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To Investigate The Association Between Chronic Functional Constipation & Serum Vitamin D Levels At A Rural Tertiary Care Centre in North India -A Case Control Study

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Abstract

Background: Chronic functional constipation (CFC) is a long lasting debilitating condition whose exact pathophysiology is still not clear.

Aim: To evaluate the association between serum vitamin D levels and chronic functional constipation.

Methods: We performed a prospective case control study in total 70 patients with & without chronic functional constipation. Their serum vitamin D levels were assessed, which were further evaluated for any association with the constipation and its severity.

Result: In this prospective case control study of 70 patients, we took 35 cases (patients with chronic functional constipation) and 35 controls (patients without chronic functional constipation) and measured their serum vitamin D level and found that patients suffering from chronic functional constipation have significantly low level of serum vitamin D level (mean value 12.829±3.92 ng/ml) as compared to patient without chronic functional constipation (mean value 18.71±6.93 ng/ml). Our study also reveal low serum vitamin D levels were positively corelated with severity of constipation p value < 0.001 (assessed using Wexner constipation score).

Conclusion: The Vitamin D deficiency is commonly associated with chronic functional constipation and its severity. A routine vitamin D measurement in CFC can play an important role in its management.

Keywords: Constipation, Fluid Secretions, Fistula Outlet Obstruction

Introduction

Constipation is common gastrointestinal disorder which affects population of all age groups. It has been defined in many ways while using self-reported and formal criteria. Its global prevalence is around 15% in adults[1], it is reported in 12% to 17% of Indian population[2] and 11.6% of rural population of Haryana[3].

The constipation can be primary (functional) or secondary to various causes. Chronic functional constipation (CFC) is found in around[4] 6% of the population. It is further divided into normal transit constipation, outlet obstruction and slow transit constipation[5]. Although normal transit constipation is the most prevalent subgroup of CFC[6], but its pathophysiology is still unclear. The changes in the colonic microbiota can alter bile acid metabolism[7], methane production[8] and epithelial functions which can further alter colonic motility and fluid secretions. An incoordination between abdominal wall muscles, pelvic floor muscles and anal sphincters may result to the obstructed defecation. In slow transit constipation, there is a limited increase in postprandial motor activity, along with impairment of normal retrograde colonic propulsion. The vitamin D has been reported to play a momentous role in maintaining the gut microbiota by regulating expression of antimicrobial peptide and the barrier function of gut mucosa[12]. Moreover, it also plays a critical role in modulation of adaptive and innate immunity. Its deficiency has been reported to be associated with pathophysiology of IBS and depression. The vitamin D receptors are expressed in the gut and regulates epithelial barrier function and bowel inflammation and hence directly impact bowel functions[9] Despite having a significant burden of CFC and vit D deficiency in Indian population, there is paucity of literature about their association. Therefore, the present study has been planned to evaluate the association of CFC with serum vitamin d deficiency in Indian population.

Methodology

It was a case control study conducted in the department of general surgery. All patients of CFC fulfilling the inclusion criteria were enrolled in the study as cases while similar number of healthy individuals of comparable demographic profile were enrolled as controls.

A detailed history of all patients of chronic functional constipation was noted. Bristol Stool Scale was used to describe the stool form.

Physical examination included palpation of the abdomen in search for palpable lump/ fecaliths. A careful digital rectal examination was done to identify any anal diseases such as, fissures, fistula, inflammation, strictures or any

masses. A digital rectal examination (DRE) involves inspecting the anus and surrounding tissue for abnormalities, followed by digital palpation to assess anal resting and squeeze pressures. Patients were then asked to bear down, evaluating anal sphincter relaxation, abdominal push effort, and perineal descent. These were classified into various categories like normal, impaired, or excessive. DRE has a sensitivity of 93.2%, specificity of 58.7%, and a positive predictive value of 91.0% in diagnosing dyssynergia[10].

The blood samples of all the cases were taken at the time of first visit and sent for 25(OH) vitamin d levels, complete blood count, blood sugar level, thyroid function test, blood urea and serum calcium levels.

