



Serum vitamin D3 levels, Demographic characteristics and anthropometric measurements in patients with irritable bowel syndrome-A prospective hospital based observational study.

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ABSTRACT: Background: Vitamin D has been found to be strongly associated with many inflammatory systemic disorders. Present century has witnessed an augmented interest within the medical community in vitamin D deficiency in various systemic disorders, IBS being one among them. Irritable bowel syndrome (IBS) is a gastrointestinal disorder characterized by disorganized bowel function due to neurohormonal gut- brain axis dysfunction. Although the role of vitamin D deficiency in irritable bowel syndrome (IBS) has not yet been clearly established, studies are underway to establish its role in the disease. Various studies have suggested a role for vitamin D in IBS, but this has not been evaluated in a detailed and analytical way.

Material and Methods: This study is a prospective hospital based observational study of vitamin D deficiency in patients with IBS diagnosed with ROME 3 criteria of classification (the third ROME foundation classification). The 80 patients with IBS (43 males and 37 females) were included in the study and their demographic characteristics and anthropometric measurements were taken. The serum Vitamin D (ng/ml) levels were tested by radioimmunoassay.

Results: Vitamin D deficiency was detected in 45 patients (56.25%). Of 43 male patients 22 (51.1%) were having vitamin D deficiency, and among 37 females, 23 (62.1%) were found to have vitamin D deficiency. 54 patients (67.5%) belonged to the rural areas, and 26 patients belonged to urban areas. The average BMI in males was 25 and females was 22.86.

Conclusion: Our study shows that vitamin D deficiency is highly prevalent in patients with IBS and these results seem to have therapeutic implications. Vitamin D supplementation could

play a therapeutic role in the control of IBS, and hence improve the quality of life in these patients.

Key words: IBS-Irritable bowel syndrome; Serum Vitamin D Deficiency, Neurohormonal gut-brain axis dysfunction.

I. INTRODUCTION:

Irritable bowel syndrome (IBS) is a gastrointestinal disorder characterized by disorganized bowel function due to neurohormonal gut-brain axis dysfunction¹.

The patients afflicted with IBS predominantly present with abdominal pain and altered bowel habits, with either predominantly diarrhea (IBS-D), constipation (IBS-C), or both (IBS-M). There is no definite investigation as no biomarker has been found to correlate, so IBS is diagnosed clinically, with ROME 3 criteria of classification (the third ROME foundation classification). It is hence a diagnosis of exclusion².

Nowadays it's a fairly commonly reported medical disease with its prevalence being reported approximately 4.6% to 21.2% in adults in Asia, and 10% to 15% in North America and Europe. Second, third and fourth decades are the most frequent ages of onset with a significant female predominance³.

There are three recognized sub-types of IBS: diarrhea-predominant (Type D), constipation-predominant (Type C) and alternating diarrhea and constipation (Type A). The other clinical features of this commonly diagnosed condition include, bloating, passing of mucus from the rectum, irregular stool habits and urgency of evacuation. This condition has a significant impact on the patient's quality of life as is evident with the frequent occurrence of psychiatric issues such as anxiety and depression in these patients⁴.



Various studies have observed low vitamin D levels in a number of medical conditions including some cancers, neurologic disorders, and cognitive disorders in the elderly age group. Researchers have postulated a possible role of vitamin D deficiency in the development of inflammatory response in gut, making the connection between vitamin D and IBS a feasible speculation. Treatment for IBS consists of dietary modifications, behavioral therapy, and pharmacotherapy depending on the predominant symptoms. Treatment is based on a patient's symptoms and may need to be altered according to a patient's needs⁵.

Vitamin D is a hormone that is mainly produced in the skin as a response to sunlight. The dominant form of vitamin D that circulates throughout the body is 25-hydroxyvitamin D (25[OH]D). According to the Institute of Medicine (IOM), vitamin D deficiency is defined as a serum 25(OH)D level <12 ng/mL⁶. The Endocrine Society defines vitamin D deficiency as 25(OH)D levels ranging from 21 to 29 ng/mL (Table 3). The recommended measurement of vitamin D is the 25(OH)D level using a reliable assay. Vitamin D deficiency in the general population has numerous causes, including lack of sunlight, poor dietary choices, and comorbidities such as diabetes, inflammatory bowel disease, or gastric bypass⁷. Symptoms of deficient vitamin D levels include fatigue, muscle weakness, chronic musculoskeletal pain, leg heaviness, and joint pain, all of which are common complaints in a primary care setting. Vitamin D deficiency has been linked to an increased risk of colon cancer, ovarian cancer, and prostate cancer. Vitamin D has been known to inhibit T-cell proliferation, thereby decreasing the potential for an immune response. Interestingly, 70% to 80% of vitamin D absorption in the gut occurs in the ileum with most vitamin D receptors (VDRs) and regulatory mechanisms in the cecum and large intestine. VDR is a protein that regulates physiologic processes and is present in most tissues of the body. The presence of VDRs in the gut suggests that vitamin D is needed to maintain normal function. The effects of vitamin D on gut function may be due to VDR expression in the gut and the neurologic system that regulate the epithelium barrier, neurotransmitters, and serotonin synthesis, causing a decrease in visceral hypersensitivity and abdominal pain^{8,9}.

II. MATERIAL AND METHODS

This prospective observational study was conducted in a private hospital after taking informed consent from the patients. 80 diagnosed

cases of IBS (diagnosed by ROME III criteria, Table 2)¹⁰ were included in the study falling in the age group of 20-70 years. The serum concentration of vitamin D level was measured by chemiluminescence method on immunoassay analyzer. On the basis of multiple guidelines serum 25(OH)D level of <20 ng/mL has been defined as vitamin D deficiency.

