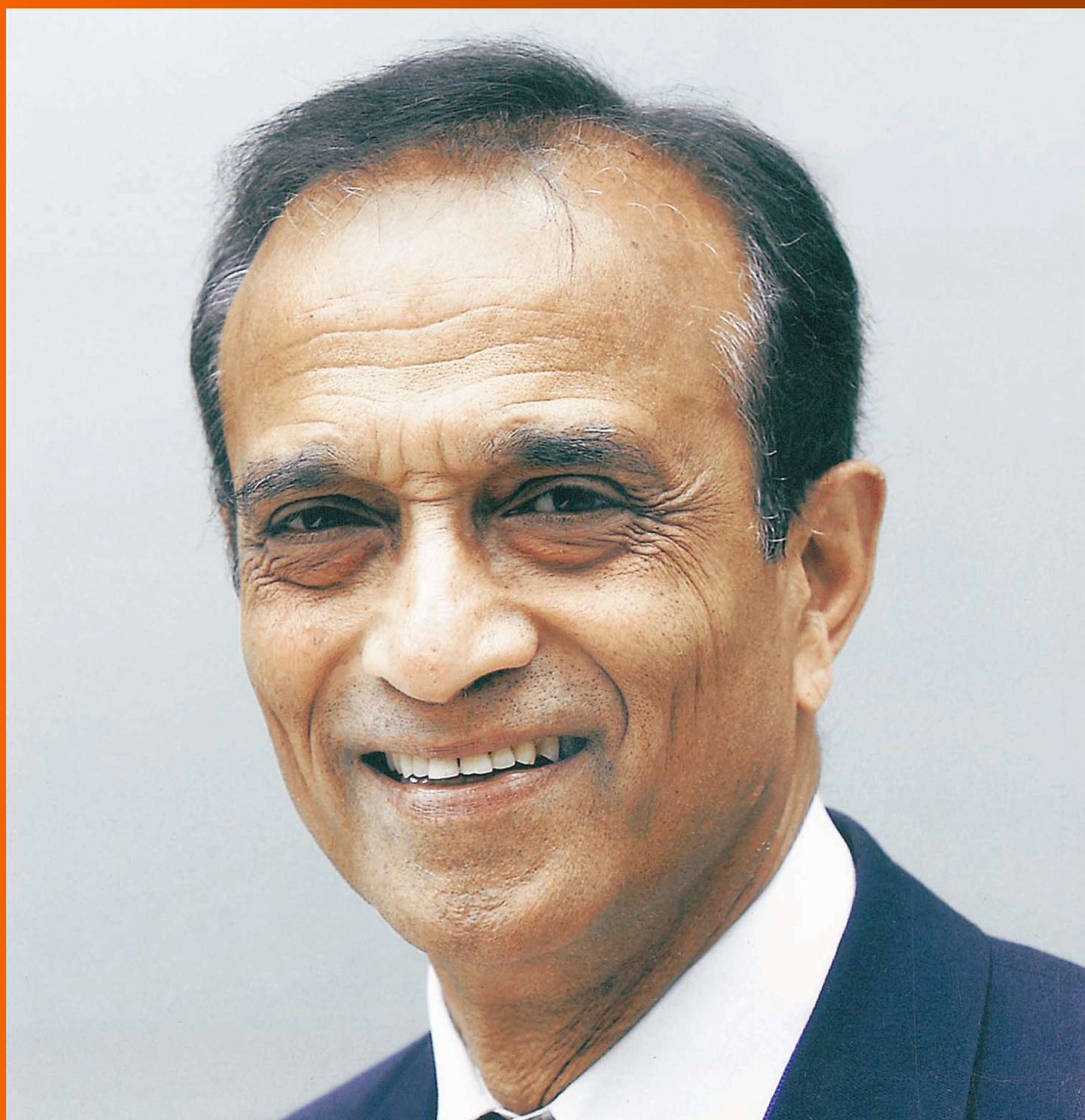


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Observational Study

Fatigue is not associated with vitamin D deficiency in inflammatory bowel disease patients

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Abstract

AIM

To investigate if vitamin D deficiency is associated with fatigue in patients with inflammatory bowel disease (IBD).

