INTRODUCTION

Osteoporosis is a disease characterized by low-bone mass and micro-architectural deterioration of bone tissue, leading to enhanced bone fragility and a consequent increase in fracture risk (2). Osteoporosis and low-bone mineral density (BMD) have important implications in terms of morbidity—population based studies from Nottingham, UK have shown a 60% increased risk of fracture in IBD patients (3).

The estimated prevalence of osteoporosis in the IBD population ranges widely from 13% to greater than 50% (1,4–7). The marked difference in the prevalence of osteoporosis between these data sets reflects patient selection, method and location of DEXA imaging, patient age, duration from diagnosis to DEXA scan and study size.

The etiology of low BMD in IBD is multifactorial. Risk factors include low-body mass index (BMI) (4,8,9). Recent pertinent data from Bartram and colleagues in Newcastle, UK showed that CD patients with osteoporosis had a mean BMI of 22 compared to those without osteoporosis where the BMI was 25 (p < 0.0001) (4). A number of studies have shown that
corticosteroid use is also a risk factor for the development of osteoporosis in patients with IBD (5,10–12) and other factors that have been implicated include smoking, hypogonadism, increased secretion of osteoclast stimulating cytokines, calcium and vitamin D deficiency, disease location and duration (4,7–14).

Twin studies have suggested that up to 80% of a patient’s BMD is genetically determined and in view of its chromosomal location and function there has been sustained interest in the contribution of germline variation of the vitamin D receptor (VDR) gene (15).

In our recently published study we aimed to investigate the prevalence of osteoporosis in our IBD cohort, and to evaluate the contribution of specific environmental and genetic factors on the development of osteoporosis in this IBD population (1).

A cohort of 440 IBD patients who attended the Western General Hospital, Edinburgh and had demographic data collected and DNA stored as part of the IBD database were recruited. DEXA scans were undertaken between 1997–2006. The T-score at the lumbar spine was selected for analysis as tight correlation was observed between T scores from the femoral neck and lumbar spine. Using the WHO criteria osteoporosis was defined as a T-score of below −2.5 and osteopenia when the T score was between −1.0 and −2.5 (2). All the IBD patients and 240 healthy controls (HC) were genotyped for VDR variants Taq-1 and Apa-1 using RFLP-PCR.

RESULTS

Our retrospective data show that in this well phenotyped cohort of IBD patients, relatively low levels of osteoporosis and osteopenia were observed (Figure 1). In IBD 15% were osteoporotic, 18% had osteopenia and 67% had normal T scores at their lumbar spine. In the CD patients, 16% were osteoporotic, 18% were osteopenic and 66% had normal T scores at their lumbar spine and in the UC patients, 13% were osteoporotic, 19% were osteopenic and 68% had a normal T score.

When environmental risk factors were considered in CD patients a low BMI (<18.5) was associated with osteoporosis (p = 0.048, OR 4.9 CI 1.2–19.8) and furthermore a linear correlation between T score at the vertebral spine and BMI was observed. R2 = 0.034, p = 0.0009).

Further analysis was carried out to include CD patients at increased risk of fracture—those with osteoporosis and osteopenia. Low BMI (p = 0.0008) and history of being a current or ex-smoker (p = 0.005) were associated with osteoporosis and osteopenia. No association was observed between the number of months a CD patient was on corticosteroid therapy and osteoporosis and no environmental associations were observed with osteoporosis in the UC cohort.

Multivariate analysis showed low BMI (<18.5) was independently associated with osteoporosis (p = 0.021, OR = 5.83, CI = 1.31–25.94). No clinically significant genetic associations were observed between the IBD, CD, UC and osteoporosis disease groups and the VDR Apa-1 and Taq-1 variants.

