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BRIEF ARTICLES

Osteoporosis in adult Sri Lankan inflammatory bowel disease patients

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Abstract

AIM: To determine if inflammatory bowel disease (IBD) is a risk factor for osteoporosis in adult Sri Lankans.

METHODS: We identified eligible subjects from among consecutive patients diagnosed with IBD who attended our outpatient clinic. We included only patients aged between 20 and 70 years. Patients who were pregnant, had significant comorbidity, or were on calcium supplements or treatment for osteoporosis within the past 6 mo, were excluded. Healthy, age- and sex-matched controls were also recruited, in a control to patient ratio of 3:1. Both groups were screened for osteoporosis using peripheral dual energy X-ray absorptiometry scanning.

RESULTS: The study population consisted of 111 IBD patients (male:female = 43:68; mean age 42.5 years) and 333 controls (male:female = 129:204; mean age 43.8 years). The occurrence of osteoporosis among IBD patients (13.5%) was significantly higher than among controls (4.5%) (P = 0.001). The frequency of osteoporosis was not significantly different between ulcerative colitis (14.45%) and Crohn's disease (10.7%). However, on multivariate analysis, only age (P = 0.001), menopause (P = 0.024) and use of systemic steroids (P < 0.001) were found to be associated independently with the occurrence of osteoporosis, while IBD, severity of disease, number of relapses, duration of illness or treatment other than systemic steroids were not.

CONCLUSION: IBD does not appear to be an independent risk factor for the occurrence of osteoporosis in this population. However, the use of systemic steroids was a risk factor.

Key words: Osteoporosis; Inflammatory bowel disease; Asians; Crohn's disease; Ulcerative colitis

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INTRODUCTION

The incidence of inflammatory bowel disease (IBD)

is rising in Asian populations[1]. IBD, both ulcerative colitis (UC) and Crohn's disease (CD), is a recognized risk factor for development of osteoporosis among Caucasians[2-4] but this association does not seem to have been investigated adequately in Asian populations[5].

Osteoporosis is usually diagnosed by dual energy X-ray absorptiometry (DEXA) scanning[6]. However, peripheral DEXA (pDEXA), quantitative computed tomography (QCT), radiographic absorptiometry, and ultrasound have become useful in community screening[7-9]. In the literature, the reported prevalence of osteoporosis/osteopenia in IBD varies from 7% to 56%[10,11]. A retrospective study of a Caucasian population showed a 40% increase in the risk of fracture compared to healthy controls[12]. CD seems to be associated with a slightly higher risk than UC does for osteoporosis and subsequent fractures, although this has been disputed in some studies[13,14]. The mechanism for development of osteoporosis in IBD patients seems to be multifactorial[15]. The slightly higher incidence of osteoporosis in CD could be attributed to the presence of ileal disease or small intestinal resection causing vitamin D malabsorption, malnutrition or estrogen deficiency[16]. Some studies have shown a genetic predisposition to osteoporosis in IBD patients[17]. The identified genes involve the pro-inflammatory cytokine interleukin-6[18,19]. It is important to identify IBD patients with osteoporosis, as treatment with bisphosphonates has been found to be effective[20,21].

There have been no large published studies regarding an association between osteoporosis and IBD in Asian populations[22]. It is important to investigate such an association because IBD among Asians seems to be genetically and phenotypically different to that in the West[23].

MATERIALS AND METHODS

Patients

Consecutive patients with previously diagnosed IBD from a single tertiary care center in Sri Lanka were eligible for inclusion in the study. IBD was diagnosed using standard criteria[24]. Inclusion criteria were age > 20 and < 70 years and the presence of IBD. Exclusion criteria were pregnancy; uncontrolled diabetes; renal, hepatic, cardiovascular or psychiatric disease; rheumatoid arthritis; ankylosing spondylitis; primary sclerosing cholangitis; or treatment with teriparatide, calcitonin, bisphosphonates, fluoride, androgens, anabolic steroids or active metabolites of vitamin D within the past 6 mo.

