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Evaluation of Serum Vitamin D Level and its Effect on the Severity of Disease in Patients with Inflammatory Bowel Disease

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Abstract

Background: Evolving evidence indicates the role of vitamin D deficiency in the progression of IBD and its impact on the severity of the disease, but it remains unclear whether vitamin D deficiency causes IBD or vice versa.

Methods: This cross-sectional study was conducted to determine the serum levels of vitamin D and its effects on the severity of disease in patients with inflammatory bowel disease in the Imam Khomeini Hospital complex. A questionnaire containing demographic information, records on the use of supplements and medications, disease complications, and criteria for determining the severity of the disease based on the Mayo score and Crohn's Disease Activity Index (CDAI) and 25 hydroxy vitamin D levels was completed and evaluated.

Results: Of the 101 participants, 21 were with Crohn's disease and 80 had ulcerative colitis. The mean age of Crohn's patients was 33.80±9.5 years and ulcerative colitis was 38.43±10.2 years. Among patients with ulcerative colitis, 37 (46.8%) had a mayo score less than 3 and 42 (53.2%) were 3 and more. Mean vitamin D in the mayo score less than 3 was 32.14 and the mayo score 3 and more was 23.99. Of the Crohn's patients, 12 (57.1%) were in the recovery phase and 9 (52.9%) were in a non-recovery phase. The mean of vitamin D in the recovery phase was 29.10 and in the others was 27.04

Conclusion: There is a significant relationship between the level of vitamin D supplementation, the final value of CDAI, and the identification of the patients with the Mayo score.

Keywords: Crohn's disease, Inflammatory bowel disease, Ulcerative colitis, Vitamin D deficiency

Introduction

Inflammatory Bowel Diseases (IBD) including Crohn's Disease (CD) and Ulcerative Colitis (UC) are chronic disorders of the gastrointestinal tract. The pathogenesis of these diseases is unknown (1). However, it seems to be due to the complexity of the interactions of gut microbes, host immune system regulation, genetic sensitivity, and environmental factors (2).

CD often involves the ileum and colon but can affect any area of the digestive tract, while UC is often confined to the colon and rectum (3). The severity of UC according to the Mayo score index, includes information on the frequency of fecal excretion, daily bleeding from the anus, endoscopic findings and a general assessment of the physician, and a total score of between 0 and 12, that a higher score indicates more severe disease.

The severity of CD is based on the CD activity index, in which the shape of the stool (use or non-use of loperamide), abdominal pain, general condition, side effects, abdominal mass, anemia, and weight changes over a period of 7 days are asked. This criterion is 0-1100 points, with a score of between 0-149 means asymptomatic remission, from 220 to 150 means mild to moderate, and from 221 to 450, indicates moderate to severe disease, and 451-1100 shows severe disease to fulminant form.

Vitamin D is a fat-soluble vitamin that the active form, calcitriol, or 1,25 hydroxyvitamin D3, regulates bone metabolism, calcium, and phosphorus. In humans, vitamin D comes from 2 sources of diet and ultraviolet radiation that acts on the skin's epidermis through the breakdown of D-hydro cholesterol 7 to vitamin D. After producing vitamin D with 2 steps of hydroxylation, the first step Carbon No 5 is activated by the hydroxylase 25 in the liver and the second step by the 1α-hydroxylase in the kidney, and this active form activates its function by contacting the Vitamin D Receptor (VDR). The binding to the recipient causes the transcription of several replicating genes to vitamin D, which are located on one piece. Different tissues, and especially immune-dependent cells, express these receptors and are capable of producing an active form of vitamin D, which means that vitamin D plays a role beyond the classical role of the endocrine hormone to the role of autocrine (4).

In the IBD, the function of the epithelial barrier is impaired and causes a leak flux and permanent inflammation due to increased antigen reabsorption within the lumen. The intestinal epithelial barrier is composed of intracellular junctional complexes, such as Tight Junctions (TJs), adherent junctions, and desmosomes (1).