METHODS

IBD patients were recruited from nine hospitals in the southeastern and western regions of Norway to participate in a multicenter cross-sectional study lasting from March 2013 to April 2014. Data were collected by interviews, from medical records and laboratory tests. The Fatigue Questionnaire (FQ) was used to measure fatigue. Linear and logistic regression models were applied to explore the possible association between vitamin D deficiency and total fatigue scores and chronic fatigue, respectively. The analyses were adjusted for age, gender, disease activity, depressive symptoms and sleep disturbance.

RESULTS

In total, 405 patients were included in the analyses, of which 227 (56%) had Crohn's disease (CD) and 178 (44%) had ulcerative colitis (UC). Vitamin D deficiency (< 50 nmol/L) was present in half (203/405) of the patients. Chronic fatigue was reported by 116 (29%) of all included patients with substantial fatigue reported by 194 (48%). Vitamin D levels were neither associated with total fatigue nor with chronic fatigue. Higher total fatigue scores and chronic fatigue were both associated with increased disease activity scores in patients with UC and CD, but not with increased CRP or fecal calprotectin. In UC patients, female gender was associated with fatigue in the univariate analysis, but no such difference was found when adjusted for elevated disease activity scores. Sleep disturbance and more depressive symptoms were associated with total fatigue scores in both UC and CD patients, but with chronic fatigue only in CD patients.

CONCLUSION

In this study, no significant association between fatigue and vitamin D deficiency in IBD patients was revealed.

Key words: Inflammatory bowel disease; Crohn's disease; Ulcerative colitis; Fatigue; Chronic fatigue; Vitamin D deficiency

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Core tip: Fatigue is common in inflammatory bowel diseases (IBD) and is especially prevalent in active disease. We wanted to investigate if vitamin D deficiency was associated to fatigue in IBD as this is a common belief among both patients and physicians. To the best of our knowledge, no previous studies have investigated this possible association in IBD patients. We also wanted to take into account the multidimensional approach in understanding fatigue making it difficult to single out any one contributing factor. In this study, no significant association between fatigue and vitamin D deficiency in IBD patients was revealed.

Frigstad SO, Høivik ML, Jahnsen J, Cvancarova M, Grimstad T, Berset IP, Huppertz-Hauss G, Hovde Ø, Bernklev T, Moum B, Jelsness-Jørgensen LP. Fatigue is not associated with vitamin D deficiency in inflammatory bowel disease patients. *World J Gastroenterol* 2018; 24(29): 3293-3301 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v24/i29/3293.htm> DOI: <http://dx.doi.org/10.3748/wjg.v24.i29.3293>

INTRODUCTION

Inflammatory bowel diseases (IBD), including ulcerative colitis (UC) and Crohn's disease (CD), are characterized by chronic, recurrent inflammation of the gastrointestinal tract^[1-3]. IBD may present a variety of symptoms such as diarrhea with or without blood, abdominal pain, and fatigue. Patients with IBD often report the latter as one of their most troublesome symptoms^[4].

Fatigue is common in IBD, with a prevalence of 44%-86% in active disease and 22%-41% in remission^[5-7]. The patients usually report an overwhelming feeling of tiredness, reduced energy levels, reduced muscle strength, and cognitive impairment, which supports a multidimensional approach to understanding and measuring fatigue^[5,6,8,9]. Chronic fatigue has been defined as severe fatigue persisting for at least six months leading to substantial impairment of daily life^[10,11].

