Int J Clin Exp Med 2011;4(2):157-163
www.ijcem.com /ISSN:1940-5901/IJCEM1102009

Original Article

The prevalence and risk factors of decreased bone mineral density in firstly diagnosed ulcerative colitis patients in the eastern region of Turkey

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Received February 26, 2011; accepted March 31, 2011; Epub April 3, 2010; published may 15, 2011

Abstract: The prevalance of osteoporosis or osteopenia in Turkish population with ulcerative colitis (UC) at the diagnosis time has not been evaluated so far. Therefore we aimed to determine the prevelance and risk factors of decreased bone mineral density (BMD) in UC patients at the diagnosis time in Turkey. We retrospectively evaluated dexa results, demographic and clinical characteristics, and some biochemical markers of bone turnover of the UC patients at the diagnosis time between June 2005 and February 2010 from the gastroenterology clinic records of the university hospital. The study population consisted of firstly diagnosed 63 UC patients (male: female = 27: 36; mean age 41.8 years). 38.1% at lumbar spine and 44.4% at femoral neck of the Turkish UC patients patients had low BMD at the diagnosis time. The occurrence of osteoporosis among Turkish UC patients at the diagnosis time were 8% at lumbar spine and 11% at femoral neck. 30.1% at lumbar spine and 33.3% at femoral neck of the patients had osteopenia at the diagnosis time. Pearson's coefficient of correlation showed significant correlations between low BMD and pancolitis ($p<0.01$), age, menopause, and symptom duration before the diagnosis ($p<0.05$).In conclusion, the prevelance of low bone density at the diagnosis time in Turkish UC patients is in accordance with Western and Eastern societies. Pancolitis, age, duration of symptoms, and menopause are predictive factors for low bone density in these patients.

Keywords: Ulcerative colitis, low bone density, osteoporosis, osteopenia, prevelance, risk factors, Turkey

Introduction

Ulcerative colitis (UC), referred to as inflammatory bowel disease (IBD), is chronic aggressive disorder, which has world-wide annual incidence and prevalence of about 15–25/100 000 and 200-300/100 000 respectively [1]. Osteopenia and osteoporosis are recognized complications of a multifactoral etiology associated with IBD. The prevalence of reduced bone mineral density (BMD) has been demonstrated in IBD patients [2]. Reported prevalence rates in these patients range from 40 to 50% for osteopenia and from 2 to 40% for osteoporosis and [3]. The prevalance of osteopenia or osteoporosis in Turkish population of IBD at the diagnosis time has not yet been evaluated so far.

Although the magnitude of the problem, major risk factors, and therapeutic approach remain controversial, and the exact pathogenic mechanisms for the lower BMD in IBD patients have not been clearly understood, a number of conditions have been suggested. Several factors such as corticosteroid therapy, calcium, vitamin D and vitamin K deficiency, sex-hormone deficiency, malnutrition, smoking, alcohol use, inflammatory cytokines, and physical inactivity, small intestinal resection, ileal involvement, low body mass index (BMI); have been correlated with bone loss in IBD [4,5].

Studies about which of these factors really acts in determining bone loss in IBD patients are inconsistent, likely as a consequence of small

sample size and heterogeneous disease populations. In some of these studies, corticosteroid therapy appeared as the main osteopenic factor [6,7], whereas in others low BMD was found in the absence of past or present steroid treatment [8].

Bone mineral density is strongly influenced by ethnic differences in body mass, diet, physical activity and genetics [10-12]. The Turkish population has distinct cultural, nutritional and genetic aspects from other Asian and Western populations. Although a recently reported literature about osteoporosis and osteopenia in Turkish IBD patients who were under treatment [13], there are no published data about the prevalence and clinical relationships of low bone mineral density at the diagnosis time in UC patients in Turkish population.

The aim of this study was to assess the prevelance and risk factors of decreased bone mineral density prevelance in Turkish UC patients at the diagnosis time by retrospectively evaluating the results of DEXA, clinical and demographic characteristics and some biochemical markers of bone turnover.

