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Original Article

Impact of Oral Vitamin D3 Supplementation on Quality of Life in Patients with Irritable Bowel Syndrome (IBS)

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ABSTRACT

Irritable Bowel Syndrome (IBS) is the most prevailing complicated gastrointestinal disorder with an approximate 11.2% global prevalence, indicating a critical need for an improved understanding of the condition. Several studies suggested that adult IBS patients' symptoms and quality of life are markedly improved by vitamin D supplementation. **Objective:** To analyze the impact of oral Vitamin D3 supplementation on quality of life in patients with Intestinal Bowel Syndrome. **Methods:** A randomized control trial (RCT) was conducted for 9 months. Non-probability purposive sampling technique was used to allocate 24 participants aged between 25 to 35 years and BMI of 18-25. The participants were separated into two groups, G1 and G0. G1 received 50,000 IU of vitamin D weekly for 6 weeks. **Results:** Before the intervention, values of IBS-QOL for G1 were estimated as 1.8±0.71 while at the end of the intervention, there was a visible improvement in the values of IBS-QoL with the mean and SD determined as 2.4±0.51. The p-value for G1 was 0.002 which shows that there were significant improvements in the G1. **Conclusions:** The present study concluded that vitamin D supplementation can benefit patients with IBS by adding 5000 IU of vitamin D supplementation.

INTRODUCTION

Irritable bowel syndrome (IBS) shows a cluster of symptoms which are chronic stomach pain and discomfort and changes in bowel habits like diarrhea and constipation, which are best explained by functional bowel disorders rather than structural or metabolic abnormalities [1]. Psychological problems, intestinal dysmotility, genetic or environmental factors, visceral hypersensitivity, or a misaligned brain-gut axis have all been proposed as causes of IBS symptoms [2]. IBS is the most prevailing complicated gastrointestinal disorder with an approximate 11.2% global prevalence, indicating a critical need for an improved understanding of the condition [3]. One of the most prevalent gut-brain illnesses, IBS is thought to impact one in ten people worldwide. Studies conducted in Southeast Asia and the Middle East found a prevalence of 7.0%, whereas North European, Australian Asian, and North American, studies found a prevalence of between 11.8 - 14.0%, and South American, African, and South European studies found a prevalence of between 15.0 - 21.0% [4]. According to a survey, there were 14.1% of IBS cases in the USA. In 2019, a study was out in Pakistan found that 33.2% of the general population had IBS [5]. Conferring to the kind of stool produced, IBS is further

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classified into four subtypes: IBS with diarrhea (IBS-D), IBS with constipation (IBS-C), unsub typed IBS (IBS-U), and mixed IBS (IBS-M) [6, 7]. It is diagnosed using symptom-based criteria, the elimination of worrying structures (warning signs beginning after the age of fifty, family history of certain organic gastrointestinal ailments, unexplained weight loss, unexplained anemia, and signs of gastrointestinal bleeding), and the outcomes of some tests (Age-appropriate colorectal cancer C-reactive protein or faecal calprotectin, complete blood count, serologic testing for celiac disease). In choosing diagnostic procedures and therapies, the primary symptom (IBS-D, IBS-C, or mixed IBS) is crucial [8, 9]. The clinical diagnosis of IBS typically employs the Rome IV criteria [10]. The following two or more of the following must be present along with recurring abdominal pain for the condition to be met: 1) connected to feces; 2) connected to a shift in stoma frequency; and 3) connected to a shift in stoma appearance [11]. A physiologically activated form of vitamin D3 is 1,25-dihydroxy vitamin D3 [1,25(OH)2D3], the main functions of which are to modulate cell development, immunological function, and inflammation reduction [12]. Numerous studies have found that IBS patients have low vitamin D levels [13]. Numerous causes, such as an altered digestion pattern or an aversion to dairy and fatty foods, might be blamed for this deficit. Adult IBS patients' symptoms and quality of life are markedly improved by vitamin D supplementation [14]. The management of the microbiome, the intonation of the immune system, inflammation activity, and the generation of anti-microbial peptides are just a few of the cellular mechanisms that vitamin D may affect [15]. These activities, in turn, may favorably affect the altered gut function [16]. The study suggests that vitamin D insufficiency may be related to IBS because of the function it plays in the disorder, and supplementation may help regulate and maintain remission [17]. Numerous studies have found that IBS patients have low vitamin D levels. Numerous causes, such as an altered digestion pattern or an aversion to dairy and fatty foods, might be blamed for this deficit [18-20]. VD may help reduce the symptoms of IBS by modulating the immune system and inflammatory activity, which may then positively interfere with the altered gut function [21]. Additionally, IBS patients who are deficient in this vitamin frequently have pain, anxiety, and despair. These factors suggest that those with IBS may benefit from using VD supplements [22, 23]. Adult IBS patients' symptoms and quality of life are markedly improved by vitamin D supplementation [14]. The current study aimed to analyze the impact of oral Vitamin D3 supplementation on quality of life in patients with intestinal bowel syndrome.