Fatigue is associated with reduced health-related quality of life (HRQoL) and work ability^[4,10,12-15]. In IBD, factors such as disease activity, disturbed sleep, anemia, pain and depression have all been associated with fatigue^[5,6,10,16-19]. Anemia and pain are both related to more active disease, and nocturnal symptoms in IBD may be associated with sleep disturbance, a

known factor predisposing to fatigue. In addition, patients with severe fatigue are more likely to suffer from mood disorders such as depression, and there is an association between fatigue and psychological comorbidity^[20].

Vitamin D deficiency has been reported to be associated with fatigue in cancer patients^[21]. Moreover, vitamin D supplementation has been shown to be significantly associated with the improvement of fatigue symptoms in other chronic inflammatory conditions^[22,23]. Several studies have shown that vitamin D deficiency is common in patients with IBD, that it is seen more often in patients with CD than in those with UC and that it is more frequent in these patients than in the general population^[24-29].

Furthermore, vitamin D deficiency has been associated with disease activity in IBD patients^[24,27,28,30-32]. Low vitamin D levels in IBD may result in increased fatigue that is partly due to more active disease. However, fatigue often persists after the patient has achieved clinical remission, without any objectively measured signs of intestinal inflammatory activity. This indicates that fatigue is not only a symptom related to inflammation^[5].

The high prevalence of vitamin D deficiency may also be of potential importance in fatigue, as muscle weakness has been linked to vitamin D deficiency^[33]. Skeletal muscle has vitamin D receptors and may require vitamin D for maximal function, and thus vitamin D deficiency may result in physical fatigue, one of the dimensions frequently measured in the assessment of fatigue^[33].

The aim of this study was to investigate the possible association between vitamin D deficiency and fatigue in patients with IBD.

MATERIALS AND METHODS

Study area and population

Patients were recruited from nine hospitals in the southeastern and western part of Norway as part of an observational, multicenter cross-sectional study. Inclusion criteria were: Age ≥ 18 years, a verified diagnosis of IBD based on endoscopic, biochemical and histological findings according to the Lennard-Jones criteria^[34], ability to read and understand Norwegian and to give written informed consent. The inclusion period lasted from March 2013 to April 2014. At each of the included centers, a senior gastroenterologist was responsible for the study.

Clinical, socio-demographic and laboratory variables

Data were collected by interviews, from medical records and laboratory tests. All data were collected at inclusion.

Serum 25-OH-D from all patients was analyzed by one central accredited laboratory with liquid chromatography tandem mass spectrometry (LC-MS/MS), and the method used for vitamin D analysis has

been compared to the LC-MS/MS method used in the vitamin D standardizing Program VDSP and showed good compliance^[35]. Vitamin D deficiency was defined as 25-OH-D concentration < 50 nmol/L, and vitamin D insufficiency was defined as a 25-OH-D concentration of 50-75 nmol/L^[33].

All other biochemical analyses were performed at the local laboratories at the participating centers. C-reactive protein (CRP) levels of 5 mg/L or higher were chosen to indicate active inflammation^[36,37].

The stool samples for the measurement of fecal calprotectin were sent by mail and analyzed with Calpro Easy Extract (Calpro AS, Norway). Fecal calprotectin < 100 mg/kg was set as the cut-off for disease in remission, while higher levels were defined as active inflammation^[38].

Clinical disease activity was measured with the Simple Clinical Colitis Activity Index (SCCAI) for UC and the Harvey Bradshaw Index (HBI) for CD^[39,40]. For UC, an SCCAI score ≥ 5 was defined as active disease^[36,37,41,42], and in CD, an HBI score ≥ 5 was defined as active disease^[39,43].

Assessment of fatigue, depressive symptoms and quality of sleep

Fatigue was measured with the Fatigue Questionnaire (FQ)^[8,44]. The FQ has been found to be suitable both for clinical and epidemiological purposes and has been translated into Norwegian and validated^[8]. Two dimensions of fatigue are measured, physical fatigue (items 1-7) and mental fatigue (items 8-11). The sum of all items produces the total fatigue score. Each item score can be dichotomized (0 to 1 = 0, 2 to 3 = 1), giving a total score between 0 and 11. Chronic fatigue (CF) was defined as dichotomized FQ scores ≥ 4 with a duration > 6 mo, in accordance with previous studies^[8,10,44,45].