Materials and methods

Subjects

We retrospectively evaluated only UC patients because Crohn's disease is very uncommon in the eastern region of Turkey. The diagnosis of ulcerative colitis was established based on endoscopic, histological, radiological and clinical criteria [14]. Only, UC patients at the dignosis time were included in the study. Exclusion criteria were: inadequte data of the patients about the study parameters in the university hospital records, age<18 year, hepatic or renal disease (creatinine> 1.5 mg/dl), thyroid and parathyroid diseases, diabetes mellitus, previous corticosteroid use for any reason, inflammatory joint disease (ankylosing spondylitis, rheumatoid arthritis etc.), treatment for osteoporosis (bisphosphonates, calcium, vitamin D, fluoride, calcitonin and hormone replacement therapy). 41 out of 104 retrospectively evaluated firstly diagnosed UC patients excluded from the study (36 patients because of the lack of the records about the study parameters, 1 patient because of hyperparathyroidism, 2 patients because of previously steroid use, 2 patients because of hyperthyroidism). Remained 63 firstly diagnosed UC patients included in the study. The demographic and clinical characteristics of the patients at the diagnosis time including age, gender, body mass index (BMI), menopause, disease location and duration of symptoms were recorded from the hospital records.

Measurement of bone mineral density and some biochemical parameters

The DEXA investigation and laboratory tests on some biochemical markers of bone turnover that affect bone metabolism in IBD patients at the diagnosis time has been a routine part of clinical investigations in the gastroenterology clinic of our university hospital since 2004. The reason of that is the increased prevelance of osteoporosis (up to 50% in the literature) in these patients. But the prevalance of osteoporosis or osteopenia in Turkish population with IBD at the diagnosis time has not yet been evaluated. So we retrospectively evaluated DEXA, demographic characteristics, and some biochemical markers of bone turnover that affect bone metabolism of the ulcerative colitis patients at the diagnosis time between June 2005 and February 2010 from the gastroenterology clinic records of the university hospital.

Bone mineral density was measured by dual energy X-ray absorptiometry (DXA-Norland XR-46 Fort Atkinson, WI, USA) at the spine (L2-L4) and the neck of the left proximal femur. Results were expressed as absolute BMD values (g/cm^2), Z-scores and T-scores obtained by comparison with values of age- and young- sex-matched persons of the healthy population. Osteopenia and osteoporosis were diagnosed using WHO criteria [15]. Osteopenia was defined as a T score between -1 to -2.49, while osteoporosis was diagnosed with a T score of -2.5 or below. Number of patients with low BMD was defined the total number of osteopenic and osteoporotic cases. Biochemical analysis were performed with autoanalyser (Cobas Integra 800). Serum alkaline phosphatase, calcium and phosphorus levels at the diagnosis time were recorded from the hospital records. The study protocol was performed in accordance with the Declaration of Helsinki.

Statistical analysis

Results are expressed as mean (SD) for

Table 1. Demographic and some clinical and laboratory features of the patients with ulcerative colitis (UC) at the diagnosis time

Characteristics	UC patients included in the study (n=63)
Age (years) (mean(SD))	41.8 (14.6)
Gender (male/female)	27/36
Duration of symptoms before the diagnosis (months) (mean(SD))	21.2 (18.7)
Body mass index (BMI) (kg/m2) (mean(SD))	25.7 (4.9)
Postmenopausal women (n)	10
Alkaline phosphatase (normal range 80–306 IU/l) (mean(SD))	194.92 (77.16)
Calcium (normal range 8.1–10.4 mg/dl) (mean(SD))	8.9 (0.96)
Phosphorus (normal range 2.5–5 mg/dl) (mean(SD))	3.64 (0.59)
Rectal involvement (n)	11
Rectosigmoid involvement (n)	14
Descending colon involvement (n)	17
Pancolitis involvement (n)	21

Table 2. Measurements of bone mineral density (BMD) and calculated T and Z scores (mean(SD)) in 63 UC patients

DEXA measurement area	BMD (g/cm^2) (mean(SD))	T score (mean(SD))	Z score (mean(SD))
Femoral neck	0.792 (0.168)	-1.06(1.42)	-0.23(1.34)
Lumbar spine (L2-4)	0.813 (0.147)	-0.82(1.85)	-0.12(1.76)

continuous variables, unless otherwise stated. Correlations were investigated by Pearson's coefficient of correlation. Significance was defined as $p<0.05$ (95% confidence interval). Tests were performed using SPSS package version 13.

