(International Print/Online Journal)

SJIF IMPACT FACTOR: 5.565
PUBMED-National Library of Medicine ID-101739732

ISSN (Print): 2209-2870
ISSN (Online): 2209-2862

International Journal of Medical Science and Current Research (IJMSCR)
Available online at: www.ijmscr.com
Volume 4, Issue 4, Page No: 46-51
July-August 2021

IJMSCR

Association of Vitamin D with Irritable Bowel Syndrome, In Indian Perspective

[1]Dr Omna Shaki, [2]Dr Atul Abhishek Jha, [3]Dr SK Rai, [4]Dr Tp Gupta, [5]Dr Amit Kale

[1]Medical officer, [2]Gastroenterologist, [3]Associate Professor, [4]Asst Professor, [5]orthopaedic Surgeon
[1]Department of Trauma and Emergency. [2]Department of Medicine, [3, 4, 5]Department of orthopaedics, Base Guwahati, Assam India

***Corresponding Author:**
Dr Omna Shaki
Department of Trauma and Emergency Base Guwahati, Assam India

Type of Paper: Research Paper
Conflicts of Interest: Nil

ABSTRACT

Objectives

Many systemic disorders have been associated with Vitamin D. However, data is available regarding its role in irritable bowel syndrome (IBS). Whether Vit D plays any role in this disease is not yet clear. Our study aimed to establish the role of vitamin D deficiencyin patients with IBS compared to a healthy control group.

Methods

This study is a comparative case-control study of vitamin D deficiency in patients with IBS who fulfilled ROME 3 criteria of classification to age and gender-matched healthy control group. The vitamin D level was measured in both cohorts for comparison, and the results were interpreted statistically. One hundred twenty patients with IBS and 100 healthy individuals were included as test and control groups, respectively, in the study. The mean serum vitamin D level (nmol/L) of IBS patients was compared to the control group.

Results

Vitamin D deficiency was detected in 82 patients (68.2%) in the IBS group and 29 patients (29%) in the control group. There was a statistically significant difference in the mean vitamin D level (p=0.022) between the IBS and control groups.

Conclusion

A high prevalence of vitamin D deficiency is in patients with IBS in our study, and these results might have therapeutic implications. Its supplementation could play a therapeutic role as well.

Keywords: Vitamin D, Irritable Bowel Syndrome, Vitamin D Deficiency, Indian population.

INTRODUCTION

Irritable bowel syndrome (IBS) is one of the common gastrointestinal disorders.[1,2] It is a functional gastrointestinal disorder characterized by disorganized bowel function due to neurohormonal bowel wall-gut axis dysfunction.[2] its clinical feature comprises varying degrees of abdominal discomfort, abdominal bloating, altered bowel habits, and excessive flatulence. There are three subtypes according to bowel habits –IBS with diarrhea (IBS-D), IBS with constipation (IBS-C), and IBS with mixed bowel habits (IBS-M). The incidence of IBS has been increasing over the last two decades. [3]

Vitamin D has been found to be strongly associated with many systemic disorders. [4,5] The association of vitamin D in skeletal and extra-skeletal health is an established medical fact. More than 80% of metabolic vitamin D is derived from sunlight and the rest through dietary supplementation. [6]

A pharmacological regimen and modified dietary protocol are being followed for the management of

IBS. The milk and milk-derived products and other calcium-rich dairy products are being avoided in the majority of the patients. However, there are published comparative study reports from Sweden that contradict the efficacy of these modified dietary protocols in IBS patients. [7]

Although the role of vitamin D deficiency in IBS has not yet been fully established, the recent report on the successful treatment of diarrhea-predominant IBS with high doses of oral vitamin D supplementation with the resolution of the associated anxiety and depression. This has sparked a gush in the medical and scientific community.[8]

The present study's objective is to establish the role of vitamin D deficiency in IBS patients compared to a healthy control group.

