SHORT COMMUNICATION

Varied Presentation of Celiac Disease in Pakistani Adults

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Abstract

The objective of this retrospective study was to evaluate presentation of celiac disease in adults. It included 77 patients, 41 (53.2%) males with median age 26 years and median body mass index of 18 (16 – 22) kg/m^2. Typical presentation with gastrointestinal symptoms was seen in 76.6%. Atypical presentation with extra intestinal complaints in 7.8% and silent presentation in 15.6%. Major symptoms were diarrhea in 64.9%, weight loss 36.4%, abdominal pain 35.1%, vomiting 32.5%, pallor 24.7%, and weakness 13%. Iron deficiency was documented in 20.8%, B12 deficiency in 9.1%, folic acid deficiency in 6.5% and vitamin D deficiency in 10.4%. Half of the patients had haemoglobin less than 11 g/dl. Osteoporosis and osteomalacia, hypothyroidism, diabetes and atrophic gastritis were seen in 2.6% each. Raised alanine aminotransferase was documented in 23.4%. Duodenal biopsy, done in 39 patients, revealed increased intraepithelial lymphocytes in 11, along with crypt hyperplasia in 3, partial villous atrophy in 15 and sub-total villous atrophy in 10. In conclusion, celiac disease in adults should be looked for in patients with chronic diarrhea or irritable bowel syndrome like symptoms, underweight, anaemic, or having nutritional deficiencies.

Key words: *Celiac disease. Adults. Clinical presentation. Pakistan.*

Celiac disease (CD) is an autoimmune enteropathy triggered by ingestion of gluten in genetically susceptible individuals. It has extremely varied clinical presentations. Diagnosis of celiac disease is made by history and clinical presentation compatible with CD, serological screening compatible with CD, histological findings compatible with CD, obvious clinical and serological response to a gluten-free diet, and exclusion of other clinical conditions mimicking CD.[1] Exact prevalence of celiac disease in Pakistan is not known. Not much is known about presentation of this disease in Pakistani adults. We aimed to evaluate presentation of celiac disease in adults and its association with various conditions.

This is a retrospective study of patients presented to a tertiary care hospital between 1990 and 2010. The study population consisted of adolescents and adults of age 15 years or more. Subjects were identified through using ICD-9 codes. The case notes were reviewed regarding the clinical presentation, and laboratory, endoscopic and biopsy findings. The diagnosis of celiac disease was based on criteria mentioned above. Serological screening was done by ELISA technique for anti-gliadin (IgA and IgG), and tissue transglutaminase antibodies (tTG IgA and IgG). Endoscopy with distal duodenal biopsy was also done in 39 patients. Statistical analysis was done by using Statistical Package for Social Sciences (SPSS) software version 19. Descriptive statistics were used. Results were presented as median with interquartile range for quantitative variables. Frequencies for qualitative variables were reported as percentages.

Case records of 77 consecutive adult CD patients attending the clinics fulfilled the criteria for inclusion in this study. The median age at diagnosis was 26 years (mean 29.9 $\pm$ 12.7 years) with a range of 15 – 67 years (interquartile range 20 – 39). Forty-one (53.2%) were males. Typical presentation with gastrointestinal symptoms was seen in 59 (76.6%) patients, atypical presentation with extra intestinal complaints in 6 (7.8%) and silent presentation with no symptoms in 12 (15.6%). Two patients were initially diagnosed to have irritable bowel syndrome and found to be suffering from celiac disease after investigations. Two patients were referred to evaluate positive fecal occult blood. Presenting symptoms and routine laboratory investigations are summarized in Table I.

Median haemoglobin was 11.0 g/dl. There was iron deficiency in 16 (20.8%), followed by B12 deficiency in 7 (9.1%) and folic acid deficiency in 5 (6.5%). Vitamin D deficiency was seen in 8 (10.4%), osteoporosis and osteomalacia 2 (2.6%), hypothyroidism 2 (2.6%), diabetes 2 (2.6%) and atrophic gastritis 2 (2.6%). Other associated conditions identified were renal calculi, muscular pain, joint pain, dermatitis, Addison's disease, autoimmune cholangiopathy, subacute combined degeneration of spinal cord in one each. Clubbing was present in 4 (6.5%). Raised alanine aminotransferase (ALT) > 40 IU/L was present in 18 patients (23.4%), elevated bilirubin > 2 mg/dl in 2 (2.6%), raised gamma glutamyl transferase (GGT) > 50 IU/L in 7 (9.1%)

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Table I: Presenting symptoms and routine laboratory results in adult patients with celiac disease (n = 77).

