

Investigating the relationship between Vitamin D and Bone Mineral Density among Coeliac patients attending Ibn Sina Hospital

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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: February 10, 2020

Revised: May 10, 2020

Accepted: April 16, 2020

Published online: June 21, 2020

ABSTRACT

AIM: To investigate the correlation between vitamin D and bone mineral density among coeliac patients.

MATERIAL AND METHODS: This is a cross sectional hospital-based study carried out in Ibn-Sina hospital from July - November 2019. Forty-two participants with coeliac disease were recruited in this study aged 18 years or above who attended the coeliac clinic. Data was collected using well-constructed questionnaires. Their laboratory investigations along with serum 25(OH)D levels were done. Bone mineral density was measured using Furuno's CM-200

light ultrasound bone densitometer. Data was analyzed by using Statistical Packages for Social Sciences (SPSS) software.

RESULTS: A total of 42 participants were enrolled. Eighty one percent of the sample were female and 19% were male. The mean age of our sample was $27.3095 \pm 9.47780SD$. This study demonstrated a moderate positive relationship between vitamin D level and T- score level with ($r = 0.437$), and statistically significant ($p < 0.004$). There was a significant relation between T -score and adherence to gluten free diet ($p < 0.012$). All the participants stated no previous history of bone fracture. Moreover, the results revealed no coeliac patients with osteoporosis.

CONCLUSION: There was correlation between vitamin D and BMD. Our results suggest, there is an underlying factor related to bone fracture among patients with coeliac disease. Furthermore, we suggest that serum calcium investigation is not predictive of low BMD in coeliac patients.

Key words: Coeliac; Vitamin D; Bone Mineral Density

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Basheer MO, Khojali FM, Kheir OO, Mohammed SA, Abdalla HIA. Investigating the relationship between Vitamin D and Bone Mineral Density among Coeliac patients attending Ibn Sina Hospital. *Journal of Gastroenterology and Hepatology Research* 2020; 9(3): 3191-3195 Available from: URL: <http://www.ghrnet.org/index.php/joghr/article/view/2800>

INTRODUCTION

Coeliac disease (CD) is one of the most prevalent malabsorptive syndromes, of either one or more nutrients. It was initially thought to be a disease of Caucasians, until realizing it was also common in non-Caucasians and other parts of the world, including Asian and African countries^[1,2].

CD is a highly frequent disease^[3] that affects around 1% of the world population according to serology-based screening studies^[4].

When CD is diagnosed through the childhood period it estimated

during this period, one-third of affected children have osteoporosis, one-third have osteopenia and only the remaining third recall a normal bone mineral density (BMD)^[5].

In fact, coeliac patients without gastrointestinal symptoms may have low BMD, which increases after start of the gluten free diet (GFD)^[6].

Untreated adult coeliac patients have shown a 45 % decline in calcium absorption followed by an improvement of 52 % after 6 months of gluten free diet(GFD) adherence^[7]. Previous Spanish study reveal that vitamin D, at the time of diagnosis, less than 5 % of Spanish adult CD patients had normal serum levels^[8].

Vitamin D deficiency is common among patients with CD, although there are no changes in the expression of vitamin D receptors^[9] or a greater number of receptor gene mutations interfering with the metabolism of this vitamin^[10] in this population.

Several authors have suggested that deficits in other fat-soluble vitamins (A, K and E) and even water-soluble vitamins (C, B12, folic acid and B6) or minerals (such as iron, calcium, phosphorus, copper, zinc, boron, fluoride), which are all required for normal bone metabolism^[8,11], also consequence from the intestinal malabsorption displayed by coeliac patients.

In any case, once the glutenfree diet (GFD) is instituted, most coeliac children catch up to their height-weight growth curve and accelerate their rate of bone mineralization, so that most achieve normal peak bone mass by the time bone growth is completed. The main problem arises when CD is diagnosed during adulthood, once bone growth is complete and peak bone mass has been reached. Among these patients, the prevalence of osteoporosis is at least twice that of the unaffected population in the same age range^[12,13]. There is scarce information about the vitamin d and BMD among coeliac patients in Sudan. Therefore, the purpose of this study was to examine the correlation between vitamin D and BMD among patients with coeliac disease.