The presence of depressive symptoms was measured with the Hospital Anxiety and Depression Scale (HADS), which has been translated into Norwegian and validated^[46]. HADS is a 14-item questionnaire designed to screen for depression (7 items) and anxiety (7 items). Each item is scored from 0 to 3, and consequently the total score ranges from 0 to 21 for either depression or anxiety^[46]. A higher score indicates an increased level of symptoms. In this study, depressive mood was defined as a HADS-D subscore ≥ 8 , which is considered to be the most relevant score for the screening of depressive symptoms in chronic disease^[47].

Sleep disturbance was measured with the first dimension of the Basic Nordic Sleep Questionnaire (BNSQ) on a 5-point Likert scale and dichotomized into normal sleep (scores 4 to 5) or sleep disturbance (scores 1 to 3)^[48].

Statistical analysis

Normally distributed continuous variables were described with means and standard deviation (SD), and variables with skewed distributions were described with medians

and ranges. Crude differences between pairs of continuous variables were analyzed using Student's *t*-test when normally distributed, otherwise a non-parametric test (Kruskal Wallis test) was used. The crude association between pairs of categorical variables was analyzed with Chi-square test. To explore possible associations between the selected variables and fatigue, multiple regression models were fitted using fatigue as the dependent variable. For chronic fatigue, a logistic regression was fitted, and for total fatigue scores, a linear regression was used. Age and gender plus the variables that were statistically significant ($P < 0.1$) in univariate analyses were entered into the final multiple models. *P*-values < 0.05 were considered statistically significant in the multivariate analyses. As our analyses were considered as exploratory, no corrections for multiple testing were applied. All tests were two-sided. IBM SPSS Statistics for Windows version 24.0 (IBM Corp. Armonk, NY, United States, Released 2016) was used for all statistical analyses.

Ethical considerations

The Regional Committee for Medical and Health Research Ethics approved the study (2012/845/REK). All the study participants gave written, informed consent before inclusion in the study, and the study was performed in accordance with the Declaration of Helsinki.

RESULTS

In total, 452 patients were eligible, and their participation was requested; of these, 414 (92%) gave written consent. Nine of these 414 patients were excluded due to missing data, leaving 405 patients available for the analyses, of which 227 (56%) had CD and 178 (44%) had UC. There were no statistically significant differences between the UC and CD patients regarding age or gender, but the CD patients had significantly longer disease duration than the UC patients (median 11 vs 6 years, $P < 0.01$). Approximately half (203/405) of the patients had vitamin D deficiency^[28]. For further details see Table 1.

The median score for total fatigue was similar in patients with UC and those with CD, see Table 1. There were no significant associations between vitamin D deficiency and mental, physical, and total fatigue scores. In addition, no significant differences in mean vitamin D levels between patients with and patients without chronic fatigue were found. Chronic fatigue was reported by 116 (29%) of all included patients with substantial fatigue (dichotomized FQ scores ≥ 4) reported by 194 (48%).

When separating patients into four groups according to (1) only chronic fatigue, (2) only depressive symptoms, (3) both chronic fatigue and depressive symptoms or (4) no chronic fatigue or depressive symptoms, there was no statistically significant association between the groups and their vitamin D levels, including when the data were adjusted for gender. No differences in total fatigue scores

or in the number of chronic fatigue cases were reported between patients receiving different medical treatments (data not shown).

In the multivariate linear regression analysis, when adjusted for age, gender, depressive symptoms, sleep disturbance and vitamin D level, higher total fatigue scores were associated with elevated disease activity scores in comparison to the total fatigue scores of patients in clinical remission in both UC and CD, but not with increased CRP or fecal calprotectin. In UC patients, female gender was associated with higher total fatigue scores in the univariate analysis, but this association disappeared in the multiple regression. Sleep disturbance and more depressive symptoms were associated with higher total fatigue in patients with UC and those with CD. The analyses are summarized in Tables 2 and 3.