Methods

This prospective comparative analysis was conducted at the two tertiary care hospitals Guwahati Assam and Ambala Haryana, India, between Aug 2019 and Feb 2021. Informed consent of all the participants was taken and ethical approval was obtained from the institutional ethical committee.

Patients presenting to the Medicine clinic with symptoms of IBS diagnosed by ROME 3 criteria were compared to a healthy control group. The control group was age and gender-matched; otherwise, healthy patients attended Ortho clinic.

Vitamin D deficiency is characterized by According, lower serum 25(OH) D (<20 ng/mL) with consequent and consistent elevation of parathyroid hormone and a decrease in intestinal calcium absorption, according to US Endocrine Society.[9]

The desirable and safe range of serum 25(OH) D level would be 30–100 ng/mL as at serum 25(OH) D levels of 30 ng/mL intestinal calcium absorption reaches its peak, and PTH levels continue to fall until this level of 25(OH) D is attained.[9,10]

Table 1: Demographical characteristics of study and control groups.

Characteristic	IBS (n=120)	Control group (n=100)	P value
Mean Age	32.6±26.3	31.2±28.8	0.361
Sex (M:F)	48:72	31:69	0.422
BMI			
<18.5 kg/m^2	62	32	0.034
18.5 - 25 kg/m^2	43	38	0.451
>25 kg/m^2	15	30	0.542
Vit D(ng/mL)			
Mean 25(OH)D level (nmol/L)*	18.77±9.31	37.71±19.52	0.032
Deficiency <20	82(68.3%)	29(29%)	0.024
Insufficiency 21 -30	38(31.6%)	57(57%)	0.013
Sufficient > 30	-	14(14%)	

* mean±SD; ** n(%)

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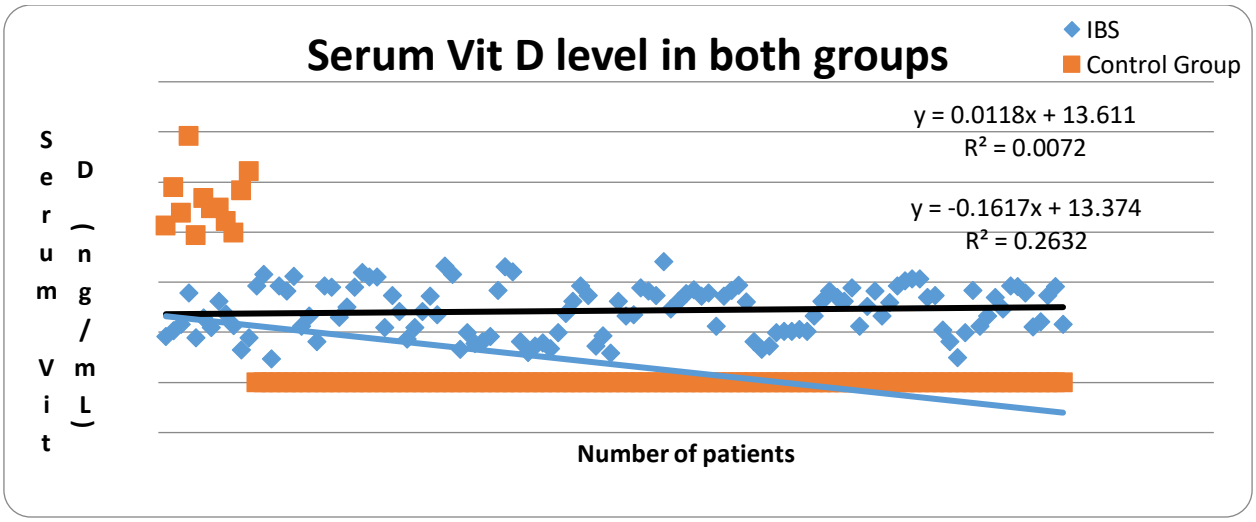

The distribution of serum level of Vit D in both groups has been shown in Fig 1. The majority of IBS patients have a deficient of Vit D as compared to the control group. None of the IBS patients had sufficient Vit D levels; however, only 14% of the population had a sufficient level (> 30ng/mL) of Vit D in the control group.