Claudine's protein consists of a family of TJ proteins that differentially permeate adjacent cells through their hemophilic and heterophilic relationships with other claudine's of adjacent cells. Claudins play a significant biological role in the consolidation of intestinal barrier function so that changes in TJ protein levels, in particular, decrease in Claudine 4 and 7 and increase in Claudine 2 can cause dysfunction in the active phase of UC. Vitamin D can play a vital role in the function of the barrier by reducing Claudine 2 and redistributing Claudine 4 and 7 (1).

While the diagnosis of macronutrient deficiencies is based on clinical symptoms, micronutrient does not always have clinical evidence, and laboratory testing is usually required to diagnose them. The best measure of vitamin D is the measurement of 25 hydroxyvitamin D levels. In this criterion, a level below 20 indicates deficiency, and levels between 20-30 are insufficiency and 30-100 is normal (5).

The prevalence of vitamin D deficiency in IBD is different in various studies. in some studies, more than 60-70% of IBD patients seem to have insufficient levels of vitamin D. However, this depends on various factors such as the location of the study, the season of measurement, and the degree of disease in individuals in the active phase of the disease (6-9). Reproductive studies have shown that every 100 units of increase in total vitamin D levels per day reduce the risk of developing UC by 10% and reduce the risk of CD by 7% (10).

Various factors play a role in vitamin D deficiency in IBD patients, some of which are specifically linked to the underlying bowel disease, while others are common in non-IBD populations. Some of these causes include exposure to inadequate sunlight due to a pattern of life or chronic disease symptoms that limit physical activity, inadequate dietary intake due to symptoms of intestinal disease, absorption impairment, impairment of vitamin D conversion to Active form, increasing catabolism, and increasing

secretion (5).

Lack of vitamin D in the IBD has different interpretations, especially in all of these two situations, common environmental factors such as air pollution, industrialization, higher latitudes and seasons are effective. Vitamin D deficiency in IBD can be a result of malabsorption due to inflammation of the intestine or resection of the surgery. Reducing out-of-home activity by reducing exposure to sunlight or increasing vitamin D intake by inflammatory cells in the affected areas is a result of the symptoms of IBD (3).

The link between intestinal inflammatory disease and vitamin D deficiency was initially raised by the lower risk of IBD in people living in the southern regions compared with those living in northern areas facing less sunlight (11).

Therefore, considering that the IBD imposes a lot of burdens on the country's health system every year and also it is very important for patients to control the disease, and in previous studies, the effect of vitamin D on the severity of the disease and its prognosis has been raised, but there are ambiguities in the studies, and further studies are recommended. In this study, in addition to studying the level of vitamin D on the severity of inflammatory bowel disease, an attempt is being made to advise on the threshold of the need for vitamin D supplementation in patients with inflammatory bowel disease.

Materials and Methods

This is a cross-sectional study to evaluate the serum vitamin D level and its effect on the severity of the disease in patients with IBD (UC and CD). The research environment of this study is the Imam Khomeini Hospital complex. The instrument of this study was a questionnaire including demographic information, duration of disease, history of supplements and other drugs usage, the complications of the disease, underlying diseases as well as questions for determining the severity of the disease based on the criteria of mayo score for UC and CD Activity Index (CDAI) for CD. Then levels of 25 hydroxyvitamin D were measured in all the participants in this study. Our research sample included 101 patients with UC or CD at Imam Khomeini Hospital.

The research tool was designed by the project leader and completed for all the participants. In the second stage, after explaining the research objectives, all participants received informed consent and then the level of vitamin D in patients who did not have a trial was studied. The level of vitamin D was measured by measuring the amount of 25 hydroxyvitamin D by hormone analysis. After collecting the data from the questionnaires and the results of the experiments and data categorization, statistical analysis was performed by SPSS 18 software. Then the results were discussed and the final report of the plan was compiled and published.

