

Original article

Prevalence of Vitamin D Deficiency and Its Association with Disease Activity among Libyan Patients with Inflammatory Bowel Disease

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Vitamin D Deficiency, Disease, Libyan Patients, Inflammatory Bowel Disease.

ABSTRACT

Vitamin D deficiency is a recognized non-skeletal concern in patients with inflammatory bowel disease (IBD) due to its immunomodulatory roles. However, regional data on vitamin D status in North African IBD cohorts, particularly in Libya, remain scarce. This study aimed to evaluate the prevalence of low serum 25-hydroxyvitamin D (25(OH)D) levels in Libyan IBD patients and examined its association with disease activity state. A cross-sectional study was conducted involving 71 adult IBD patients and 20 age-, sex-, and BMI-matched healthy controls. Demographic, clinical, and laboratory data, including serum 25(OH)D, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR), were collected. Disease activity (active flare vs. clinical remission) was evaluated using a composite assessment of clinical symptoms, medical records, laboratory biomarkers, and endoscopic findings. Statistical comparisons were performed using Mann-Whitney and Fisher's exact tests. The IBD cohort had a mean age of 36.35 ± 15.78 years and a mean BMI of 25.51 ± 4.54 kg/m². Results revealed a high prevalence of vitamin D deficiency among the IBD cohort, where 86% of patients presented with suboptimal vitamin D levels (serum 25(OH)D < 30 ng/ml) and exhibited substantially lower levels (mean 20.32 ng/ml) compared to controls (mean 31.20 ng/ml) ($p < 0.0001$). A statistically significant association between active disease state and lower vitamin D levels compared to remission periods (median 16.90 ng/mL vs 21.50 ng/mL, $p < 0.05$) with patients presenting with active disease having nearly six-fold increased odds of vitamin D deficiency than those in remission. In conclusion, suboptimal vitamin D status is highly prevalent among IBD patients in Misurata, Libya, with disease activity acting as the primary driver of vitamin D depletion regardless of patient gender, underscoring the critical need for continuous assessment and the implementation of effective supplementation strategies to improve therapeutic outcomes across all IBD cohorts.

Introduction

Inflammatory Bowel Disease (IBD), encompassing two main conditions: Crohn's disease and ulcerative colitis, is a chronic, relapsing inflammatory disorder of the gastrointestinal tract (GIT), characterized by immune-mediated inflammation that may affect any part of the digestive tract from the mouth to the anus [1,2]. Micronutrient deficiencies occur in more than half of patients with IBD, which is often exacerbated by an attenuation of nutrient absorption within the intestinal lumen coupled with both inadequate intake and malabsorption [3]. The most commonly encountered deficiencies are deficiencies of vitamin D, iron, vitamin B12, vitamin K, folic acid, selenium, zinc, vitamin B6, and vitamin B1. Micronutrient deficiency has been frequently associated with prolonged and complicated course of disease [3].

Although vitamin D is crucially important for bone health, its deficiency has emerged as critical non-skeletal concern in chronic inflammatory conditions, particularly in IBD. This deficit is driven by multiple factors including malabsorption, dietary restriction and limited sun exposure [3,4]. In fact, the relationship between IBD and vitamin D is considered one of the most complex among micronutrient interactions in IBD because 1,25 dihydroxy vitamin D act as a potent immunomodulator through enhancing epithelial barrier, suppressing cytokine production and regulating innate and adaptive immunity [5-7]. Consequently, vitamin D deficiency may lead to several clinical consequences in IBD patients as low levels are linked to increased clinical and endoscopic activity, as well as a higher risk of relapse, poorer response to therapy and higher risk of extraintestinal complications [8,9].