Vitamin D levels measurement

Serum vitamin D [25-(OH)-D] levels were measured in all the patients. The levels were further categorized as (deficiency less than 20 ng/mL, insufficiency from 20 to 29 ng/mL and sufficient when equal or higher than 30 ng/ml)[10].

Statistical analysis

The collected data was compiled and analysed. The mean ±SD was calculated for quantitative data, percentage and proportion was calculated for qualitative data. The Shapiro- wilk test was used to check the normality of data. The Student t- test was used to compare the mean difference between vitamins d levels (for normally distributed data) while the Mann-Whitney u- test was used for the non-parametric data. The chi square test was used to find out any association between serum vitamin D levels and chronic constipation. The SPSS software (? Version) was used for data compilation and the p value <0.05 was considered as statistically significant.

Results

Out of the total 70 patients (35 cases and 35 controls) were finally included in study. The cases were labelled as group 1(patients of chronic functional constipation) while the controls were labelled as group 2 (patients without constipation).

Table1: Demographic profile of patients

DEMOGRAPHIC DATA	CASES	CONTROL	P VALUE
Age in years (Mean±S.D.)	40.057±11.417	37.34±16.52	0.423

The mean age of the patients in group 1 was 40.057±11.417 years while in Group 2, it was 36.771±15.232 years which are comparable as depicted in table 1.

Table 2: Wexner Constipation Score

Variable	Group1 Mean±S.D	Group2 Mean±S.D	P value
WCS 1	0.31±0.53	0.06±0.23	**<0.001**
WCS 2	1.17±1.38	0.03±0.16	**<0.001**
WCS 3	2.06±1.49	0.06±0.33	**<0.001**
WCS 4	0.71±0.62	0±0	**<0.001**
WCS 5	1.57±1.33	0.06±0.23	**<0.001**
WCS 6	1.03±0.82	0.09±0.28	**<0.001**
WCS 7	1.09±0.95	0±0	**<0.001**
WCS 8	0.71±0.45	0±0	**<0.001**
Total (Wexner constipation score)	8.66±4.23	0.29±0.71	**<0.001**

There is a significant difference in the severity of constipation (Wexner Constipation Score) between the groups with mean score of 8.65±4.23 in group 1, while it was 0.286±0.71 in group 2 as shown in table 2.

Table 3: Bristol stool scale comparison between cases and controls

Variable	Group1 Mean±S.D	Group2 Mean±S.D	P value
Bristol stool scale (mean)	2.71±1.44	3.80±0.83	**<0.001**

The mean Bristol stool scale was 2.71±1.44 and 3.80 ±0.83 among group1 and group 2 respectively which is highly significant as depicted in table 4.

Table 4: The serum vitamin D levels

Vitamin D category	Group 1	Group 2	Total	P value
Mean serum vitamin D levels (ng/ml)	12.829±3.92	18.71±6.93		<0.001
Deficient (<20 ng/ml)	34 (97.1%)	18 (51.4%)	52 (74.3%)	χ^2 =
Non deficient (≥20 ng/ml)	1 (2.9%)	17 (48.6%)	18 (25.7%)	19.14 p<0.001
TOTAL	35	35	70	

In group1, the mean vitamin d level was 12.829±3.92 ng/ml compared to 18.71±6.93 ng/ml in group 2 which is statistically significant as illustrated in table 4. In group 1, 97.1 % patients were vitamin D deficient compared to group 2 where only 51.4% patients were having vitamin D deficiency with an odds ratio of 32.11 (95% CI: 3.94 to 26.122).

Discussion

Constipation is a common entity that has been defined most commonly in terms of a decreased frequency of stool. The prevalence of chronic functional constipation increases with age [9,11].

Vazquez et. al. in 2015 have reported that the cumulative incidence of chronic constipation (CC) is higher in the elderly (~20%) compared to a younger population.58. In our study, the mean age group of patients in group 1 (patients with constipation) was 40.05±11.47 years, which was higher compared to the mean age of 36.77±15.32 years of group 2, but statistically it is non-significant (p value > .05, Table 1). Involvement of younger patients by the constipation in our study might reflect that it might be due to some pathological condition like vitamin D deficiency rather than age-related decreased gut motility.