METHODS

The sample size calculation was based on irritable bowel syndrome symptom severity score as a primary variable according to the reference article. We considered the probability of a type I error of 5% (α= 0.05) and a type II error of 20% (β= 1, power= 99%). The mean of the treatment group as well as the control group was 61.4 and 35.5 respectively. The standard deviation of this variable was 14.5 and 13.5. The following formula was used to calculate the sample size.

$$n=\frac{(Z_1-\beta+Z_1-\alpha/2)^2(S_1^2+S_2^2)}{(\mu_1-\mu_2)^2}$$

This resulted in a minimum sample size in each group of 12 patients. A randomized control trial (RCT) was conducted for 9 months after taking the approval for synopsis. Non-probability purposive sampling technique was used to allocate 24 participants aged between 25 to 35 years and BMI of 18–25. Participants who fall in the severe category (>300) of IBS-SSS with low Vitamin D levels were selected. Pregnant and nursing women were excluded from the study. Subjects with serum Vitamin D levels of >30 ng/ml were also excluded from the study. Also, subjects taking vitamin D supplements and those with chronic conditions like renal failure or diabetes mellitus were not selected. Participants were selected from the gastroenterology department of Hijaz Hospital, Lahore. This study was a clinical trial, so written permission was taken from Hijaz Hospital, Lahore for data collection. After obtaining informed consent in written form from participants, data were collected. The participants were randomly allotted to take 50,000 IU of vitamin D weekly for 6 weeks. Initial data were based on anthropometric measurements, and serum Vitamin D levels were taken at the baseline of the study. After screening, participants were separated into two groups, the control group (G0), and the treatment group (G1). The participants were evaluated based on ROME IV for the diagnosis of IBS. We filled out a validated IBS-SSS questionnaire, IBS-QOL questionnaire, gastrointestinal symptom evaluation form and total score of IBS at the beginning of the study period. The follow-up for patients was conducted after 3 weeks. The anthropometric measurements and vitamin D screening tests of both the control and treatment groups were collected in the last follow-up. Data were tabulated and analyzed using SPSS version 25.0. The quantitative variables like age, BMI etc. were reported by using mean and standard deviation. To find out the mean difference in the impact of oral vitamin D_3 supplementation on the quality of life in patients with intestinal bowel syndrome, a paired sample T-test was used and $p \leq 0.05$ was considered significant.

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RESULTS

The demographic characteristics of the participants of the study are demonstrated in Table 1. Out of 24 participants, 19 (79.2%) were males while 5 (20.8%) were females. 11 (45.8%) out of 24 participants fell in the age range of 25-30 years while 13 (54.2%) ranged between 31-35 years. The majority of the participants were well-educated. 8 (33.3%) participants had completed their education to a master's or bachelors. While 4 (16.7%) had a matric or intermediate level of education. 18 (75%) participants were married while 6 (25%) were unmarried.

Table 1: Frequency Distribution of Demographic Profile

Demographic Profile of Participants		
Variable	**Frequency (%)**	**Mean ± SD**
Age		
25-30	11(45.8)	1.54±0.50
31-35	13(54.2)	
Gender		
Male	19(79.2)	1.20±0.41
Female	5(20.8)	
Education		
Matric	4(16.7)	2.83±1.09
Intermediate	4(16.7)	
Bachelors	8(33.3)	
Masters	8(33.3)	
Marital Status		
Unmarried	6(25.0)	1.75±0.44
Married	18(75.0)	

Serum vitamin D levels are presented in Table 2. It shows that before the intervention, serum vitamin D levels of G0 were 1.5±0.52 and at the end of the intervention there was no improvement in vitamin D levels as 1.5±0.52 while the p-value was 1.00. Before intervention, serum vitamin D levels for G1 were determined as 1.75±0.45 while at the end of the intervention, vitamin D levels were elevated as 2.66±0.49 with a p-value of 0.001 which shows significant improvements in G1.

