalence of CD among patients with otherwiseunexplained IDA, to determine the sensitivity of endoscopy to detect celiac disease .and to identify the GIT causes of anemia in those patients.**

**Setting: Al-Nasirrhea & Al-Hussien Teaching Hospitals in Thi-Qar for the period from Augest to December2018.**

**Methods: This was a cross sectional study of patients with IDA. Esophageo Gastroduodenoscopy& colonoscopy were performed**

**to determine the cause of anemia. Four to six biopsies were taken from the second part ofduodenum. Small intestinal histologic features were interpreted according to the modified Marshcriteria. Total number of patients was 308 ,**

**82 males and 226 females . in all age groups.**

**Results: 78 of 308 patients (25.3%) had biopsy result consistent with CD. Most CD patients were at between**

**15 and 45 years(72 %) , 23% were bove 45 year of age. And 4.5% below !5**

**Out of 78 CD patients, 35 were**

**having Marsh grade III A ,23 had Marsh III B ,14 with Marsh grade IIIC, 5with Marsh II and one patients had Marsh I. Twenty were males and fifty-eight were females.**

**Conclusion:Clinicians should consider celiac disease as a possible cause of anemia in all patientswith iron deficiency anemia of obscure origin, even in menstruating women. Serologic screening tests should be performed in premenopausalwomen with iron deficiency anemia, especially when anemia is refractory to oral iron treatment All patients with other wise unexplained IDA should have upper gastrointestinal endoscopywith at least four biopsies from the duodenum to exclude CD.**