In the multivariate logistic regression analysis, when adjusted for age, gender, depressive symptoms, sleep disturbance and vitamin D level, chronic fatigue was associated with elevated disease activity scores but not with increased CRP or fecal calprotectin, in contrast to patients in clinical remission regardless of diagnosis. In UC patients, female gender was associated with higher odds for chronic fatigue in the univariate analysis, but no such difference was found when adjusted for elevated disease activity scores. Self-reported sleep disturbance and depressive mood (HADS-D ≥ 8) were associated with higher odds for chronic fatigue in CD patients but not in UC patients in the multivariate analyses adjusted for disease activity and gender. The analyses are summarized in Tables 4 and 5.

DISCUSSION

In this cross-sectional study of IBD patients, neither total fatigue scores nor chronic fatigue were associated with vitamin D deficiency. Both higher total fatigue scores and chronic fatigue were associated with elevated disease activity scores, indicating clinically active disease in both UC and CD patients, but not with objective inflammatory markers. Moreover, higher total fatigue scores were associated with more depressive symptoms, as well as disturbed sleep in both disease groups.

Vitamin D deficiency was reported by half of the patients in this study, and as reported in a previous paper, this is more common than in the general population^[28]. Furthermore, vitamin D deficiency was associated with higher disease activity scores and relapse rates in CD, as well as increased inflammatory markers in UC^[28]. The prevalence of fatigue and mean total fatigue scores were similar to those reported in previous studies in IBD patients^[5,7,10].

To the best of our knowledge, no previous studies have investigated if vitamin D deficiency is associated with fatigue in IBD patients. However, vitamin D deficiency has been linked to fatigue in cancer patients^[21].

Table 1 Socio-demographic and clinical data *n* (%)

	UC (<i>n</i> = 178)	CD (<i>n</i> = 227)	<i>P</i> value
Age median, years (range)	40 (18-76)	40 (18-77)	0.92
Gender			
Female	87 (48)	112 (49)	0.77
Disease duration median, years (range)	6 (0-46)	11 (0-50)	< 0.01
Total fatigue, median (range)	16 (3-30)	15 (0-33)	0.55
Chronic fatigue	52 (29)	65 (28)	0.93
25-OH-D concentration nmol/L			
< 50	78 (44)	125 (55)	0.07
50-75	76 (43)	68 (30)	< 0.01
> 75	24 (13)	34 (15)	0.61
HADS-D ≥ 8	25 (14)	32 (14)	0.99
Sleep disturbance	44 (25)	36 (16)	0.03
Disease activity			
SCCAI ≥ 5	53 (29)		
HBI ≥ 5		103 (46)	
Fecal calprotectin ≥ 100 mg/kg (missing <i>n</i> = 82)	61 (34)	86 (38)	
CRP ≥ 5 mg/L (missing <i>n</i> = 10)	50 (28)	76 (33)	
UC extent, Montreal classification			
E1 - Proctitis	19 (11)		
E2 - Left-sided colitis	58 (32)		
E3 - Extensive colitis	101 (56)		
CD localization, Montreal classification			
L1 - Terminal ileum		74 (32)	
L2 - Colon		48 (21)	
L3 - Ileocolon		75 (33)	
L4 - Upper GI		31 (14)	
Current use of medication			
Biologics	52 (29)	113 (50)	< 0.01
5-ASA	137 (77)	23 (10)	< 0.01
Prednisolone	26 (14)	19 (8)	0.05
AZA / MTX	46 (26)	87 (38)	0.02

UC: Ulcerative colitis; CD: Crohn's disease; SCCAI: Simple Clinical Colitis Activity Index; HBI: Harvey Bradshaw index; ASA: Aminosalicic acid; AZA: Azathioprine; MTX: Methotrexate; CRP: C-reactive protein; HADS-D: Hospital Anxiety and depression score - depression subscore.

