

# Journal of Gastroenterology and Hepatology Research

Online Submissions: <http://www.ghrnet.org/index./joghr/>  
doi: 10.17554/j.issn.2224-3992.2022.11.1044

Journal of GHR 2022 February 21; **11**(1): 3676-3681  
ISSN 2224-3992 (print) ISSN 2224-6509 (online)

## ORIGINAL ARTICLE

## Low Bone Mineral Density in Inflammatory Bowel Disease Patients

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**Conflict-of-interest statement:** The authors declare that there is no conflict of interest regarding the publication of this paper.

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**Received:** January 27, 2022

**Revised:** February 8, 2022

**Accepted:** February 10, 2022

**Published online:** February 21, 2022

### ABSTRACT

**BACKGROUND AND AIMS:** Inflammatory Bowel Disease (IBD) is associated with low bone mineral density (BMD). Several purported risk factors contribute to this risk, however there is still lack of consensus on criteria for screening in Australia. This study aims to assess screening and identify risk factors for low BMD in IBD patients at a single tertiary centre in the Asia-Pacific region

**METHODS:** A retrospective review of IBD patients who attended an Australian tertiary centre between 2013 to 2018 was conducted. Risk factors for low BMD such as age, gender, BMI, type of IBD, smoking,

steroid therapy, serum calcium and vitamin D levels were evaluated.

**RESULTS:** A total of 236 of 544 (43%) IBD patients had a DEXA scan performed. Of those patients, 46.6% had low BMD on initial DEXA. Follow up DEXAs occurred in 33.1% of those 236 patients with an average time of 5 years between scans. Risk factors for low BMD were age  $\geq 50$  years ( $p \leq 0.001$ ) and BMI  $< 25$  kg/m<sup>2</sup> ( $p < 0.001$ ). There were 21 of 236 (9%) patients who sustained a fracture in this study.

**CONCLUSION:** Screening rates for BMD in IBD patients was low at 43% at this single tertiary centre in the Asia-Pacific region. Approximately 47% has low BMD and age  $\geq 50$  years and BMI  $< 25$  kg/m<sup>2</sup> were identified as significant risk factors for low BMD. Early identification of those at risk of low BMD is important in order to prevent osteoporosis and related adverse skeletal events.

**Key words:** Bone mineral density; Inflammatory bowel disease; Osteoporosis; Dual-energy X-ray absorptiometry; Body mass index

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Lin MCP, Eddy C, Stanton S, Subramaniam K. Low Bone Mineral Density in Inflammatory Bowel Disease Patients. *Journal of Gastroenterology and Hepatology Research* 2022; **11**(1): 3676-3681 Available from: URL: <http://www.ghrnet.org/index.php/joghr/article/view/3254>

### INTRODUCTION

Patients with inflammatory bowel disease (IBD) are at high risk of low bone mineral density (BMD) and associated skeletal complications such as fractures<sup>[1-6]</sup>. Several purported mechanisms contribute to loss of BMD in IBD patients, including a chronic inflammatory state, corticosteroid use, and intestinal malabsorption resulting in vitamin D and calcium deficiency<sup>[7,8]</sup>. Other possible risk factors such as low body mass index (BMI), older age, male gender, smoking, alcohol consumption, low physical activity, history of fractures and hypogonadism have also been explored<sup>[6-9]</sup>. Whilst international guidelines recommend screening for osteoporosis and osteopenia in IBD patients, there is lack of consensus in Australia on screening criteria.

The pathogenesis of bone mineral loss in IBD patients is multifactorial, with chronic inflammation's effect on bone

homeostasis playing a major role. Chronic intestinal inflammation hastens bone loss as pro-inflammatory cytokines such as interleukin-1 (IL-1), IL-6 and tumour necrosis factor alpha (TNF- $\alpha$ ) impair osteoblastic bone formation whilst inducing osteoclastic bone resorption<sup>[9]</sup>. The role of TNF- $\alpha$  in the pathogenesis of Crohn's Disease (CD) and impact on loss of BMD has recently come to light as studies demonstrated clinically significant improvements in BMD and disease activity in patients on infliximab, a monoclonal antibody against TNF- $\alpha$ <sup>[10,11]</sup>. This suggests the importance of TNF- $\alpha$  therapy in IBD to induce remission and reduce bone loss.

