Indian Journal of Gastroenterology (January–February 2024) 43(1):254–263
https://doi.org/10.1007/s12664-024-01539-9

ORIGINAL ARTICLE

Comprehensive assessment of nutritional and functional status of patients with ulcerative colitis and their impact on quality of life

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Received: 29 November 2023 / Accepted: 22 January 2024 / Published online: 23 February 2024

Abstract

Introduction Patients with ulcerative colitis (UC) are likely to have poor nutritional intake and increased gut losses. This study was designed to study the prevalence and predictors of nutritional deficiencies in patients with UC and their impact on the quality of life (QOL).

Methods A prospective study was conducted among consenting patients with UC (cases) and healthy relatives of the cases (controls) visiting a university teaching hospital. They were assessed for clinical, demographic, endoscopic (Mayo score) and histological profile (Robart's score). They were assessed for the presence of macronutrient and micronutrient deficiency, anthropometry, functional status (muscle strength by dynamometer and sit-to-stand test) and the quality of life (short inflammatory bowel disease questionnaire [SIBDQ]). A SIBDQ score of ≤ 50 was considered poor QOL.

Results We studied 126 cases and 57 healthy controls (age [mean ± SD] 37.7 ± 13.2 years vs. 34.40 ± 11.05 years; [$p=0.10$] females [38.1% vs. 38.7%]; $p=0.94$). Cases more often were underweight (28% vs. 3.5%; $p<0.001$), had low mid arm circumference (45% vs. 12%; $p<0.0001$), lower functional status in the form of weaker hand grip strength (67% vs. 45.6%; $p=0.007$) and weaker lower limb strength (80% vs. 42%; $p<0.0001$). Cases more often had the evidence of macronutrient deficiencies: total serum protein deficiency (31% vs. 3.5%; $p<0.0001$), serum albumin deficiency (25.4% vs. 0.00%; $p<0.0001$) and cholesterol deficiency (63% vs. 28%; $p<0.0001$). Micronutrient deficiencies were highly prevalent among cases: calcium (44%), phosphate (21%), magnesium (11%), zinc (76%), iron (87%), folate (16%), vitamin B_{12} (10%) and vitamin D (81%). Most cases had a poor quality of life (85/126; 67.5%). Factors associated with poor QOL were low hemoglobin, serum albumin, zinc and vitamin D levels and histologically active disease. On multi-variate analysis, low vitamin D levels (odds ratio [OR] = 6.1; 95% confidence interval [CI]: 1.9–19.7) and histologically active disease (OR = 4.0; 95% CI: 1.6–9.9) were identified as independent predictors of poor QOL.

Conclusions Macronutrient deficiency, micronutrient deficiency, lower functional status and poorer QOL are highly prevalent among patients with UC. The independent predictors of poor QOL were histologically active disease and low serum vitamin D levels. Identifying and correcting the deficiencies may help in improving the QOL of patients with UC.

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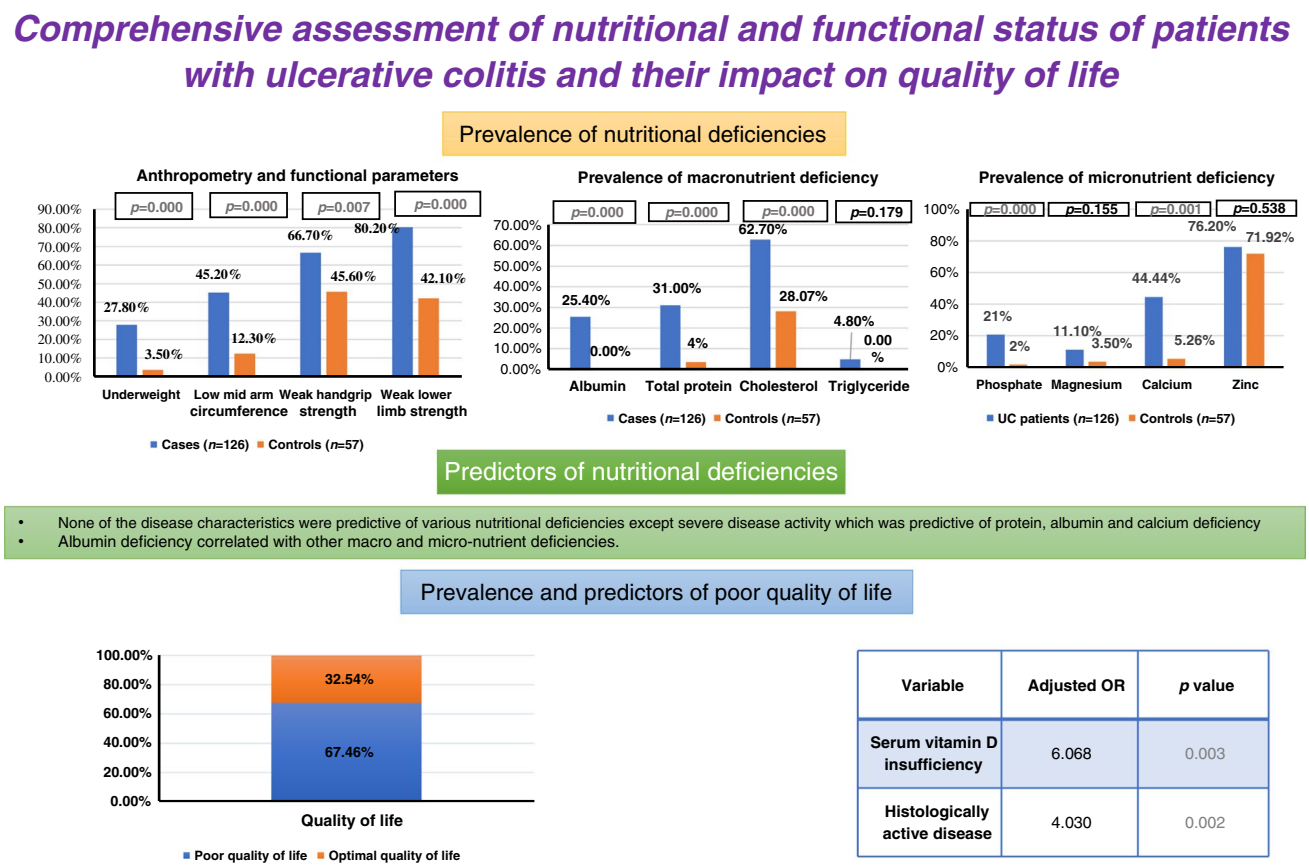
Graphical Abstract