***Introduction***

**Celiac disease is a chronic, small intestinal, immune-mediatedenteropathy that is precipitated by dietary gluten in genetically predisposed individual[[1]](#footnote-1).Gluten is the commonly usedterm for the complex of water-insoluble proteins from wheat,rye, and barley that is harmful to patients with celiac disease.Celiac disease is characterized by villus atrophy of the smallintestinal mucosa associated with malabsorption of nutrients,prompt clinical and subsequent histological improvementafter strict adherence to a gluten-free diet (GFD), and clinicaland histological relapse when gluten is reintroduced[[2]](#footnote-2).Traditionally patients with CD presented with malabsorptiondominated by diarrhea , steatorrhoea, weight loss or failure tothrive (‘classical CD’)[[3]](#footnote-3) but over time the proportion of newlydiagnosedpatients withmalabsorptivesymptomshas’decreased[[4]](#footnote-4),and ‘non-classical including anaemia , vague abdominal symptoms (often similar)to irritable bowel syndrome (IBS ,neuropathy ,ataxia ,Depression ,short stature , osteomalacia and osteoporosis ,,outcome liver disease adverse pregnancy and lymphoma[[5]](#footnote-5).Asymptomatic patients are typically diagnosed through screening.Screening may be initiated because the individual has a CD-associated disorder or has symptoms and is a first-degreerelative to a patient with CDNewly diagnosed patients withCD can present with a wide range of symptoms and signs,Celiac disease affects the mucosa of the small intestine;the submucosa, muscularis propria, and serosa usually arenot involved. The mucosal lesion can vary considerably inseverity and in extent.Examination under magnification ofthe small intestinal mucosal surface in severe untreatedceliac disease reveals a flat mucosal surface with completeabsence of normal intestinal villi. Histological examination oftissue sections confirms this loss of normalvillus structure .The intestinal crypts are markedly elongatedand open onto a flat absorptive surface. The total thicknessof the mucosa may be reduced only slightly, becausecrypt hyperplasia compensates for the absence or shorteningof the villi. These architectural changes decrease theamount of epithelial surface available for digestion and absorption[[6]](#footnote-6).Celiac disease is a histological diagnosis, and, in patientsin whom there is certainly a clinical concern of theproblem, small bowel biopsy remains the first diagnosticmethod. Some assays for the diagnosis of celiac relevantantibodies are available, and, although these serologicaltests do not exchange the require for small intestinal biopsy for recognition, they could be extremely helpful an adjunct to diagnosis. Positive antibody tests mighthelp guide clinicians towards biopsy in patients at highrisk of improving celiac disease or inpatients with a lowindex of suspicion for the disease[[7]](#footnote-7).Iron Deficiency Anemia (IDA) is one of themost common presenting features of CD[[8]](#footnote-8).IDAis also common at the diagnosis in patients with CD[[9]](#footnote-9).Iron deficiency with or without anemia,typically refractory to oral iron supplementation,can be the only presenting sign ofCD[[10]](#footnote-10). although as many as one half of anemicpatients with untreated CD have iron deficiency[[11]](#footnote-11).In 2000, The British Society of Gastroenterologyproposed that all adult male patients andpostmenopausalfemale patients, without overtblood loss or any other obvious cause of IDA,should undergo upper gastrointestinal endoscopy,including duodenal biopsy, andcolonoscopy or barium enema, with or withoutflexible sigmoidoscopy[[12]](#footnote-12).Anemia is a common manifestation of celiac disease in childrenand adults and usually is caused by impaired iron orfolate absorption from the proximal intestine; in severe disease with ileal involvement, vitamin B12 absorption also is impaired.Coagulopathy resulting from impaired intestinal absorptionof fat-soluble vitamin K occurs rarely, and in such casesbleeding can aggravate preexisting anemia[[13]](#footnote-13).Iron deficiency anemia is experienced by 2-5% of men and postmenopausal women and 5-12%of premenopausal women in the UK at any time[[14]](#footnote-14), but occurs in some 30-50% of patients with coeliac disease at diagnosis[[15]](#footnote-15). NICE Guidance for the recognition, assessment and managementof coeliac disease recommends that GPs screen patients with recurring or unexplained iron, B12or folate deficiency anaemia for celiac disease[[16]](#footnote-16).].Diagnosis of CD is by serology and duodenal biopsy, ideallywith the patient on a normal, that is, gluten-containing diet.Biopsy remains essential for the diagnosis of adult CD andcannot be replaced by serology. Exceptions are patients withcoagulation disorders and pregnant women, in whom biopsymay not be feasible or should be postponed until postpartum.To state definite diagnosis of CD, villous atrophy is required.However, lesser degrees of damage(=25 IELs but no villous atrophy)combined with positive serology (IgA-EMA, tissuetransglutaminase (TTG) or IgG-DGP) may also represent CD(‘probable CD’), and in these circumstances a trial with GFDmay be considered to further support the diagnosis of CD. HLAstatus may also aid diagnosis. Differential diagnoses of lymphocyticduodenosis should be ruled out if there is no response toGFD while consuming a gluten-containing diet, have positive serologyand a duodenal biopsy with obvious coeliac histology (increasedintraepithelial lymphocytosis, crypt hyperplasia and villousatrophy; table 1). These patients can immediately initiate a GFD with confidenc. The aim of this study was to to define the prevalence of CD in the gastroentology department of Al-Hussein teaching hospital in patients with IDA ,to determine the sensitivity of endoscopy to detect the changes in celiac disease and to identify the gastrointestinal pathology in patients with IDA .**

 ***Methods***

**this cross sectional study was conducted in Al-Nasirrhea city which is the main city of Thi-Qar govrnorate .All patients presented to the gastroentology department of Al -Hussein teaching hospital, from Augest to December were candidated for entery to this study. Inclusion criteria was IDA which defined as Hb < 12g/dl in women [normal 12 -16 g /dl] and less than 14 g/dl in men [normal 14 -18g/dl ] .Serum Ferriten<25 ng /ml [normal 25 -300 ng/ml ] . And mean corpuscular volume (MCV) <80 fl , with hypochromic microcytic morphology . Patients with obvious blood loss, such as those with a history of melena, hematochezia, hemoptysis,recurrent epistaxis, hematuria, trauma, pregnancy, hypermenorrhea (cycles ≥7 days), or menometrorrhagia, and those with alcoholism, gastric surgery, known chronic diseases (e.g. chronic liver disease, chronic renal failure, heart failure, collagen vascular disease, etc.), and hematologic diseases were excluded from the study. , upper gastrointestinal (GI) endoscopy was performed in all of the patients. In this study from 1763 patients who referred from private clinics and hospital,we found about 405 patients had unexplained IDA .age ,gender ,complaints , presence of other autoimmune diseases ,and serology if performed.**