A total of 80 IBS patients were included in the study, which took place over a period of 6 months. The study population was mostly males 43 (53.75%) with a mean age of 42±5 years and 37 (46.25%) were females. The mean serum level of 25(OH)D in IBS patients was 17±7 ng/mL.

Vitamin D deficiency was detected in 45 patients (56.25%). Of 43 male patients 22 (51.1%) were having vitamin D deficiency, and among 37 females, 23 (62.1%) were found to have vitamin D deficiency. 54 patients (67.5%) belonged to the rural areas, and 26 patients belonged to urban areas. The average BMI in males was 25 and females was 22.86 (Table 1).

III. DISCUSSION

Irritable bowel syndrome (IBS) is one of the most common gastrointestinal conditions encountered in day to day practice characterized by chronic abdominal pain, discomfort, bloating, and alteration of bowel habits without any known organic cause. Two recent clinical trials have shown promising effects of Vitamin D supplementation on IBS symptoms. Furthermore, a recent review article has shown that immune system activation is more frequent in IBS patients in comparison to healthy controls¹¹.

Although the exact pathophysiology of IBS has not yet been elucidated, it has been shown that alterations in the gut microbiome, intestinal permeability, gut immune functions, visceral sensation, brain-gut interactions, and psychosocial factors are involved in the development of this intriguing condition. Furthermore, it has been shown previously that Vitamin D can modulate all of these probable mechanisms involved in IBS pathogenesis. The effects of Vitamin D on the improvement of intestinal barrier function have been demonstrated in *in vitro* studies also. Moreover, it has been shown that Vitamin D regulates immune cell trafficking and differentiation, gut barrier function, and antimicrobial peptide synthesis, all of which, has been shown that play a role in the development of IBS. Vitamin D regulates the innate immune response to the microbiota^{12,13}. Vitamin D is a critical regulator of T-cell function, and the expression of several pattern recognition receptors



involved in intestinal inflammation is regulated by Vitamin D. In the absence of Vitamin D, there are many effector T-cells that produce inflammatory cytokines in the intestine. Vitamin D promotes regulatory T-cell development and function to turn off the Th1 and Th17 cells and to control inflammation in the intestine. The ability of Vitamin D to inhibit Th1, Th17 cells, induce regulatory T-cells, and reduce inflammation resulted in a shift in the microbiome and maintenance of tolerance in the gut. Thus, Vitamin D can improve the IBS symptoms through reduction in all known risk factors that are involved in the pathogenesis of this syndrome¹⁴.

The present study revealed statistically significant vitamin D deficiency in patients with IBS. The mean serum level of 25(OH)D in IBS patients was 17 ± 7 ng/mL. Secondly the frequency of vitamin D deficiency was found to be high in rural patients and females with IBS. However no significant positive correlation between BMI and vitamin D level with IBS was found.

The link between IBS and vitamin D deficiency can be theoretically established to the alterations in the immune response as vitamin D has been demonstrated to have an anti-inflammatory role in various disease processes. More recently vitamin D deficiency has been proposed as a causative factor in the pathogenesis of IBS. The present study has shown significant difference in the mean level of vitamin D in the IBS group compared to controls. However there is a paucity of clinical studies about the pathophysiological role of vitamin D in the

development of IBS. Food avoidance behaviour patterns have been observed in these patients as IBS severely impacts the psyche of these patients, which leads to an altered vitamin D absorption mechanism^{15,16}. Sprake et al has shown a probable treatment response associated with active diarrhea symptoms of IBS¹⁷.

This study is limited by the fact that vitamin D balance is dependent on numerous physiological and social factors like exposure to sunlight, physical activity, and dietary habits that serve as the determinants of serum vitamin D levels.

Statistical analysis was accomplished using SPSS (version 19). Qualitative data were presented in the form of number and percentage values. The quantitative data were presented in the form of mean and standard deviation (\pm SD) values. Chi-square test was employed as a test of significance for ordinal data.

IV. CONCLUSION

Vitamin D deficiency in the present study as well as previous studies points towards a possible role of vitamin D in the pathogenesis of IBS. More research is needed to establish the therapeutic role of vitamin D in the management of IBS patients and deficiency should be addressed in the diagnosis and the treatment of the condition. Vitamin D supplementation should be considered as a part of the therapeutic protocol in patients with IBS henceforth.

Table 1. Demographic characteristics and anthropometric measurements.

S.NO	Number	Percentage
1.	80	100%
Number of males	43	53.75%
Number of Females	37	46.25%
No of males with Vitamin D deficiency	22	51.1%
No of females with vitamin D deficiency	23	62.1%
No of rural patients	54	67.5%
No of Urban patients	26	32.5%
Mean BMI in males	25.00	
Mean BMI in females	22.86	

Table 2. Rome 3 criteria for the diagnosis of IBS.

IRRITABLE BOWEL SYNDROME (ROME 3 CRITERIA) FOR DIAGNOSIS
Recurrent abdominal pain or discomfort for at least three days/month in the last three months associated with two or more of the following:



1.	Improvement with defecation.
2.	Onset associated with a change in frequency of stool.
3.	Onset associated with a change in form (appearance) of stool.
* Criterion fulfilled for the last three months with symptom onset at least six months prior to diagnosis	

Table 3. Vitamin D deficiency levels according to Endocrine Society.

VITAMIN D (25-hydroxyvitamin D [25(OH)D] levels)	ENDOCRINE SOCIETY (ng/ml)
Deficient	0-20
Insufficient	21-29
Sufficient	30-50
Adverse effects	>100

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