Whilst screening recommendations for low BMD in IBD patients exist, the criteria for screening varies internationally. Dual energy X-ray absorptiometry (DEXA) scans are globally recognised as the screening tool for low BMD. The British Society of Gastroenterologists (BSG) advised scanning patients who take  $\geq 7.5$ mg per day of prednisolone for 6 months, whereas the American College of Gastroenterologists (ACG) advised scanning patients on at least 3 months of high dose steroids at an unspecified dose. Moreover, both guidelines recommend screening of high-risk patients identified with two or more of the following risk factors: BMI  $< 20$  kg/m<sup>2</sup>, weight loss  $> 10\%$ , continuing active disease and age  $> 70$  years<sup>[12,13]</sup>. The European Crohn and Colitis Organisation (ECCO) recommends scanning IBD patients who are on steroids for  $> 3$  months without defining dosage, whilst the Gastroenterological Society of Australia (GESA) advised that DEXA should be considered for patients newly started on steroids and patients on long-term steroids or weight loss<sup>[14,15]</sup>. The Asian Organisation for Crohn's and Colitis (AOCC) and Asia Pacific Association of Gastroenterology (APAGE) recommends calcium and vitamin D3 supplements for IBD patients who have osteoporosis, but does not specify when to screen for and review BMD at follow-up<sup>[16]</sup>.

A 2018 survey of Australian Gastroenterologists found variable rates of screening and treatment of osteoporosis in IBD patients<sup>[17]</sup>. This study aims to assess screening and identify risk factors for low BMD in IBD patients at a single tertiary centre in the Asia-Pacific region.

## METHODS

A retrospective review of 544 IBD patients who attended the IBD clinic at the Canberra Hospital between January 2013 and January 2018 was performed. Inclusion criteria were all adult patients identified with an IBD diagnosis from the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (ICD-10-AM). Patients who had DEXA scans performed at the Canberra Hospital were included. For patients with a DEXA scan, additional information regarding steroid usage two years prior to the scan, smoking history, age, gender, BMI, menopausal status, fracture history, serum calcium and vitamin D levels at the time of scan were collected by reviewing medical records. For patients who had a second DEXA scan, the years between scans and BMD results were collected. BMD outcomes between the two DEXA scans were evaluated.

Osteoporosis was defined as T-score  $< -2.5$  standard deviations (SD), osteopenia between  $-1$  and  $-2.5$ , and normal BMD  $\geq -1$  and  $\leq +1$  as per the World Health Organisation (WHO) guidelines<sup>[18]</sup>. In cases where only a Z-score was measured, osteopenia was defined as a Z-score  $\leq -2.0$  SD. For statistical purposes, osteopenia and osteoporosis were grouped together as low BMD. The majority of patients had DEXA measurements taken from the lumbar spine and/or femur (total hip and/or femoral neck) with one patient scanned

solely at the wrist. Ulna Z-score was used in place of spine Z-score for that patient. BMI was defined as underweight at  $< 18.5$  kg/m<sup>2</sup>, normal between 18.5 to 24.9 kg/m<sup>2</sup>, overweight between 25 and 29.5 kg/m<sup>2</sup>, and obese if  $\geq 30$  kg/m<sup>2</sup>.

Statistical analysis was performed using Statistical Package for Social Sciences for Mac Version 28 (SPSS, INC., Chicago, IL, USA). Descriptive statistics were performed. After adjusting for assumptions, binomial logistic regression model was applied to assess the relationship between potential risk factors and low BMD. Results of bivariate and multivariate analysis was presented as odds ratio (OR) and 95% confidence interval (CI), with statistical significance defined as  $p < 0.05$ . Variables that were not routinely obtained for all IBD patients (e.g., serum calcium and vitamin D levels) were evaluated separately.

Ethics was obtained through Australian National University Medical School and Australian Capital Territory Health.