Results

Of the total of 101 participants in this project, 21 people were with CD and 8 people with UC. The mean age of the participants with CD was 33.87±9.5 years and those with UC were 38.43±10.2 years. Of the patients with UC in this project, 41 people (51.2%) were female and 39(48.8%) were male (Tables 1 and 2). Among the patients with UC, 37 (46.8%) had mayo score less than 3 and 42 (53.2%) were 3 and more. Mean vitamin D in the mayo score less than 3 was 32.14 and the mayo score 3 and more was 23.99. Of the patients with CD, the participants in this project were 12 (57.1%) females and 9 (42.9%) males (Table 3). Of the Crohn's patients, 12 (57.1%) were in the recovery phase and 9 (52.9%) were in a non-recovery phase. The mean of vitamin D in the recovery phase was 29.10 and in the others was 27.04. There is no significant correlation between vitamin D levels of patients with UC with a few variables such as age, ESR, CRP, Calprotectin, WBC, HB, Plt and Mayo score ($p<0.05$). There is no significant correlation between vitamin D level of CD with variables such as age, ESR, CRP, Calprotectin, WBC, HB, and Plt ($p> 0.05$). There was no significant correlation between the vitamin D level of patients and the mean of disease in patients with CD and UC ($p> 0.05$).

Between levels of vitamin D in two groups of patients with UC and Crohn's by sex, smoking, taking loperamide and diphenoxylate tablets, abdominal pain severity, general patient, arthritis and arthralgia, itching, uveitis, erythema, pyoderma, stomatitis, fishers and fistulas, anal abscess, high fever, abdominal mass, anemia, weight loss, colitis, defecation and bleeding status, endoscopy, and assessment of the patient's condition were not significantly related ($p>0.05$).

Table 1. Demographic characteristics of UC patients

		Frequency	Percent
Sex	Female	12	57.1
	Male	9	42.9
Cigarette	NO	19	90.5
	YES	2	9.5
Supplemental Tab	NO	6	28.6
	YES	15	71.4
Drug history	5-ASA	2	9.5
	ASA+immuno modulator	9	42.9
	Immuno modulator+Anti TNF	1	4.8
	ASA+immuno modulator+Anti TNF	7	33.3
	ASA+immuno modulator+prednisolone	1	4.8
	ASA+immuno modulator+Anti TNF+prednisolone	1	4.8
Frequency of recurrence	0	2	9.5
	1	6	28.6
	2-5	7	33.3
	5-10	3	14.3
	>10	3	14.3
Loperamide intake	NO	19	90.4
	Yes	2	9.6
Taking diphenoxylate	NO	19	90.5
	YES	2	9.5
The severity of abdominal pain in the last 7 days	Low	5	23.8
	Negative	15	71.4
	Severe	1	4.8

Table 2. Demographic characteristics of UC patients

		Frequency	Percent
General patient	Good	15	71.4
	Moderate	4	19.0
	Severe	1	4.8
	Very Severe	1	4.8
Arthritis	No	20	95.2
	Yes	1	4.8

Cont Table 2.

Arthralgia	No	20	95.2
	Yes	1	4.8
Iritis	No	21	100.0
Uveitis	No	21	100.0
Erythema	No	21	100.0
Pyoderma	No	21	100.0
Stomatitis	No	21	100.0
Fisher	No	19	90.5
	Yes	2	9.5
Fistula	No	17	81.0
	Yes	4	19.0
Anal abscess	No	21	100.0
Fistula A	No	21	100.0
High fever	No	21	100.0
Abdominal mass	No	21	100.0
Anemia	No	6	28.6
	Yes	15	71.4
Weight Loss	No	18	85.7
	Yes	3	14.3

Table 3. Demographic characteristics of Crohn's patients

		Frequency	Percent
Sex	Female	41	51.9
	Male	38	48.1
Cigarette	No	72	91.1
	Yes	7	8.9
Supplemental Tab	No	13	16.5
	Yes	66	83.5
Frequency of recurrence	>10	8	10.1
	0	14	17.7
	1	14	17.7
	2-5	33	41.8
	5-10	10	12.7

Cont Table 3.