**All patients with IDA of obscure origin underwent upper GI endoscopy . This procedure carried out byspecialist endoscopist using [Olympus EVIS GIT -Q24 OZ or SP 240] Gastroduodenal endoscopic examination, after an overnight fasting .Whole procedure was explained to the patients and informed consent was obtained. This examination was done by conscious sedation ( Diazepam , pethidine IV)and with general anesthesia for pediatrics. ,with 10% xylocaine pharyngeal spray was administered to regress the gag reflex , patient lied in left lateral position on the endoscopy couch with flexion of the head mouth piece was applied, monitoring devices for blood pressure , heart rate and oxygen saturation were performed during the procedure.Then the doctor placed the flexible tube through the mouth,when the patient swallow ,then the doctor gently advanced the scope down to the esophagus ,stomach , then when reached the duodenum ,the endoscopist gave special attention to the first and second part of the duodenum**

**Endoscopic features of celiac disease include mosaic pattern ,scalloped folds ,reduction in number or loss of fold and visible under lying blood vessels. For histopathological examination, 4-6 biopsies were obtained from the second section of the duodenum by endoscopic biopsy forceps. The duodenal biopsy specimens were fixed immediately in formalin solutions for 4-6 hours (h) at room temperature and were routinely processed for conventional histological evaluation. Small intestinal histologic features were interpreted according to the modefied Marsh criteria. 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 of celiac disease .then we went to the central laboratory in Al-Hussein teaching hospital to get the duodenal biopsy results.**

**Patient Demographics**

**Three hundred forty consecutive patients with iron-deficiency anemia were screened for the study. Three hundred eight of these patients met the inclusion and exclusion criteria and had follow-up data available for analysis. Thirty-five patients were excluded because of the following: history of overt gastrointestinal bleeding in the previous 3 months (n = 14), history of gastrointestinal malignancy (n = 10), uncooperative patients (n = 4), and non fasting patients(n = 4),in adequate biopsy ( n=3),**

**Statistical analysis was performed using Statistical Package for the SocialSciences (SPSS) software version 15.0, t-test for comparison of**

**the means of quantitative variables, chi-Square test for comparison**

**of qualitative variables and pearson’s chi-square test**

**for determine correlation of between two categorical variables.**

**P<0.05 was considered statistically significant**

**Results**

**From 1763 patients that attended the gastroentology department of Al\_Hussein teaching hospital in 2018 .about 308 patients had IDA , 226 were female (73.4%) and 82 were male (26.6%) ..with different age group fom 6 to 100 years.table 1 shows the age groups with obscure IDA .the mean serum ferriten was 8.6 ,HB was 8.04, MCV was 63.04 .Only 86 of these patients had brought with them their tests prior to endoscopy.72 had positive results .30 of them had positive ATTG IGA While 13 of them had positive ATTG IGg ,and 29 had positive both ATTG. All 308 patients with IDA underwent OGD examination .the endoscopy findings show in table 3 . we found that 111 patients (36.0) had**

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| --- | --- | --- | --- | --- |
| ***groups*** | ***frequency*** | ***male*** | ***female*** | ***percentage*** |
| **Less than 15** | **14** | **6** | **8** | **4.5%** |
| **15 to 30** | **127** | **37** | **90** | **41.2%** |
| **31 to 45** | **95** | **17** | **78** | **30.8%** |
| **46 to 60** | **39** | **9** | **30** | **12.7%** |
| **Above 60** | **33** | **13** | **20** | **10.7%** |
| **total** | **308** | **82** | **226** | **100.0%** |