Controls

For each case, three age- (± 5 years) and sex-matched healthy controls were selected from among individuals who were selected randomly from the community for a large population study that screened for non-communicable diseases. The controls were screened for diabetes and were not taking active metabolites of vitamin D or calcium supplements.

Steroid use

Steroid use was defined as the continuous use of systemic steroids for > 3 mo. Others were considered steroid naïve.

Ethics

The study protocol was approved by the Ethics Committee of the Faculty of Medicine, University of Kelaniya. Written informed consent was obtained from all participants.

Study design

A comparative study involving IBD cases and age- and sex-matched community controls at ratio of 1:3.

DEXA scanning

Both cases and controls underwent pDEXA with the accuDEXA (ADXA-finger) (Schick, New York, NY, USA) using the right index finger. The bone mineral density (BMD) and *T* scores were recorded.

Diagnosis of osteoporosis and osteopenia

Osteoporosis and osteopenia were diagnosed using WHO criteria[25]. Osteoporosis was defined as a *T* score of -2.5 or below, while osteopenia was diagnosed with a *T* score between -1 to -2.49.

Statistical analysis

Previous studies have reported a 56% prevalence of osteoporosis among Caucasian IBD patients, and we assumed a 40% prevalence of osteoporosis among controls. We calculated that a sample size of 111 IBD patients and 333 controls was required to have 80% power to detect this difference at a significance level of 0.05. Quantitative data were compared using the *t* test, and categorical data were compared using a χ^2 test. Multiple logistic regression was used to identify independent risk factors for osteoporosis. The analysis was carried out using the statistical program SPSS version 16 (Chicago, IL, USA).

RESULTS

One hundred and eleven IBD patients [male:female = 43:68; mean age 42.5 years; 83 (74.8%) with UC, 28 (25.2%) with CD, and 333 age- and sex-matched healthy controls (male:female = 129:204; mean age 43.8 years) were recruited (Table 1). The site of disease was mainly proctitis for UC and colonic for CD (Table 2). Osteopenia was significantly more common among IBD patients (13.51%) than the controls (4.5%) (P = 0.001). Osteopoenia (T < -1) was also significantly more common in IBD patients than in controls (35.1% *vs* 22.5%, P = 0.008). The prevalence of osteoporosis was not significantly different between patients with UC (14.45%) and CD (10.71%) (P = 0.616). On bivariate analysis, age, female sex, menopause, presence of IBD, severity of disease and use of systemic steroids were found to be associated independently with the

Table 1 Characteristics of inflammatory bowel disease (IBD) patients and controls *n* (%), mean ± SD

	IBD patients (*n* = 111)	Controls (*n* = 333)	*P* value
Male:Female	43:68	129:204	1.000
Age (yr)	42.5 ± 14.19	43.8 ± 11.2	0.368
Postmenopausal women	29 (42.6)	83 (40.7)	0.778
Fractures	12 (10.8)	20 (6)	0.073
BMI (kg/m^2)	21.3 ± 4.45	23.8 ± 4.47	< 0.001
Disease duration (yr)	5.66 ± 5.72		
Corticosteroid use	74 (66.7)	3 (0.9)	< 0.001
Current smokers	4 (3.6)	29 (8.7)	0.094

Table 2 Disease location in IBD patients

	Frequency	Percent
Ulcerative		
Distal	46	56.8
Left sided	23	28.4
Total	12	14.8
Total	81	100.0
Crohn's disease		
Upper GI	2	6.7
Small bowel	4	13.3
Colon	21	70.0
Small bowel & colon	3	10.0
Total	30	100.0

Table 3 Summary of multiple logistic regression analyses

Variable	Regression coefficient	*P* value	OR (95% CI)
Constant	-7.478		
Age	0.78	0.001	1.081 (1.032-1.133)
Sex[1]			
Female (pre-menopausal)	0.898	0.213	2.456 (0.597-10.108)
Female (menopausal)	1.271	0.024	3.563 (1.179-10.763)
Using steroids[2]	2.082	< 0.001	8.021 (2.693-23.891)

[1]Comparison group is males; [2]Comparison group is not using steroids.

occurrence of osteoporosis. In the multivariate logistic regression model, age, sex, menopausal status and use of steroids were significant predictors of osteoporosis (Table 3). IBD was not a significant predictor of osteoporosis. With each advancing year of age, there was a 1.081 times increase in the likelihood of the development of osteoporosis. Premenopausal women were 2.5 times more likely to have osteoporosis than men, and menopausal women were 3.6 times more likely to have osteoporosis than men. Steroid use increased the risk of osteoporosis by eightfold.