## RESULTS

In a cohort of 544 known IBD patients, females accounted for 51.5% of the total cohort with 48.4% being male (Table 1). The proportion of CD patients was almost double that of UC patients (65.8% of CD vs 34.2% UC). There were more females with CD at 55.6% and more males with UC at 56.6%. DEXA scans were performed on 43.4% ( $n = 236$ ) of the study population (Table 1).

Table 2 highlights demographics of the 236 patients who had an initial scan (DEXA 1) and the 78 patients with a follow-up scan (DEXA 2). Out of the 236 patients, 110 had low BMD (osteopenia,  $n = 94$ ; osteoporosis,  $n = 16$ ). Patient characteristics were compared with BMD status. The median time between scans was 5 years (range 1 to 8 years). The median age of patients who had an initial DEXA scan was 40 years old (range 18 - 78 years), and that of patients with a follow-up scan was 42 years old (range 23 - 75 years). A total of 171 patients were younger than 50 years of age (normal BMD,  $n = 104$ ; low BMD,  $n = 67$ ), and 65 patients were aged 50 and above at time of first DEXA (normal BMD,  $n = 22$ ; low BMD,  $n = 43$ ). More women than men had a first DEXA (52% women vs 48% men), of which 21% of women ( $n = 51$ ) and 25% of men ( $n = 59$ ) were found to have low BMD. Follow-up scans occurred at the same rate of 33% for both genders. More patients with CD had an initial DEXA compared to patients with UC (total CD vs total UC,  $n = 166$  vs  $n = 70$ ), with a similar trend on follow-up (CD vs UC,  $n = 57$  vs  $n = 21$ ).

Of the 135 patients on steroid therapy, 48% ( $n = 65$ ) had low BMD at first scan. Rates of follow-up were almost double for patients on steroids than those without at 41% versus 21%. The breakdown of BMI to BMD status demonstrates 5 out of 7 underweight patients and 55 out of 96 with normal BMI have low BMD at first DEXA. Interestingly, more people who had BMI  $\geq 25$  kg/m<sup>2</sup> had normal BMD (overweight and normal BMD,  $n = 47/80$ ; obese and normal BMD,  $n = 36/53$ ). Similar findings for BMI and BMD were noted on DEXA 2, with 62% of overweight ( $n = 18$  out of 29) and 64% ( $n = 7$  out of 11) of obese patients having normal BMD, whereas only 33% of those whose BMI  $< 24.9$  kg/m<sup>2</sup> had normal BMD. In terms of smoking exposure and BMD, 72 non-smokers and 38 smokers (current smokers,  $n = 17$ ; ex-smokers,  $n = 21$ ) had low BMD on first DEXA; on follow-up, 23 non-smokers and 17 smokers (current smokers,  $n = 5$ ; ex-smokers,  $n = 12$ ) had low BMD. Comparing fracture history to BMD status, only 10 patients of the 110 patients with low BMD sustained a fracture at first DEXA, and only 3 patients out of the 40 with low BMD at second DEXA had a fracture. Lastly, serum calcium and vitamin D levels were not routinely collected for

all patients (Table 2). At initial DEXA, only 211 of 236 patients had serum calcium levels checked and 123 of 236 with serum vitamin D levels; at DEXA 2, serum calcium was checked for 69 of 78 patients and serum vitamin D was checked for 41 of 78 patients. Of note, none of the patients with low BMD at both DEXA 1 and 2 had low calcium levels. Low vitamin D levels was noted in 21 patients with low BMD at DEXA 1, and 9 patients at DEXA 2.

Table 3 compares BMD outcomes between initial and follow-up DEXA scan. “Better” is defined as progression of at least one standard deviation towards normal BMD, “same” being no change in outcome, and “worse” defined as left-shift of at least one standard deviation away from initial BMD. Of the 33 patients with osteopenia at DEXA 1, 48% ( $n = 16$ ) remained osteopaenic, 42% ( $n = 14$ ) had improved BMD to normal range, and 9% ( $n = 3$ ) had become osteoporotic. Of the 7 patients with osteoporosis on initial scan, 43% ( $n = 3$ ) had improved BMD to either osteopaenia or normal, and 57% ( $n = 4$ ) remained osteoporotic. Of the 38 patients with normal BMD at first scan, 79% ( $n = 30$ ) stayed within normal range, and 21% ( $n = 8$ ) had either developed osteoporosis or osteopenia.

