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Vitamin D Status in Inflammatory Bowel disease

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ABSTRACT

Background: There were many studies reported deficient vitamin D in patients with inflammatory bowel disease.

Objective: Our study aimed to examine the relationship between vitamin D levels and clinical disease activity in patients with inflammatory bowel disease (IBD).

Patients and Methods: A prospective study was conducted at IBD Outpatient Clinic of Al-Rajhi University Hospital of Assiut University Hospitals in period from May 2018 to May 2019. The study enrolled 54 patients with known IBD. In addition to reviewing the demographic and clinical data, serum vitamin D was measured in all patients.

Results: Mean age of enrolled patients was 34.24 ± 11.71 years with range between (14 - 67) years. Females were more than half of participants (51%). Mean serum vitamin D level was 43.45 ± 33.91 ng/ml. 20 IBD patients (37%) were deficient in vitamin D, 4 (7.4%) patients had insufficient level and 30 (55.6%) patients had normal level. Patients with deficient vitamin D had significantly higher C-reactive protein in comparison with those with insufficient level and those with normal level. Patients on conventional therapy or biological therapy had insignificant differences as regard level of vitamin D and its status ($P > 0.05$). There is a non-significant differences as regard level of vitamin D and disease activity, but the level of vitamin D were lower in active patient than non-active one.

Conclusion: Vitamin D insufficiency was uncommon among IBD patients, especially in those with Crohn's disease, and was linked to a stronger inflammatory response as well as more active illness.
Keywords: IBD, C-reactive protein, vitamin D.

INTRODUCTION

The incidence of inflammatory bowel disease (IBD) is on the rise. 1.5 million Americans, 3 million individuals in Europe, and the Asia-Pacific region are all impacted. The primary pathogenic mechanism for both illnesses is a dysregulated host immune response to commensal gut flora in genetically susceptible people [1, 2]. In addition to encouraging the development of Th2 immune responses and the shift to antimicrobial peptide synthesis, vitamin D also controls autophagy and the epithelial barrier's integrity.

In IBD patients, vitamin D insufficiency has been estimated to be as high as 60% [3]. Low blood ionised calcium levels as a result of insufficient vitamin D leads to secondary hyperparathyroidism, osteoclastogenesis, abnormally rapid bone resorption, osteopenia, and osteoporosis. Metabolic bone disease occurs significantly more frequently in IBD patients [4].

In this study, we looked at the association between vitamin D levels and the severity of the disease in people with IBD (Crohn's disease or ulcerative colitis).

PATIENTS AND METHOD

This prospective study was conducted at IBD Outpatient Clinic and Inpatient Department of Internal Medicine of Al-Rajhi University Hospital of Assiut University Hospitals. It was performed in period between May 2018 and May 2019 to assess the vitamin D status among patients with IBD including UC or Crohn's disease (CD) patients. It included 54 patients presented and diagnosed with IBD.

Selection criteria: Any patient with IBD was eligible for the study. Cancer patients or those with therapy that affect the blood level of vitamin D weren't eligible to be recruited.

Methods:

Thorough history taking and full evaluation including systemic examination for presence of signs of anemia, systemic toxicity or weight loss, abdominal examination for any abdominal tenderness, distension and any abnormal sign. Baseline laboratory data was done for all patients.

According to The entire Mayo Clinic Score (MCS), the four criteria of stool frequency, rectal bleeding, endoscopic examination, and physician's overall assessment are used to measure the stage of the UC [5, 6].

To evaluate the severity of the condition, the Crohn's Disease Activity Index, or CDAI, is widely utilised (7). ELISA was used to do a quantitative analysis of blood total 25-OH vitamin D levels (Vitamin D2 and Vitamin D3) and to subclassify the results into deficient, inadequate, and normal groups [8, 9].