 ***table 1 : the frequency of age groups according to the gender in IDA Patients***

**endoscopic features of celiac** disease ,and 197 patients (64.0)had normal duodenum. other common findings on upper endoscopy included gastropathy in 112 (37.1%),duodenal ulcer in15 (4.9%),hiatus hernia in 14 (4.5%) ,gastric erosions in 11 (3.6%),GERD in 7 (2.3%) ,gastric polyps in 5 (1.6%) ,esophageal web in 5 (2.3%) ,gastric ulcer in 4 (1.3%) ,gastric tumor in 3 (1.0%) ,bulb erosions in 3 (1.0%) ,diverticulae in 2 (0.6%)patients ,Brunner gland hyperplasia in2 (0.6%) esophageal candidiasis ,thick gastric mucosa and gastric mucosal atrophy also in 2 patients for each of them. gastric &duodenal ulcer in one patient 0.3 %, and esophageal varices ,GEJ lesion ,bulb duodenitis in one patient for each of them

|  |
| --- |
| **endoscopy** |
|  **Findings** | **Frequency** | **Percent** | **male** | **female** |
|  | **normal** | **115** | **37.3** | **22** | **93** |
| **gastropathy** | **112** | **36.4** | **34** | **78** |
| **gerd** | **7** | **2.3** | **3** | **4** |
| **haitus hernia** | **14** | **4.5** | **2** | **12** |
| **duodenal ulcer** | **15** | **4.9** | **4** | **11** |
| **gastric ulcer** | **4** | **1.3** | **0** | **4** |
| **gastric erosion** | **11** | **3.6** | **5** | **6** |
| **gastric &duod.ulcers** | **1** | **.3** | **0** | **1** |
| **brunner gland hypertrophy** | **2** | **.6** | **1** | **1** |
| **esophageal web** | **5** | **1.6** | **1** | **4** |
| **gastric polyp** | **5** | **1.6** | **3** | **2** |
| **diverticulum** | **2** | **.6** | **2** | **0** |
| **bulb erosions** | **3** | **1.0** | **2** | **1** |
| **gastric tumor** | **3** | **1.0** | **1** | **2** |
| **esophageal varices** | **1** | **.3** | **1** | **0** |
| **thick gastric mucosa** | **2** | **.6** | **0** | **2** |
| **GEJ lesion** | **1** | **.3** | **0** | **1** |
| **bulb duodenitis** | **1** | **.3** | **0** | **1** |
| **esophageal candidiasis** | **2** | **.6** | **1** | **1** |
| **gastric mucosal atrophy** | **2** | **.6** | **0** | **2** |
| **Total** | **308** | **100.0** | **82** | **226** |

***Table 2 : the OGD findings in the IDA patients.***



***Figure 1 :the endoscopic findings in the 2ndpart of the duodenum in IDA patients***

**.in the biopsy Celiac disease was found in 78 patients (20 male and 58 females), which accounted for 25.3% of all patients with iron-deficiency anemia in this study ,from 78 CD ,76 of them had serrated duodenal mucosa and only two patients had normal mucosa so the sensitivity of endoscopy is 97.4% and specificity is 29.7%. 55 of them had already positive serology and the rest was recommended to do the tests after biopsy**



***Figure 2 : the frequency of celiac disease in duodenal biopsy***



***figure 3 : the frequency of celiac disease in comparsionwith endoscopic feature***

**. From those 78 patients the most common finding in biopsy was Marsh III A in 35 (44.9 %)patients ,followed by 23(29.5 %) patients had Marsh III B , while Marsh III C in 14 (17.9 %) patients , 5 (6.5 %) had Marsh II ,and one patient(1.2 %) had Marsh I. We found also there were 12 patients with positive and endoscopic feature of celiac disease but had negative biopsy this may goes with potential celiac disease. we found about 6 patients had DM type one ,one patient with thyroid disease and one patient had wilsone disease & auto immune hepatitis . None of the most patients had diarrhea, skin rash, or other evidence of celiac disease, emphasizing the occult nature of this disease.**

