

Malnutrition Prevalence in Newly Diagnosed Patients with Inflammatory Bowel Disease – Data from the National Romanian Database

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ABSTRACT

Background & Aims: Prevalence of malnutrition in inflammatory bowel diseases (IBD) varies between 16% and 75%. Data on the nutritional status at initial diagnosis of ulcerative colitis (UC) or Crohn's Disease (CD) are scarce. It is believed that more than 50% of IBD patients suffer significant weight loss prior to diagnosis. The aims of our study were to assess malnutrition in patients recently diagnosed with IBD and to determine its predictive factors.

Methods: We retrospectively included 625 IBD patients registered in the Romanian "IBD Prospect" database between January 2006 and July 2017. All patients were diagnosed within 6 months prior to registration. We defined malnutrition as weight loss of more than 5% of the initial weight during the 3 months prior to registration.

Results: There were 361 new cases of UC, 241 CD and 23 cases of unclassified IBD. There was a slight male predominance (M/F=1.2). Prevalence of overall malnutrition was 36.3%. It was significantly more frequent in CD than in UC patients (41.1% vs. 32.4%, $p=0.031$). In multivariate analysis, malnutrition in UC patients was associated with male gender ($p=0.001$), more severe disease ($p<0.0001$) and more extensive disease ($p=0.027$), while in CD it was associated with younger age ($p=0.013$) and more severe disease ($p<0.0001$).

Conclusions: About 1 in 3 newly diagnosed IBD patients presents with malnutrition at the time of diagnosis.

Key words: weight loss – malnutrition – inflammatory bowel diseases – recent diagnosis.

Abbreviations: BMI: body mass index; CD: Crohn's disease; CDAI: Crohn's Disease Activity Index; ESPEN: European Society for Clinical Nutrition and Metabolism; IBD: inflammatory bowel disease; IL: interleukin; TNF- α : tumor necrosis factor α ; UC: ulcerative colitis.

INTRODUCTION

The prevalence of malnutrition in inflammatory bowel diseases (IBD) has been reported between 16% and 75%, both for patients with prior diagnosis as well as at their initial presentation [1-3].

The etiology of malnutrition in IBD patients is complex. There may be an inadequate nutritional intake due to anorexia, nausea, vomiting, abdominal pain and/or psychosocial factors. Maldigestion and malabsorption may be the consequence of enterocyte damage or small

bowel resections [4-6]. Also, there is a hyper-catabolic state characterized by high levels of pro-inflammatory cytokines such as interleukin (IL) 6, IL-10, tumor necrosis factor α (TNF- α) [4].

Malnutrition in IBD is an independent risk factor for unfavorable disease prognosis (longer duration of active disease, increased risk of infections, post-surgical complications including late healing and prolonged hospitalization) and altered quality of life [2, 3, 7].

Data on nutritional status at IBD initial diagnosis are scarce. Elsherif et al. [8] found that 57% of the patients with CD and 51% of the patients with UC experienced significant weight loss prior to diagnosis.

The primary aim of our study was to assess the nationwide prevalence of malnutrition in recently diagnosed patients with CD and UC. Secondary aims were to identify the predictive factors for malnutrition.

METHODS

Patients

We performed a retrospective study on IBD patients registered in the Romanian national IBD register - the "IBD Prospect" database [9]. This database has developed gradually since 2006 and currently 14 centers from 8 Romanian cities have access to register adult and pediatric patients.

Inflammatory bowel disease phenotype, pattern, extension, severity, complications and therapy with their corresponding clinical, laboratory, endoscopic, imaging and histological parameters were recorded.

Crohn's disease behavior was classified according to the Montreal classification: non-stricturing non-penetrating (inflammatory, B1), stricturing (B2) and penetrating (B3) [10]. Extension of CD is labeled as ileal (L1), colonic (L2), ileocolonic (L3) or involving the upper gastrointestinal tract (L4), with or without perianal complications (p) [10].

Ulcerative colitis was classified as disease limited to the rectum (proctitis, E1), extending to the splenic flexure (left sided colitis, E2) or more proximally (extended colitis, including pancolitis, E3) [11].

Severity of IBD was defined according to activity scores (CDAI - Crohn's Disease Activity Index) for CD [12] and a partial Mayo score for UC [13].

Patients were included as a "new case", if the diagnosis had been made in the 6 months prior to inclusion.