Keywords Anthropometry · Inflammatory bowel disease · Macronutrient · Micronutrient · Quality of life

Introduction

The incidence and prevalence of ulcerative colitis (UC) is on the rise in developing world proportional to increasing adaptation to western lifestyle [1]. In developing countries, macronutrient and micronutrient deficiencies are likely to be more common due to limited food availability, low micronutrient levels in natural food and lack of national food fortification programs [2, 3]. Assessment of nutritional deficiencies is important in the management of patients with UC as it is likely to impact inflammation, healing and overall quality of life (QOL) in them [4]. Patients with UC are at an increased risk of nutritional deficiencies due to poor intake, food restrictions, increased endogenous losses of cellular constituents into the intestinal lumen, drug-induced side effects and ongoing inflammation. Total dietary intake and protein intake are reduced in UC patients than normal persons [5–8].

Corticosteroids suppress intestinal absorption, increase albumin synthesis at the expense of body protein stores and increase urinary excretion of calcium [7]. Sulfasalazine reduces folate absorption while cyclosporine and azathioprine are associated with nausea, vomiting, esophagitis and diarrhea [7]. Patient with Crohn's routinely undergoes evaluation for nutritional status in contrast to all those with ulcerative colitis [4, 8]. However, nutrient deficiencies are also common among patients with UC, especially in those with active disease. Preliminary studies from some developing countries have indicated high prevalence of nutritional deficiencies in patients with UC [4, 5, 8]. However, there is lack of comprehensive studies in a large population of patients with UC using validated methods to assess macronutrient and micronutrient status in the developing world.

Undernutrition can be due to macronutrient and/or micronutrient deficiency, both of which need to be assessed by validated, cost-effective methods in all patients. Macronutrient deficiency or protein energy malnutrition assessment includes the anthropometry measures, functional status and laboratory parameters such as serum albumin and cholesterol [9].

Functional status can be assessed using validated tests such as hand dynamometer, sit stand test and six-minute walk test [10, 11].

Micronutrient assessment is often expensive, needs more sophisticated technology and often not available at all centres. The previously identified micronutrient deficiencies in the setting of UC include iron, calcium, magnesium, vitamin A, B_{12}, folate and vitamin D [12]. Zinc is a vital micronutrient which plays an important role in maintaining gut barrier and gut immunity; both of which are deranged in the setting of UC. There are only limited studies that have evaluated the zinc levels in patients with UC. The quality of life is often poor in the setting of UC. Studies have shown that the QOL is related to disease activity.

We thus planned to conduct a comprehensive assessment of micronutrient and macronutrient deficiencies in patients with ulcerative colitis and compare it with healthy controls living in the similar environment. We also planned to study the QOL and its determinants using validated specific short inflammatory bowel disease questionnaire score developed by McMaster University [13].

Methods

A prospective case-control study was conducted at a university teaching hospital. Consecutive adult patients with UC attending the gastroenterology services from February 2021 to October 2021 were evaluated for enrolment. The study was approved by the Institute's Ethics Committee (NK/6875/DM/711). Those fulfilling the study criteria were recruited after a written informed consent. The study was conducted in full compliance with the guidelines of good clinical practice of the World Medical Assembly declaration of Helsinki and the Indian Council of Medical Research guidelines. Cases were defined as consecutive patients with ulcerative colitis as defined by European Crohn's and Colitis Organisation (ECCO) criteria [14]. Consenting healthy relatives/attendants of the recruited cases belonging to similar demographic profile were enrolled as controls (Fig. 1).