Valid Colitis	Extensive	7	8.9
	One side	27	34.2
	Pan	28	35.4
	Proctitis	8	10.1
	Recto sigmoiditis	9	11.4
Stool defecation	Blood most of the time	15	19.0
	Blood oftenly	40	50.6
	No	14	17.7
	Only bloody defecate	10	12.7
Bleeding	0	58	73.4
	1	12	15.2
	2	8	10.1
	3	1	1.3
Endoscopy	Moderated	47	59.5
	Normal	7	8.9
	Semi Severe	20	25.3
	Severe	5	6.3
Assessment	Moderated	18	22.8
	Normal	54	68.4
	Severe	7	8.9
	Total	79	100.0

Table 4. The relationship between vitamin D and CDAI

		CDAI
VITD	Pearson Correlation	-0.199
	Sig. (2-tailed)	0.0387

Table 5. The relationship between vitamin D and supplementation

Supplemental tab	GROUP	Mean	Std. deviation	Sig.
NO	CD	24.5000	19.01810	0.016
	UC	18.4238	12.05104	
	Total	20.3426	14.34251	
YES	CD	29.7033	12.57350	0.016
	UC	29.6533	15.59640	
	Total	29.6626	15.01017	

Table 6. Vitamin D cut off to detect mayo score less than 3

CUT VIT	SEN	1-SPSIF	Asymptotic sig/[b]	Area	Asymptotic 95% confidence interval	
					Lower bound	Upper bound
19.2	0.595	0.73				
19.65	0.571	0.73	0.008	0.672	0.207	0.499
20.6	0.548	0.73				

There is no significant relationship between the level of vitamin D and the diagnosis of patients with CD and UC ($p>0.05$). There is no significant relationship between a certain level of vitamin D and a recovery phase in CD. There is a significant correlation between vitamin D and CDAI in patients ($p<0.05$) (Table 4). There was a significant correlation between vitamin D levels in two groups of patients with UC and CD using supplemental pills ($p<0.05$) (Table 5). There is a significant relationship between a certain amount of vitamin D and a Mayo score of less than 3 (Table 6).

Discussion

In 2013, Gilman J *et al* stated in their study that there is a significant relationship between vitamin D levels and supplementation in different seasons, and there is no significant relationship between male sex and smoking with vitamin D levels, which is consistent with the results of the present study. The strength of Gilman's study is the measurement of vitamin D levels in different seasons, which is itself an important factor that has not been considered in our study (12).

In the study of Suibhne TN *et al* in 2012, they noticed a higher vitamin D deficiency in winter, as well as the relationship between smoking and vitamin D levels, which did not match the outcome of this study, and this difference could be observed in the season or type of sampling (13).

In another study by Tajik M *et al* in 2004, there was a correlation between vitamin D levels with the duration of CD, Crohn's activity index, and CRP. Also, they state that the duration of the disease and CDAI can predict vitamin D deficiency. In the same part of our study, we found only a significant relationship between the level of vitamin D and CDAI, and the other items in this study were not significant (14).

In another study in 2016, as in the current study, any relation between vitamin D levels and other variables such as age and sex, and inflammatory factors have not been reported. The only difference was in the basic characteristics of supplementary consumers that most of the users were female. In the present study, there was a significant relationship between supplementation and vitamin D levels, which is more indicative of the accuracy of the study (15).

In a study by Sharifi A *et al* in 2018, 38.9% of the patients with mild-to-moderate levels of UC based on Truelove and Witts' severity index simultaneously have a vitamin D deficiency, Also, there was no significant relationship between vitamin D level and ESR and CRP. In the present study, we evaluated the Mayo index for UC patients, and we reported a significant association between a certain amount of vitamin D and a Mayo score of less than 3 (11).

In a prospective cross-sectional study by Mohammed AS *et al* in 2019 in the Duhok Governorate of Iraq, 82.4, 76.9, and 100%, respectively, of IBD, UC, and CD patients had the serum Vitamin D deficiency and had a significantly lower level of Vitamin D compared with healthy controls (23.4%). However, the study did not show that vitamin D levels between UC and CD patients were substantially different. Each patient's disease activity was measured using the Harvey–Bradshaw Index (HBI) (16).

Conclusion

In this study, we examined the relationship between vitamin D levels with different criteria in Mayo score

and CD activity index, blood factors such as white blood cells and platelets, and inflammatory factors, and only between vitamin D levels with consumption of vitamin D supplements and the final score of CDAI and also a certain level of vitamin D in order to identify the Mayo score of less than 3 were significant.

Conflict of Interest

The authors declare no conflict of interest related to this work.

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