While vitamin D deficiency has been historically defined and recently recommended by the Institute of Medicine (IOM) as a 25-hydroxyvitamin D (25(OH)D) of less than 20 ng/mL. Vitamin D insufficiency has been defined as a 25(OH)D of 21–29 ng/mL [10,11]. However, the definition of optimal serum 25(OH)D concentration still an ongoing debate. Endocrine Society, for example, consider optimal levels are (≥ 30 ng/mL). These recommendations were based on evidence suggesting that maintaining serum 25(OH)D concentrations > 30 ng/mL significantly lower disease and mortality risks in healthy subjects [11]. Nevertheless, in patients with inflammatory diseases; most experts aim for higher targets in vitamin D levels; as an example, a large cohort published in 2024 suggests 30–50 ng/mL as target range as such levels were linked to lower inflammatory state [12]. Moreover, from a disease prevention perspective, levels between 40–80 ng/mL were found to

reduce infections, autoimmunity and mortality rates [13, 14]. Despite evidence from a number of high-quality trials, there is no universally accepted clear inflammation-specific vitamin D targets. Nevertheless, there is broad agreement that serum 25(OH)D concentrations should be maintained within the range of approximately 30–50 ng/mL, particularly in populations at increased risk of deficiency and in those with chronic medical conditions, where higher vitamin D levels may confer additional health benefits.

Despite the growing recognition of vitamin D anti-inflammatory properties and the fact that vitamin D hypovitaminosis may contribute to disease exacerbation, low circulating levels of 25(OH)D remain highly prevalent across patients with IBD [15–18]. In a five-year longitudinal study in the USA, Kabbani et al. found that patients who were vitamin D deficient at the start were more likely to require surgery 29.2% compared to those with sufficient levels 19.4% [16]. This link between low vitamin D and poorer outcomes was also seen in a Canadian pediatric study, where López-Muñoz et al. showed a strong inverse relationship between vitamin D deficiency and inflammatory markers like fecal calprotectin and CRP [17]. This confirms the significant role of vitamin D in regulating the body's inflammatory response.

Despite these insights, regional data on vitamin D hypovitaminosis in North African IBD cohorts remain limited; furthermore, data directly linking serum 25(OH)D levels to inflammatory disease activity in Libyan patients are scarce. To address this gap, the study evaluated the prevalence of low vitamin D levels among patients with IBD in Misurata, Libya and assessed its association with disease activity state.

Methods

Study design and setting

This observational cross-sectional study was conducted at the Misurata Center for Gastrointestinal Endoscopy and Liver Diseases, Misurata, Libya. To obtain the data required to meet the study objectives, a structured questionnaire was administered, followed by blood sample collection. We collected all data and samples from participants, including patients and healthy controls, over a single period of four and a half months.

Study sample and data validity

The study included two groups: an IBD patient group comprising 71 Adult patients with a confirmed diagnosis of IBD and a healthy control group of 20 subjects (both groups aged ≥ 18 years).

Exclusion criteria included pregnancy, breastfeeding or menorrhagia; active or severe infections, chronic kidney failure, liver cirrhosis, any type of malignancy and the presence of other chronic inflammatory diseases, such as rheumatoid arthritis, lupus, or psoriasis. Patients with an ileostomy, colostomy, a past colectomy, a history of IBD-related surgery or any malabsorption syndromes unrelated to IBD were also excluded. Additionally, individuals following a special diet, taking iron supplements, having a recent blood transfusion, or using unverified high doses of vitamin D were excluded as well.

To ensure consistency and reduce analytical errors, all samples were processed and analyzed in the Misurata Center for Gastrointestinal Endoscopy and Liver Diseases laboratory using standardized equipment, reagents, and testing procedures. The healthy controls were carefully selected to match the demographic and anthropometric characteristics of the IBD patient group to minimize the influence of gender, age, and BMI on micronutrients and inflammatory marker results.

Data collection and clinical assessment

Data were collected through face-to-face interviews with the patients using a structured questionnaire, followed by laboratory investigations. To assess disease state and accurately categorize patients into active disease or clinical remission states, a multi-disciplinary approach combining patient-reported symptoms, clinical records, and objective clinical data was utilized. Patients were interviewed in person by the research team in collaboration with their attending physicians. During these evaluations, a structured questionnaire was administered to record patient symptoms over the preceding 7 days, specifically tracking abdominal pain severity, daily frequency of loose stools, and current medication regimens.