All consecutive patients with UC (recently diagnosed and previous follow-ups) between 12 and 70 years of age were screened for eligibility. Those who fulfilled the selection criteria were enrolled. Patients who were unable to provide informed consent, having serious life-threatening co-morbidities (malignancy, heart failure, renal or hepatic failure), pregnant or breastfeeding women were excluded. The 24-hour diet recall (the amount of food, beverages and supplements consumed by patients during each meal [i.e. breakfast, lunch, snacks and dinner] was noted down in terms of household measures [standard cup set] or numerical [e.g. chapatis] which was used to calculate total calorie intake as per nutritive value of Indian foods) and history of medication intake were noted [6]. Detailed physical examination, blood investigations and data collection were performed to

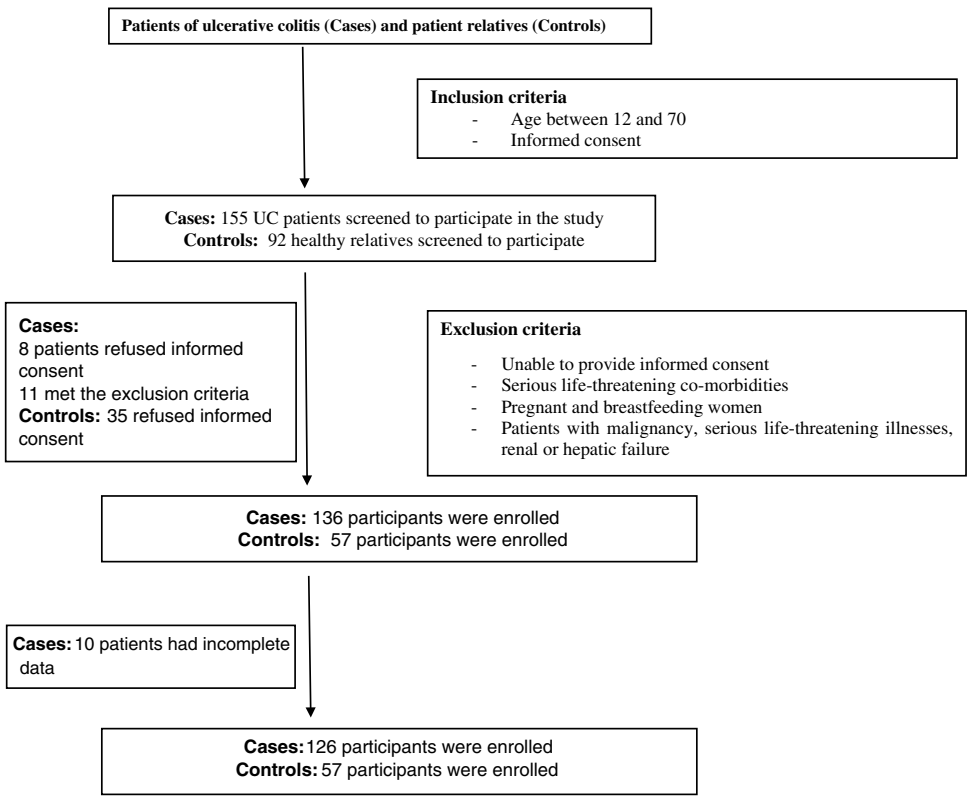


Fig. 1 Study design and methods

evaluate for micronutrient (calcium, magnesium, phosphate, zinc, iron, folate, vitamin B_{12} and vitamin D) and macronutrient (24-hour diet recall, functional status, anthropometry, protein, albumin, triglyceride and cholesterol) deficiencies and QOL, Supplementary Fig. 1. Modified Kuppuswamy scale 2021 was used for assessing socioeconomic status [15].

Assessment of disease characteristics

All patients underwent comprehensive clinical, demographic profiling and detailed assessment of UC status with respect to duration, extent, course and treatment in a structured case report form. The severity of disease was graded as per Mayo scoring system [16]. All patients underwent sigmoidoscopy/colonoscopy to assess disease activity. Multiple mucosal biopsies were obtained with sterilized biopsy forceps; these biopsies were placed in formalin vial and sent for histopathological examination. An experienced gastrointestinal histopathologist reported the activity as per Robarts histological index (RHI). Score of ≤ 3 was taken as criteria for remission [17]. Colonoscopic findings of mucosal changes were graded according to Mayo scoring system [18].

Macronutrient and anthropometric evaluation

Macronutrient deficiency was assessed by levels of serum albumin, total serum protein, serum triglycerides and serum cholesterol. All cases and controls were assessed for their body mass index (BMI), mid arm circumference (MAC), triceps skinfold thickness (TSFt), mid arm muscle circumference (MAMC), handgrip strength (HGS) and sit to stand test (STS). BMI was categorized as per Asian guidelines (< 18.5 kg/m^2 for underweight,18.5–22.9 kg/m^2 for normal weight, 23.0–24.9 kg/m^2 for overweight, > 25 kg/m^2 for obese) [19]. Low BMI was defined as BMI < 18.5 kg/m^2 [18]. Mid arm circumference (MAC) was measured at the midpoint between the acromioclavicular joint and olecranon process using a standard tape. MAC < 24.5 cm was considered low MAC for both male and female [16]. MAMC was calculated using standard formula (MAMC = MAC–3.14*TSFt) [10, 20].