Table 1: Frequency Distribution of Demographic Profile

Groups	Parameters	Mean ±SD	Mean Difference	p-value
G0 Control Group	Serum Vitamin D test (Pre)	1.5±0.52	0.15	1.00
	Serum Vitamin D test (Post)	1.5±0.52	0.15	
G1 Treatment Group	Serum Vitamin D test (Pre)	1.75±0.45	0.13	0.001
	Serum Vitamin D test (Post)	2.66±0.49	0.14	

Table 3 shows the changes in quality of life in patients with intestinal bowel syndrome. It showed that before the intervention, IBS-QoL for G0 were 2.6±0.49 and at the end of the intervention there was a little improvement in the values of IBS-QoL with mean and SD as 2.3±0.65 while p-value was 0.39. Before the intervention, values of IBS-QoL for G1 were estimated as 1.8±0.71 while at the end of the intervention, there was a visible enhancement in the values of IBS-QoL with the mean and SD determined as 2.4±0.51. The P-value for G1 was 0.002 which shows that there were significant improvements in the G1.

Groups	Parameters	Mean ±SD	Mean Difference	p-value
G0 Control Group	IBS-QoL (Pre)	2.6±0.49	0.14	0.39
	IBS-QoL (Post)	2.3±0.65	0.18	
G1 Treatment Group	IBS-QoL (Pre)	1.8±0.71	0.14	0.002
	IBS-QoL (Post)	2.4±0.51	0.20	

DISCUSSION

Demographic characteristics of the participants stated that out of 24 participants 19 (79.2%) were males while 5 (20.8%) were females. Likewise, Linsalata *et al.*, (2021) conducted a study with ninety-three participants, 82 were females and 11 were males [24]. A similar study was conducted by Sikaroudi *et al.*, (2020) with participants of which 39 were women and 35 were men [25]. Another study was conducted by Naderpoor *et al.*, (2019) which included 38 individuals of which 22 were males and 16 were females [26]. 11 (45.8%) out of 24 participants were 25 to 30 years old while 13 (54.2%) were between 3 to 35 years of age. Similarly, a study was conducted by Ibrahim *et al.*, (2020) with participants who fall in the range of mean age=22.33±1.37 [27]. Likewise, Quigley *et al.*, (2016) conducted a randomized, double-blind, placebo-controlled trial study with participants between the ages of 18 to 65 years old [28]. In another study that was conducted by Linsalata *et al.*, (2023) the mean age of the subjects was with mean age 43.3 ± 10.11 [24]. Before the intervention, changes in weight of G0 were estimated as 5.91±2.35 and at the end of the intervention, there was no improvement in weight change as 5.58±2.10 while the p-value was 0.266. Before intervention, weight change for G1 was estimated as 1.75±0.45 while at the end of the intervention, weight changes were elevated as 2.66±0.49 with a p-value of 0.001 which shows significant improvements in weight changes of G1. In the study conducted by Chao *et al.*, (2013) out of 2714 participants 1.19% were underweight, 28.5% had normal weight, 36.5% were overweight and 33.7% had obesity from the control group. In the treatment group, 0.52% were underweight, 73 24.01% had normal weight, 37.09% fell in the category of overweight and 38.3% had obesity [29]. Other than that, table 2 shows that before the intervention, serum vitamin D levels of G0 were 1.5±0.52 and at the end of the intervention no improvement in vitamin D levels was shown as the mean and SD remained 1.5±0.52 while the p-value was 1.00. Whereas for the treatment group (G1), serum vitamin D levels for G1 were determined as 1.75±0.45 before the intervention. At the end