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| --- | --- | --- |
| Marsh classification | Frequency | Percentage |
| Marsh I | 1 | 1.2 % |
| Marsh II | 5 | 6.5 % |
| Marsh III A | 35 | 44.9 % |
| Marsh III B | 23 | 29.5 % |
| Marsh III C | 14 | 17.9 % |
| Total | 78 | 100 % |

 |

***Table 3 : the Marsh classification of celiac disease & frequency***

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| --- |
| **Endoscopy \* biopsy Crosstabulation** |
|  | biopsy | Total |
| celiac | non celiac |
| Endoscopy | normal | Count | 2a | 195b | 197 |
| Expected Count | 49.9 | 147.1 | 197.0 |
| serrated | Count | 76a | 35b | 111 |
| Expected Count | 28.1 | 82.9 | 111.0 |
| Total | Count | 78 | 230 | 308 |
| Expected Count | 78.0 | 230.0 | 308.0 |
| Each subscript letter denotes a subset of biopsy categories whose column proportions do not differ significantly from each other at the .05 level. |

|  |
| --- |
| **Chi-Square Tests** |
|  | Value | df | Asymptotic Significance (2-sided) | Exact Sig. (2-sided) | Exact Sig. (1-sided) |
| Pearson Chi-Square | 170.814a | 1 | .000 |  |  |
| Continuity Correctionb | 167.266 | 1 | .000 |  |  |
| Likelihood Ratio | 187.869 | 1 | .000 |  |  |
| Fisher's Exact Test |  |  |  | .000 | .000 |
| Linear-by-Linear Association | 170.259 | 1 | .000 |  |  |
| N of Valid Cases | 308 |  |  |  |  |
| a. 0 cells (.0%) have expected count less than 5. The minimum expected count is 28.11. |
| b. Computed only for a 2x2 table |

**The most common colonoscopic findings were hemorrhoids. Colorectal cancer was found in only 3 (2.6%) of the 114 patients presenting with iron-deficiency anemia.44 were male and 66 were female**

|  |  |  |
| --- | --- | --- |
| *Colonoscopical findings* | *Frequency* | *Percentage* |
| Normal | **51** | **44.7 %** |
| Hemorrhoid | **31** | **27.2 %** |
| Polyps | **9** | **7.9 %** |
| Diverticulae | **4** | **3.5 %** |
| Colitis | **3** | **2.6 %** |
| Proctitis | **1** | **0.9 %** |
| Tumor | **3** | **2.6 %** |
| Polyps &diverticulae | **3** | **2.6 %** |
| Colonic erosion | **1** | **0.9 %** |
| Aphthus ulcer | **3** | **2.6 %** |
| Angectasiae | **2** | **1.8 %** |
| Worms infestation | **2** | **1.8 %** |
| Anal fissure & pile | **1** | **0.9 %** |
| Total | **114** | **100 %** |

***Table 4 :the colonoscopical findings in 114 patients with IDA***



***Figure 5 : the frequency of age groups among patient with IDA whom underwent colonoscopy***



***Figure 6 :the frequency of colonoscopic findings in IDA patients***

**Discussion**

**Celiac Disease may be a surprisingly frequent cause of IDA, which requires duodenal biopsyto confirm the diagnosis. The finding of endoscopiclesions such as esophagitis and gastritis,that may otherwise explain IDA should notpreclude small bowel biopsy and thus delay the discovery of CD [[17]](#footnote-17).Guidelines from the British Societyof Gastroenterology recommend that duodenalbiopsies should be taken during endoscopy if no obvious cause of IDA can be found [[18]](#footnote-18).To increase the diagnostic yield of CD wehave obtained 4 -6 biopsies from the second partof the duodenum, since histological changescan be patchy[[19]](#footnote-19).However some patients withCD had biopsies which are not consistent withCD, the so-called potential CD. These patients**