Assessment of micronutrient status

Micronutrient deficiency was assessed by levels of zinc (atomic absorption spectrometry), magnesium, calcium, phosphate (Beckman-coulter autoanalyzer), iron, vitamin B_{12}, folate and vitamin D (Roche™ ELISA, Cobas e 60, Basel, switzerland). Based on the institutional laboratory cut-offs, the patient was classified as deficient or normal, Supplementary Table 1. Serum samples were procured and stored in iron free vials for vitamin D, vitamin B_{12}, folate and iron levels. Presence of anemia was characterized as per World Health Organization (WHO) classification for males and females (hemoglobin [hb] levels < 12.0 gm/dL in women and < 13.0 gm/dL in men) [21].

Evaluation of functional status

Handgrip strength was measured using a validated dynamometer (Camry™ dynamometer, Camry Scale, Zhongshan, China). A mean of three readings (3 seconds each) was taken from the dominant hand. Handgrip strength was categorized as weak or normal based on the established criteria as per gender and weight category [10]. Lower limb muscle strength was graded using a standard five times repetition sit to stand (STS) test. The test incorporates a standard height armless chair and involves documenting the time required to complete five repetitions of sitting to standing. The patients were demonstrated the procedure by the instructor for uniformity. Patients would begin by sitting forward on the chair with their feet flat on the floor. They were asked to stand up completely and sit down as firmly as fast as possible while their upper limbs are folded across their chests. The time was recorded by standard stopwatch. It was categorized as weak or normal or above as per charts provided by Bohannon et al [11].

Quality of life assessment

The QOL score was assessed according to the Short Inflammatory Bowel Disease Questionnaire (SIBDQ) after due permission from McMaster University for its usage. The SIBDQ is a disease-specific health-related QOL instrument that consists of 10 questions to measure the effect of IBD on social, emotional and physical well-being. Total scores range from 10 (worst health) to 70 (best health) [13]. A SIBDQ score ≤ 50 denoted poor QOL [22].

Statistical analysis

All data was analyzed on Statistical Package for the Social Sciences (SPSS) 26.0, (IBM Corporation, New York, USA). Data was represented as mean ± standard deviation or median and interquartile range if it had a non-parametric distribution. Continuous variables were compared using Student's '*t*' test or the Mann-Whitney *U* test. Discrete variables were analyzed using Chi-square test or Fisher's exact test and expressed as proportions (percentage). A two-tailed p-value < 0.05 was considered to be significant in all statistical evaluations. Correlation statistics were performed using Pearson's *r* or Spearman's rho depending on the distribution to study the relationship of continuous variables. Univariate followed by multivariable regression analysis was used to determine the predictors of micronutrient deficiencies and the quality of life.

Results

As many as 126 cases and 57 healthy controls were included. The mean age of patients with UC (cases) was 37.71 ± 13.24 and females constituted 38.1%. The mean age of controls

Table 1 Table showing comparison of demographic characteristics of cases and controls

Clinical feature	Cases ($n=126$)	Controls ($n=57$)	p-value
Mean age	37.71 ± 13.24	34.40 ± 11.05	0.102
Gender			0.948
Male	78 (61.9%)	35 (61.4%)	
Female	48 (38.1%	22 (38.6%)	
Marital status			0.212
Unmarried	31 (24.6%)	15 (26.3%)	
Married	95 (75.4%)	42 (73.7%)	
Religion			0.805
Hindu	91 (72.2%)	39 (68.4%)	
Sikh	30 (23.8%)	18 (31.6%)	
Muslim	5 (4.0%)	0%	
Socioeconomic scale (Kuppuswamy scale)			0.075
Upper	0%	0%	
Upper middle	57 (45.2%)	35 (61.4%)	
Lower middle	40 (31.7%)	17 (29.8%)	
Upper lower	27 (21.4%)	4 (7.0%)	
Lower	2 (1.6%)	1 (1.8%)	
History of smoking			0.061
Yes	25 (19.8%)	5 (8.8%)	
History of alcohol			0.054
Yes	34 (27.0%)	8 (14.0%)	
Dietary type			0.522
Vegan	22 (17.5%)	13 (22.8%)	
Lacto-vegetarian	35 (27.8%)	19 (33.3%)	
Ovo-vegetarian	24 (19.0%)	7 (12.3%)	
Non-vegetarian	45 (35.7%)	18 (31.6%)	

Continuous data is expressed as mean ± SD, categorical data as *n* (%)

was 34.40 ± 11.05 and females were 38.6%. The study flow and enrolment is shown in Fig. 1. The baseline demographic, socioeconomic and social habits were comparable between both groups (Table 1).

Disease characteristics

The most common disease phenotype was left-sided colitis 38.1% ($n=48$) followed by pancolitis 34.1% ($n=43$), 11.1% ($n=14$) had proctitis and 16.7% ($n=21$) could not be evaluated for complete extent due to severe disease at presentation. The disease duration was ≤ 2 years in 50% of the cases and > 2 years in 50%. The disease activity by complete Mayo score was in remission in 24 (19.0%), mild disease activity in 38 (30.2%), moderate disease activity in 52 (41.3%) and severe disease in 12 (9.5%) patients. Severe disease by endoscopic Mayo score (EMS) was seen in 26.2% ($n=33$), while remission (EMS = 0/1) was seen in 38.09% ($n=48$) cases. Only 23.8%($n=30$) were in remission by RHI of ≤ 3. Only 9.5% ($n=12$) cases classified as having severe disease and 19.05% ($n=24$) patients were in remission by complete Mayo score. History of 5-ASA compound was present in 86.57% ($n=109$), steroids use was in 39.68% ($n=50$) and history of immunomodulators was in 34.12% ($n=43$) of cases. Twenty-two (17.46%) patients had extraintestinal manifestation. Of these, 16 (12.7%) patients had arthritis/arthralgia, two (1.6%) had pyoderma gangrenosum, one patient each had uveitis, ichthyosis and thromboembolic disorder and one patient had both uveitis and arthritis.

