



EVALUATION OF BONE MINERAL DENSITY AMONG PATIENTS WITH INFLAMMATORY BOWEL DISEASE IN A TERTIARY CARE HOSPITAL

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ABSTRACT

To evaluate bone mineral density among patients with IBD, to determine and correlate the prevalence of osteopenia and osteoporosis by measuring BMD in IBD patients with severity of disease with modifiable risk factors. The present study is carried out in the Department of Gastroenterology, Gandhi Medical College / Hospital, Hyderabad, from November 2017 to October 2019. In the present study, it was observed that 40% patients were in the age group of 20-29 years. The age range of subjects in the study was between 18 years to 59 years. The mean age of the study population was 31.48 ± 8.73 years. Continuous variables were expressed as mean \pm SD values, categorical variables were expressed as frequencies and percentages. Statistical test such as unpaired t-test was used to evaluate mean differences between groups for continuous variables and Fisher test/Chi square test was used to assess association between categorical variables. Probability value (p value) was used to determine the level of significance. p value < 0.05 was considered as significant and p value < 0.01 was considered as highly significant. BMD in patients with recently diagnosed IBD was not significantly decreased compared with population controls. Subsequent development of osteoporosis in patients with IBD seems to be a phenomenon related to the disease process and the treatment modalities of IBD.

KEYWORDS : Bone mineral density, Ulcerative colitis, Crohn's disease, inflammatory bowel disease, Osteoporosis

INTRODUCTION

Inflammatory bowel disease (IBD) is a chronic inflammatory condition of the colon characterized by relapsing and remitting episodes of inflammation requiring long term therapy¹. Due to the chronic nature of the disease, frequent monitoring is required to assess the disease severity, response to treatment and to predict relapse².

Clinical indices are subjective, with a great deal of interobserver variation. At present, colonoscopy and biopsy is considered the gold standard for the evaluation of mucosal inflammation. Patients with inflammatory bowel disease are no more immune to development of osteoporosis than the general population. Initial estimates suggest that 30% of patients with severe Crohns disease & somewhat fewer patients with ulcerative colitis had metabolic disease either osteopenia or osteoporosis. With the introduction of dual energy x ray absorptiometry (DEXA), to quantitate bone mineral density, reliably, reproducibly and with ease and its application to patient with IBD, prevalence of bone mineral density (BMD) was increased to 60%. Pathogenesis of low BMD in IBD was due to ileal & small intestinal involvement of disease, surgical resections causing vitamin D and or calcium malabsorption, malnutrition in Crohns disease and corticosteroids in ulcerative colitis^{3,4}.

Aims & Objectives

1. To evaluate bone mineral density among patients with IBD
2. To determine the prevalence of osteopenia and osteoporosis by measuring BMD in IBD patients
3. To correlate BMD with severity of disease
4. To correlate BMD with modifiable risk factors

Material & Methods

A total of 50 patients with Inflammatory Bowel diseases were included in this study and carried out in the Department of Gastroenterology, Gandhi Hospital, Hyderabad.

After obtaining an informed consent, detailed medical history was obtained, and physical examination was done. Those who qualified for the study underwent a colonoscopy and blood investigations for further characterization. Further, patients were divided into groups based on severity by clinical

and endoscopic criteria as mild, moderate and severe UC & Crohns disease according to Montreal classification. Various clinical and laboratory indices were compared between these groups.

BMD was measured by DEXA scan at two sites, i.e. the lumbar spine and femoral neck using Hologic DEXA scan. BMD was defined according to World Health Organization (WHO) criteria. 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.

Vitamin D levels were estimated using chemiluminescence method. Based on the recommendation of the World Endocrine Society, a level of 30 ng/ml or above is considered as vitamin D sufficiency and patients are categorized as normal (≥ 30 ng/ml), insufficient (20-29.9 ng/ml), deficient (< 20 ng/ml).