Results

A total of 104 patients diagnosed as UC at the university hospital retrospectively evaluated for low BMD and study parameters at the diagnosis time. According to the inclusion and exclusion criteria, 41 patients excluded from the study. Remained 63 UC patients who matched the inclusion criteria of the study included in the trial. The demographic and some clincal and biochemical data of UC patients are summarized in **Table 1**. Number of postmenopausal women was 10 (15.8%). Distrubition of disease locations was rectum 11 patients, rectosigmoid 14 patients, descending colon 17 patients and pancolitis 21 patients.

The mean BMD, T score and Z score at femoral neck represented as mean(SD) were 0.792 (0.168) g/cm^2, -1.06(1.42) and -0.23(1.34), respectively. And the mean BMD, T score and Z score at lumbar spine (L2-4) were 0.813 (0.147) g/cm^2, -0.82(1.85) and -0.12(1.76), respectively (**Table 2**).

Of 63 Turkish UC patients, twenty-one (33.3%) had osteopenia and seven (11%) patients had osteoporosis at the diagnosis time acccording to the femoral neck T scores based on world health organisation (WHO) guidelines, while nineteen (30.1%) had osteopenia and five (8%) patients had osteoporosis acccording to the lumbar spine (L2-4) T scores (**Table 3**, **Figures 1, 2**).

Pearson's coefficient of correlation showed significant correlations between low BMD and pancolitis ($p<0.01$), age, menopause, and symptom duration before the diagnosis ($p<0.05$) in 63 Turkish UC patients (**Table 4**).

Discussion

Low bone density is a significant complication associated with ulcerative colitis (UC) and

Table 3. Number and percentages of osteoporotic and osteopenic UC patients according to the T scores based on WHO guidelines

DEXA measurement area	Normal	Osteopenia	Osteoporosis	Total number of patients who have low BMD
Femoral neck	35 (55.5%)	21 (33.3%)	7 (%11)	28 (44.4%)
Lumbar spine (L2-4)	39 (61.9%)	19 (30.1%)	5 (8%)	24 (38.1%)

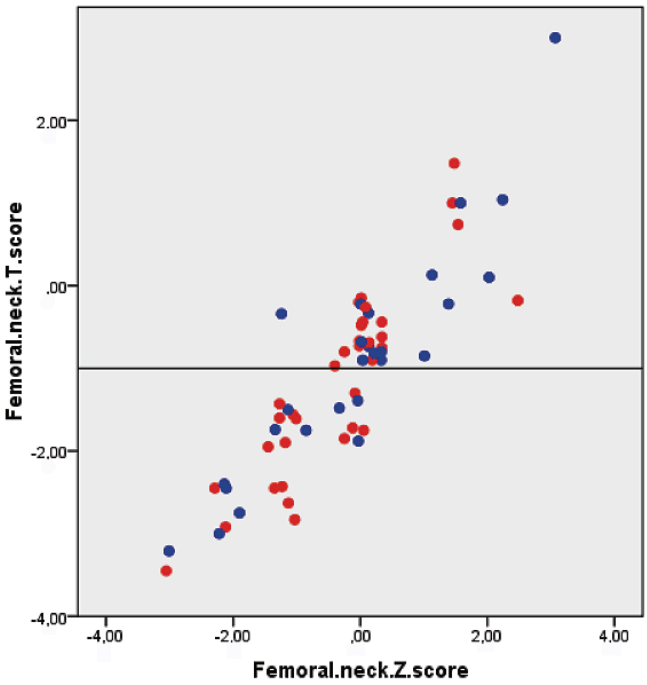

Figure 1. Bone mineral density (BMD) of the femoral neck in patients with ulcerative colitis (UC). The BMD measurements are given as T and Z scores. Cases under the horizantal line (T-score<-1) have low BMD. Blue dots: males, red dots: females.