Table 4 compares risk factors associated with low BMD. Age and BMI were found to be statistically significant risk factors to BMD in both bivariate and multivariate analysis. Those older than 50 years of age are at three times the risk of having low BMD (OR 3.962, 95% CI: 2.058 - 7.626,  $p < 0.001$ ). A BMI  $< 25 \text{ kg/m}^2$  also tripled one's risk for low BMD (OR 2.929, 95% CI: 1.630 – 5.265,  $p < 0.001$ ). Gender was not found to be a significant risk factor for low BMD ( $p = 0.126$ ) along with type of IBD ( $p = 0.187$ ), steroid exposure ( $p = 0.584$ ) and smoking history ( $p = 0.209$ ).

Table 5 compares fracture risk with serum calcium, serum vitamin D and BMD status for the 236 patients who had an initial DEXA scan. The serum calcium and vitamin D levels were not measured routinely for all patients. Of the 21 patients who sustained a fracture, 17 had normal serum calcium levels and 8 had normal vitamin D levels. One patient with a fracture had high measured calcium and none of the fracture patients had low calcium levels. Three patients with a fracture had low measured vitamin D levels. There were more patients with normal BMD than low BMD sustained a fracture (52 % vs 48%). Of the 215 patients who did not have a fracture, 188 had normal calcium levels and 68 had normal vitamin D levels. Neither serum calcium or vitamin D levels or BMD status were clinically significant risk factors for fractures.

## DISCUSSION

IBD is a relapsing and remitting condition characterised by chronic intestinal inflammation. Compared to the general population, IBD

**Table 1** Patient Demographics ( $n = 544$ ).

	n	%
Female	280	51.50%
Male	264	48.40%
CD <sup>a</sup>	358	65.80%
Female	199	55.60%
Male	159	45.30%
UC <sup>b</sup>	186	34.20%
Female	81	43.40%
Male	105	56.60%
DEXA <sup>c</sup>	236	43.40%
No DEXA	308	56.60%

<sup>a</sup> CD = Crohn's disease, <sup>b</sup> UC = ulcerative colitis, <sup>c</sup> DEXA = dual-energy X-ray absorptiometry

**Table 2** Demographics of patients with initial and follow-up DEXA scans Time between scans (Median 5 years, range 1-8 years).

	DEXA 1 (n = 236)			DEXA 2 (n = 78)		
	Total	Normal (n=126)	Low BMD (n=110)	Total	Normal (n=38)	Low BMD (n=40)
	Age (median 40, range 18-78)			Age (median 42, range 23-75)		
<50	171	104	67	60	31	29
≥ 50	65	22	43	18	7	11
<b>Gender</b>						
Male	114	55	59	38	13	25
Female	122	71	51	40	25	15
Post-menopausal	14	4	10	3	2	1
Pre-menopausal	108	67	41	37	23	14
<b>IBD</b>						
CD	166	84	82	57	26	31
UC	70	42	28	21	12	9
<b>Steroids</b>						
Yes	135	70	65	56	29	27
≥ 20 per day	77	42	35	29	15	14
<20 per day	58	28	30	27	14	13
No	101	56	45	22	9	13
<b>BMI</b>						
Underweight	7	2	5	2	1	1
Normal	96	41	55	36	12	24
Overweight	80	47	33	29	18	11
Obese	53	36	17	11	7	4
<b>Smoking</b>						
Current	34	17	17	12	7	5
Ex-smoker	38	17	21	14	2	12
Non-smoker	164	92	72	52	29	23
<b>Fracture</b>						
Yes	21	11	10	6	3	3
No	215	115	100	72	35	37
Calcium	(n=211)	(n=113)	(n=98)	(n=69)	(n=34)	(n=35)
High	4	1	3	1	0	1
Normal	205	110	95	68	34	34
Low	2	2	0	0	0	0
Vitamin D	(n=123)	(n=67)	(n=56)	(n=41)	(n=21)	(n=20)
Normal	76	41	35	24	13	11
Low	47	26	21	17	8	9