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Ethical approval:

The 2013 Seventh Revision of the Declaration of Helsinki's recommendations and the Code of Good Practice were both followed during the completion of this study. Additionally, Assiut University's Faculty of Medicine's Institutional Review Board gave its clearance. NCT03496246 is the clinicaltrials.gov identifier assigned to the study. Consents was formally signed by patients.

Statistical analysis: SPSS was used for the analysis (Statistical Package for the Social Science, version 20, IBM, and Armonk, New York). While continuous data were represented as mean ± SD and compared using the Student t test. Nominal data were expressed as number and percentage and compared using the chi square test. If $P \leq 0.05$, it was significant.

RESULTS

Vitamin D status among the enrolled data (table 1):

It was noticed that 20 (37%), 4 (7.4%), and 30 (55.6%) patients had deficient, insufficient and normal 25(OH) vitamin D level respectively.

Table (1): Vitamin D status of enrolled patients

	N= 54
Serum 25(OH) vitamin D (ng/ml)	43.45 ± 9.82
Vitamin D status	
Deficient	20 (37%)
Insufficiency	4 (7.4%)
Normal	30 (55.6%)

Data expressed as frequency (percentage), mean (SD).

Baseline data of enrolled patients based on status of vitamin D (table 2): Patients with deficient vitamin D had significantly lower hemoglobin level (10.05 ± 1.75 g/dl) in comparison with those with insufficient level (10.95 ± 1.50 g/dl) and those with normal level (11.24 ± 1.67 g/dl). Also, patients with deficient vitamin D had significantly lower calcium level (8.16 ± 0.44 mg/dl) in comparison with those with insufficient level (9.27 ± 0.28 mg/dl) and those with normal level (9.93 ± 0.40 Mg/dl). In contrast, those patients with deficient vitamin D had significantly higher CRP (11.45 ± 2.75 mg/dl) in comparison with those with insufficient level (6.55 ± 1.59 mg/dl) and those with normal level (5.11 ± 1.10 mg/dl).

Table (2): Baseline data of enrolled patients based on status of vitamin D

	Status of 25(OH) vitamin D			*P* value
	Deficient (n=20)	Insufficient (n= 4)	Normal (n= 30)	
Age	35.50 ± 12.89	40.25 ± 10.87	32.60 ± 11.04	0.40
Sex				0.11
Male	6 (30%)	2 (50%)	18 (60%)	
Female	14 (70%)	2 (50%)	12 (40%)	
Type of IBD				0.28
Ulcerative colitis	12 (60%)	4 (100%)	21 (70%)	
Crohn's disease	8 (40%)	0	9 (30%)	
Presentation				
Follow up	11 (55%)	3 (75%)	12 (40%)	0.31
Diarrhea	8 (40%)	0	15 (50%)	0.15
Bleeding	5 (25%)	1 (25%)	13 (43.3%)	0.37
Fever	1 (5%)	0	4 (13.3%)	0.48
Type of therapy:				
Conventional	9 (45%)	3 (75%)	11 (36.7%)	0.33
Biological	11 (55%)	1 (25%)	19 (63.3%)	
Hemoglobin (g/dl)	10.05 ± 1.75	10.95 ± 1.50	11.24 ± 1.67	**0.01**
Platelets (10^3/ul)	314.95 ± 76.63	372 ± 8.72	327.83 ± 8.08	0.52
Leucocytes (10^3/ul)	6.76 ± 1.52	6.02 ± 1.48	7.12 ± 1.70	0.68
Urea (mg/dl)	37.45 ± 9.01	35.75 ± 4.94	32.36 ± 8.07	0.14
Creatinine (mg/dl)	0.79 ± 0.19	0.68 ± 0.08	0.71 ± 0.07	0.22
Sodium (mmol/l)	139.50 ± 3.57	141.75 ± 5.61	139.46 ± 3.63	0.51
Potassium (mmol/l)	4.32 ± 0.54	4.10 ± 0.39	3.93 ± 0.40	0.05
Calcium (mg/dl)	8.16 ± 0.44	9.27 ± 0.28	9.93 ± 0.40	**0.01**
Phosphorous (mg/dl)	4.26 ± 0.58	4.37 ± 0.33	4.19 ± 0.49	0.78
Albumin (g/dl)	4.22 ± 0.66	4.80 ± 0.29	4.14 ± 0.65	0.17
ALT (u/l)	22.5 ± 5.51	21.25 ± 5.42	22.80 ± 5.32	0.91
AST (u/l)	25.78 ± 2.45	26.89 ± 3.33	27.01 ± 1.87	0.34
RBS (mg/dl)	142.70 ± 32.96	142.50 ± 25.82	131.60 ± 23.82	0.35
INR	1.09 ± 0.01	1.06 ± 0.04	10.08 ± 0.02	0.31
1st hour ESR (ml/hour)	33.30 ± 4.02	18.25 ± 4.22	28.90 ± 7.11	0.38
2nd hour ESR (ml/hour)	69.40 ± 6.67	40.75 ± 9.99	70.50 ± 6.56	0.40
CRP (mg/dl)	11.45 ± 2.75	6.55 ± 1.59	5.11 ± 1.10	**0.03**

