Inflammatory bowel disease (IBD) has been associated with increased risk of osteoporosis and osteopenia.1-6 The prevalence of osteoporosis and osteopenia using the World Health Organization (WHO) diagnostic criteria varies from 13% to 77% among Caucasian patients with IBD.1–6 The pathogenesis of osteoporosis in patients with IBD is likely to be multifactorial including factors such as genetic, current or cumulative use of corticosteroids, systemic inflammation, calcium and vitamin D deficiency, small bowel involvement or intestinal resection, smoking, and older age.1-6

Bone mineral density (BMD) is strongly influenced by ethnic differences in body mass, physical activity, nutritional intake and genetic factors.1,3,4,5,7 Therefore, there is a potential for bias resulting from factors such as socioeconomic, demographic and genetic on the prevalence of osteoporosis and osteopenia among Caucasians and Asians. There is a single report from Asia where Lee et al in a study including 39 patients reported low values of BMD in 36% of newly diagnosed Korean patients with IBD.8

This cross-sectional study aimed to determine the prevalence of osteopenia and osteoporosis in patients with IBD and to identify the potential risk factors.

Methods

We included 46 randomly selected patients with IBD (22 with ulcerative colitis (UC) and 24 with Crohn’s disease (CD). The diagnosis of UC was established on the clinical...
evidence of large bowel diarrhea, hematochezia and tenesmus; endoscopic evidence of diffuse pattern of involvement of the colonic mucosa characterized by loss of vascular pattern, erythema, friability or ulcerations; and histological evidence of acute on chronic colitis. The diagnosis of CD was established on the presence of characteristic clinical manifestations (chronic diarrhea, hematochezia, abdominal pain, and intestinal obstructive manifestations), endoscopic features (skip lesion, asymmetrical involvement, deep ulcers, ileocecal valve involvement, and terminal ileum involvement), and histological evidence (acute or chronic colitis, presence of inflammation extending beyond muscularis mucosae, lymphoid follicles, and non-caseating granuloma). Involvement of the small intestine was assessed by using barium meal follow-through, small bowel enema, and/or retrograde ileoscopy. The extent and behavior of CD was classified according to the Montreal classification. Those excluded were patients <16 years and >70 years of age, pregnant women, alcoholics, smokers and those with diabetes mellitus, hypo- or hyperthyroidism, hypertension, ischemic heart disease, cardiac arrhythmias, chronic pancreatitis, chronic liver disease, and epilepsy. None of the patients was taking antidepressants, muscle relaxants or analgesics and they were included only if they had stopped using these medicines at least 3 weeks before the study. None of the patients had undergone any bowel resection. All the patients were in remission phase of disease and were on stable form of 5-ASA and/or immunosuppressive drugs at the time of measurement of BMD.

Details were recorded about the duration of disease, extent of disease, cumulative steroid use, dietary or supplemental calcium intake (using the Indian Council of Medical Research guidelines). Daily calcium intake was assessed by the standard 3-day diet recall system and divided into three groups; calcium intake <200 mg/day, 200–400 mg/day, and >400 mg/day.

To compare values of BMD for patients, data from 46 age- and sex-matched healthy controls were selected from an existing database of healthy Indian volunteers whose BMD had been measured in a community-based survey carried out among people residing in Delhi (unpublished data). The mean age of patients (28 men) and healthy controls (28 men) was 40.5 (14.7) years and 40.5 (14.6) years, respectively.

**Measurement of BMD**

BMD was measured at the spine (antero-posterior), and the hip regions using dual energy X-ray absorptiometry (DXA, Hologic QDR 4500, USA).

Since the reference values of BMD for Indians have not been defined yet, the WHO guidelines were used for the definition of osteoporosis and osteopenia. BMD values of patients with IBD were compared with those of healthy sex- and age-matched controls and standard deviation scores (Z-score) were calculated. As per the standard WHO criteria, the Z-scores used to define BMD of patients were: less than -2.5 for osteoporosis, between -1.0 and -2.5 for osteopenia, and more than -1.0 for healthy individuals. Since the WHO criteria are race-specific as well, we have not compared BMD values of our patients with that of Caucasians.

**Statistical analysis**

Statistical analysis was done using SPSS version 10 for Windows (SPSS Inc, USA). The data are presented as mean (SD). Mean values of the different parameters of subjects were compared using the independent Student t-test. Proportions were compared using the chi-square test. Difference was considered significant at a p value of <0.05.