Dual-energy X-ray absorptiometry, DEXA; inflammatory bowel disease, IBD; Crohn's disease, CD; ulcerative colitis, UC; Bone mineral density, BMD; osteopenia: T-score  $< -1$  SD or Z-score  $\leq -2$  SD; osteoporosis: T-score  $\leq -2.5$  SD; milligrams, mg; body mass index, BMI; underweight  $< 18.5 \text{ kg/m}^2$ ; normal BMI  $18.51$  to  $\leq 24.9 \text{ kg/m}^2$ ; overweight:  $25 \leq \text{BMI} \leq 29.9 \text{ kg/m}^2$ ; obese: BMI  $\geq 30 \text{ kg/m}^2$ ; high calcium  $> 2.6 \text{ mmol/L}$ ; normal calcium  $2.1$ - $2.6 \text{ mmol/L}$ ; low calcium  $< 2.1 \text{ mmol/L}$ ; low vitamin D  $< 50 \text{ nmol/L}$ ; normal  $\geq 50 \text{ nmol/L}$ .

**Table 3** BMD outcomes between DEXA 1 and DEXA 2.

	Better <sup>a</sup>	Same <sup>b</sup>	Worse <sup>c</sup>
Osteopenia	14	16	3
Osteoporosis	3	4	n/a
Normal	n/a	30	8

<sup>a</sup> better defined as improved BMD by at least one standard deviation.

<sup>b</sup> same defined as no change in BMD.

<sup>c</sup> worse defined as left shift of BMD by minimum of one standard deviation.

**Table 4** Risk factors for low BMD in DEXA patients (n=236).

	Bivariate Analysis		Multivariate Analysis	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Gender(Male vs female)	1.493 (0.893 – 2.497)	0.126	0.658 (0.376 – 1.152)	0.143
Age(≥ 50 years vs <50 years)	3.034 (1.668 – 5.520)	<0.001*	3.962 (2.058 – 7.626)	<0.001*
IBD <sup>a</sup> type (CD vs UC)	0.683 (0.387 – 1.204)	0.187	1.380 (0.735 – 2.588)	0.316
BMI <sup>b</sup> (BMI <25 kg/m <sup>2</sup> vs BMI ≥ 25 kg/m <sup>2</sup> )	2.316 (1.369 – 3.919)	0.002*	2.929 (1.630 – 5.265)	<0.001*
Steroids use (Yes vs No)	0.865 (0.516 – 1.452)	0.584	0.785 (0.449 – 1.372)	0.395
Ever smoked <sup>c</sup> (Yes vs No)	1.428 (0.819 – 2.490)	0.209	1.170 (0.637 – 2.147)	0.613

\*statistical significance defined as  $p < 0.05$ . <sup>a</sup> IBD, Inflammatory bowel disease, including crohns disease (CD) and ulcerative colitis (UC). <sup>b</sup> BMI, body mass index. <sup>c</sup> Smoking exposure, yes inclusive of ex- and current smokers.

**Table 5** Fracture and Bone Mineral Density.

	Fracture (n=21)		OR (95% CI)
	n, %	n, %	
Calcium <sup>a</sup> (n=211)	18, 85%	193, 90%	2.21 (0.24-20.03)
Normal	17, 94%	188, 97%	
High	1, 6%	3, 2%	
Low	0, 0%	2, 1.0%	
Vitamin D <sup>b</sup> (n=123)	11, 52%	112, 52.1%	0.58 (0.15-2.30)
Normal	8, 73%	68, 61%	
Low	3, 27%	44, 39%	
BMD <sup>c</sup> (n=236)			1.05 (0.43-2.56)
Normal	11, 52%	115, 53%	
Low	10, 48%	100, 47%	

<sup>a</sup> Corrected calcium in blood, reference range 2.10-2.60 mmol/L.