METHODS

This is a cross sectional hospital-based study carried out in Ibn-Sina hospital from July - November 2019. This Hospital is a tertiary referral hospital concentrated on 3 specialties: Gastroenterology (GI), Nephrology-Urology, and Ear, Nose, Throat. The institution of the GI unit at Ibn-Sina Hospital was a fundamental in the development of gastroenterology services in Sudan^[14]. A study protocol was submitted to the ethics committee of the Sudanese Medical Specialization Board (S.M.S.B) and Ibn-Sina hospital for approval, ensuring adherence to ethical principles such as those specified by the World Medical Association Declaration of Helsinki, and ethical approval was granted. Following an explanation of the study, each participant signed an informed consent form. The participants were assured anonymity and confidentiality and that declining to participate would not affect their current and future treatment.

Forty-two participants with coeliac disease were recruited in this study aged 18 years or above who attended the coeliac clinic. Patients on steroids, or with other diseases affecting the bone or refused to participate in this study were excluded from the study. The sample size was calculated using epi info software (www.cdc.gov/epiinfo). Convenience nonprobability sampling method was used for recruitment.

Data was collected using well-constructed questionnaires. These questionnaires were filled by trained medical doctors. The questionnaire includes the following variables age, gender, residence, level of education, employment, adherence to gluten free diet, previous history of pathological fracture, body mass index (BMI),

vitamin D level, Bone mineral density and serum calcium.

The BMI was calculated as weight/height² (kg/m²). Based on WHO criteria^[15]. Bone mineral density was measured using Furuno's CM-200 light ultrasound bone densitometer (Furuno electric Co.LTD, Japan)^[16]. T-score criteria which is similar to WHO's^[17] criteria T- score is divided into three groups : Normal is a T-score of -1.0 or higher, Osteopenia is defined as between -1.0 and -2.5 and Osteoporosis is defined as -2.5 or low Vitamin D deficiency is categorized as a serum 25-hydroxyvitamin D level of less than 20 ng per mL (50 nmol per L), and insufficiency is categorized as a serum 25-hydroxyvitamin D level of 20 to 30 ng per mL (50 to 75 nmol per L)^[18].

Data was entered, coded, and cleaned in excel master sheet. Data was analyzed by using Statistical Packages for Social Sciences (SPSS) 23.0 software. Shapiro-Wallis test was used to assess the normality. Tests used for analysis spearman's for correlation test, Mann Whitney u test, Kruskal-Wallis test and Dunnett's teste for pairwise comparison, as appropriate. $p < 0.05$ is considered statistically significant (Confidence Interval: CI 95%).

RESULTS

A total of 42 participants were enrolled by a response rate of 85.7%. all sample were collected after excluding patients did not meet the eligible criteria or refuse to participate among which 81% of the sample were female and 19% were male. Ninety percent of participants live in urban area and 78% of them with university education or higher education (Table 1). Regarding the occupation 47, 6% of the sample was unemployed, 23.8% of the individuals are housewife and 28.6% were employed showed in table^[1]. Twenty-eight participants stated that the diseases started less than 5 years, while 7 individuals stated that diseases started between 5-10 years and the last group stated they had the disease for more than 10 years. Regarding the adherence to gluten free diet 45.2% were good adherence, 45.2% were average adherence and 9,5% were bad adherence. The sample distribution according t-score 42.9% were osteopenia, while 57.1% were normal bone density. (Table 1). All participants stated that no previous history of bone fracture (100%) (Table1).

The mean age of our sample was $27.3095 \pm 9.47780SD$, BMI mean was $19.7588 \pm 4.40561 SD$, vitamin D level mean was $31.7531 \pm 14.47192 SD$, T- score mean was $-0.9779 \pm 0.64518 SD$ and the mean for serum ca⁺⁺ $9.1791 \pm 0.65584SD$ (Table 2).

This study demonstrated a moderate positive relationship between vitamin D level and T- score level with ($r = 0.437$), and statistically significant ($p < 0.004$) displayed in (table 3). So was the vitamin d and body mass index (BMI), also showed a moderate positive relationship with ($r = 0.328$), and statistically significant ($p < 0.034$) (Table 3).

There was no correlation between vitamin D level and age $r = -0.46$ and statistically not significant ($p > 0.773$) (Table 3). Also, there was no correlation between vitamin D and serum calcium ($r = -0.06$) and statistically not significant ($p > 0.704$).

This study negative a moderate correlation between T-score level and age ($r = -0.356$), and statistically significant ($p < 0.021$) (Table 4).

There was no correlation between t-score and the BMI $r = -0.109$ and statistically not significant ($p > 0.493$) (table4). Furthermore, the was no correlation between t-score and serum calcium ($r = 0.007$), and statistically not significant ($p > 0.962$).