DISCUSSION

The prevalence of osteoporosis and osteopenia in our IBD patients was significantly higher than in community controls. However, on multiple logistic regression analysis, only use of systemic steroids, age and menopause were found to be significant independent risk factors for osteoporosis. The presence of IBD and its severity were not, nor were the number of relapses, duration of illness, or treatment other than systemic steroids. The increased frequency of osteoporosis in our IBD patients was likely to have been caused by use of systemic steroids rather than by IBD itself. This is different to western studies, and we cannot explain this difference.

We did not find a significant difference in prevalence of osteoporosis between patients with UC and CD, although we admit that the number of CD patients in our sample was small, with mainly colonic involvement. This is in agreement with some but not all western data[26,27]. Our finding that there was no association between the occurrence of osteoporosis and severity of IBD, number of relapses, duration of illness, and treatment other than systemic steroids, agrees with the findings of Western studies[28,29].

We also noted a difference in the fracture risk between the two groups: 10.8% in the IBD group and 6% in the control group. However, this did not reach statistical significance, as our study was probably not adequately powered to investigate this complication. This finding is not surprising and could be attributed to steroid use as in western studies[30].

There are several methodological weaknesses in our study. We designed this as a comparative study rather than a case-control study, as that would have been difficult to perform in an Asian country where the prevalence of IBD is much lower than in the West. We also used pDEXA scanning instead of central DEXA to diagnose osteoporosis. However, although central DEXA scanning is accepted widely as the gold standard for diagnosis of osteoporosis, there have been many studies showing that pDEXA is a good alternative, especially in the community setting[7,8].

In conclusion, IBD does not appear to be an independent risk factor for the occurrence of osteoporosis in this population. The increased frequency of osteoporosis in our IBD patients is likely to be related to the use of systemic steroids. However, our finding that osteoporosis is more common in IBD patients, even though it may only be related to steroid use, has a direct bearing on patient management, as new guidelines advise the routine use of bisphosphonates in IBD patients with a BMD of < -1.5[31].

COMMENTS

Background

Inflammatory bowel disease (IBD) is a well-recognized risk factor for osteoporosis in Caucasian patients. However, there have been very few studies on Asian patients that have investigated this problem. To the best of our knowledge, there have been no studies on this topic in Southern Asians. However, since there are obvious genetic differences between the two populations it an important area of study that has been neglected.

Research frontiers

The genetics of IBD is a rapidly expanding field. To support this type of work, good phenotypic data from different cohorts of patients across continents are important. In studying osteoporosis, it is important to have similar data that will help in subsequent genetic studies.

Innovations and breakthroughs

In the present study, the authors showed that IBD was not an independent risk

factor for osteoporosis, but rather the use of systemic steroids was a risk factor for the development of osteoporosis.

Applications

It is important to know that not all Asian patients with IBD need routine bisphosphonates, as these are expensive drugs. This study will help to target whom to treat. Also, in future genetic studies, phenotypic racial differences will be important in the search for specific genes.

Terminology

Osteoporosis is a metabolic bone disease that is characterized by reduced bone mineral density. It is usually asymptomatic until it results in fractures. It is diagnosed using dual energy X-ray absorptiometry. IBD is a chronic disease of unknown etiology that comprises Crohn's disease and ulcerative colitis.

Peer review

This study dealt with the prevalence and risk factors of osteoporosis in adult Sri Lankan IBD patients. It is a well conceived and analyzed study.

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