<sup>b</sup> Serum vitamin D, reference range for normal levels ≥ 50 nmol/L, low < 50 nmol/L. <sup>c</sup> Bone mineral density.

patients are at greater risk for vertebral fractures<sup>[3,19]</sup>, hence the importance of early screening and prevention of osteoporosis amongst this patient group. In our cohort of 544 patients, nearly half (46.6%,  $n = 110$ ) of the 236 patients who had DEXA scans were identified with low BMD, with osteopenia and osteoporosis comprising 39.8% ( $n = 94$ ) and 6.8% ( $n = 16$ ) respectively. Similar rates were reported in a Brazilian IBD population ( $n = 128$ ), with 40% diagnosed with osteopenia and 7% osteoporosis<sup>[6]</sup>, and other studies reporting osteoporosis rates between 12% to 42% and osteopenia rates as high as 77%<sup>[3,4,9,20,21]</sup>. In a meta-analysis of twelve studies reviewing 3661 IBD patients, the prevalence of osteoporosis varied between 4% to 9% in IBD, with slightly higher proportions seen in CD (7%-15%) versus UC (2%-9%), not too dissimilar findings amongst 12789 healthy controls (3%-10%)<sup>[22]</sup>.

This study found that BMI ≥ 25 kg/m<sup>2</sup> was a protective factor against low BMD ( $p < 0.001$ ). The physiological impact of weight-related gravitational loading on bone remodelling is well established, and explains why being underweight is an independent risk factor for osteopenia and osteoporosis<sup>[23,24]</sup>. However, the relationship between BMI and osteoporosis is not linear. Firstly, BMI does not reflect differences in body composition (e.g., lean body mass and fat mass), which have variable association depending on skeletal sites. For example, one study found positive association between lean mass and BMD in normal and overweight women except in the radius, but found negative association between femoral neck and spine BMD in obese women despite positive association between fat mass and radius BMD<sup>[25]</sup>. Secondly, fat mass in particular visceral fat, is associated with higher levels of bone-active hormones such as leptin and adiponectin that can either induce osteoclastic bone resorption or osteoblastogenesis depending on oestrogen levels, ghrelin and IGF-1<sup>[26,27]</sup>. The complex interplay between oestrogen, ghrelin and IGF-1 depends on menopausal status, presence of estrogen replacement and

also nutritional status which is beyond the scope of this study.

In our study, age ≥ 50 years was a significant risk factor for low BMD ( $p \leq 0.001$ ). Perhaps the older age bracket reflected post-menopausal women who are known to experience accelerated bone loss in the first 10 years of menopause<sup>[28]</sup>. However, given the small sample size of post-menopausal women ( $n = 14$ ), it was difficult to conclude whether menopause made IBD patients more susceptible to BMD loss. It is important to note that 107 patients who did not have a DEXA scan were above the age of 50, and therefore could have missed out on being identified with low BMD.

Gender was not a significant risk factor in this study, which was not in keeping with other studies purporting male IBD patients are at higher risk for osteoporosis<sup>[29]</sup>. Similar to other studies<sup>[30,31]</sup>, we also found no difference in osteoporosis risk between UC and CD patients, although our cohort was not assessed for history of bowel resections, which was attributed as a risk factor by Hoffman and colleagues<sup>[29]</sup>. Smoking was also not a notable risk factor, although this may be inaccurate as smoking history was based on self-reported data.

This study did not find a history of steroid-use a significant risk factor for low BMD ( $p = 0.584$ ) despite the well-known effect of glucocorticoids on stimulating osteoclast differentiation, heightening osteoclastic resorptive capacity, and prolonging osteoclast survival by suppressing apoptosis. Whether daily dose or cumulative lifetime steroid exposure plays a bigger role on loss of bone density remains contentious. In an IBD specific population of 152 patients, one study found that high lifetime corticosteroid dose >10g was associated with greater BMD loss<sup>[32]</sup>. However, a Danish study on 513 IBD patients, 338 of which received ≥500 mg corticosteroid within a year, did not find corticosteroid therapy a considerable risk factor<sup>[33]</sup>. Instead, hospitalization, a reflection of disease activity correlated more with osteoporosis amongst CD patients, suggesting the role chronic inflammation has in bone density loss<sup>[33]</sup>. Moreover, a meta-analysis on fracture risks in the general population found steroid dose ≥ 7.5mg per day increased one's risk of osteoporotic fractures, but cumulative lifetime steroid exposure does not, as fracture risk reduced upon cessation of steroids<sup>[34]</sup>. Interestingly, rheumatoid arthritis patients who received a higher lifetime dose of steroids at >20g per day did not experience more loss of BMD compared to IBD patients<sup>[32,35]</sup>. This suggests additional factors contribute negatively to bone homeostasis.