In view of the high prevalence of low BMD in ulcerative colitis patients, the knowledge of a risk factor profile may be beneficial for monitoring of the individual patient. Our study showed significant correlations between low BMD and pancolitis ($p<0.01$), age, menopause, and symptom duration before the diagnosis ($p<0.05$) in 63 newly diagnosed Turkish UC patients (**Table 4**). Our results failed to show any correlation between BMD and gender, calcium, phosphorus or alkaline phosphatase level, and BMI.

In a previous study from Turkey [13], relationship between bone mineral density and clinical features in IBD patients who were under treatment were evaluated. Since we evaluated newly diagnosed Turkish UC patients, the current study differs from this study. In the mentioned study, Poturoglu et al. [13] found osteopenia in 38.6% of Turkish UC patients under the treatment. But they didn't report osteoporosis prevelance for Turkish UC patients. This reported prevelance for osteopenia is a bit higher than that of the current study (33.3%).

Crohn's disease (CD) in adults and even in children [16]. In the current study, the prevalence of low BMD and the relationship between patients characteristics have been assessed in the Turkish population of newly diagnosed UC patients. The current study confirms the prevalence of osteopenia and osteoporosis in Turkish UC patients is close to the eastern and western societies. Our findings of 33.3% osteopenia and 8% osteoporosis within the patient population is close to the ranges seen in previously published trials. Reported prevalence rates range from 30 to 50% for osteopenia and from 2 to 30% for osteoporosis in western and eastern societes [3,17-21].

In contrast of our results, in the study of Poturoglu et al. [13] in Turkish IBD patients, BMI showed a significant positive correlation with BMD in UC patients. Disease localization and disease duration had no influence on BMD in their study. These different results between two studies may be due to firstly distinct nutritional and sociodemographic aspects of the study regions that our study was performed in the eastern region of Turkey while the other was performed in the western region of Turkey. Secondly we included only first time diagnosed UC patients, while Poturoglu et al included patients under treatment for UC.

We found positive correlation between low BMD

Table 4 Pearson's correlation coefficient of bone mineral densitometry in 63 Turkish ulcerative colitis patients, comparing clinical characteristics and some biochemical parameters to the T scores of the lumbar spine, femoral neck at the diagnosis time

Parameters	Lumbar spine (L2–L4)	Femoral neck
Age (years) –	-0.315[b]	-0.289[b]
Gender	0.067	0.045
Body mass index (kg/m2)	0.113	0.124
Duration of the symptoms before diagnosis (months)	-0.236[b]	-0.258[b]
Calcium (mg/dl) Phosphorous (mg/dl)	0.056	0.032
Phosphorus	0.036	-0.056
Alkaline phosphatase (IU/l)	0.012	-0.034
Colits location (Partial or Pancolitis)	0.332[a]	0.364[a]
Menopause	0.267[b]	0.281[b]

[a]Correlation was significant at the 0.01 level; [b]Correlation was significant at the 0.05 level