CONCLUSIONS

The prevalence of osteoporosis in our CD (16%) and UC (13%) population is in line with recent CD data pub-
Low Body Mass is Associated with Osteoporosis

INFLAMMATORY BOWEL DISEASE: A PRACTICAL APPROACH, SERIES #41

Table 1
Prevalence of osteoporosis in adult inflammatory bowel disease cohorts

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of Patients</th>
<th>Prevalence of Osteoporosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compston, et al (5) 1987</td>
<td>75</td>
<td>30.6%</td>
</tr>
<tr>
<td>Bjarnason, et al (16) 1997</td>
<td>79</td>
<td>17%–28%</td>
</tr>
<tr>
<td>Pollak, et al (7) 1998</td>
<td>104</td>
<td>41%–42%</td>
</tr>
<tr>
<td>Frei, et al (6) 2006</td>
<td>88</td>
<td>5%–14%</td>
</tr>
<tr>
<td>Bartram, et al (4) 2006</td>
<td>258</td>
<td>11.6%–13.6%</td>
</tr>
<tr>
<td>Noble, et al (1) 2008</td>
<td>440</td>
<td>15%</td>
</tr>
</tbody>
</table>

lished from Newcastle, UK where 11.6% of Crohn’s disease patients were osteoporotic at either the lumbar spine or femoral neck (4) (Table 1). The data are also comparable to data from London, where in patients with CD and UC the incidence of osteoporosis of the vertebrae and the hip was between 17%–28% (16).

Low BMI was the strongest risk factor for osteoporosis in our CD population and increasing data are emerging in both patients with IBD and in the healthy population that low BMI is a significant independent risk factor for osteoporosis. In a recent study of postmenopausal women in the USA, Asomaning, et al observed a linear decrease of 12% in BMD for each point decrease in BMI. (17) Low BMI has also been observed to predict risk of hip fracture even after adjustment for BMD. In a meta-analysis of 60,000 patients from 11 prospective studies the relative risk of fracture rose from 1.4 in females with a BMI of 20 to 2.2 in females with a BMI of 15 (18).

In the present study being a current or ex-smoker was also associated with osteoporosis and osteopenia on univariate analysis. The mechanisms underlying smoking-associated bone loss and fracture risk remain poorly understood and previous studies have suggested that the effect of smoking appears to be dose-dependent, and may be reversible (19).

No association was observed between corticosteroid use and osteoporosis when the osteoporotic CD patients were compared to a matched non-osteoporotic CD group. Although the role of corticosteroids in the development of osteoporosis in patients with IBD remains controversial, this result is in line with previous data published from our centre in 1994 where low-bone mineralization was observed in patients with CD at diagnosis and prior to any corticosteroid therapy (20).

In the present study, when variants of the VDR gene and osteoporosis were examined no association was observed and it will be of great interest to look for further evidence of association in the present cohort with genes identified as being associated with osteoporosis in the healthy adult population by genome wide association studies (21).

In conclusion, our results show relatively low incidences of osteoporosis in a large cohort of Scottish patients with inflammatory bowel disease. Low body mass index was the strongest risk factor associated with osteoporosis. Longitudinal follow-up studies to assess the benefits of nutritional intervention in these patients, on BMI, bone density and fracture risk will be of great interest.

References
Low Body Mass is Associated with Osteoporosis

(continued from page 34)

World Health Organ Tech Rep Ser, 1994; 843, 1-129.


Practical Gastroenterology REPRINTS
Visit our web site at www.practicalgastro.com

Fellows’ Corner is a New Section in Practical Gastroenterology open to Trainees and Residents ONLY.
Section Editor: C. S. Pitchumoni, M.D.

Send in a brief case report. No more than one double-spaced page. One or two illustrations, up to four questions and answers and a three-quarter to one-page discussion of the case. Case to include no more than two authors. A $100.00 honorarium will be paid per publication.

Case should be sent to:
C. S. Pitchumoni, M.D.
Chief, Gastroenterology, Hepatology and Clinical Nutrition
St. Peter’s University Hospital
254 Easton Avenue, Box 591
New Brunswick, NJ 08903
E-mail: pitchumoni@hotmail.com