Patients with IBD are reported to have more nutritional deficiencies than the general population<sup>[36]</sup>. Calcium is vital for normal bone formation and vitamin D plays an important role in maintaining adequate calcium levels by stimulating intestinal calcium absorption, renal calcium reabsorption and osteoclast-mediated bone resorption. Calcium deficiency in IBD is often attributed to intestinal malabsorption and poor oral intake. Similarly, vitamin D deficiency in IBD is due to reduced intake, but also due to ileopathies



(e.g. ileitis, terminal ileal resection) that disrupt enterohepatic circulation<sup>[37,38]</sup>. Moreover, reduced sun exposure and renal insufficiency also contribute to low serum vitamin D levels. Based on this data set, hypocalcaemia (OR 0.14, 95% CI: 0.17, 11.97) and low vitamin D (OR 0.57, 95% CI: 0.15, 2.15) are not associated with increased fracture risk (Table 5).

There was an overall low rate of screening for low BMD in IBD patients. Only 43% ( $n = 236$ ) of the total cohort ( $n = 544$ ) had a DEXA scan at the Canberra Hospital with CD patients slightly more likely to have one than UC patients (70% CD vs 30% UC). This may be due to CD patients receiving higher rates of steroid therapy, a well-established risk factor for low BMD, than UC patients. Of the 236 patients who had an initial DEXA scan, 78 (33%) had a follow up scan. Inconsistency in screening may be due to a lack of straightforward Australian guidelines. For example, GESA's 2018 guidelines did not specify a threshold for minimum steroid dosage or course length to prompt screening<sup>[15]</sup>. Additionally, the guidelines do not include recommended intervals for repeat DEXA scans, which has not changed since the last update in 2013<sup>[39]</sup>. One study found that by educating gastrointestinal (GI) fellows and by incorporating a reminder template in clinic notes significantly improved screening rates by 56%<sup>[40]</sup>. This highlights the importance of education and having reminders to improve screening.

It is difficult to make inferences about causation of low BMD in a cross-sectional study. There are a few limitations to this study. This was a retrospective study and cannot account for unmeasured confounders in determining risk factors for low BMD in IBD patients. The decision to obtain a DEXA scan was at the discretion of the clinician based on the clinical history and individual patient's risk. There was potential selection bias as patients who had investigations done external to this single tertiary centre, which could not be accessed by the principal investigators, were excluded from the study cohort. Moreover, as there was no control group, confounding bias could not be assessed. In addition, given the retrospective nature of this study, complete data on variables such as serum calcium and vitamin D levels as well as drug therapy and gonadal status, were not consistently collected.

## CONCLUSIONS

This study found that over the course of five years, only 43% of IBD patients were screened for low BMD at a single centre in the Asia-Pacific region. Approximately 47% were identified with low BMD amongst those who had an initial screening DEXA. In particular, age  $\geq 50$  years and BMI  $< 25$  kg/m<sup>2</sup> were identified as significant risk factors for low BMD, and should be highlighted as indications for screening. Early identification of those at risk of low BMD is extremely important in order to prevent osteoporosis and related adverse skeletal events. To improve screening rates, it could be worthwhile implementing reminders to prompt the timely screening of low BMD in IBD patients. Future studies could benefit from a prospective approach to ensure complete collection of relevant data and including age-matched control groups without IBD to address confounding bias.

## Declarations

This work is not under active consideration for publication, has not been accepted for publication, nor has it been published, in full or in part (except in abstract form). I confirm that the study has been approved by the Human Research and Ethics Committee at the Australian Capital Territory (ACT) Health.

## Author contribution

Conceptualization: KS. Methodology: KS, SS, CE. Formal analysis: ML. Project administration: KS, CS, ML. Visualization: KS, ML. Writing-original draft: ML, CE. Writing-review and editing: ML, KS. Approval of final manuscript: all authors.

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