The association of vitamin D deficiency with chronic functional constipation has been reported in the literature. Vaes et al. in an intriguing hypothesis stated that STC and/or delayed small intestinal transit time could negatively modify the gut microbiota [12], or conversely, altered microbiome could primarily affect mucosal barrier and gut motility due to microbial-derived metabolites [13]. Autier et. al. suggested that vitamin D deficiency could predispose to gastrointestinal infections. Clark et. al. and Ge et. al. has reported that it could be responsible for the “leaky gut” alteration and for the loss of immune homeostasis [13,15]. Clark et. al., He et. al., and Shahini et. al. has reported that the presence of vitamin D receptor on gut epithelial cells, macrophages, and lymphocytes suggests a possible link between vitamin D deficiency, the dysfunction of its receptor, and gut microbiota composition, leading to the onset of autoimmune diseases [13,15,16]. Chia et. al. in a study in multiple sclerosis cases, whose pathogenesis has been linked to vitamin D deficiency, have reported a slow colonic motility in the proximal tract as well as autonomic rectal dysfunction. [17]. The intestinal motility disorder could be the “primum movens” of an underlying autoimmune process in a specific genetic background and unmasked by chronic vitamin D deficiency, which could exert metabolic/immunologic damage on epithelial and neuromuscular structures of the gut. The latter alterations could include gut hyper permeability and bacterial translocation, whose degree of injury and extension could be influenced by the severity of vitamin D deficiency.[18]. Tazzyman et. al. in 2015 found that the IBS population exhibits significant levels of vitamin D insufficiency and would benefit from screening and possible supplementation, and the impact of IBS on quality of life may be by vitamin D level. [19]. Marginean et. al. in their study found that vitamin D levels were independently

related to intestinal motility disorders. In addition, the symptoms of patients with functional chronic constipation were reported to worsen in parallel with decreased vitamin D levels. Tabatabaeizadeh et. al. studied the effect of vitamin D on gut microbiome and inflammatory bowel disease and concluded that there is some evidence that vitamin D can regulate gastrointestinal inflammation, with epidemiological studies showing that individuals with higher serum vitamin D have a lower incidence of IBD, particularly Crohn's disease. Vitamin D changes the transcription of cathelicidin and DEFB4 (defensin, beta 4) that can affect the gut microbiome. Several cell types of the immune system express vitamin D receptor, and hence the use of vitamin D in immune regulation has some potential. Furthermore, vitamin D deficiency leads to dysbiosis of the gut microbiome and is reported to cause severe colitis. [20]. Parul et. al. (2020) studied the potential role of vitamin D supplementation as a gut microbiota modifier in healthy individuals and found out that vitamin D supplementation significantly increased gut microbial diversity. Significant variations in the two dominant genera, Bacteroides and Prevotella, indicated a variation in enterotypes following supplementation.

The Bristol Stool Scale is a tool used to classify human stool into seven types, ranging from hard and lumpy (Type 1) to watery and liquid (Type 7). It helps assess digestive health and can indicate issues like constipation or diarrhea. Type 1 and Type 2 suggest constipation, while Type 6 and Type 7 indicate diarrhea. Type 4, which is smooth, soft, and sausage-like, is considered the ideal and healthiest stool type.

The mean Bristol stool scale was 2.71±1.44 in group 1, while it was 3.80±0.83 in group 2, with a p-value of <0.001, which is highly significant, as depicted in Table 4. In our study, it was found that the BSS score was significantly low in constipated patients, but vitamin D deficiency is not significantly associated with the BSS score.

Conclusion

In the present study CFC has not only reflected a significant association with its serum vitamin d levels but also the severity of constipation (WCS) has revealed a significant association with the serum vitamin d levels. Therefore, a larger, multicentric study on a heterogenous population is required for further supporting the findings for definite recommendations.

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