Moreover, supplementation of vitamin D decreased fatigue scores in a Swedish study in patients with neurological disease^[23]. In a study from the US of patients with different chronic conditions, not including IBD, vitamin D supplementation was also significantly associated with the improvement of fatigue symptoms^[22]. These findings may suggest a possible role of vitamin D deficiency in the development of fatigue. As previously discussed, one explanation behind such an effect may be that insufficient vitamin D levels predispose patients to muscular weakness and physical fatigue. In the current study, however, no association between physical fatigue and vitamin D deficiency was found.

In addition, vitamin D has immunoregulatory properties, which may attenuate intestinal inflammation^[30,33,49]. As fatigue is more often reported in patients with active disease, one could speculate that vitamin D deficiency may contribute to disease activity, which in turn increases fatigue^[5,10,16]. In the current study, however, vitamin D deficiency was not independently associated with fatigue. However, there was an association between fatigue and elevated disease activity scores in patients with UC and those with CD, but not with objective inflammatory markers such as CRP and fecal calprotectin. This suggests that factors other than inflammation may play an important role and that the total burden from

clinical disease activity may contribute relatively more to the experience of fatigue by the patient than just the intestinal inflammation.

Previous studies have also found pain and disturbed sleep to be of importance for the perception of fatigue in IBD^[17,50]. This is in accordance with our results, where symptoms of disturbed sleep were consistently associated with both total fatigue scores and chronic fatigue for both UC and CD patients. Sleep disturbance has been shown to be highly prevalent in inflammatory conditions including IBD and has also been associated with higher fatigue scores^[17,50]. Furthermore, there is evidence that sleep deprivation may increase inflammatory activity, but this has not been studied in IBD patients^[50].

The finding that several symptoms not directly related to intestinal inflammation may influence fatigue is supported by a Swedish study on fatigue in gastrointestinal disorders that reported more severe fatigue in patients with functional gastrointestinal disorders than in those with organic gastrointestinal disorders^[18]. Another Swedish study in irritable bowel syndrome has shown that patients with more severe symptoms report higher fatigue severity, supporting the importance of symptom burden in fatigue^[51].

In contrast to previous studies, however, we found that clinical disease activity, depressive symptoms and

Table 2 Univariate and multivariate analysis of total fatigue and selected variables in ulcerative colitis (*n* = 178)

	Univariate B	95%CI	P value	Multivariate B	95%CI	P value
Age	-0.07	-0.13, -0.01	0.03	-0.05	-0.10, 0.00	0.04
Sex (ref. male)	2.30	0.80, 3.80	< 0.01	1.29	0.01, 2.57	0.05
25-OH-D < 50 nmol/L	Ref.					
25-OH-D 50-75	-0.27	-1.92, 1.39	0.75			
25-OH-D > 75	-0.93	-3.33, 1.47	0.45			
SCCAI ≥ 5	5.66	4.20, 7.12	< 0.01	4.25	2.75, 5.75	< 0.01
CRP ≥ 5 mg/L	0.35	-1.37, 2.07	0.69			
Calprotectin ≥ 100 mg/kg	0.61	-1.18, 2.40	0.50			
Depressive symptoms ¹	4.78	2.68, 6.88	< 0.01	2.37	0.44, 4.30	0.02
Sleep disturbance	4.17	2.50, 5.84	< 0.01	2.07	0.47, 3.67	0.01

¹HADS: Hospital Anxiety and depression score - depression subscore ≥ 8. UC: Ulcerative colitis; SCCAI: Simple Clinical Colitis Activity Index; CRP: C-reactive protein; B: Regression coefficient.