An informed consent was signed by each patient prior to inclusion in the IBD Prospect and each center ensured local Ethics Committee approval before including patients.

Method

In the present study, we included all adult IBD "new cases" recorded in the IBD Prospect between January 2006 and July 2017 (over 18 years old at IBD diagnosis, established in the 6 months prior to inclusion).

For each patient, we retrieved gender, age at diagnosis, smoking status (smoker, non-smoker, ex-smoker), biological parameters as well as disease phenotype, pattern, extension and severity, as they were entered by the physician who registered the patient in the database.

Information on weight loss was found on the patient's digital record. The physician filled in data concerning the "current weight", "weight loss (yes/ no)" and "number of kilograms lost during the last 3 months". No data on height, body mass index or body composition were recorded in the database. Also, no data on nutritional management or nutritional follow-up were available.

We defined malnutrition as loss of more than 5% of the patient's initial weight in the 3 months prior to IBD Prospect registration [14, 15].

Statistical analysis

Categorical variables were presented as absolute numbers and/or percentages. Differences among categorical variables were tested using the Fisher exact test for two groups and Kruskal-Wallis test for more than two groups.

Continuous variables were presented as mean, standard deviation (SD) and range. Differences between continuous

variables means were tested using the Mann-Whitney U test for two groups.

Variables that were found predictive for malnutrition at diagnosis in univariate analysis were included in multivariate analysis using logistic regression. In multivariate analysis, results were presented as odds ratios (OR) and 95% confidence intervals.

A p-value less than 0.05 was considered statistically significant.

For statistical analysis IBM SPSS Statistics 25 software was used.

RESULTS

There were 815 newly diagnosed adult IBD patients included in the IBD Prospect during the above-mentioned timeframe. Of these, 625 had complete data regarding weight loss and fulfilled our inclusion criteria.

Demographic data are shown in Table I. Incidence of IBD had a slight male predominance with a sex ratio of 1.2. Disease characteristics for UC and CD patients are presented in Table II. There were more UC than CD patients, with an UC/CD ratio of 1.49. Mean age at diagnosis was slightly higher in UC. None of the included patients were in clinical remission (Table II).

Overall malnutrition was found in 36.3% of patients and was significantly more frequent in CD than in UC patients (41.1% CD vs. 32.4% UC, $p=0.031$).

Table I. Demographic data and type of disease

	Patients
No.	625
Sex ratio Men / Women, no. (%)	341 (54.6%) / 284 (45.4%)
Age, mean \pm SD [range], years	42.1 \pm 14.9 [18 - 81]
Type of disease	
UC, no. (%)	361 (57.8%)
CD, no. (%)	241 (38.6%)
IBD type Unclassified, no. (%)	23 (3.7%)

Malnutrition in UC was significantly associated with a higher serum C reactive protein value (72 ± 123 mg/dl vs. 34.8 ± 92.8 mg/dl, $p=0.035$), a lower serum albumin value (3.6 ± 0.9 g/dl vs. 3.9 ± 0.8 g/dl, $p=0.032$) and a lower hemoglobin value (11.9 ± 1.9 g/dl vs. 12.6 ± 2.2 g/dl, $p=0.006$). In CD, malnutrition was associated with a lower serum albumin value (3.6 ± 0.0 g/dl vs. 3.9 ± 0.6 g/dl, $p=0.021$) and a lower hemoglobin value (11.7 ± 2.2 g/l vs. 13.4 ± 1.7 g/dl, $p=0.001$).

The predictive factors of malnutrition observed at CD and UC diagnosis are shown in Table III.

On multivariate analysis, a more severe disease was predictive for malnutrition at diagnosis for both CD and UC. In addition, in UC patients, malnutrition at diagnosis was significantly more frequent in men and for patients with more extensive disease, while in CD patients, malnutrition at diagnosis was significantly more frequent in the younger ones.

Prevalence of malnutrition was not significantly associated with a particular extension of CD ($p=0.203$) nor with a specific CD pattern ($p=0.68$).