Macronutrient and anthropometry evaluation

The patients more often had lower mean levels of albumin, total protein and total cholesterol as compared to controls ($p<0.0001$) (Table 2). Cases more often had protein deficiency ([30.95% vs. 3.50%], $p=0.0001$), albumin deficiency (25.39% vs. 0.00%, $p=0.0001$) and cholesterol deficiency (62.69% vs. 28.07%, $p=0.0001$) as compared to controls. However, triglyceride deficiency was similar in both groups (4.76% vs. 0%, $p=0.179$) (Table 2).

The mean weight (58.79 ± 13.016 kgs) was significantly lower in cases than controls (71.17 kgs) ($p=0.0001$). The mean height was comparable between cases and controls (1.64 ± 0.085 vs. 1.65 ± 0.092 m, $p=0.542$). The median BMI (21.60 [5.88] vs. 27.00 [6.32] kg/m^2, $p=0.0001$), mean MAC (24.83 [5.74] vs. 29.99 [4.32] centimetres, $p=0.0001$) and mean MAMC (19.09 ± 5.30 vs. 23.56 ± 4.45 cm, $p=0.0001$) were significantly lower in the cases than controls. The median triceps skin fold thickness (TSFt) was numerically lower in cases than controls, however, did not reach statistically significant difference between the two groups (1.85 [1.20] vs. 2.00 [1.23], $p=0.342$). Cases more often had evidence of malnutrition than controls with the prevalence of low BMI (27.8% vs. 3.50%, $p=0.000$) and low MAC (45.23% vs. 12.28%).

Micronutrient assessment

Cases had lower levels of calcium (8.90 [0.66] vs. 9.4 [0.37] mg/dL, $p=0.000$) than controls. Cases had higher levels as compared to controls of vitamin B_{12} (462 [686.75] vs. 200.80 [153.5] pg/mL, $p=0.0001$), folate (7.8 [9.95] vs. 4.98 [2.27] mg/dL, $p=0.0001$) and vitamin D (20.99 ± 10.33 vs. 14.80 ± 14.61 mg/dL, $p=0.0001$). Levels of magnesium (2.08 [0.47] vs. 2.05 [0.23] mg/dL, $p=0.966$), phosphate (3.40 [0.97] vs. 3.68 [0.69] mg/dL, $p=0.713$) and zinc) 64 [24.25] vs. 61.16 [31.9] µg/dL, $p=0.641$) were similar between cases and controls.

The prevalence of calcium deficiency (44.44% vs. 5.26%, $p=0.000$) and phosphate deficiency (20.63% vs.

Table 2 Table showing comparison of various nutrition parameters and prevalence of deficiencies between cases and controls

Clinical feature	Cases ($n=126$)	Controls ($n=57$)	p-value
24-h diet recall			
Total 24-h calorie intake (kcal)	1340 ± 277.75	2330 ± 325.61	**0.0001****
Anthropometry and functional parameters			
Height (metres)	1.642 ± 0.085	1.651 ± 0.092	0.542
Weight (kilograms)	58.790 ± 13.016	71.165 ± 14.418	*0.0001***
Body mass index (BMI) (kg/m^2)	21.60 (5.88)	27.00 (6.32)	*0.0001***
BMI			**0.0001***
Underweight (< 18.5 kg/m^2)	35 (27.8%)	2 (3.50%)	
Normal (18.5–22.9 kg/m^2)	51 (40.5%)	12 (21.1%)	
Overweight (23–24.9 kg/m^2)	17 (13.5%)	6 (10.5%)	
Obese (> 25 kg/m^2)	23 (18.3%)	37 (64.9%)	
Mid arm circumference (MAC) (cms)	24.826 ± 5.745	29.991 ± 4.321	*0.0001***
Low MAC < 24.5 cm	57 (45.23%)	7 (12.28%)	**0.0001****
Triceps fold thickness (cms)	1.85 (1.20)	2.00 (1.23)	0.342
Mid arm muscle circumference	19.092 ± 5.308	23.556 ± 4.453	*0.0001***
Mean handgrip strength (cms)	24.88 (13.66)	29.30 (12.20)	*0.026**
Weak handgrip strength	84 (66.66%)	26 (45.61%)	**0.007***
STS test time (seconds)	10 (5)	7.00 (2.00)	*0.0001***
Weak lower limb strength	101 (80.15%)	24 (42.10%)	**0.0001****
Macronutrient parameters			
Total protein levels (gm/dL)	6.79 (1.30)	7.29 (0.63)	*0.0001***
Protein deficiency	39 (30.95%)	2 (3.50%)	**0.0001****
Albumin levels (gm/dL)	4.01 (0.98)	4.78 (0.48)	*0.0001***
Albumin deficiency	32 (25.39%)	0 (0.00%)	**0.0001****
Cholesterol levels (mg/dL)	139.242 ± 35.726	171.963 ± 36.022	*0.0001***
Cholesterol deficiency	79 (62.69%)	16 (28.07%)	**0.0001****
Triglycerides levels (mg/dL)	102 (50.05)	141 (95.3)	*0.0001***
Triglyceride deficiency	6 (4.76%)	0 (0%)	**0.179**
Micronutrient parameters			
Calcium deficiency	56 (44.44%)	3 (5.26%)	**0.0001****
Magnesium deficiency	14 (11.11%)	2 (3.5%)	**0.155**
Phosphate deficiency	26 (20.63%)	1 (1.75%)	**0.001****
Zinc deficiency	96 (76.19%)	41 (71.92%)	**0.538**
Iron levels (mg/dL)	39.55 (31.37)	-	
Iron deficiency	110 (87.3%)	-	
Folate deficiency	20 (15.9%)	25 (43.85%)	**0.0001****
Vitamin B_{12} deficiency	13 (10.3%)	27 (47.36%)	**0.0001****
Vitamin D deficiency	25 (19.8%)	22 (38.59%)	**0.007***
Vitamin D insufficiency	110 (87.3%)	50 (87.71%)	**0.937**

