



Original research

Fatigue in inflammatory bowel diseases: Relationship with age and disease activity



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ABSTRACT

A higher rate of patients suffering from inflammatory bowel diseases (IBD) are reported to experience the symptom of fatigue compared with general population. Fatigue can impair quality of life of IBD patients by limiting their daily functioning.

However, this problem is poorly understood and addressed. Our aim was to investigate the impact of fatigue in IBD patients compared with controls, and to seek for relation between age and disease activity.

IBD patients aged between 16 and 75 years observed at our Unit from June 2011 through June 2012 were evaluated for fatigue. Patients were asked to fill the fatigue impact scale (FIS) questionnaire. A cohort of age- and sex-matched patients observed for other-than-IBD diseases were prospectively enrolled to act as controls. Patients diagnosed with malignancies were excluded from evaluation.

Each group included 16 patients, of whom half aged over 65 years.

Fatigue was more severe in IBD patients than in controls ($p = 0.02$), irrespective of age and disease activity. IBD patients with moderate to severe disease activity showed worse fatigue compared with controls at any age ($p < 0.0001$). Young IBD patients with low disease activity showed a trend toward worse FIS score when compared with old IBD counterparts ($p = 0.06$).

IBD significantly impacted on fatigue in our series. Considering IBD patients in remission, younger patients may experience worse fatigue. Further studies are needed to explore the effects of fatigue on quality of life and the potential of appropriate intervention strategies.

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1. Introduction

Inflammatory bowel diseases (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), are chronic conditions

characterized by periods of remission and relapse, affecting people at any age [1–3]. The aetiopathogenesis of IBD relies on complex immune mechanisms, and is mediated by a genetic/epigenetic predisposition and environmental factors [4–7]. Symptoms of IBD include diarrhoea, abdominal pain, fatigue, appetite and weight loss [8]. Moreover, IBD patients may often require both treatment with immunodepressants [1,2,9–12], which may be associated with significant side-effects [13–15], and invasive/repeated surgical procedures for primary disease [1,2,16–19] as well as for potential complications of the treatments [3,20–25]. Furthermore, IBD patients and their relatives are at increased risk of immune-driven cancerogenesis [26–28]. These observations justify the consistent impact of IBD on health related quality of life [20,29].

Even if fatigue is known to be a common concern in chronic diseases of the digestive system [30], there is lack of knowledge as

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List of abbreviations

CD	Crohn's disease
CDAI	Crohn's disease activity index
IBD	inflammatory bowel diseases
SD	standard deviation
UC	ulcerative colitis
UCDAI	Ulcerative Colitis Disease Activity Index

well as of effective therapeutic interventions to treat fatigue in IBD. The condition is still unjustifiably overlooked in IBD patients, as clinicians tend to concentrate on controlling problems related to inflammation [31]. Our aim was to assess patient-reported fatigue in IBD patients and in controls, seeking for potential influences of age and disease activity.

2. Material and methods

All consecutive patients diagnosed with CD or UC aged between 16 and 75 years observed at our Unit from June 2011 through June 2012 were evaluated for inclusion.

Diagnosis of IBD was made following the accepted criteria [32,33]. Patients willing to participate were included. IBD patients with prior or current malignancies were excluded from the study. Patients observed for perianal CD were excluded.

A control group of patients diagnosed with other-than-IBD conditions was prospectively enrolled. Patients underwent surgery for benign diseases, hence excluding cancer patients [34–38], and were age- and sex-matched with IBD patients.

IBD patients and controls who were previously operated on for any disease were not included.

Each group comprised half patients aged over 65 years to allow sub-analyses.

2.1. Disease assessment

All patients underwent complete clinical examination. All IBD patients underwent endoscopy with biopsies to confirm the diagnosis [32,33]. Imaging modalities were selectively advocated [17,32,33,35,37–40]. Disease activity assessment in CD and UC patients was performed by means of Crohn's disease activity index (CDAI) [41] and Ulcerative Colitis Disease Activity Index (UCDAI) [42], respectively.