Simultaneously, the attending physicians reviewed each patient's comprehensive medical records to verify objective markers of inflammation. Group assignment into active disease or in remission was confirmed based on a synthesis of the questionnaire responses alongside recent laboratory biomarkers including CRP and endoscopic findings extracted from the patient's file. To evaluate vitamin D status for participants, blood samples were collected and analyzed for serum 25(OH)D and inflammatory markers including CRP and ESR.

Ethical considerations

Ethical approval was obtained from the administration of the Misurata Center for Gastrointestinal Endoscopy and Liver Diseases before the start of the study. All participants were informed about the study objectives and procedures and provided informed consent before blood sample collection. Participant confidentiality was maintained by assigning a unique identification code to each participant. No personal identifying information was recorded, and all data were analyzed anonymously.

Statistical analysis

Data were organized in Excel and analyzed using GraphPad Prism 8.0.2, employing appropriate statistics based on the type of data and data distribution.

Results

Demographic and anthropometric characteristics of both the IBD patients and the healthy control group, outlined in Table 1 illustrate that the examined groups had comparable characteristics (all p-values < 0.05), thereby eliminating any potential confounding effects that gender, age, or weight might exert on the evaluated laboratory parameters.

Table1. Demographic and anthropometric characteristics of IBD patients and healthy controls

Characteristic	Patients	Healthy controls	p-value
Men/Women	37/34	11/9	N/A
Age (year) Mean (SD) Median Q1-Q3	36.35±15.78 33.00 23.00-45.00	36.95 ±14.33 33.50 24.00-49.00	0.67
BMI (kg/m²) Mean (SD) Median Q1-Q3	25.51± 4.54 24.91 22.41-27.39	26.6± 4.30 25.31 24.11-28.57	0.11

Data presented in Table 2 reveal highly significant statistical differences in serum vitamin D and CRP levels between the two cohorts, as confirmed by their respective p-values ($p < 0.0001$). Specifically, the vitamin D third quartile of the IBD group was below the cutoff of optimal levels ($\geq 30 \mu\text{g/L}$), which was used in this research as a cutoff to indicate vitamin D sufficiency, while CRP levels were markedly elevated, indicating a strong association with the disease state. In the healthy control group, better vitamin D statistics are observed, indicated by median and mean values ($\geq 30 \mu\text{g/L}$).

Table 2. Comparative analysis of laboratory parameters in IBD and healthy control groups

Laboratory parameter	IBD patients	Healthy controls	p-value
Vitamin D (ng/ml) Mean ±SD Median Q1-Q3 90th percentile RSE	20.32 ± 8.49 20.60 13.90-25.90 32.78 4.96%	31.20 ± 10.26 29.69 25.26-32.93 40.19 7.33%	< 0.0001
CRP (mg/L) Mean ± SD Median Q1-Q3 90% percentile RSE	10.37 ± 20.77 2.90 1.40-9.20 29.48 23.32%	1.23 ± 0.80 1.00 0.8- 1.45 2.09 13.82%	< 0.0001
ESR (mm/hr) Mean ± SD Median Q1-Q3 90% RSE	23.56 ± 21.73 15.50 7.00-35.00 60.00 10.93%	12.85 ± 6.75 12.00 8.50-15.75 20.70 22.367%	0.11

**All p-values were calculated by Mann-Whitney test*

Descriptive statistics revealed comparable vitamin D deficiency across both genders, as indicated by low median values and lower quartile distribution in both male and female groups.

Table 3. Descriptive statistics of serum vitamin D concentrations in male and female patients

Statistics	Males	Females	p-value
Mean $\pm$ SD	20.41 $\pm$ 7.35	20.23 $\pm$ 9.70	0.93
Median	19.70	20.95	
Q1-Q3	14.95-24.90	11.10-28.80	
90th percentile	28.90	33.50	

*P-value was calculated by Mann-Whitney test.

The pie chart in Figure 1 illustrates that nearly half of the cohort presents with vitamin D deficiency (49%) followed by insufficiency (37%) while only 14% maintain sufficient vitamin D levels. Suboptimal vitamin D status (combines both deficiency and insufficiency) accounts for 86% of the overall patient sample.