Normally distributed data has been expressed as mean ± SD. **Non-normal data has been expressed as median (IQR), *$p < 0.05$,**$p < 0.005$**. *Categorical data is expressed as n (%),* *$p < 0.05$,**$p < 0.005$

1.75%, $p=0.001$) was significantly higher in cases; however, no statistically significant difference in magnesium deficiency (11.11% vs. 3.5%, $p=0.155$) and zinc deficiency (76.19% vs. 71.92%, $p=0.538$) was found. The prevalence of vitamin B_{12} deficiency (10.3% vs. 47.36%, $p=0.0001$), folate deficiency (15.9% vs. 43.85%, $p=0.0001$) and vitamin D deficiency (19.8% vs. 38.59%, $p=0.007$) was significantly more in the control population ($p<0.05$) (Table 2).

Functional status

The median handgrip strength (24.88 [13.66] vs. 29.30 [12.20] kilograms, $p=0.03$) was lower among the cases than the controls. The median STS time (10 [5] vs. 7 [2] seconds, $p=0.0001$) was prolonged in cases than controls (Table 2). Cases more often had weak hand grip strength (66.66% vs. 45.61%0, $p=0.007$) and weak lower limb

Table 3 Table showing prevalence of nutrition parameters with disease severity by complete MAYO score

Clinical feature	Severe activity ($n=12$)	Non-severe activity ($n=114$)	p-value
BMI < 18.5 kg/m^2	6 (50%)	29 (25.43%)	**0.092**
Low MAC < 24.5 cm	5 (41.66%)	52 (45.61%)	**0.794**
Weak handgrip strength	8 (66.66%)	76 (66.66%)	**1.000**
Weak lower limb strength	11 (91.66%)	90 (78.94%)	**0.457**
Protein deficiency	9 (75%)	30 (26.31%)	***0.001*****
Albumin deficiency	10 (83.33%)	22 (19.29%)	***0.0001*****
Cholesterol deficiency	10 (83.33%)	69 (60.52%)	**0.208**
Triglyceride deficiency	1 (8.33%)	5 (4.38%)	**0.459**
Calcium deficiency	10 (83.33%)	46 (40.35%)	***0.004*****
Phosphate deficiency	5 (41.66%)	21 (18.42%)	**0.125**
Magnesium deficiency	3 (25%)	11 (9.64%)	**0.108**
Zinc deficiency	8 (66.66%)	88 (77.19%)	**0.478**
Iron deficiency	11 (91.66%)	99 (86.84%)	**1.000**
Anemia	11 (91.66%)	74 (64.91%)	**0.101**
Vitamin B_{12} deficiency	2 (16.66%)	11 (9.64%)	**0.358**
Folate deficiency	4 (33.33%)	16 (14.03%)	**0.098**
Vitamin D deficiency	5 (41.66%)	20 (17.54%)	**0.061**

Categorical data is expressed as n (%), *p < 0.05,**p < 0.005

MAC mid arm circumference, *BMI* body mass index

strength (80.15% vs. 42.10%, $p=0.0001$) than controls, respectively (Table 2).

Predictors of macronutrient deficiencies and functional status

Total protein deficiency (26.31% vs. 75%; $p=0.001$) and albumin deficiency (19.29% vs. 83.33%; $p=0.0001$) were significantly more in patients with severe activity of disease (Table 3). However, there was no difference as per disease duration or extent in the prevalence of macronutrient deficiencies ($p>0.05$). Mean handgrip strength levels positively correlated with albumin levels ($r=0.198$; $p=0.007$) and serum iron levels ($r=0.306$; $p=0.0001$). Time taken for sit to stand test negatively correlated with serum albumin levels ($r=-0.391$; $p=0.0001$), calcium levels ($r=-0.269$; $p=0.0001$), phosphate levels ($r=-0.202$; $p=0.008$), cholesterol levels ($r=-0.230$; $p=0.002$) and vitamin B_{12} ($r=-0.330$; $p=0.0001$).