Male: female	41:36
Age: years	26 (20 – 39)
Height (cm)	155.5 (144 – 181
Weight (kg)	48.5 (31 – 84)
Body mass index (kg/m^2)	18 (16 – 22)
Presenting symptoms	
Diarrhea	50 (64.9%)
Weight loss	28 (36.4%)
Abdominal pain	27 (35.1%)
Vomiting	25 (32.5%)
Pallor	19 (24.7%)
Weakness	10 (13.0%)
Constipation	06 (7.8%)
Jaundice	03 (3.9%)
Failure to gain weight	02 (2.6%)
Routine laboratory results	
Haemoglobin % (g/dl)	11.0 (9.0 – 13.0)
MCV (fl)	80 (69 – 89)
MCH (pg)	28 (23 – 30)
Total leucocyte count (x 10^9 /L)	7.0 (5.3 – 10.0)
Platelets (x 10^9 /L)	245 (180 – 431)
Bilirubin (mg/dl)	0.7 (0.47 – 1.07)
Alanine aminotransferase (IU/L)	42 (24 – 70)
Gamma glutamyl transferase (IU/L)	19 (10 – 59)
Alkaline phosphatase (IU/L)	107 (83 – 229)
Albumin (g/dl)	3.3 (2.1 – 4.0)

Values are frequencies with percentages or median with interquartile range in bracket.

patients whereas hypokalemia, hyponatremia, hypocalcemia and hypomagnesemia were observed in 4, 3, 2 and 1 patients respectively. Stool detailed report showed occasional pus cells in 8 patients and moderate in 2 cases. One patient had co-existent blastocystis hominis and 2 had positive occult blood.

Endoscopy was done in 39 patients. Duodenal findings were decreased number of duodenal folds in 4 cases, nodularity of mucosa in 3 cases, flattening of folds, fissuring and erythema in 2 cases each; and erosions, oedema and granularity were seen in one case each. Ulcer in the bulb of duodenum was seen in 4 patients. Other endoscopic findings include pangastric erythema in 14 and antral erythema in 4 cases. Two patients had hiatal hernia and one had a gaping lower esophageal sphincter. To further investigate symptoms, colonoscopy was done in 9 patients, which was normal in 7. One patient showed aphthous ulcers with proctitis and another had internal haemorrhoids. Duodenal biopsy findings revealed increased intraepithelial lymphocytes in 11 cases (Marsh 1), along with crypt hyperplasia in 3 cases (Marsh 2); and partial (n = 15) or sub-total villous atrophy (n = 10) in 25 cases (Marsh 3); giardiasis was seen in one case. *H. pylori* infection in gastric biopsies was seen in 15 patients.

Celiac disease is now being diagnosed more frequently in adults and elderly.[2] The delayed presentation in adulthood may be typical with gastrointestinal symptoms or atypical with short stature, anaemia, metabolic bone disease, dental enamel defects, arthritis, increased transaminases, neurological symptoms, or infertility. There is a rising trend of diagnosis of celiac disease in the Asian countries.[3] The disease in adults has not been well documented in Pakistan. There is only one study available in a local journal. In this study, 44 (88%) adult patients presented with typical symptoms and 6 (22%) with atypical features.[4]

The adult patients presented mostly in 3rd and 4th decade. Probably they had celiac disease since their childhood and adolescence. However, mechanism of de-novo celiac disease during later decades is not clear. The presenting features of our patients were chronic diarrhea sometimes mimicking IBS, short stature, being under weight, iron deficiency anaemia, B12 deficiency, transaminasemia and osteoporosis. This is in contrast to the childhood celiac disease where malabsorbtion, chronic diarrhea and failure to thrive are the major features.[2]

Celiac disease may be an important cause of anaemia.[5] In this study, median haemoglobin was 11 g/dl which means about half of our patients were anaemic. Iron deficiency anaemia was seen in 21%, followed by B12 deficiency in 9.1% and folic acid deficiency in 6.5%. There are few reports to suggest that celiac disease can be associated with occult gastrointestinal bleeding.[6] Two patients had positive fecal occult blood.

The extra-intestinal involvement in CD may be related to autoimmunity and genetic pre-disposition. This series had hypothyroidism, diabetes and atrophic gastritis in 2 cases each and Addison's disease in one case. A meta-analysis found abnormal serum transaminases in 27% of patients with newly diagnosed CD.[7] Raised ALT more than 40 was present in 23.4% of these patients. These patients were not suffering from hepatitis B or C. The spectrum of liver impairment in CD is particularly wide and includes mild inflammation of the liver parenchyma reversible on a gluten-free diet (celiac hepatitis), chronic inflammatory liver injury that may lead to fibrosis or cirrhosis irreversible on gluten-free diet and severe liver failure potentially reversible on a gluten-free diet.[8] In celiac hepatitis, increase in the liver enzymes (ALT, AST) is mild to moderate. One patient was suffering from autoimmune cholangiopathy or seronegative primary biliary cirrhosis.

Not all the patients in this study had endoscopy. They were diagnosed on the basis of clinical presentation, sensitive positive serological tests and response to gluten-free diet.[1] Findings of the histopathology are non-specific and are present in other conditions as well. So the role of biopsy for the diagnosis has been questioned. An adequate number of biopsy samples should be taken patchy involvement in CD. Currently, biopsy is not always necessary for the diagnosis of celiac disease.[9]

In conclusion, celiac disease may present at any age and has diverse presentation. It should be looked for in patients with chronic diarrhea, patients who have irritable bowel syndrome like symptoms, underweight, anaemic, or having nutritional deficiencies and in patients with unexplained hypertransaminasemia.

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