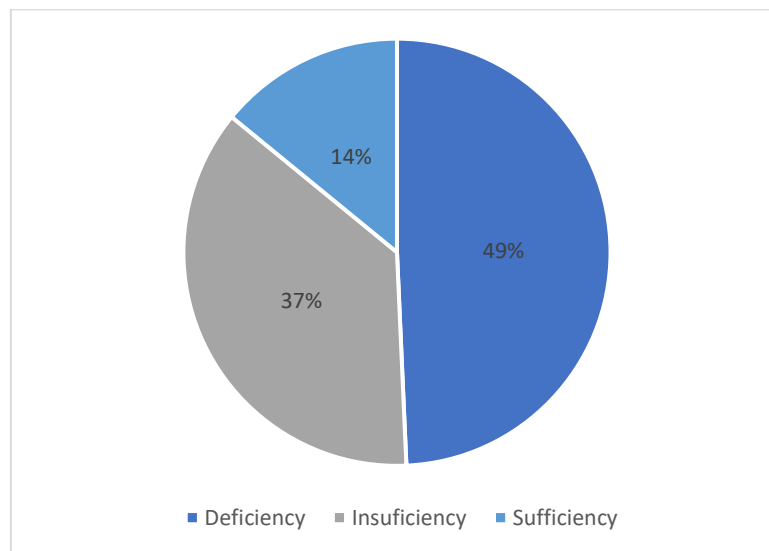


Figure 1. Prevalence of vitamin D deficiency (≤ 20 ng/mL), insufficiency (between 20–30 ng/mL) and sufficiency (≥ 30 ng/mL) among patients with IBD.

Serum vitamin D levels were significantly lower in patients with active IBD (mean 18.00 ± 9.02 ; median = 16.90 ng/mL, IQR 11.10-25.25 ng/mL) compared to those in clinical remission (mean = 22.46 ± 8.51 ; median = 21.50 ng/mL, IQR 16.95-28.55 ng/mL; p-value = 0.04). These differences in serum vitamin D levels across disease activity states are further illustrated in Figure 2.

Table 4. Comparison of serum vitamin D levels between patients with active flare and those in remission periods

Vitamin D (ng/ml)	Active disease	In remission	p-value
Number of cases	34	37	0.04
Mean $\pm$ SD	18.00 $\pm$ 9.02	22.46 $\pm$ 8.51	
Median	16.90	21.50	
Q1-Q3	11.10-25.25	16.95-28.55	
90% percentile	27.95	36.22	
RSE	7.59 %	6.23 %	

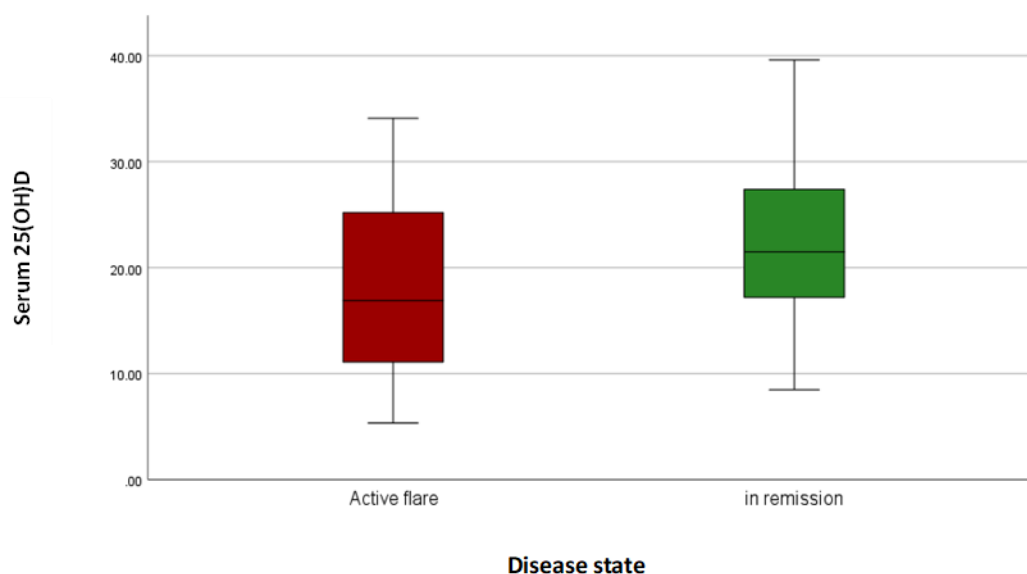


Figure 2. Comparison of serum 25 (OH)D concentrations between patients presenting with active flare and those in remission. Horizontal lines within the boxes represent median values, box boundaries represent the quartiles, and the whiskers extend to the minimum and the maximum observed concentrations.