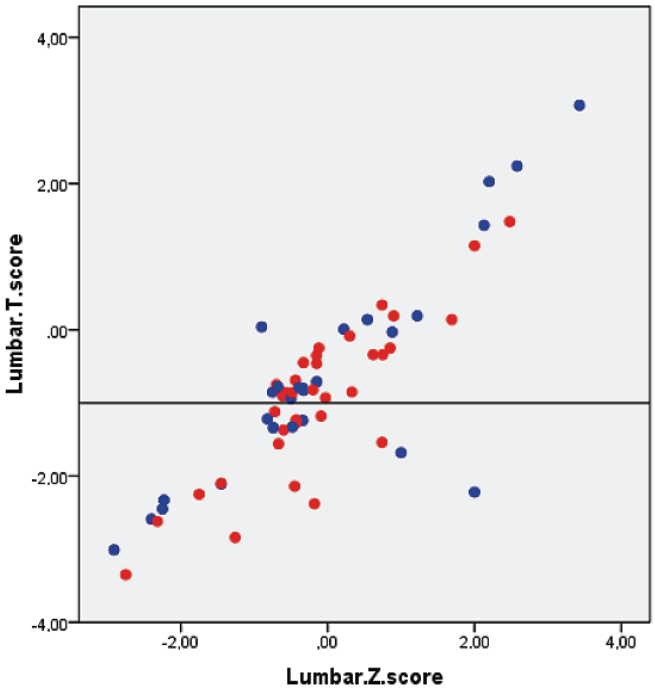

Figure 2. Bone mineral density (BMD) of the lumbar L2-4 in patients with ulcerative colitis (UC). The BMD measurements are given as T and Z scores. Cases under the horizantal line (T-score<-1) have low BMD. Blue dots: males, red dots: females.

and pancolitis rather than less widespread disease at the diagnosis time. This positive correlation may be associated with more deleterious systemic consequences of pancolitis. There are also studies in the literature provide evidence that the disease itself contributes to reduced BMD. In a study, reduced BMD was also found in inflammatory bowel disease patients who had never received steroids [22].

As in our study, Lee et al. showed low BMD was common in newly diagnosed IBD Korean patients [23]. Duration of symptoms may affect BMD. Because malabsorption and pro-inflammatory cytokines released due to bowel inflammation contribute to low bone density associated with UC [24]. Orlic et al suggested that it is most important to achieve disease remission as soon as possible in addition to nutritional support [25].

We found positive correlation between low BMD and symptom duration. Dresner-Pollak et al. found an inverse correlation between BMD and disease duration in their IBD patients [26]. Sakellariou et al also showed that recently diagnosed young male patients with inflammatory bowel disease had lower bone density values than healthy controls. According to their findings, duration of disease above 6 months was the major risk factor for low bone density in these patients [27]. We also found positive correlation of low BMD with age. Zali et al. [21] also found positive correlation between age and low BMD in Iranian IBD patients. Low BMD was associated with certain risk factors, some of which may be modifiable and low BMD may also be an early supportive diagnostic tool in this patient population.

Healthy control subjects were not used in this study and comparisons were made according to the WHO osteopenia and osteoporosis criteria based on DEXA results. Lack of a control group in our study is a limitation. But, as in our study, Zali et al. [21], Tsironi et al. [28] and Van Schaik et al. [29] also did not use healthy control subjects in their studies.

Majority of our UC patients were in a normal group of BMD, based on T scores of L2-4 (61.9%) and femoral neck (55.5%) compared to osteopenia and osteoporosis groups. It could be due to the initial stage of UC as they were newly diagnosed. As in our study, Lee et al. [23] showed 64% of newly diagnosed IBD patients had normal BMD. But the disease progresses, the prevalence of reduced BMD increases because of corticosteroid use, nutritional deficiency and the presence of chronic inflammation [30]. For example, Van Schaik et al. [29] performed a retrospective chart review in 474 followed IBD patients (259 with UC, 210 with CH and 5 with indeterminate colitis) without including healthy controls and found osteopenia in 64.3% (T-score<-1) and osteoporosis in 23.8% (T-score<-2.5).

Limitations of the current study; a) the small sample size (n=63) which inevitably leads to the limited statistical power, b) Turkish CD patients and a healthy group were not included in the study, c) The study was done retrospectively. However, data was sufficient to demonstrate the prevelance and the risk factors of low BMD in Turkish UC patients at the diagnosis time.

In conclusion, our study showed that a significant number of Turkish patients with UC at the time of initial diagnosis had low bone density. Pancolitis, duration of symptoms, age and menopause were major risk factors. Early therapeutic management focused on disease itself and low BMD may prevent bone loss in patients with UC.

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