According to Mann-Whitney U there was no significant relationship between the vitamin D and the gender ($p > 0.785$), so

was vitamin D and occupation, also statistically not significant ($p > 0.302$) (Table 5). Kruskal Wallis test showed there was no significant relationship between vitamin D level and level of education ($p > 0.148$), moreover, There was no significant relationship between vitamin D and adherence to gluten free diet with ($p > 0.81$) (Table 5). so was the t-score and duration of coeliac disease, also statistically not significant ($p > 0.400$) (Table 5).

However, there was a significant relation between t -score and adherence to gluten free diet ($p < 0.012$). pairwise comparison test was performed and adjust it Bonferroni showed a significant between the good adherence to gluten free diet group and bad adherence to gluten free diet group ($p < 0.32$) (Table 6).

Table 1 Sociodemographic and exposure characteristics ($n = 42$).

Variable	Subgroup	Frequency	Percentage
Gender	Male	8	19.00%
	Female	34	81.00%
Residence	Rural	4	9.50%
	Urban	38	90.50%
Education level	non educated	1	2.40%
	primary	4	9.50%
	Secondary	4	9.50%
	university and above	33	78.60%
Occupation	unemployed	20	47.60%
	housewife	10	23.80%
	employee	12	28.60%
Adherence to Gluten free diet	good	19	45.20%
	average	19	45.20%
	bad	4	9.60%
Duration of Coeliac disease	less than 5 years	28	66.60%
	5- 10 years	7	16.70%
	more than 10 years	7	16.70%
previous history of bone fracture	yes	0	0%
	no	42	100

Table 2 Age, BMI, Vitamin D level, T-score and serum calcium (in means \pm SD).

	N	Mean	Std. Deviation
AGE	42	27.310	9.478
Body Mass Index	42	19.759	4.406
Vitamin D Level	42	31.753	14.472
T-Score	42	-0.978	0.645
Serum calcium	42	9.179	0.656

Table 3 Correlation coefficients and P-value between Vitamin D , T- score, age, serum calcium and BMI.

	Correlation Coefficient	P-value
Vitamin D Level / T-Score	0.437*	< 0.004
Vitamin D Level / Serum Calcium	-0.06	> 0.704
Vitamin D level/ Age	-0.046	> 0.773
Vitamin D/ Body Mass Index	0.328*	< 0.034

Table 4 Correlation coefficients and P-value between T- score, age, serum calcium and BMI.

	Correlation Coefficient	p-value
Age /T- score	-0.356*	< 0.021
Serum Calcium/T-score	0.007	> 0.962
Body Mass Index/t-score	-0.109	> 0.493

DISCUSSION

The study should be considered with its limitations. The sample was made up of participants attending the hospital with coeliac disease; a random sample population would have been more representative. However, the study design was made to obtain information on vitamin D and BMD on patients with coeliac disease.

Our study revealed that there is a significant correlation between vitamin D and Bone Mineral Density which agreed to previous studies conducted by Ardawi et al^[19,20].

The prevalence of osteopenia and osteoporosis is lower in blacks as compared to that seen in the whites^[21]. Our data showed that no participants had osteoporosis this may be due to our sample been taken from patients who are doing follow up in the hospital and they started counseling and following the gluten free diet. Also, our

Table 5 Analysis of Characteristics according to vitamin d level ($n = 42$).

Variable	Subgroup	Frequency	Mean rank	P-value
Gender	Male	8	22.56	>.785
	Female	34	21.25	
Residence	Rural	4	20	>0.797
	Urban	38	21.66	
Education level	non educated	1	7	>0.148
	primary	4	17.75	
	Secondary	4	33	
	university and above	33	21	
Occupation	unemployed	20	21.33	>0.966
	housewife	10	20.95	
	employee	12	22.25	
Adherence to Gluten free diet	good	19	25.68	>0.81
	average	19	19.21	
	bad	4	12.5	
Duration of Coeliac disease	less than 5 years	28	19.54	>0.267
	5- 10 years	7	27.71	
	more than 10 years	7	23.14	

A-P-value ($p < 0.05$) results from Mann-Whitney and Kruskal-Wallis tests for the differences between subgroups.

Table 6 Analysis of Characteristics according to T- score ($n = 42$).