Table 3 Univariate and multivariate analysis of total fatigue and selected variables in Crohn's disease (*n* = 227)

	Univariate B	95%CI	P value	Multivariate B	95%CI	P value
Age	-0.01	-0.07, 0.05	0.75	0.00	-0.06, 0.05	0.84
Sex (ref. male)	1.30	-0.16, 2.75	0.08	0.63	-0.67, 1.93	0.34
25-OH-D < 50 nmol/L	Ref.					
25-OH-D 50-75	-1.04	-2.79, 0.63	0.22			
25-OH-D > 75	-0.66	-2.79, 1.48	0.55			
HBI ≥ 5	4.17	2.81, 5.54	< 0.01	3.26	1.92, 4.59	< 0.01
CRP ≥ 5 mg/L	0.68	-0.89, 2.25	0.40			
Calprotectin ≥ 100 mg/kg	0.00	1.61, 1.61	1.00			
Depressive symptoms ¹	5.99	4.02, 7.94	< 0.01	4.72	2.82, 6.63	< 0.01
Sleep disturbance	4.04	2.10, 5.99	< 0.01	2.21	0.40, 4.03	0.02

¹HADS-D: Hospital Anxiety and depression score - depression subscore ≥ 8. CD: Crohn's disease; SCCAI: Simple Clinical Colitis Activity Index; CRP: C-reactive protein; B: Regression coefficient.

sleep disturbance are independently associated with fatigue. Depressive symptoms have consistently been associated with fatigue, mainly due to an overlap of symptoms between these conditions. We believe that these are separate conditions, even if fatigue has been shown to predict the onset of depression^[52]. Similar to our study, fatigue is often seen in patients with no history or current signs of psychological comorbidity^[53]. In a Canadian study, perceived psychological stress was associated with the presence of fatigue, but depressive symptoms were not measured^[17].

Previous studies in IBD patients have shown that fatigue is more commonly reported in female patients^[6,7]. A similar observation has been made in a Norwegian study on fatigue in the general population^[8]. In other studies, however, gender has not been shown to have a significant impact on fatigue^[10,19]. The latter is in accordance with the current study, where female gender was not associated with fatigue when adjusted for disease activity.

Even with a cross-sectional design of our study, the number of patients included is relatively high, and the patients were recruited from several hospitals. The patients included can therefore be assumed to be representative of IBD patients treated in specialist care settings. The sample size and completeness of data, with few missing data from questionnaires, are important

strengths in this study. The choice of questionnaire used to measure fatigue may be of relevance when comparing results from different studies as this may influence both the number of cases and severity reported. We used the Fatigue Questionnaire because it has been validated in the general Norwegian population^[8].

The duration of disease was longer in CD patients, and this may influence patient-reported outcomes such as fatigue, depressive symptoms and sleep disturbance. It is not known how disease duration influences these outcomes in chronic disease, but it may result in under-reporting, as patients may get used to fatigue symptoms over time. With self-reporting of symptoms, there is also a risk of recall bias.

Approximately 40% of the patients in the current study were treated with biologics. This may represent a selection bias of patients with more severe disease, with an expected higher prevalence of fatigue. On the other hand, effective medical treatment reducing the symptom burden may have improved fatigue scores in several patients. Only a few patients were treated on corticosteroids, not allowing for analyses on the effect use of steroids has on fatigue.

In conclusion, fatigue is common in IBD and is associated with clinical disease activity, depression and sleep disturbance. Our data did not reveal any association between vitamin D deficiency and fatigue, supporting

Table 4 Univariate and multivariate analysis of chronic fatigue in ulcerative colitis (*n* = 178)

	Univariate OR (95%CI)		P value	Multivariate OR (95%CI)		P value
Age, years	0.59	0.07, 1.02	0.59			
Gender (ref. male)	2.12	1.10, 4.11	0.025	1.80	0.90, 3.62	0.10
25-OH-D < 50 nmol/L (ref.)	1.00					
25-OH-D 50-75	0.93	0.45, 1.84	0.80			
25-OH-D > 75	1.20	0.45, 3.18	0.72			
SCCAI ≥ 5	4.81	2.39, 9.67	< 0.01	4.47	2.20, 9.07	< 0.01
CRP ≥ 5 mg/L	1.20	0.57, 2.52	0.63			
Calprotectin ≥ 100 mg/kg	1.57	0.73, 3.39	0.25			
Depressive symptoms ¹	3.92	1.64, 9.36	< 0.01	2.55	0.98, 6.64	0.06
Sleep disturbance	2.71	1.33, 5.53	< 0.01	1.40	0.61, 3.19	0.43