**might show immunologic abnormalities characteristicfor the disorder (e.g., positive IgA orIgG to endomysium, and IgA or IgG tissuetrans glutaminase antibodies, now recognized as the offending endogenous antigen in CD )[[20]](#footnote-20),a “celiac intestinal antibody pattern,”. Studies usingserologic tests and small-bowel biopsies in patientsreferred for evaluation of IDA have reported CD in1.8%-14.6% of patients [[21]](#footnote-21),[[22]](#footnote-22).This prevalencemay be especially high in those unresponsive to oral iron therapy [[23]](#footnote-23).In a sub-group study of patientswho did not respond to iron replacement, theprevalence of CD was found as 20% [[24]](#footnote-24),[[25]](#footnote-25).A positive CD-specifi c serology (TTG, DGP, and EMA) inpatients with villous atrophy confirms the diagnosis of CD[[26]](#footnote-26).A positiveserological test is supportive of the diagnosis but no single testis 100% specific for CD and the diagnostic accuracy varies dramatically between laboratories .The reasonwhy both IgA and IgG antibodies are usedin the diagnosis of CD, is that those people areat least five times more frequently IgA deficientthan healthy control subjects, and appropriatescreening for CD requires measurement ofendomyseal or tissue transglutaminase antibodies and IgA[[27]](#footnote-27).The prevalence 0f CD in this study is 4.3 % in 2018.while the prevalence of CD in IDA is 19.5 %.For instances in some centersthe presence of a few inflammatory cellsin an otherwise normal epithelium is sufficientto make the diagnosis in a seropositive patient[[28]](#footnote-28),[[29]](#footnote-29),[[30]](#footnote-30).In this study 12 of the patients seropositive and had normal or non specific duodenitis in histopathology. duodenosis[[31]](#footnote-31)Lymphocyticis a common condition (3.8% of aserology[[32]](#footnote-32))population negative for celiac seen in association with infection(particularly Helicobacter pylori),altered immune states, for example, common variable immune deficiency,autoimmune and chronic inflammatory disorders, drugs[[33]](#footnote-33),[[34]](#footnote-34)and neoplasiaThe villous architecture is normal, typicallythere is no crypt hyperplasia and IELs are=25/100enterocytes. Of note, in a single study 16% of cases of lympho Cyticduodenosis were found to have CD.A biopsy finding of villousatrophy is not specific for CD. Although CD is the commonest cause of villous atrophy, there are other causes for this reason the addition of coeliac-specific serology seals the diagnosis.The biopsies must be properly oriented (usually by anexperienced laboratory technician) as correct orientation isnecessary for assessment of villous height crypt depth ratio(derived from the well oriented fields of the biopsies).the following feature should state in report:Number of biopsies (including those from the duodenal)[[35]](#footnote-35)bulband orientation.The architectural features (normal, partial, sub-total or total villous atrophy).Comment on the content of the lamina propria (in CD theseare lymphocytes, plasma cells and eosinophils, and occasionallyneutrophils, but cryptitis and crypt abscesses shouldsuggest other pathology).Presence of Brunner’s glands.Presence of crypt hyperplasia, villous height: crypt depth[[36]](#footnote-36)ratio (3:1).The absence of plasma cells suggests commonvariable immunodeficiency.Evaluation of IELs (with immunocytochemical staining for Tcases[[37]](#footnote-37))cells (CD3) in equivocalis vital.Whilst the classic presentation of CD with diarrhoea and malabsorption has become relativelyrare (prevalence from 1 in 2000 to 1 in10 000 in the west), atypical, oligosymptomatic,or even asymptomatic manifestations (withpatients having villous flattening of variousdegrees) are frequent, with an estimated prevalenceof 1 in 200 in Europe and the USA, makingCD one of the most common inherited disorders.Untreated patients witholigosymptomatic like IDA or asymptomaticCD are of concern, since they might have anincreased risk of disease exacerbation later,secondary autoimmune disorders, and gastrointestinal or hematological cancers[[38]](#footnote-38),[[39]](#footnote-39)**