Inclusion Criteria

Age more than 18 years, selected patients with IBD with Ulcerative colitis (UC) and with Crohn's disease (CD) (Clinical, histological, biochemical)

Exclusion Criteria

Patients < 18 years and > 70 years of age, Pregnant women, Alcoholics & smokers, Diabetes mellitus, Hypo- or hyperthyroidism, Hypertension, Ischemic heart disease, Chronic pancreatitis, Chronic liver disease

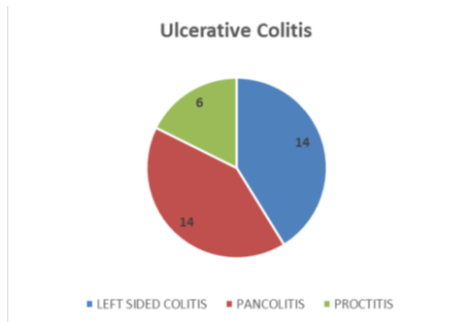
RESULTS

DISTRIBUTION OF IBD BASED ON GENDER

Sex	UC		CD	
	NO	%	No	%
Male	23	67.6%	7	43.8%
Female	11	32.4%	9	56.2%
Total	34	100.0%	16	100.0%
Chi square	2.59		p value 0.108	

In the present study it was observed that 67.6% were males in

patients with UC compared to 43.8% in Crohn's disease. 32.4% were females with UC compared to 56.2% females with Crohn's disease. There was no statistically significant difference in between groups ($p > 0.05$). Over all Male: Female ratio was 1.5:1.



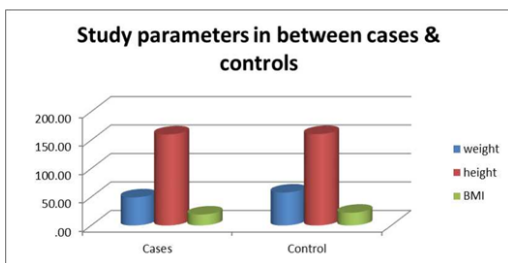
DISTRIBUTION BASED ON EXTENT OF DISEASE ON COLONOSCOPY IN UC

In the present study it was observed that 41.2% each had Pan colitis and left sided colitis, 17.6% had proctitis.

COMPARISON OF MEAN HEIGHT, WEIGHT AND BMI IN BETWEEN GROUPS (CASES & CONTROLS)

Parameters	Cases		Control		t value	p value
	Mean	SD	Mean	SD		
Weight	49.38	8.79	57.94	9.32	4.72	<0.001
Height	160.02	6.74	160.64	7.26	.44	.659
BMI	19.30	2.94	22.42	3.03	5.22	<0.001

In the present study it was observed that the mean weight was 49.48 ± 8.79 and mean height was 160.02 ± 6.74 and mean BMI was 19.30 ± 2.94 . In the present study it was observed that the Mean weight and BMI was significantly lower in cases compared to controls ($p < 0.05$).



DISTRIBUTION OF SURGERIES IN IBD

History of Surgery	UC		CD	
	No.	%	No.	%
No	34	100.0%	13	81.2%
Diversion ileostomy	0	.0%	2	12.5%
Ileal Resection	0	.0%	1	6.3%
Total	34	100.0%	16	100.0%
chi square	6.78		p value 0.034	

In the present study it was observed that 12.5% of patients with Crohn's disease had history of diversion ileostomy, 6.3% had history of ileal resection which was significantly higher than ulcerative colitis ($p < 0.05$).

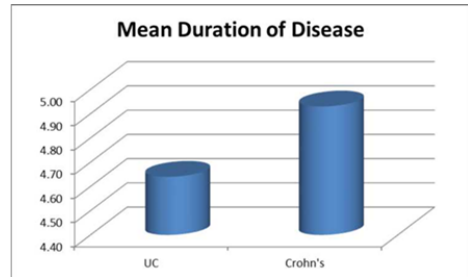
COMPARISON OF MEAN STUDY PARAMETERS (Ca, Po4, VITAMIN D) IN BETWEEN GROUPS (CASES & CONTROLS)

Parameters	Cases		Control		t value	p value
	Mean	SD	Mean	SD		
Calcium (mg/dl)	8.19	1.09	8.53	.58	1.91	.058
Phosphorus (mg/dl)	2.70	.35	3.71	.39	13.65	<0.001
Vitamin D (ng/ml)	27.06	6.55	35.99	11.24	4.81	<0.001

Mean phosphate and Vitamin D was significantly lower in

cases compared to controls ($p < 0.05$). There was no statistically significant difference in the mean Calcium in between groups ($p > 0.05$).

Duration of Disease (UC & CD)

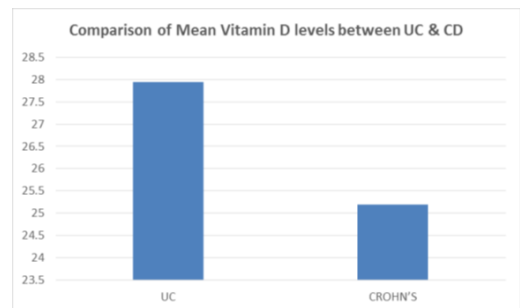


In the present study mean duration of disease for UC was 4.64 yrs and mean duration of crohn's disease was 4.93yrs. There was no statistically significant difference in the mean duration of disease between ulcerative colitis and Crohn's disease ($p > 0.05$).