Predictors of micronutrient deficiencies

The micronutrient deficiency did not differ as per disease extent (E1/E2/E3) or duration (≤ 2 years and > 2 years) ($p>0.05$). Calcium deficiency was the only micronutrient that differed significantly between cases and with severe and non-severe disease activity ($p=0.004$) (Table 3). Only prevalence of lower limb muscle strength, anemia and albumin deficiency showed significant difference between patients having remission and active disease ($p<0.05$), Supplementary Table 2.

Quality of life and its predictors

Eighty-five (67.46%) cases had poor quality of life with SIBDQ score ≤ 50. When the prevalence of malnutrition parameters and disease characteristics was compared between poor and optimal quality of life patient sub-group, anemia) (74.1% vs. 53.65%; $p=0.022$), vitamin D insufficiency (94.11 vs. 73.17; $p=0.001$) and severe disease by complete Mayo score (14.11 vs. 0.00; $p=0.027$) were statistically more prevalent in poor QOL group. The patients with optimal QOL were more often in clinical (8.23% vs. 41.46%; $p=0.0001$) or histological remission (15.29% vs. 41.46%; $p=0.0001$) (Table 4).

Table 4 Table showing prevalence of nutrition and disease parameters which showed significant difference with optimal quality of life

Clinical feature	Poor QOL ($n=85$)	Optimal QOL ($n=41$)	p-value
Anemia	63 (74.11)	22 (53.65)	***0.022****
Vitamin D insufficiency (< 32 ng/mL)	80 (94.11)	30 (73.17)	***0.001****
Severe disease by CMS	12 (14.11)	0 (0.00)	***0.027****
Remission by CMS	7 (8.23)	17 (41.46)	***0.0001****
Remission by RHI	13 (15.29)	17 (41.46)	***0.001****

Categorical data is expressed as n (%),*p < 0.05,**p < 0.005

CMS complete Mayo score, *RHI* Robarts histological index

Table 5 Table showing adjusted odds ratio of predictors of poor quality of life after multivariate regression analysis

Variable	Adjusted OR	Lower level (95% CI)	Upper level (95% CI)	*p*-value
Serum vitamin D insufficiency	**6.068**	1.859	19.705	*0.003*
Histologically active disease	**4.030**	1.645	9.875	*0.002*

Categorical data is expressed as *n* (%)

CI confidence interval

After univariate analysis, presence of anemia, serum albumin deficiency, serum zinc deficiency, vitamin D insufficiency and histological active disease was incorporated in the model used for stepwise backward regression analysis. Vitamin D insufficiency (< 32 ng/mL) (OR = 6.1 [1.9–19.7]; $p = 0.003$) and histologically active disease (OR = 4.0 [1.9–19.7]; $p = 0.003$) were independent predictors of quality of life (Table 5).

Discussion

In this study, patients with UC were nutritionally and functionally poor than the healthy controls. Patients were found to have a lower anthropometric measurement by BMI, MAC and MUAC. Both MAC and MAMC were low in our patients despite comparable TSFt suggesting that it is a decrease in the muscle mass causing low MAC. Total calorie intake and serum macronutrient deficiencies were predominantly eminent in cases as compared to the healthy controls. Cholesterol and total protein levels have a role in inflammation and healing cascade; so, their deficiencies need to be identified and rectified with proper dietary and disease management [23, 24]. The patients with UC had poor micronutrient status. Muscle strength parameters such as weaker handgrip and weaker lower limb strength were more prevalent in patients with UC impacting their functional status. The poor nutritional and functional status resulted in poor QOL of patients with UC.

This was the first study to the best of our knowledge that studies the prevalence of zinc deficiency in patients with UC in India. Although the UC patients are more prone for micronutrient deficiencies, vitamin B_{12}, folate, zinc and vitamin D deficiencies were not more prevalent in UC patients than the healthy controls. This is due to the already prevalent micronutrient deficiency in the Indian population [25–27]. Another reason could be the presence of the cases under medical follow-up and intermittent supplementation of these nutrients if deficient in a tertiary care setup, whereas the controls were out of this medical radar. Specific micronutrient deficiencies although prevalent in patients with UC and more likely to occur with active disease are hard to predict. Although available evidence in literature is not robust, serum albumin levels may be used as a biomarker of malnutrition in resource-constraint settings [28].

The median BMI and proportion of patients with BMI > 25 kg/m^2 were higher when compared to previous studies in the Asian region [6, 29]. It is significantly less than the Australian cohort with 60% of patients in overweight or obese category [30]. Even patients in normal BMI range had lower MAC in this study, which may be explainable by a study by Adams et al. who have shown that 41% of patients with normal range BMI and 20% of patients with BMI in overweight category may have sarcopenia [31]. So, BMI alone may be a poor predictor of nutrition status and functional parameters should be added to assessment.