**conclusion**

**we found that the prevalence of CD in IDA patients was 25.4% and in all patients the prevalence was 4.4% in 2018 in this study, this outcomes**

**was obtained in conditions that the majority of patients**

**had not gastro intestinal symptoms. Therefore, serological**

**screening is recommended for early detection of CD in all**

**patients with u IDA. There are some important benefits**

**of CD screening in patients with IDA. It may prevent the**

**need for other often useless tests, treatment failure, and**

**intestinal lymphoma, since CD may easily be treated with**

**a gluten-free diet**.**.**

***references***

1.. Ludvigsson JF, Leffler DA, Bai JC, et al. The Oslodefinitions for coeliac disease and related terms. Gut 2013;

62:43-52..

2 .. Farrell RJ, Kelly CP. Celiac sprue. N Engl J Med 2002;346:180-8..

3.. Ludvigsson JF, Leffler DA, Bai JC, et al. The Oslo definitions for coeliac diseaseand related terms. Gut 2013;62:43–52 .

4.Rampertab SD, Pooran N, Brar P, et al. Trends in the presentation of celiacdisease. Am J Med 2006;119:355 e9 -14..

5.Bergamaschi G, Markopoulos K, Albertini R, et al. Anemia of chronic disease anddefective erythropoietin production in patients with celiac disease. Haematologica2008;93:1785–91

6.Rubin CE, Brandborg LL, Taylor HC Jr. Studies of celiacdisease: I. The apparent identical and specific nature of the

duodenal and proximal jejunal lesion in celiac disease andidiopathic sprue. Gastroenterology 1960; 38:28-49

7..Fasano A, Catassi C. Current approaches to diagnosis and treatment of celiacdisease: an evolving spectrum. Gastroenterology. 2001;120(3):636–51

8.Hin H, Bird G, Fisher P, et al. Coeliac disease in primarycare: case finding study. BMJ 1999; 318:164–7

9.Cluysenaer OJJ, vanTongerenJHM. MalabsorPtionin celiac sprue. The Hague: MartinusNijhoff, 1977

10. Carroccio A, Iannitto E, Cavataio F, Montalto G,Tumminello M, Campagna P et al. Sideropenic anemia

and celiac disease: one study, two points of view.Dig Dis Sci 1998;43:673–8

11.Hoffbrand AV. Anemia in adult celiac disease. ClinGastroenterol 1974;3:71-89 .

12.Goddard AF, McIntyre AS, Scott BB. Guidelines forthe management of iron deficiency anaemia. BritishSociety of Gastroenterology. Gut 2000; 46(IV):1–5

13. O’Grady JG, Stevens FM, Harding B, et al. Hyposplenismand gluten-sensitive enteropathy: Natural history,

incidence, and relationship to diet and small bowelmorphology. Gastroenterology 1984; 87:1326-31.

14. Goddard AF et al. (2011) Guidelines for the management of iron deficiency anaemia.

15.Ludvigsson J F et al. (2013) Use of computerised algorithm to identify individuals in need to testing for coeliac disease, J Am Med InformAssoc 20: e2; e306-e310

16.NICE Guideline NG20 Coeliac disease: recognition, assessment and management, September 2015.

17. Ackerman, Z, Eliakim, R, Stalnikowica, R,Rachmilewitz, D. Role of small bowel biopsy in the

endoscopic evaluation of adults with iron deficiencyanemia. Am J Gastroenterol 1996; 91: 2099

18.Goddard AF, McIntyre AS, Scott BB. Guidelines for themanagement of iron deficiency anaemia. British Society ofGastroenterology. Gut 2000; 46 (Suppl 3-4): IV1-IV5. Erratumin: Gut 2000 Dec; 47: 872..