Fisher's Exact Test (Table 4) revealed a statistically significant association between vitamin D status and inflammatory disease activity (p-value= 0.025, OR= 5.93, 95% confidence interval (CI) [1.35- 28.28]. Among patients with active disease state the vast majority were vitamin D deficient (n=32, 45.07% of the overall cohort), while only 2 patients maintained sufficient levels. Conversely, in the remission group, vitamin D sufficiency was observed in 10 patients (14.08%) compared to 27 patients (38.03%) with deficiency. Patients presenting with active disease had nearly a six-fold increase in the odds of vitamin D deficiency compared to those in remission.

Table 4. Association between vitamin D status and disease state using Fisher's exact test

Disease state	Vitamin D deficient Number/ (% of grand total)	Vitamin D sufficient Number/ (% of grand total)	Total
Active disease	32 (45.07%)	2 (2.82%)	34
In remission	27 (38.03%)	10 (14.08%)	37
Total	59 (83.09%)	12 (16.91%)	71
Fisher's Exact Test	P= 0.025, OR= 5.93, 95% CI [1.35- 28.28]		

Discussion

The study revealed a high prevalence of suboptimal vitamin D status, with 86% of the cohort exhibiting either deficiency or insufficiency. This finding is consistent with, yet slightly higher than, rates reported in similar studies, such as the 73.8% prevalence observed in a pediatric IBD cohort in Bahrain [15] and the 60–80% range frequently cited in broader IBD populations [16,19]. These results underscore that vitamin D deficiency remains a widespread clinical challenge in IBD management.

While general healthy populations often exhibit higher rates of vitamin D deficiency among females [20-22], gender does not appear to influence deficiency rates among individuals with IBD. In the studied patient cohort vitamin D depletion affects both genders at comparable rates. In fact, these results align with the results published by Kabbani et al. where male patients with IBD exhibited lower vit D levels compared to females (p<0.0001) [16].

In terms of association with disease activity, patients presenting with an active flare exhibited lower serum 25(OH)D concentrations compared to those in remission. These results align with existing literature establishing that systemic inflammation and mucosal damage during active IBD flares significantly impair nutrient absorption and alter vitamin D metabolism [17,18]. Active inflammation can downregulate intestinal absorption sites and increase the consumption of circulating 25(OH)D [3,4]. Conversely, maintaining higher serum 25(OH)D levels may exert an immunomodulatory effect, promoting mucosal healing and aiding in the maintenance of clinical remission through the suppression of pro-inflammatory cytokine pathways and reinforcement of gut epithelial barrier integrity.

Conclusion

Vitamin D deficiency is highly prevalent among the IBD population in Misurata, affecting approximately 86% of patients. Disease activity significantly exacerbates this nutritional deficit, with patients experiencing active flares exhibiting lower serum 25(OH)D levels compared to those in remission. Overall, disease activity drives the vitamin D depletion regardless of gender, making routine monitoring and targeted supplementation essential for all IBD patients.

Recommendations and limitations

Routine vitamin D screening should be integrated into standard care for all IBD patients. Given the strong link between active disease flares and profound vitamin D depletion, early nutritional assessment and supplementation are essential during active inflammatory phases to avoid severe deficiency risks. Furthermore, prospective, multi-center, longitudinal studies are needed to better understand how vitamin D levels change over the course of IBD.

This study is limited by its small, single-center cohort, which may constrain the generalizability of the findings. Future prospective multi-center studies involving larger patient populations are needed to track the long-term dynamics of vitamin D over the course of IBD.

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Conflict of interest. Nil

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