The handgrip strength was weaker in significantly high number of patients, which may be due to the associated protein energy malnutrition in these patients. However, hand dynamometer was used in this study whose ranges have not been validated in Indian population. Another novel parameter evaluated in this study was the presence of lower limb weakness with STS and patients had almost double the prevalence of weakness than the healthy controls as per the available western cut-offs. However, this has not been previously studied in UC patients and regional cut-offs are not yet validated. Poor functional status with increased STS correlated with poor quality of life and we suggest that improving the functional status with nutrition and required physiotherapy may help improve the QOL.

Significant prevalence of protein energy malnutrition and micronutrient deficiency in patients with UC is multifactorial. Being in a developing country, the nutritional status of large proportion of patients is inherently poor with multiple micronutrient deficiencies. Also, patients when not properly counselled about dietary habits often exclude multiple food items and resultant malnutrition occurs [6, 32]. Nutritional deficiencies are combined action of decreased intake as well as increased requirements and losses due to disease activity as well as medications [33]. Serum albumin has pleiotropic actions with roles as a carrier protein, oncotic protein, anti-inflammatory, anti-oxidant and buffer agent. It also affects drug concentrations of anti-inflammatory medications and deficiency predicts poor surgical outcomes [34, 35]. Hence, albumin deficiency should be monitored and restored with proper dietary as well as disease-controlling interventions.

Another revelation of the study was that two-thirds of the patients had poor quality of life in spite of only less than 10% having severe disease. SIBDQ score used is a well-validated score in UC and has previously been used in drug trials also [36]. In a few other studies with a slightly smaller sample size, they have demonstrated that endoscopic and clinical disease activity correlated well with SIBDQ but histological activity

has been studied for the first time in this study [37, 38]. It was found that patients with active disease are likely to have poor quality of life with presence of anemia and vitamin D deficiency predominantly more in this subset of patients. This can be explained with the resulting fatigue and weakness associated with these deficiencies. Vitamin D insufficiency and active histological disease were good predictors of poor quality of life; hence, supplementing vitamin D and inducing deep remission would be suggestible for improving QOL in patients with UC regardless of disease extent or duration. In another previous study, vitamin D deficiency has been associated with lower SIBDQ scores [39]. It is imperative to understand that the management of nutrition is two pronged, i.e. control the disease activity by appropriate treatment as well as active surveillance for nutrient deficiencies and adequate supplementation for optimal quality of life. Clinician should target for better QOL of patient.

This study highlights that patients with UC have poor quality of life. The holistic improvement in patient QOL needs comprehensive evaluation and addressal of the nutritional and functional component with the control of disease activity. All patients should not be tested for each micronutrient deficiency as this strategy would be very cost intensive. Recommended dietary allowances (RDA) dose of these vitamins can be supplemented in patients with poor functional status. In admitted patients, low serum albumin can act as a simple marker for starting supplementation of essential micronutrients. OPD patients can be started with standard multi-vitamin with multi-mineral supplementations for short durations. One of the studies has already shown benefit of adding nano preparation of vitamin D with the disease control agents showing better disease control [40].

Strengths of this study include that it is one of the largest prospective studies of ulcerative colitis patients from a developing country for malnutrition analysis, including micronutrient deficiency and the assessment of quality of life, which is again novel in this study. Objective assessment of quality of life was obtained with a well-validated SIBDQ score. Assessment of lower limb strength and zinc levels in patients with UC was novel in this study. Risk factors and predictors of micronutrient deficiencies as well as quality of life were evaluated in the study. However, the limitations of this study were that it was conducted at a single centre, healthy controls were not screened for sub-clinical UC, iron deficiency could not be studied in healthy controls due to logistic reasons, intake of multivitamin supplements in cases and less number of controls.

In conclusion, this large prospective comprehensive study, patients with ulcerative colitis more often had macronutrient and micronutrient deficiency compared to healthy controls. They are more likely anthropometrically weak with increased prevalence of being underweight and decreased muscle circumference. They also have weaker muscle strength than healthy controls affecting their functional status. Patients with UC have high prevalence of micronutrient deficiencies. Significant proportion of patients with UC have poor quality of life. Histologically active disease and insufficient vitamin D are predictors of poor quality of life.

Implications: To improve QOL of patient, improve both disease activity as well as nutrition. Vitamin D level and disease in remission are best predictors of QOL. Serum albumin levels may be a surrogate marker for poor nutritional status even in OPD patients.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s12664-024-01539-9.

Acknowledgements Mr. Harish and Ms Deepa for helping with sample collection and storage.

Author Contribution UD and AS provided the concept and design of the study. MT, RSJ, Arun KS and HK were involved in the sample processing and data validation. KV and KKS were involved in histology scoring and final data validation. VS, AJ, Anupam KS, JS and SB were involved in manuscript writing and final editing of the manuscript. All authors approved the final manuscript.

Funding None.

Data availability Data is available as required with the authors.

Declarations

Conflict of interest AS, MT, HK, KKP, RSJ, VS, AJ, AKS, KV, JS, ArKS, SKB and UD declare no competing interests.

Ethics statement The study was performed conforming to the Helsinki Declaration of 1975, as revised in 2000 and 2008 concerning human and animal rights, and the authors followed the policy concerning informed consent as shown on Springer.com.

Ethical approval and consent to participate The study was approved by the Institute's Ethics Committee (NK/6875/DM/711). Informed consent was taken from each participant for participation in the study.

Consent for publication All authors gave consent for publication.

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