¹HADS-D: Hospital Anxiety and depression score - depression subscore ≥ 8. UC: Ulcerative colitis; SCCAI: Simple Clinical Colitis Activity Index; CRP: C-reactive protein.

Table 5 Univariate and multivariate analysis of chronic fatigue in Crohn's disease (*n* = 227)

	Univariate OR (95%CI)		P value	Multivariate OR (95%CI)		P value
Age, years	1.02	1.00, 1.04	0.10			
Gender (ref. male)	1.27	0.71, 2.26	0.41	1.11	0.61, 2.01	0.74
25-OH-D < 50 nmol/L (ref.)	1.00					
25-OH-D 50-75	0.65	0.33, 1.29	0.22			
25-OH-D > 75	1.25	0.56, 2.78				
HBI ≥ 5	2.71	1.50, 4.91	< 0.01	2.67	1.47, 4.87	< 0.01
CRP ≥ 5 mg/L	1.18	0.64, 2.19	0.59			
Calprotectin ≥ 100 mg/kg	0.56	0.29, 1.10	0.56			
Depressive symptoms ¹	4.77	2.19, 10.39	< 0.01	3.65	1.61, 8.27	< 0.01
Sleep disturbance	4.18	2.00, 8.74	< 0.01	3.02	1.38, 6.61	< 0.01

¹HADS-D: Hospital Anxiety and depression score - depression subscore ≥ 8. CD: Crohn's disease; HBI: Harvey Bradshaw index; CRP: C-reactive protein.

a multidimensional approach in the understanding of fatigue. The possible associations we report need to be explored in further clinical studies before any certain conclusions can be drawn.

ARTICLE HIGHLIGHTS

Research background

Fatigue is common in inflammatory bowel diseases (IBD) and is especially prevalent in active disease. Also sleep disturbance, anemia, pain and depression all seem to influence fatigue. However, a relationship between vitamin D and fatigue has not been established.

Research motivation

We wanted to investigate if vitamin D deficiency was associated to fatigue in IBD as this is a common belief among both patients and physicians. To the best of our knowledge, no previous studies have investigated this possible association in IBD patients.

Research objectives

A relationship between vitamin D and fatigue has not been established. We wanted to explore this association and discover possible implications for our patients and further research.

Research methods

The research question was explored in a fairly large cohort of IBD patients from specialist care. The study was designed as an observational study, and all data were collected at inclusion. Linear and logistic regression models were applied to explore the possible association between vitamin D deficiency and total fatigue scores and chronic fatigue, respectively. All vitamin D analyses were done at the same laboratory.

Research results

In this study fatigue was commonly reported. Vitamin D levels were, however, neither associated with total fatigue nor with chronic fatigue. Higher total fatigue scores and chronic fatigue were both associated with increased disease activity scores, but not with objective markers of inflammation. Sleep disturbance and depressive symptoms were associated with total fatigue scores in both ulcerative colitis and Crohn's disease (CD) patients, but with chronic fatigue only in CD patients.

Research conclusions

In this study, fatigue was associated with clinical disease activity, depression and sleep disturbance. Our data did not reveal any association between vitamin D deficiency and fatigue, supporting a multidimensional approach in the understanding of fatigue.

Research perspectives

The possible associations we report need to be explored in further clinical studies. A randomized controlled trial with an interventional group receiving vitamin D supplementation may shed light on the possible benefits of vitamin D in patient reported outcomes in IBD.

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