Table 2: Subtypes of IBS and Vit D level

Subtypes of IBS	IBS-C (n = 32)	IBS-D (n= 39)	IBS-M (n=49)
Mean 25(OH)D level (nmol/L)*	17.81±11.52 (26.6%)	19.27±9.63 (32.5%)	15.22±9.72 (40.8%)
P value	0.761	0.762	0.682

IBS –C (Constipation), IBS –D(Diarrhea), IBS –M (Mixed type)

Demographical parameters regarding age, gender, and BMI were collected from both groups. The serum concentration of vitamin D was measured by 25-hydroxycholecalciferol (25(OH)D levels, Vitamin D assay was performed with cobase 602 analyzer (Roche Diagnostics, USA) in both groups.

Statistical analysis

We used SPSS (version 19, IBM, Inc USA). Number and percentage values used for, Qualitative data and for quantitative data mean and standard deviation (±SD) values used. Chi-square test was used as a test of significance for ordinal data. Student's *t*-test and linear correlation (Pearson's coefficient-2-tailed) was utilized to compare the mean vitamin D levels in both groups with a *p*-value set at less than 0.05 for significance.

Results

In the present study, 120 IBS patients and 100 healthy individuals from the control group were included. The 72(60%) patients were female, and 48 (40%) were male in the study group with a mean age of 32.6±26.3 years. The mean serum level of 25(OH) D in IBS patients was 18.77±9.31 nmol/L compared to the control group of 37.71±19.52 nmol/L. There was a statistically significant difference in the mean 25(OH) D level between the IBS and control groups (*p*=0.032) (Table 1).

Vitamin D deficiency was detected in 82 (68.3%) in the IBS group and 29 (29%) patients in the control group. However, Vitamin D insufficiency was noted in 38(31.6%) in the IBS group and 57(57%) in the control group.

The majority of participants had baseline 25OHD levels considered insufficient/severely deficient with an overall sample mean 25OHD of 18.77±9.31 nmol/L. We noted no significant differences in Vit D level in the subtypes of IBS (Table 2).

A positive Pearson's correlation coefficient (r=0.242, *p*=0.001) was found to exist between age and serum 25(OH) D levels indicating a proportionality of 25(OH)D levels to age. Scatter plotting showed a linear relationship between age and

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vitamin D levels. Gender had no significant effect on vitamin D levels. In terms of consumption, Vitamin D supplementation over the study period was excluded in both groups due to inadequate recollection response.

Discussion:

Irritable bowel disease is a common health problem affecting the gastrointestinal tract of nearly all age groups across the globe. The pathogenesis of IBS is still not well understood. Most studies regarding pathogenesis and management of IBS were done in adult patients, and to our knowledge, this is the first study evaluating the effect of vitamin D supplementation on adolescent IBS patients.

Our study revealed statistically significant results. Firstly, the mean serum level of 25(OH) D in IBS patients was 18.77±9.31 nmol/L compared to the control group 37.71±19.52 nmol/L. Secondly, the frequency of vitamin D deficiency was found to be high in the IBS group 82 (68.3%). However, we did not find any significant difference in the level of Vit d and subtype of IBS.

Vitamin D deficiency and osteoporosis have been observed in many inflammatory bowel diseases such as celiac disease, Crohns disease, inflammatory bowel disease, and post-gastrectomy cases. Sprake et al. [11] noted that the areas of the gut involved in vitamin D absorption are located predominantly in the ileum (70–80%). Vestergaard [12], Holick [13] , and Christakos [14] noted that vitamin D receptors and regulatory mechanisms are mostly located in the cecum and colon regions. Many authors pointed out that the Vitamin D receptor (VDR) is expressed through the nervous system and in the gastrointestinal tract, where its activation is linked to neurotransmitter levels, serotonin synthesis, intestinal epithelial barrier function, and bowel inflammation.[15,16,17] They also suggested that vitamin D deficiency needs to be addressed in IBS patients.