Variable	Subgroup	Frequency	Mean rank	P-value
Gender	Male	8	21.5	>0.100
	Female	34	21.5	
Residence	Rural	4	23.38	>0.748
	Urban	38	21.3	
Education level	non educated	1	1	>0.403
	primary	4	20.75	
	Secondary	4	22.88	
	university and above	33	22.05	
Occupation	unemployed	20	24.63	>0.282
	housewife	10	18	
	employee	12	19.21	
Adherence to Gluten free diet	good	19	27.08	<0.012
	average	19	18.37	
	bad	4	9.88	
Duration of Coeliac disease	less than 5 years	28	22.54	>0.400
	5- 10 years	7	23.07	
	more than 10 years	7	15.79	

A-P-value ($p < 0.05$) results from Mann-Whitney and Kruskal-Wallis tests for the differences between subgroups.

sample was small; if we took a larger sample and more diverse may include patients with osteoporosis.

Vitamin D deficiency is relatively uncommon in healthy young patients; the deficiency is common in elderly population, particularly individuals where sunlight is limited^[22]. Also, vitamin D deficiency is common on patients with coeliac disease^[9].

This study examined the relationship between vitamin D levels and age but there was no significant difference in the vitamin D levels of different age group. Most of our age sample includes young patients. Our result is supported by previous study carried out by Lbronicietal which had similar result^[23].

The prevalence of vitamin D deficiency and insufficiency were high among CD patients. This is can be due to dietary vitamin D is absorbed as a fat-soluble vitamin in small intestine, and because of intestinal involvement in CD its absorption decreases thus leading to deficiency of particular vitamin D^[24].

This study showed a negative moderate relationship between t-score and age. Previous study demonstrated a negative correlation between age and BMD namely, greater age was correlated with lower BMD, corroborating the work of Biana et al^[25] who claimed that this mainly occurs at the end of the last decade of life, and may correspond to 5-10% of total bone mass/decade. The reasons for this may include nutritional deficiencies, some chronic diseases, and lack of exercise.

Vitamin D is also deficient among CD patients despite the fact that diet only provides 5-10% of required vitamin D^[26,27].

Our study revealed that no significant relationship between t-score and BMI however, Previous studies concluded that when BMI increases, BMD levels will also increase^[28,29], which disagree with our findings. The reason for this our sample was taken from patients with coeliac disease, therefore most of the patients with normal weight or underweight.

One study has evaluated vitamin D status in children living in Northern Italy and found out that almost half of the study population who were obese had vitamin D deficiency^[30].

Our results discovered that there was a significant association between vitamin D level and BMI. A previous study showed that there was an inverse relationship between vitamin D and BMI^[18,31,32].

Previous study stated that there was no significant change in fracture risk after diagnosis of coeliac disease. These results suggest that the concerns about fracture risk in patients with coeliac disease have been overstated^[33]. Our study revealed that our entire sample had no previous history of bone fracture which supported by K Thomson et al^[33].

One study has reported an increased risk of peripheral fractures in those with coeliac disease. However, most fractures were recorded prior to diagnosis or in those non-compliant with their gluten-free diet^[34]. Our result revealed that there is no history of bone fracture among patients with coeliac disease including patients stated that didn't adhere to GFD. These results suggest that there is may be underlying factor that may influence bone fracture among coeliac patients.

Jadwiga Szymczak et al. noticed that gluten-free diet improves calcium and vitamin D absorption, diminishes secondary hyperparathyroidism, and increases BMD, but does not guarantee full recovery^[35].

Our study found that there is no significant relationship between vitamin d and adherence to gluten free diet.

However, there was significant relationship between t- score and adherence to free gluten diet. the significant different occur between poor adherence group and good adherence group where the bone

density increase with good adherence to gluten free diet. These finding supported by previous study^[36-39]. Regarding vitamin d and serum there was no significant relationship, there was no relationship between BMD and serum calcium, also statistically not significant. In Sudan measuring the serum calcium is routine investigation for those with coeliac disease. Our result suggested the serum calcium investigation is not necessary in routine investigation and may help to reduce the cost for coeliac patients.

Khartoum is classified as hot desert climate (hot, dry and sunny) with dry season occur in winter according to Köppen climate classification^[40,41]. We suggest further study to examine the relationship between bone mineral density and life style, mode of transportation, physical activity, and sun exposure among coeliac patients.

CONCLUSION

There was a correlation between vitamin D and BMD. There were no pathological fractures or osteoporosis among diagnosed coeliac disease sample which suggest that is an underlying factor related to bone fracture. In this study, serum calcium level was not predictive of low BMD in coeliac patients.

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