Correlations of 25(OH) vitamin D level with other variables (table 3, figures 1-3):

Vitamin D had positive significant correlations with hemoglobin level (r= 0.35, P< 0.001) and calcium level (r= 0.44, P< 0.001). It also, had negative significant correlations with C - reactive protein (CRP) (r= -0.56, p< 0.001).

Table (3): Correlations of 25(OH) vitamin D level with other variables

Correlation of 25(OH) vitamin D level with	r value	*P* value
Age (years)	-0.12	0.35
Hemoglobin (g/dl)	**0.35**	**< 0.001**
Platelets (10^3/ul)	-0.09	0.50
Leucocytes (10^3/ul)	-0.06	0.62
Urea (mg/dl)	0.28	0.06
Creatinine (mg/dl)	-0.23	0.08
Sodium (mmol/l)	0.02	0.85
Potassium (mmol/l)	-0.37	0.09
Calcium (mg/dl)	**0.44**	**< 0.001**
Phosphorous (mg/dl)	-0.03	0.78
Albumin (g/dl)	-0.14	0.31
ALT (u/l)	-0.06	0.63
AST (u/l)	0.30	0.08
RBS (mg/dl)	-0.18	0.19
INR	0.10	0.34
1st hour ESR (ml/hour)	-0.04	0.73
2nd hour ESR (ml/hour)	0.05	0.71
CRP (mg/dl)	**-0.56**	**< 0.001**