DISTRIBUTION OF PATIENTS ACCORDING TO STEROID INTAKE

History of Steroids	UC		CD	
	No.	%	No.	%
Prednisolone	19	55.9%	4	25.0%
Budesonide	0	.0%	12	75.0%
No	15	44.1%	0	.0%
Total	34	100.0%	16	100.0%
chi square	34.81		p value <0.001	

It was observed that 55.9% patients with UC had history of intake of prednisolone which was significantly compared to 25% patients in Crohn's disease. 75% of patients with Crohn's disease had history of budesonide intake compared to 0% in patients with UC ($p < 0.05$).



In the present study it was observed that mean Vitamin D (25.19 ng/ml) was significantly lower when compared to mean Vitamin D (27.94 ng/ml) in UC. There was no statistically significant difference in the mean vitamin D levels in between cases ($p > 0.05$).

COMPARISON OF BMD BETWEEN UC & CD IN THE LUMBAR SPINE & FEMUR

BMD	UC			CD		
	Normal BMD	Osteop enia	Osteop orosis	Normal BMD	Osteop enia	Osteop orosis
Lumbar Spine	13(38.2)	17(50)	4(11.8)	4(25)	7(43.8)	5(31.3)
Femoral neck	19(55.9)	13 (38.2)	2(5.9)	5(31.3)	8(50)	3(18.8)

In the present study it was observed that in UC patients 50% had osteopenia in the spine compared to 38.2% in the hip whereas 11.8% had osteoporosis in the spine compared to 5.9% in the hip. In CD patients 43.8% had osteopenia in the spine compared to 50% in the hip whereas 31.3% had osteoporosis in the spine compared to 18.8% in the hip.

COMPARISON OF MEAN DEXA SCORE IN BETWEEN UC & CD

Mean DEXA score for femur was significantly lower in Crohn's disease compared to ulcerative colitis ($p < 0.05$). Mean DEXA for lumbar was also observed to be lower in Crohn's disease compared to ulcerative colitis. However there was no statistically significant mean difference in the mean DEXA of lumbar in between Crohn's disease and ulcerative colitis.

DISCUSSION

The mean age of presentation of IBD in the present study was 31.48 years which is comparable with studies done by **Ismail et al**⁵ & **S-H Lee et al**⁶. In a country-wide survey of IBD from India, the mean age at diagnosis of UC was found to be 38.5 years. Although the age at IBD onset in India is similar to that in the West, the bimodal peak as observed in the West is not observed in India and other Asian countries⁷.

In the present study, it was observed that the majority of the patients had ileocolonic disease (43.8%) followed by ileal (31.2%) & Colonic (25%) which were comparable to studies conducted by **Ismail et al**, **Jahnsen et al**⁸.

A study conducted by **C. A. Lima et al**⁹ showed that 53% had ileocolonic disease followed by colonic (32.7%) & ileal (14.3%) which was higher comparable to our study.

In the present study, it was observed that mean weight was 49.3 & mean height was 160.0 whereas mean BMI was 19.3 in IBD which was comparable to a study conducted by **Khadgawat et al**¹⁰.

In UC our study showed that mean weight was 51.8 & mean height was 160.3 whereas mean BMI was 20.2 in IBD which was comparable to a study conducted by **Khadgawat et al**. Mean height, weight & BMI were lower in our study compared to a study conducted by **Ismail et al**.

In CD our study showed that mean weight was 44.1 & mean height was 159.3 whereas mean BMI was 17.3 in IBD which was comparable to a study conducted by **Khadgawat et al**. Mean height, weight & BMI were lower in our study compared to a study conducted by **Ismail et al**.

In the present study it was observed that the mean weight, BMI was significantly lower in Crohn's disease compared to ulcerative colitis ($p < 0.05$). A study conducted by **Noble et al**¹¹ found that BMI to be the strongest independent risk factor associated with osteoporosis. A study conducted by **Schoon et al**¹² showed that low body mass index at diagnosis is also a predictive factor for BMD in IBD.