Table II. Disease characteristics of patients with UC and CD

	UC	CD
No. of patients	361	241
Sex ratio, Men / Women	1.27	1.09
Age, mean \pm SD [range], years	44.1 \pm 14.6 [18- 81]	39.4 \pm 14.7 [19- 81]
Smoking status, (%)		
non-smoker/ smoker/ ex- smoker	55/ 13.7/ 31.3	47.2/ 33/ 20
CD behavior, (%)		
Inflammatory/ stricturing/ penetrating	n.a.	65.6/ 19.3/ 15
Extension (%)		
Proctitis/ left-sided colitis/ extended colitis	18.7/ 49.6/ 31.6	n.a.
Ileal/ colonic/ ileo-colonic/ UGI	n.a	24.2/35/40.7/ 1.7
Severity (%) Mild/ moderate/ severe	32.7/ 51.1/ 16.2	36.4/ 49.2/ 14.4
Malnutrition at diagnosis, no. (%)	117 (32.4)	99 (41.1)

CD: Crohn's disease; UC: ulcerative colitis; UGI: upper gastrointestinal

DISCUSSION

This is the first Romanian study that addresses the nutritional status in recently diagnosed IBD patients.

In our study population, prevalence of overall malnutrition was 36.3%. Significantly more patients with CD were malnourished compared to those with UC (41.1% vs. 32.4% UC, $p=0.031$). Other studies provided evidence that malnutrition is more frequent in CD patients than in UC patients [7, 16, 17].

Previous data on malnutrition in Romania came from a multicentric national study published in 2013 on hospitalized patients [18]. Malnutrition was defined as BMI <20 kg/m² and/ or unintentional loss of >10% of initial weight during the 6 months prior to admission. In IBD patients, malnutrition was found in 30.6% of cases, irrespective of the duration of disease, without significant differences between CD and UC. The results are partially explained by the fact that hospitalized IBD patients, with severe disease, were included in the study.

Table III. Predictive factors of malnutrition at IBD diagnosis

		Univariate analysis		Multivariate analysis		
		Malnutrition, no. (%)	p value	OR	95% CI	p value
Ulcerative colitis	Gender					
	Male	81/202 (40)				
	Female	36/159 (22.6)	<0.0001	2.5	1.5 - 4.3	0.001
	Disease extension					
	Proctitis	5/67 (7.4)				
	Lest extended colitis	57/177 (32.2)				
	Extended colitis	55/117 (46.9)	<0.0001	1.6	1.05 - 2.4	0.027
	Disease severity					
	Mild	14/117 (11.9)				
	Moderate	67/186 (36.1)				
	Severe	36/58 (62)	<0.0001	3	1.9 - 4.8	<0.0001
	Smoking status					
Crohn's disease	Ex-smoker	55/123 (44.8)				
	Non- smoker	58/191 (30.3)				
	Smoker	4/47 (8.5)	<0.0001			
	Disease severity					
	Mild	20/91 (22)				
	Moderate	59/116 (50.9)				
	Severe	20/34 (58.8)	<0.0001	2.4	1.6 - 3.7	<0.0001
	Age, mean \pm SD, years					
	36.4 \pm 14.4	Malnourished				
	41.5 \pm 14.8	Non-malnourished	0.004	0.97	0.96- 0.99	0.013

Another study on malnutrition prevalence in Eastern Europe IBD patients was published in 2010 [2]. The authors defined malnutrition as a weight loss of >10% of initial weight in 6 months or >5% in the 30 days prior to inclusion. The percentage of IBD malnourished patients was 68.4, without significant differences between CD and UC [2].

In our study population, in CD, malnutrition was associated with younger age ($p=0.004$) and with the severity of the disease ($p<0.0001$), but not with the behavior or the extension of the disease. The latter is in accordance with the results obtained in a study of 173 Hungarian IBD patients, where the extent of the disease did not have a significant impact on body composition [17].

The correlation between younger CD patients and malnutrition has been debated before in other publications [16, 19, 20]. It seemed that lower height and BMI, reduction of bone density and lean body mass were more prominent in CD than UC patients [16]. The reason for this finding may be that CD usually appears at a younger age than UC (as seen also in our patients) and has a longer evolution until diagnosis [9], therefore nutritional deficits and failure to thrive are more likely to develop.

In UC patients, malnutrition was significantly associated with the male gender (OR= 2.5), a more severe disease (OR= 3) and a more extensive disease (OR= 1.6). Similar to the results of Elsherif et al. [8], we found a correlation between malnutrition and no active smoking only in univariate analysis. Smoker UC patients had significantly milder disease than no current UC smokers.