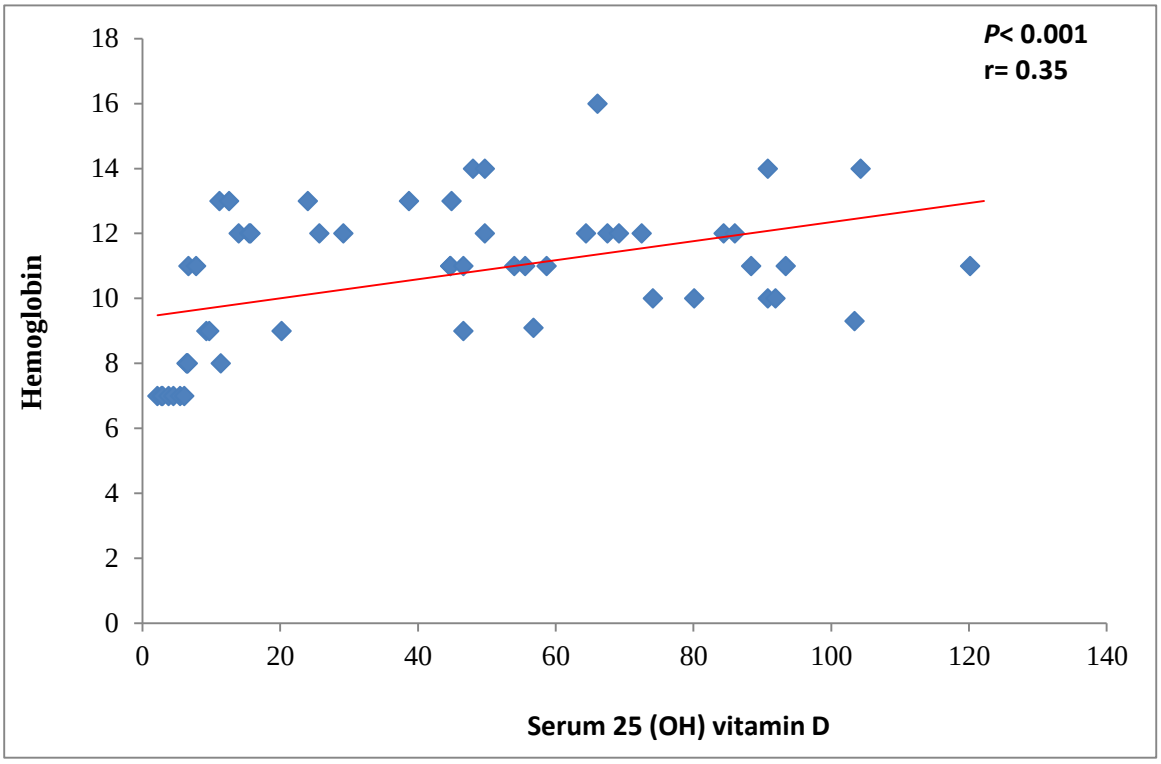

Figure (1): Correlation between 25(OH) vitamin D level and hemoglobin

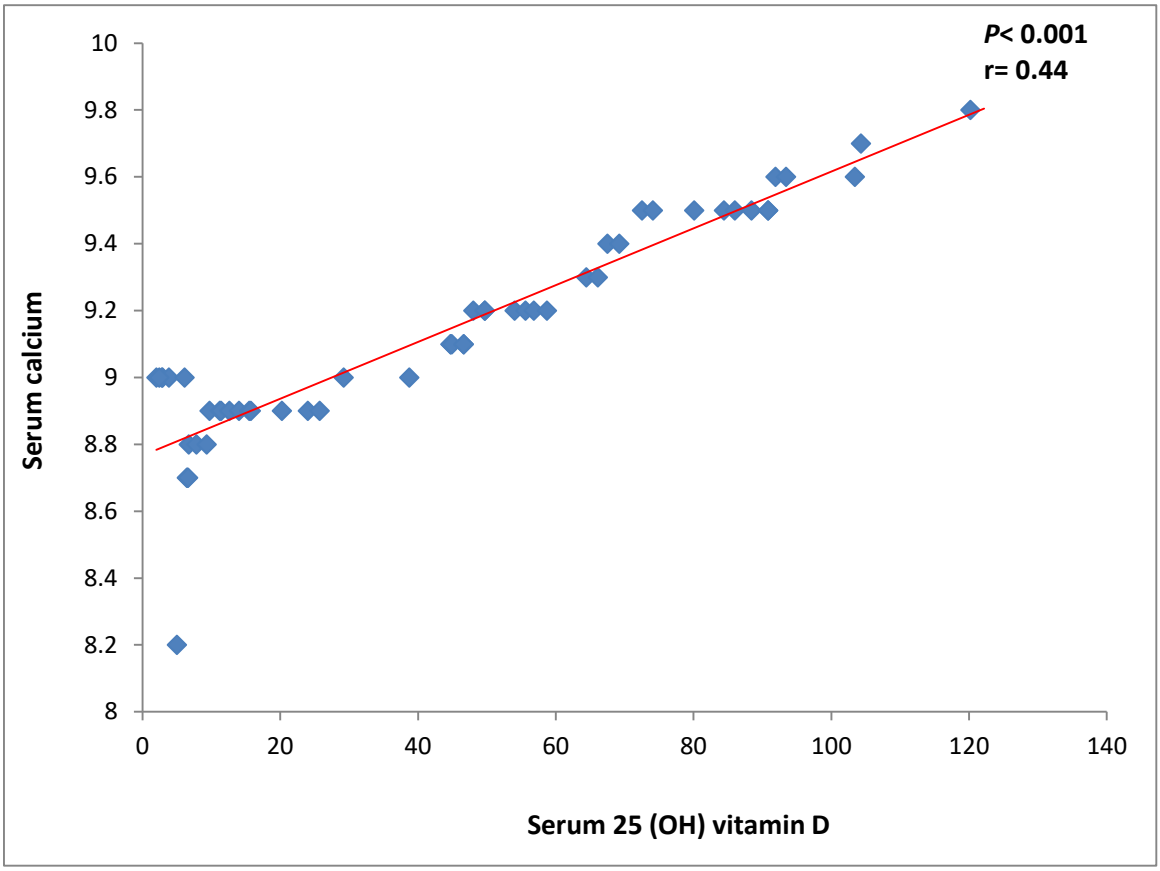

Figure (2): Correlation between 25(OH) vitamin D level and serum calcium

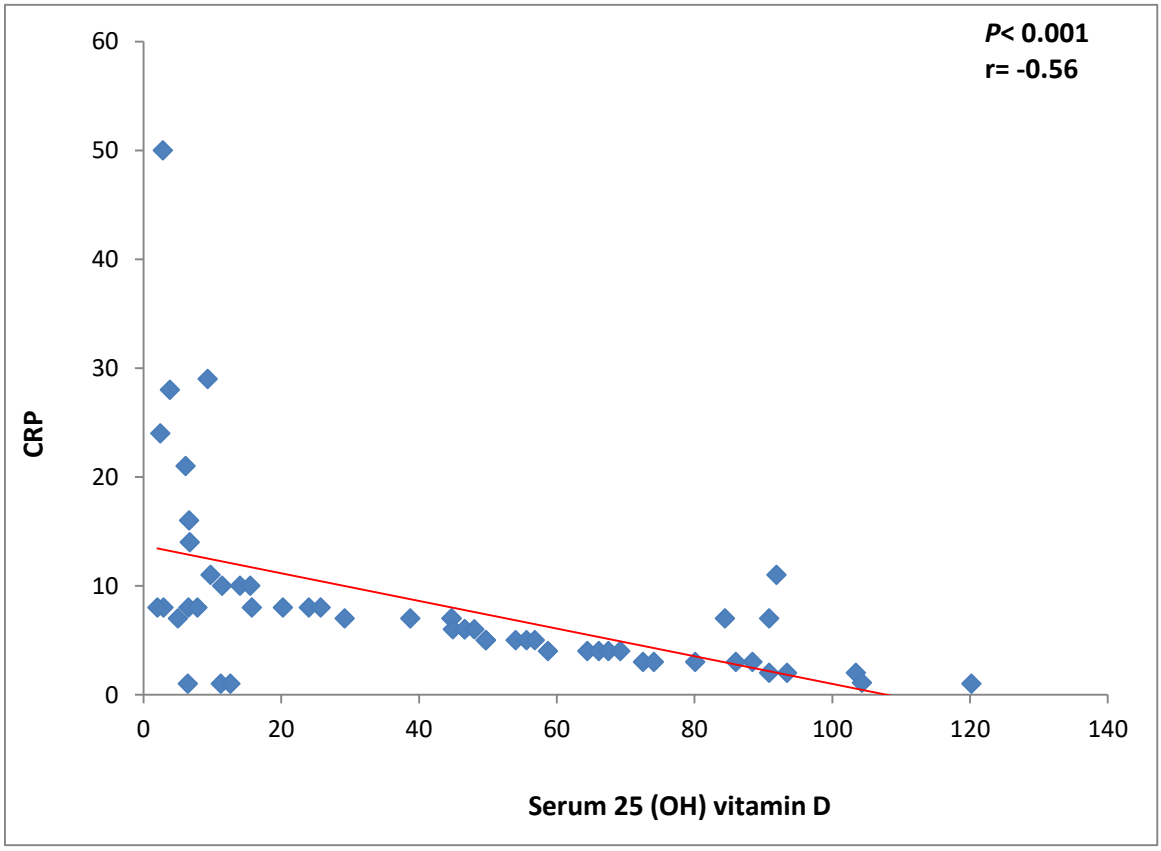

Figure (3): Correlation between 25(OH) vitamin D level and CRP.

Serum 25(OH) vitamin D level based on type of IBD (table 4):

It was noticed that both types of IBD had insignificant differences as regards level of 25(OH) vitamin D and its status (*P*> 0.05).

Table (4): Serum 25(OH) vitamin D level based on type of IBD

	UC (n= 37)	CD (n= 17)	*P* value
Serum 25(OH) vitamin D	44.53 ± 10.84	41.09 ± 9.32	0.37
Status			0.28
Deficient	12 (32.4%)	8 (47.1%)	
Insufficient	4 (10.8%)	0	
Normal	21 (56.8%)	9 (52.9%)	

Serum 25(OH) vitamin D level based on disease activity (table 5):

It was noticed that patients on with active disease and those with non-active disease had insignificant differences as regards level of 25(OH) vitamin D and its status (P> 0.05).

Table (5): Serum 25(OH) vitamin D level based on disease activity

	Non-active (n= 25)	Active (n= 29)	*P* value
Serum 25(OH) vitamin D	49.38 ± 11.21	38.34 ± 8.33	0.23