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of the intervention, vitamin D levels were elevated at 2.66±0.49 with a p-value of 0.001 which showed significant improvements in G1. Similarly, El Amrousay *et al.*, 2018 studied the effects of vitamin D supplementation in adolescents with IBS and vitamin D insufficiency. A total of 122 subjects with IBS and vitamin D insufficiency were randomly assigned to two groups in which for six months, a dosage of 2000 IU/day for vitamin D3 was given to one group and the other group a placebo. Before and six months after therapy, vitamin D levels along with IBS-QOL were assessed. When compared to the IBS placebo group, IBS patients who got vitamin D supplementation for 6 months improved significantly in IBS-QOL with a p-score of 0.001. Subjects who were given vitamin D supplementation showed double improvements in serum vitamin D levels. There serum levels increased from 17.2±1.3 to 39±3.3 ng/ml, with p-value <0.001. Serum vitamin D levels in the placebo group were not substantially different (p = 0.66) [19]. Similarly, Khalighi *et al.*, (2020) conducted a study to assess the anti-inflammatory and mental benefits of vitamin D3 supplementation on quality of life in IBS-D patients. It was a randomized controlled trial that took place at Rasoul-e-Akram Hospital in which 88 vitamin D deficient/insufficient IBS-D patients were selected. The age range of the subjects was 18-65 years. Subjects were randomized into two groups at random. For 9 weeks, a dosage of 5000 IU/week for vitamin D3 was given to the first group while the second group was given the placebo. Serum vitamin D levels in the first and second groups were 17.68 (7.69) and 17.83 (7.84) ng/mL, respectively, at the start of the trial. After 9 weeks of vitamin D supplementation, blood vitamin D3 values escalated notably ($p < 0.01$) compared to baseline values. The initial values for serum vitamin D were 46.86±12.00 ng/mL, and the second group showed no visible change. In the end, the difference in vitamin D levels between the groups was substantial (p< 0.01) [20]. Similarly, Abbasnezhad *et al.*, (2016) conducted another study to examine whether Vitamin D might alleviate the symptoms of IBS patients through its favorable effects on psychological variables and inflammation. This double-blind, randomized, placebo-controlled trial included 90 IBS subjects. For six months, subjects were randomly allotted to take either 50,000 IU vitamin D3 or a placebo. Participants documented their IBS symptoms at the start of the study and then monthly throughout the intervention period. At the baseline and postintervention assessments, the IBS and IBS-QoL questionnaires were placed. Serum 25(OH)D3 levels grew remarkably from baseline during a 6-month vitamin D treatment. But in the vitamin D group, it was never over average levels. On comparison between both groups, the mean change in serum vitamin D levels was markedly higher in the group that received vitamin D supplementation [1]. The influence of oral vitamin D3 supplementation on IBS-QOL is represented in Table 3. It shows that before the intervention, IBS-QOL for G0 were 2.6±0.49and at the end of the intervention there was a little betterment in the values of IBS-QOL with mean and SD as 2.3±0.65 while p-value was 0.39. Before the intervention, values of IBS-QOL for G1 were estimated as2.4±0.51while at the end of the intervention, there was a visible betterment in the values of IBS-QOL with the mean and SD determined as 1.8±0.71. The p-value for G1 was 0.002 which shows that there were significant improvements in the G1. Following research carried out by El Amrousy *et al.*, (2018) to evaluate the effectiveness of vitamin D supplementation in vitamin D insufficient IBS adolescents. For this purpose, 112 IBS adolescent patients were randomly allocated into two groups. Both groups have no difference in age and sex. To study the effect of vitamin D3, one group was given oral vitamin D3 supplementation with a dosage of 2000 IU per day while the other group received a placebo for 6 months. Before and after the treatment, patients were monitored for vitamin D levels along with IBS-QOL. After the completion of treatment, results showed visible improvements in IBS-QoL in the group that received vitamin D as P = 0.001. While the placebo group showed slight improvement in IBS-QOL (p= 0.47) [19]. All the scores for subscales of IBS-QOL indicated visible improvements in both groups, after the completion of the study [1]. Also, Khalighi *et al.*, (2020) conducted a similar study which showed that vitamin D supplementation helps improve the quality of life in IBS patients. At the end of the study, results showed that vitamin D supplements showed positive effects in both groups. The vitamin D group had a p-value < 0.001 and the control group showed a P-value =0.007. But vitamin D group showed more improvement than the control group (P=0.049). Other than that, for a deeper insight scores for subscales were also compared. It showed that there were significant improvements in subscales of QOL for both groups except for no change in relationship and social reaction in the control group. The vitamin D group showed more visible improvements in health worry, dysphoria, social relation and reaction, and interference with activity [20].

CONCLUSIONS

The present study concluded that vitamin D supplementation can benefit patients with IBS by adding 5000 IU of vitamin D supplementation. Vitamin D is known to reduce inflammation, immunity, gut microbiota and epithelial cell integrity by improving serum vitamin D levels. The comparison of the significance of both groups showed that vitamin D supplementation has significantly improved

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the scores of IBS-QoL. It improved the quality of life by improving dysphoria, social interactions, food choices, and health worries.

Authors Contribution

Conceptualization: AZ
Methodology: AF
Formal analysis: HA, SI, AF
Writing review and editing: BR, HA, SI

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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