19.Frenz MB, MeeAS.Making the diagnosis of celiac disease: is there a role for push enteroscopy?Eur J GastroenterolHepatol 2004, 16:1127–9.

20.Shan L, Molberg O, Parrot I, Hausch F, Filiz F, GrayGM et al. Structural basis for gluten intolerance inceliac sprue. Science 2002; 297:2275–9

21. Fernández-Bañares F, Monzón H, Forné M. A short reviewof malabsorption and anemia. World J Gastroenterol 2009;15: 4644-52. Review.

22. Zamani F, Mohamadnejad M, Shakeri R, et al. Gluten sensitiveenteropathy in patients with iron deficiency anemiaof unknown origin. World J Gastroenterol 2008; 14: 7381-5.

23. Corazza GR, Valentini RA, Andreani ML, et al. Subclinicalcoeliac disease is a frequent cause of iron-deficiency anaemia.Scand J Gastroenterol 1995; 30: 153-6

24. Karnam US, Felder LR, Raskin JB. Prevalence of occult celiacdisease in patients with iron-deficiency anemia: a prospectivestudy. South Med J 2004; 97: 30-4.

25. Carroccio A, Iannitto E, Cavataio F, et al. Sideropenic anemiaand celiac disease: one study, two points of view. DigDis Sci 1998; 43: 673-8

26. Leffler DA , Schuppan D . Update on serologic testing in celiac disease .Am J Gastroenterol 2010 ; 105 : 2520 -4 .

27. Farrell RJ, Kelly CP. Diagnosis of celiac sprue. Am JGastroenterol 2001; 96:3237–46

28. Marsh MN. Gluten, major histocompatibility complexand the small intestine: a molecular andimmunobiologic approach to the spectrum of glutensensitivity (“celiac sprue”). Gastroenterology1992;102:330-54

29. Oberhuber G, Granditsch G, Vogelsang H. The histopathologyof celiac disease: time for a standardizedreport scheme for pathologists. Eur J GastroenterolHepatol 1999; 11:1185–94

30.Marsh M, Crowe P: Morphology of the mucosal lesionin gluten sensitivity. Bailliere’s ClinicalGastroenterol 1995; 9:273–93

31. Hammer ST, Greenson JK. The clinical significance of duodenal lymphocytosis withnormal villus architecture. Arch Pathol Lab Med 2013;137:1216–19.

32.Walker MM, Murray JA, Ronkainen J, et al. Detection of celiac disease andlymphocytic enteropathy by parallel serology and histopathology in apopulation-based study. Gastroenterology 2010;139:112–19.

33.Brown I, Mino-Kenudson M, Deshpande V, et al. Intraepithelial lymphocytosis inarchitecturally preserved proximal small intestinal mucosa: an increasing diagnostic

problem with a wide differential diagnosis. Arch Pathol Lab Med2006;130:1020–5.

34.Rubio-Tapia A, Murray JA. Classification and management of refractory celiac disease. Gut 2010;59:547–57..

35. Arguelles-Grande C, Tennyson CA, Lewis SK, et al. Variability in small bowelhistopathology reporting between different pathology practice settings: impact onthe diagnosis of coeliac disease. J Clin Pathol 2012;65:242–7.

36. Villanacci V, Ceppa P, Tavani E, et al. Coeliac disease: the histology report. DigLiver Dis 2011;43(Suppl 4):S385–95.

37.Ensari A. Gluten-sensitive enteropathy (celiac disease): controversies in diagnosisand

classification. Arch Pathol Lab Med 2010;134:826–36

38.Schuppan D. Novel concepts of celiac disease pathogenesis.Gastroenterol 2000; 119: 234-42

39.Ciclitira PJ, King AL, Fraser JS. AGA technical reviewon celiac sprue. American Gastroenterological Association.Gastroenterol 2001; 120:1526–40 ..

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