Status			0.28
Deficient	7 (28%)	13 (44.8%)	
Insufficient	3 (12%)	1 (3.4%)	
Normal	15 (60%)	15 (51.7%)	

DISCUSSION

Many previous literatures stated the role vitamin D deficiency in IBD. its effect on IBD had variable results [(10)]. Regarding demographic data, mean age of enrolled patients was 34.24 ± 11.71 years with range between (14 - 67) years. Females were more than half of participants (51%). About two thirds (68.5%) of our participants had UC while and one third had CD.

In our study mean serum 25(OH) vitamin D was 43.45 ± 33.91 ng/ml, 20 (37%) of IBD patients were deficient in vitamin D, 4 (7.4%) patients had insufficient level and 30 (55.6%) patients had normal level. The deficient group of patients had 12 (60%) UC patients and 8 (40%) CD patients, with no significant difference. In accordance with many studies as **Garg *et al.*** [(11)] study, which was conducted on 40 patients with CD, and 31 with UC with (32%) of both subtype with vit D <50 nmol/L with no significant difference. Additionally, the prevalence of vitamin D insufficiency was non-significantly greater among UC participants in **Veit *et al.*** [(12)] research (50% vs. 40%, p=0.53) than among CD subjects. Other studies supported our findings [(13-18)]. This low level may be attributed to malabsorption [(19-22)].

We noticed that CRP was higher among deficient group in comparison with other groups. Other studies agree with our data [(23, 24)]. The relationship between vitamin D levels, inflammatory markers, and disease activity has been studied in many research. The majority of researches found an inverse relationship between CDAI and CRP levels and vitamin D levels [(25, 26)].

Regarding Serum 25(OH) vitamin D level based on type of therapy: patients on conventional therapy or biological therapy had insignificant differences as regard level of 25(OH) vitamin D and its status (P> 0.05). This result differs with **Ham *et al.*** [(25)]. We found insignificant differences as regards level of 25(OH) vitamin D and disease activity similar to result of **Hassan *et al.*** [(27)] and **Gubatan *et al.*** [(28)].

CONCLUSION

Vitamin D deficiency is a common issue in patients with IBD. Extent of deficiency may be related to the severity of the disease. Future studies are warranted to document these findings.

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