**Results**

The demographic characteristics including height, weight, BMI as well as disease characteristics are shown in Table 1. The overall mean duration of disease was 87.7 (78.3) months. Of those with UC, 4 patients (18.1%) had proctosigmoiditis, 7 patients (31.8%) had left-sided colitis and 11 patients (50%) had pancolitis. The extent of involvement in patients with CD was only terminal ileal disease in 4 (16.6%), only colonic in 14 (58.3%) and ileocolonic in 6 (25%). The disease behavior in patients with CD was non-stricturing, non-fistulizing in 18 (75%), stricturing in 4 (16.6%) and fistulizing disease in 2 (8.3%). Seventeen patients (36.9%) were taking steroids while 9 (19.5%) were taking a combination of steroid and immunosuppressive drugs.

**Musculoskeletal symptoms**

The musculoskeletal symptoms in patients with IBD included easy fatigability in 30 (65.2%), body ache in 22 (47.8%), diffuse bone pain in 15 (32%), joint pain in 10/45 (22.2%), proximal muscle weakness in 9 (19.5%) and gait changes in 4 (8.6%). Four patients (8.6%) were taking analgesic drugs on regular basis for relief of bone pain. Spinal tenderness in the lumbo-sacral region was present in 12 patients (26%). The BMD values in one patient, who had a fracture of the forearm on minor trauma, showed osteoporosis at both the hip and spine regions.

**Dietary calcium intake**

Two third of patients with IBD avoided or reduced milk and milk products because of the fear of worsening of symptoms due to ingestion of milk. The calcium intake
was <200 mg/day in 41 patients (89.1%), while only 2 patients (4.3%) had an intake of 200–400 mg/day and 3 patients (6.4%) of >400 mg/day. There was no significant difference in the daily calcium intake in patients with UC and CD. Similarly, there was no significant difference in the BMD of patients receiving <200 mg, 200–400 mg or >400 mg of dietary calcium.

Bone mineral density

The results of BMD measurement in patients with IBD and healthy controls are shown in Table 1. Significantly lower values of BMD at the spine and hip regions were seen in patients with IBD (both UC and CD) as compared with those in healthy controls. Osteopenia or osteoporosis was present in 29 patients (63%) and 21 patients (45.6%) at the spine and hip regions, respectively. Osteoporosis was seen in 4 patients (8.6%) at the spine and in 7 patients (15.2%) at the hip region (Table 2). When compared with BMD standards for Caucasians, the mean (SD) T scores at the spine and hip regions were -1.93 (1.3) and -1.2 (0.9) while the mean Z scores at the spine and hip regions were -1.6 (1.3 and -0.9 (0.9), respectively.

When compared with patients with normal values of BMD, patients with osteoporosis had significantly lower body weight (61.6 [20.5] vs. 46.6 [12.1] Kg; p=0.02). Similarly, significant difference in weight was observed among patients with IBD with osteopenia and those with osteoporosis (62.5 [12.8] vs 48.6 [9.6] Kg, p=0.003). A positive correlation was observed between weight and BMD values at the spine (r=0.583, p=0.0001) and BMD at the hip regions (r=0.585, p=0.0001). This correlation was persistent (p=0.009 and p=0.006) even after correction for height.

There was no difference in the BMD values for those who had received or were presently on steroids as compared with those who never received corticosteroids or immunosuppressive drugs. There was no correlation in the values of BMD with the duration of disease, and calcium intake.

Comparison of BMD in patients with CD and UC

There was no difference in the values of BMD of patients with CD and UC.

Discussion

The present study shows a high prevalence (63%) of osteopenia or osteoporosis in Indian patients with IBD in comparison with healthy age- and sex-matched Indian controls. Approximately 3% to 77% of Caucasians patients with IBD have osteopenia or osteoporosis.1–5 While there is a single report from the Asian region, there are no reports on the status of BMD in Indian patients with IBD.8 Asians and Indians in general have similar values of BMD but lower than those in Caucasians.13,14 In a study comparing BMD in Asians and Caucasians, the BMD values among Chinese and Indian women were comparable; these values were significantly lower, at all sites, than those of European women (p<0.005).14 Furthermore, healthy Indians with physically active lifestyle and adequate nutritious diet have low values of BMD at different sites in comparison with Caucasian standards.15,16 High prevalence of vitamin D deficiency, low calcium intake, and high dietary phytates intake are cited as the most important reasons for low values of BMD in the Indian population.15