Zehnder et al. noted that the binding of 25 (OH)D-VDR complex results in the expression of 1-alpha-hydroxylase, which converts 25 (OH)D to 1, 25-dihydroxyvitamin D.[18] Later, in the year 2008, McCann noted the role of 25 (OH)D metabolite in up-regulation of neutrophins, promoting survival and differentiation of nerve cells.[19] Hence, vitamin D may directly affect neurological development, gut function and consequently improve IBS symptoms and quality of life as well. They also suggested that vitamin D deficiency needs to be addressed in IBS patients.

Kong [20], in his study, noted that altered cellular growth might be triggered by alterations in the vitamin D mechanisms in the receptor cells and cause malignancy in vitro. Later on, Christakos [14] observed that the oncogenesis process was a part of immune activation with an elevation of cytokines such as tumor necrosis factor (TNF-α), and interleukins (IL-1β and IL-6). Peterlik M, and Cross HS [21] reported that the gut, rich in microflora, helps in the activation of an immune response, helps in recruitment of type-1 helper T cells and thus, maintaining hemostasis. Coussens et al. [22] noted that vitamin D inhibits T-cell proliferation and thus inhibiting the immune response.

Further, the association of Vit D with IBS can be theoretically established to the alterations in the immune response. The present study has shown a significant difference in the mean level of Vit D in the IBS group compared to the control. Khayyat [23] in his study noted that 82% patients of IBS patients had Vit D deficiency. Jesus CA [24] observed the immune response alteration in IBS and suggested more research is required to prove the association of vitamin D in the suppression of immune response by type-1 helper T cells and potentiates the function of natural killer cells.

Cho et al. [25] in study of 124 adolescents children of IBS and found that the average vitamin D level in these adolescents was <20 ng/mL, a significant lower level. Recently in the year 2019, Jalili et al. [26], in a randomized, double-blind, placebo-controlled clinical trial, 116 patients with IBS, found that Vitamin D therapy can improve the severity of symptoms and quality of life in patients with IBS.

Abbasnezhad,[27] and Tazzyman [28] noted that the Vit D deficiency might be multifactorial as these IBS patients who often tend to avoid milk and its related products, which contain calcium and vitamin D in order to avoid abdominal discomfort like bloating, flatulence, and cramps. This is added with changes in psycho-social behavioral patterns as well. This pattern is more shown by a patient suffering from IBS-diarrheal subtypes. Hence, vitamin D may directly affect neurological development and gut function and,

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consequently, improve IBS symptoms and quality of life.

Poor exposure to sunlight leads to vitamin D deficiency is a proven fact, and there has been no significant difference between the male and female population with reference to vitamin D levels in our study. However, the prevalence of vitamin D deficiency rises with advancing age and has a positive correlation.

Limitation of the study:

Both of our hospitals are a tertiary center that received a referral from different geographical locations. Variation in the season, exposure to sunlight, physical activity, and dietary habits could affect vitamin D status. The findings of our study are limited to our population, and further studies are needed.

Role of primary physician:

Primary-care physicians must be aware to recognize early alarm symptoms, such as unexplained or unintentional weight loss, abdominal discomfort, bloating, excessive flatulence, anemia, and occult blood in stool after age 50 years, family history of abdominal cancer, positive markers for IBD, inflammatory bowel disease, signs and symptoms of malabsorption. After detecting these "red flags" patients must be referred to secondary care for further investigation and management.

Conclusion

Vitamin D has been a field of interest in the pathogenesis of various inflammatory bowel disease of gastroenterological tract. Its deficiency in IBS has recently caught interest. Many published data indicate its therapeutic use in IBS in elevating symptoms. However, vitamin D deficiency should be investigated in every patient with IBS and its deficiency should be addressed in the diagnosis and the treatment. Vitamin D supplementation should be considered as a part of the therapeutic protocol in patients with IBS.

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