2.2. Fatigue assessment

Fatigue was assessed by means of the fatigue impact scale (FIS) questionnaire [43]. This is a self-reported instrument consisting of 40 questions, constructed to assess the impact of perceived fatigue on the following dimensions: physical functioning (10 items), cognitive functioning (10 items), and psychosocial functioning (20 items). Each question asks subjects to rate distress on a 5-point scale, ranging from 0 ("no problem") to 4 ("extreme problem"). The maximum total FIS score is 160, corresponding to highest fatigue perception.

2.3. Statistical analysis

Results of each group were compared, and sub-analyses were performed according to age (< and >65 years). FIS scores of young IBD patients were also compared with old IBD patients. Data are

expressed as mean $\pm$ standard deviations (SD). The Mann–Whitney test was performed for calculations of differences between groups. Values of $p < 0.05$ were considered statistically significant.

3. Results

Sixteen patients per group (10 female) were enrolled, of whom 8 (50%) were >65-year-old per group. Patients with IBD had more severe overall fatigue compared with non-IBD controls (88 ± 70 vs 40 ± 25 , $p = 0.002$). Physical (IBD vs controls: all age, 25 ± 15 vs 12 ± 8 , $p = 0.02$) and psychosocial (36 ± 22 vs 21 ± 13 , $p = 0.04$) FIS scores were higher in IBD compared with controls while no differences were observed in cognitive FIS score (9 ± 7 vs 10 ± 8 , $p = 0.12$). Results were confirmed with subgroup analyses according to age (< and >65 year-of-age).

When only considering IBD patients with moderate to severe disease activity ($n = 5$, 31.3%), differences in overall FIS scores were even more apparent (IBD vs controls: all age, 100 ± 62 vs 40 ± 25 , $p < 0.0001$).

When only evaluating IBD patients with mild to low active disease ($n = 11$, 68.7%), young IBD patients showed a trend toward higher FIS score compared with older IBD patients (73 ± 60 vs 65 ± 80 , $p = 0.06$), and significantly higher fatigue than non-IBD young counterparts (73 ± 60 vs 31 ± 42 , $p = 0.001$).

4. Discussion

With our exploratory, pilot study we were able to demonstrate that IBD-associated fatigue affects the life of IBD patients, similarly to other chronic diseases [30,43].

IBD activity significantly impacted on perceived fatigue. Interestingly, old IBD patients in remission seemed to cope better with fatigue when compared with younger IBD patients. Patients aged <65 years tended to experience more severe fatigue than non-IBD controls.

Many factors may affect patient-perceived fatigue, and chronic illnesses [30,43,44] and conditions are one of the most important. However, also cancer patients may experience fatigue [45]. For this reason, we decided to put out from analyses patients diagnosed with malignancies [34–38,46–50] as this could have biased our results.

Our findings offer interesting and practical perspectives. Many factors may be responsible for higher fatigue perception in IBD, including depression and anxiety [51]. This advocates the need of further studies also evaluating these facets of IBD patients, which are frequently overlooked.

Disease duration and activity have previously been associated with higher fatigue levels [51]. Unsurprisingly, IBD patients with more active disease were much more fatigued than both IBD patients with mild disease and non-IBD patients.

We found that age may play a role in fatigue perception, as differences were observed in overall FIS score between young and old IBD patients in remission. Even if without reaching statistical significance, these may suggest that patients with longer disease, successfully controlled, may develop more effective coping strategies than younger patients. As a matter of fact, young IBD individuals in remission had significantly higher fatigue than same-age controls. It can be hence predicted that timely, fatigue-specific treatments may be needed in such patients, potentially reducing the levels of perceived fatigue, on condition that the baseline disease is controlled.

Further researches are compulsory to seek for potential associations between other factors which may play a role in perceived levels of fatigue. These may ultimately result in the development of accepted guidelines to strengthen and validate frameworks such as

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