The risk factors for osteoporosis and osteopenia can be classified as modifiable and non-modifiable.1–5 The modifiable factors include dietary calcium intake, smoking, exercise, sedentary lifestyle, exposure to sun and drugs such as glucocorticoid, while the non-modifiable factors include age, gender and genotypes.1–5 The mean dietary calcium intake is reported to be 438.6 mg/day (range: 200–696 mg/day) in a study including 92 healthy hospital staff from northern India; furthermore, 74% of these individuals had an intake of calcium <500 mg/day.17 A majority of our patients with IBD reported that their dietary calcium intake was <200 mg/day. Milk and milk

<table>
<thead>
<tr>
<th>Region</th>
<th>Normal BMD (%)</th>
<th>Osteoporosis (%)</th>
<th>Osteopenia (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spine</td>
<td>17 (36.9)</td>
<td>4 (8.6)</td>
<td>25 (54.3)</td>
</tr>
<tr>
<td>Hip</td>
<td>25 (54.3)</td>
<td>7 (15.2)</td>
<td>14 (30.4)</td>
</tr>
</tbody>
</table>

Data are as number of patients (%). BMD: Bone mineral density.

Table 1: Bone mineral density (BMD) in patients with inflammatory bowel disease and age- and sex-matched healthy controls

<table>
<thead>
<tr>
<th>Patients with CD</th>
<th>Patients with UC</th>
<th>Healthy controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean weight (Kg)</td>
<td>53.4 (13.4)</td>
<td>58.3 (19.3)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>160.3 (10.2)</td>
<td>161.4 (9)</td>
</tr>
<tr>
<td>Duration of disease (mo)</td>
<td>82.4 (74.4)</td>
<td>92.1 (82.7)</td>
</tr>
<tr>
<td>BMD at spine (g/sq cm)</td>
<td>0.802 (0.14)*</td>
<td>0.876 (0.16)*</td>
</tr>
<tr>
<td>BMD at hip (g/sq cm)</td>
<td>0.815 (0.12)*</td>
<td>0.842 (0.13)*</td>
</tr>
</tbody>
</table>

Data are as mean (SD); CD: Crohn’s disease; UC: ulcerative colitis; *p=0.0001 when compared with controls.

Table 2: Prevalence of osteoporosis and osteopenia in patients with inflammatory bowel disease (n=46)

<table>
<thead>
<tr>
<th>Region</th>
<th>Normal BMD</th>
<th>Osteoporosis</th>
<th>Osteopenia</th>
</tr>
</thead>
<tbody>
<tr>
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</table>
products are the main source of calcium in the diet of majority of Indians. Most of our patients avoided milk and milk products because of the fear of worsening of symptoms due to ingestion of milk. The dietary restriction of milk in them was low not only during acute exacerbation but also during the remission phase of their disease. Low intake of calcium along with poor absorption of calcium because of disease activity might be an important cause of low values of BMD in these patients.

There is a common misperception including among physicians that ingestion of milk contributes to disease activity and increases symptoms in patients with IBD.\textsuperscript{18–21} Lactose intolerance in patients with UC is dependent on their age and ethnicity and not on any particular aspect of their disease. In a questionnaire-based study conducted by Bernstein \textit{et al},\textsuperscript{18} 80\% of responding physicians stated that they recommend avoidance of milk products at some time to their patients. Almost two-thirds of our patients reduced or eliminated milk products from their diet. In a previous study, of 10 patients with UC tested during a flare, only 2 (20\%) were intolerant to milk.\textsuperscript{18} In another previous study, of 10 patients with UC tested during a flare, only 2 (20\%) were intolerant to milk.\textsuperscript{18} In another study from India, Kochhar \textit{et al}\textsuperscript{18} reported no difference in the occurrence of lactose intolerance between those with UC and healthy controls (41.7\% vs. 40\%).

In conclusion, majority of patients with IBD have low values of BMD. Dietary calcium intake was inadequate in them. In place of the general practice of avoidance of milk to control the symptoms, there is a need to increase the intake of dairy products by patients with IBD.

References