In the present study, it was observed that none of the patients had surgery for UC whereas 18.8% of patients had surgery for CD. In the present study it was observed that 12.5% of patients with Crohn's had history of diversion ileostomy, 6.3% had history of ileal resection which was significantly higher than ulcerative colitis ($p < 0.05$).

In the present study, it was observed that mean serum Calcium was 8.19 mg/dl & mean serum Phosphorus was 2.7 mg/dl & mean serum Vitamin D was 27.0 ng/ml which was comparable to a study conducted by **Y.Ezzat and K. Hamdy**¹³.

In UC in our study the mean calcium was 8.35 mg/dl & mean phosphorus was 2.75 mg/dl & mean Vitamin D levels were 27.94 ng/ml comparable to studies conducted by **Kaya et al**¹⁴, **Y. Ezzat and K. Hamdy**.

In CD in our study the mean calcium was 7.84mg/dl & mean phosphorus was 2.6 mg/dl & mean Vitamin D levels were 25.19 ng/ml. The results our study was consistent with studies

conducted by **Kaya et al**, **Y. Ezzat and K. Hamdy**.

In our study mean calcium, mean phosphorus & mean Vitamin D were lower in crohns disease comparable to UC. The results our study was consistent with study conducted by **Y. Ezzat and K. Hamdy**.

A study conducted by **Y. Ezzat and K. Hamdy** found a significant positive correlation between vitamin D levels and low BMD. A study conducted by **Leichtmann et al**¹⁵ also stated that ileal and small intestine involvement in Crohn's disease, leads to increase in vitamin D malabsorption and subsequently more bone loss. Multiple factors were involved in Vitamin deficiency like age, gender, dietary intake of calcium, H/o steroids, H/o surgeries, exposure to sun, ethnicity & duration of disease.

In the present study, it was observed that mean duration of IBD was 4.7yrs and for UC 4.64 yrs and for CD 4.93 yrs which were comparable to studies conducted by **S-H Lee et al**, **Y. Ezzat and K. Hamdy**, **B Tan et al**¹⁶.

In our study CD patients have longer duration of disease than UC, these findings were consistent with study conducted by **S-H Lee et al**. A country-wide survey of IBD from India also showed mean duration for CD is 4 yrs and 2 yrs.

In our study there was no statistically significant difference in the mean duration of disease between ulcerative colitis and Crohn's disease ($p > 0.05$).

In our study in UC patients mean BMD at lumbar spine was -0.98 & mean BMD at femoral neck was -1.27 whereas in CD patients mean BMD at lumbar spine was -1.48 & mean BMD at femoral neck was -1.87. This shows that mean BMD was lower in CD compared to UC patients in our study.

The systematic review of the literature on osteoporosis in gastrointestinal diseases conducted by the American Gastroenterological Association found a low bone mass prevalence of 6% in the lumbar spine and 13% in the hip, as well as an osteoporosis prevalence of 14% in the lumbar spine and 16% in the hip.

Studies conducted by **Ghosh et al**¹⁷ & **Staub et al**¹⁸ also stated that BMD was reduced at the time of diagnosis in patients with CD but not in those with UC.

The study by **Pallone et al**¹⁹ relates the increased incidence of osteoporosis involving patients with CD more than with UC, stating that although both diseases are the consequence of T cell activation, CD inflammation is thought to be triggered by TH1 cells, increasing the levels of TNF- α and IL-6, which stimulate osteoclast activity, resulting in bone remodelling impairment.

The study by **Khadgawat et al** showed that there was no difference in the values of BMD of patients with CD and UC. A Study conducted by **B Tan et al** showed that there were no significant differences in the incidence of osteopenia and osteoporosis between the UC and CD cohorts.

CONCLUSIONS

- This study was done to know the prevalence of osteopenia & osteoporosis and its correlation to modifiable risk factors and extent & severity of disease in UC & CD.
- Low BMD occurs frequently in patients.
- Prevalence of osteopenia & osteoporosis was more in CD compared to UC patients.
- Significant correlation was found with modifiable risk factors like weight, BMI, steroids & Vitamin D levels.
- Significant correlation was found with extent of disease in

CD.

- Significant correlation was not observed with severity & extent of disease in UC.
- Increased frequency of both osteoporosis and osteopenia in this study underlines the importance of monitoring by DEXA scan, not only for high risk patients, but all inflammatory bowel disease patients, and to start initiating appropriate treatment with calcium and vitamin D in patients with low BMD values.
- Longitudinal follow-up studies are needed to assess the benefits of nutritional intervention in these patients, on BMI, bone density & fracture risk.

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