Bone mineral density in celiac patients correlates with duodenal biopsy stage

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Aims and objectives

Celiac disease (CD) is a chronic immune-based enteropathy caused by dietary gluten (protein in wheat, barley, and rye) in genetically predisposed individuals that resolves with the exclusion of gluten from the diet.1 Gastrointestinal disease is often overlooked or simply forgotten as a cause of osteoporosis. Osteoporosis is common in GI diseases, particularly those associated with malabsorption and maldigestion such as celiac disease, postgastrectomy, short gut, pancreatic insufficiency; inflammatory bowel disease(1,2,3).

Osteoporosis may also be the only presenting finding for a GI disease in an otherwise asymptomatic patient. For example, the frequency of celiac sprue in asymptomatic osteoporotic patients presenting to a metabolic bone clinic was 3%, compared to 0.3% in a general medicine clinic in the same institution (4,5).

Celiac patients are prone to vitamin D and calcium malabsorption, reduced calcium intake, secondary hyperparathyroidism, and neutralizing antibodies to osteoprotegerin (OPG), all leading to an increased fracture risk with a hazard ratio of 1.4, according to documentation (6). Asymptomatic celiac patients may present only with low bone density. Overall, risk factors for osteoporosis include disease activity, age, gender, menopausal status, and GCS (7).

Osteoporosis generally manifests in late middle age, but its causes are rooted in the years of development so prevention and timely diagnose is of fundamental importance (8,9). we aimed to asses prevalence of osteoporosis and osteopenia in newly diagnosed celiac disease and to find probable confounding factors such as degree of pathology damage in duodenal biopsy and serum anti-tTG level.
Methods and materials

Cross-sectional study was performed at the Mashhad Gastroenterology Outpatient Clinic of celiac disease from 2006-2013. We identified 195 adult patients with celiac who were diagnosed through biopsy reports of small bowel regarding marsh classification (table 1) and positive serology.

Pathology was reported by an expert gastrointestinal pathologist. All anti-tissue transglutaminase (anti-tTG) serology was checked by a Euroimmune kit in one laboratory.

Patients' data that included the mode of presentation and presence of concomitant illnesses and symptoms were collected by a questionnaire. These data included demographic characteristics, chief complaints (gastrointestinal and non-gastrointestinal), pathology, endoscopy and laboratory results.

Bone mineral density (BMD) measurements were made with a dual-energy X-ray absorptiometer (DPX-L; Lunar Radiation Corp, Madison, WI). The instrument was calibrated daily according to the manufacturer's instructions. Bone mineral density (in g/cm(2)) was measured in the lumbar spine and femoral neck. Osteoporosis was defined as a T score # -2.5 SD and osteopenia was defined as a T score between -1 and -2.5 SD.

The data was analyzed using the Statistical Package for Social Sciences (SPSS) version 16 (Chicago, IL, USA). Simple statistics were used such as frequency and standard deviation. The chi-square test and Student's t-test and the Spearman correlation were used for comparisons.
Table 1: Marsh classification of duodenal biopsy in celiac disease

<table>
<thead>
<tr>
<th>Marsh1</th>
<th>Increased intraepithelial lymphocyte</th>
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<tbody>
<tr>
<td>Marsh2</td>
<td>Crypt hyperplasia</td>
</tr>
<tr>
<td>Marsh3</td>
<td>villous atrophy</td>
</tr>
</tbody>
</table>
Results

We evaluated a total of 193 patients of which 132 were female (female to male ratio of 2.16:1). The mean age at diagnosis was 32.6 ± 13 years with a significant proportion of patients (32.3%) between 20-30 years of age. Among the all patients 24.7% (57) had hemoglobin (Hgb) level under 10mg/dl while 47.2% (92) had above 10mg/dl Hgb levels. MCV <80 was detected in 30.3% (59) and >80 in 28.2% (55) Mean anti-tTG titers were 100 ± 25 units/ml with serum anti-tTG levels >200 units/ml observed in 118 (60.5%) patients.

Among the patients, 43 (22.1%) had osteopenia in lumbar and 30 (15.4%) had osteoporosis in lumbar spine. Fortyfour (22.6%) had osteopenia in femoral neck, and 24 (12.3%) had osteoporosis in femoral neck (table 2). Marsh classification was used in Pathology reports, the results is mentioned in Table 3. In histological evaluation, 2.1% had Marsh 1 lesions, 10.8% presented with Marsh 2 lesions and 78.5% had Marsh 3 lesions. BMD, expressed as a T score, in both lumbar and femoral neck was significantly lower in patients with marsh 3 pathology than in patients with marsh <3 pathology (p<0.07). There was significant negative correlation between femoral neck bone densitometry (Tscore) and degree of marsh classification of pathology (p<0.002, r=-0.26).

Low bone mineral density (BMD), osteopenia, and osteoporosis are frequent complications of celiac disease (CD). The etiology of pathologic bone alterations in CD is multifactorial; however, two main mechanisms are involved: intestinal malabsorption and chronic inflammation (10). The incidence of osteoporosis is higher in celiac subjects (3.4%) than in the population as a whole (0.2%). Stenson et al reported that most CD patients with osteoporosis have secondary hyperparathyroidism with vitamin D deficiency, and there is strong evidence that CD is linked to vitamin D malabsorption (11,12).

The absolute prevalence of osteoporosis/osteopenia in CD patients is unclear due to the small numbers of patients studied and the varied study populations.

However, data from two studies involving adult CD patients suggest approximately one-third of adult CD patients have osteoporosis, one-third have osteopenia and one-third have normal BMD (13). another recent study in 50 celiac patients Twenty-one (39 %) patients had normal BMD, 23 (43 %) had osteopenia (T-score -1 to -2.5), and 10 (18 %) patients had osteoporosis (T-score <-2.5). A statistically significant association was seen between BMD and age of onset, duration of illness, serum tTGA levels, serum vitamin D levels, and histopathological changes. (14) in our near fifth of patients had osteopenia
in lumbar and 30 (15.4%) had osteoporosis in lumbar spine. 44 (22.6%) had osteopenia in femoral neck. and 24 (12.3%) had osteoporosis in femoral neck. and BMD, expressed as a T score, in both lumbar and femoral neck was significantly lower in patients with marsh3 pathology than in patients with marsh<3 pathology (p<0.07). there was significant negative correlation between femoral neck bone densitometry (Tscore) and degree of marsh classification of pathology (p<0.002, r=-0.26).

So duodenal atrophy leads to malabsorption of vitamin D and minerals and cause low BMD. For adults, serum calcium, albumin, 25(OH) vitamin D3, parathyroid hormone and 24 h urine calcium testing should be performed at diagnosis; patients with 'classic' CD and those at risk for osteoporosis should undergo a dual x-ray absorptiometry scan (15).

There has been a substantial change in the mode of presentation of patients with CD over recent years. There is decreased the frequency of diarrheal or classic presentation. However a significant proportion of patients with CD remain undiagnosed, which highlights the need for improved strategies in the future to better detect patients with non-gastrointestinal symptoms such as anemia, bone disorders, such as osteoporosis(16).
Table 2: Bone densitometry results in celiac patients

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Table 3: Duodenal pathology results according to Marsh classification

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Conclusion

Osteoporosis and osteopenia were common in Iranian celiac patients, femoral neck BMD expressed as T score was correlated with marsh classification of duodenal biopsy. So Duodenal villous atrophy, through malabsorption, was the main confounding factor for low BMD in adult-onset CD patients.
Personal information

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References