Gender specific differences in nutritional status have been previously acknowledged. Geerling et al. [3] performed a study on 69 patients diagnosed with IBD within the 6 months prior to inclusion. They found that alterations in body composition were statistically different in male UC patients compared to healthy controls: lower BMI ($p<0.01$), reduced body weight and fat mass ($p<0.05$). Another study published in 2008 on hospitalized IBD patients, revealed that women were less likely than men to be malnourished (OR 0.88; 95% CI: 0.83– 0.92) [7].

Furthermore, several studies focused on body composition and sarcopenia in IBD patients and its impact on disease outcome [21–24]. A recent review revealed a high variability of sarcopenia prevalence in different IBD populations (11% to 61%) [24]. Sarcopenic IBD patients were more likely to be men [21, 23], who also had a lower median BMI than patients with a normal body mass composition [21, 23]. Based on these reports and our findings, we hypothesize that the changes in body composition of male patients with UC (significant weight loss, lower BMI) might reflect predominantly their loss of muscle mass. It has been previously shown that estrogen levels in premenopausal women are protective against the loss of skeletal muscle mass when compared to men of the same age [25, 26]. Still, further research is needed to support our hypothesis.

Regarding the correlation between the presence of malnutrition and serum C reactive protein levels, although statistically significant, the differences were not clinically relevant and were not independent, being strongly correlated with disease severity ($p<0.0001$). Still, we presume that the high levels of CRP in UC are explained by the fact that patients

were registered only in tertiary centers, where more severe cases are encountered.

Our study adds a special contribution to the epidemiology of malnutrition in IBD patients. Nevertheless, there are some limitations of the study. First, our definition of malnutrition might not be considered as perfect: it was based only on weight loss during the 3 months prior to diagnosis. An excellent correlation between recalled and measured weight has already been demonstrated by other authors [27, 28]. The most recent definition of malnutrition stated by ESPEN (European Society for Clinical Nutrition and Metabolism) requires unintentional weight loss (of >5% in 3 months or >10% in 6 months) along with one of the following: low BMI or low fat free mass index [14, 29]. Nonetheless, several malnutrition screening tools recommended by ESPEN take into account recent weight loss, without low BMI or body composition: Malnutrition Screening Tool (MST) [14, 30], the Short Nutritional Assessment Questionnaire (SNAQ) [14, 31]. Weight loss alone has been used in many studies as a predictor of malnutrition [2, 8, 15, 29, 32, 33]. The Dutch definition of malnutrition involves weight loss and/or low BMI [34], while the Canadian Nutrition Screening Tool solely encompasses recent weight loss [35]. Moreover, recent research suggests the ESPEN criteria might bear a low prognostic value [36]. Second, caution is needed when assessing malnutrition in overweight or obese patients based only on BMI or weight loss. Estimates from 2008 showed that in Romania, 51% of the adult population (> 20 years old) are overweight and 19.1% are obese [37]. Our database did not grant any information about height, BMI or body composition. Hence, we believe that combining body composition techniques in future research on malnutrition will lead to more accurate results. Lastly, a possible source of bias might come from the retrospective nature of our study as we only extracted data from IBD Prospect database and multiple users registered patients' data throughout this extended period of time. We would also like to comment that only tertiary centers from Romania are actively involved in registering patients on the IBD Prospect database. As a consequence, a certain number of patients diagnosed and monitored by gastroenterologists in non-tertiary medical centers were missed.

CONCLUSION

We conclude that about 1 in every 3 newly diagnosed IBD patients already suffers from malnutrition at the time of diagnosis. Malnutrition in IBD patients was associated with more severe disease. It also was associated with male gender and more extensive disease in UC patients, while in CD patients it was associated with younger age.

Our results support the need for nutritional screening in IBD patients from the initial presentation, by enriching the IBD Prospect with new parameters, such as height, body composition or muscle strength.

Conflicts of interest: None to declare.

Authors' contributions: Maria C., Mihai C. and M.D. designed the study. R.I. and M.D. contributed to the development and design of IBD Prospect database. R.I., M.D., Alina T., L.G., C.G., D.D., G.C., C.C.,

Anca T. and A.G. collected and processed data. Maria C., Mihai C. contributed with data analysis and interpretation. Maria C. conducted the literature search and wrote the manuscript. All authors read and approved the final version of the manuscript.

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