

THE ASSOCIATION OF ANXIETY, DEPRESSION ON THE QUALITY OF LIFE OF INFLAMMATORY BOWEL DISEASE PATIENTS .docx *by F F*

Submission date: 28-Nov-2024 09:29AM (UTC+0530)

Submission ID: 2530414940

File name: Skrining-rev_without_cores.docx (62.39K)

Word count: 9130

Character count: 50082

¹
Title of the article: THE ASSOCIATION OF ANXIETY, DEPRESSION ON THE
QUALITY OF LIFE OF INFLAMMATORY BOWEL DISEASE PATIENTS

Running Title : Anxiety, Depression in IBD Patient

Abstract

Background: Inflammatory Bowel Disease (IBD), which is chronic and often recurrent, causes psychological changes in patients. This puts IBD patients at a higher risk of developing various mental disorders, especially anxiety and depression. IBD patients who had symptoms of anxiety or depression tended to show a lower quality of life than patients without those symptoms.

Methods: This research uses a cross-sectional design. Data collection was carried out using primary data obtained through interviews with IBD patients who were undergoing outpatient treatment between October and December 2023. Anxiety and depression were measured using the Hospital Anxiety Depression Scale (HADS) and quality of life for IBD patients was measured using the Inflammatory Bowel Disease Questionnaire 9 (IBDQ-9). These questionnaires have been translated into Indonesian and validated. The research sample is an accessible population that has passed the inclusion and exclusion criteria using unpaired numerical analytical sample calculations. The sample used in this research was 172 subjects.

Results: In the multivariate analysis, after controlling for confounding variables, the fully adjusted PR for anxiety was 4.241 (CI 1.292–13.924) with p-value = 0.017. Meanwhile, in the multivariate analysis, after controlling for confounding variables, the fully adjusted PR for depression was 3.276 (CI 1.033-10.387) with p-value = 0.044.

Conclusion: There is an association¹ of anxiety and depression on the quality of life of IBD patients based on the IBDQ-9 after controlling for confounding variables.

Keywords: IBD, anxiety, depression, quality of life

Judul : Pengaruh Ansietas Dan Depresi Terhadap Kualitas Hidup Pasien *Inflammatory Bowel Disease* Berdasarkan *Inflammatory Bowel Disease Questionnaire-9* (IBDQ-9)

Abstrak

Latar Belakang: *Inflammatory Bowel Disease* (IBD) terdiri atas kumpulan gejala yang bersifat kronis dan sering kambuh menyebabkan perubahan psikologis pada pasien. Hal ini menyebabkan pasien IBD memiliki risiko lebih tinggi untuk terkena berbagai gangguan jiwa, terutama ansietas dan depresi. Pasien IBD yang memiliki gejala ansietas atau depresi cenderung menunjukkan skor kualitas hidup yang lebih rendah dibandingkan pasien tanpa gejala ansietas atau depresi.

Metode: Penelitian ini menggunakan desain potongan lintang. Pengumpulan data dilakukan dengan menggunakan data primer yang diperoleh melalui wawancara dengan penderita yang sudah terdiagnosa IBD dan sedang menjalani rawat jalan di poli Gastroenterologi RSUPN Cipto Mangunkusumo antara bulan Oktober - Desember 2023. Kecemasan dan depresi diukur dengan menggunakan Hospital Anxiety Depression Scale (HADS) dan kualitas hidup pasien IBD diukur dengan menggunakan *Inflammatory Bowel Disease Questionnaire 9* (IBDQ-9). Pengukuran ansietas dan depresi menggunakan *Hospital Anxiety Depression*

Scale (HADS) dan pengukuran kualitas hidup pasien IBD menggunakan *Inflammatory Bowel Disease Questionnaire 9* (IBDQ-9). Kedua kuesioner ini sudah diterjemahkan ke dalam bahasa Indonesia dan tervalidasi. Sampel penelitian adalah populasi terjangkau yang telah melewati kriteria inklusi dan kriteria eksklusi, dengan menggunakan perhitungan sampel analitik kategorik tidak berpasangan. Sampel yang digunakan dalam penelitian ini sebanyak 172 subjek.

Hasil: Pada analisis multivariat, setelah mengendalikan variabel pengganggu, PR yang disesuaikan penuh untuk kecemasan adalah 4,241 (CI 1,292–13,924) dengan nilai $p = 0,017$. Sementara itu, pada analisis multivariat, setelah mengendalikan variabel pengganggu, PR yang disesuaikan penuh untuk depresi adalah 3,276 (CI 1,033-10,387) dengan nilai $p = 0,044$.

Kesimpulan: Ada hubungan kecemasan dan depresi terhadap kualitas hidup pasien IBD berdasarkan IBDQ-9 setelah mengendalikan variabel pengganggu.

Kata kunci: IBD, ansietas, depresi, kualitas hidup

INTRODUCTION

Inflammatory Bowel Disease (IBD) is a chronic inflammatory disease that involves inflammation of the gastrointestinal tract and has both intestinal and extraintestinal symptoms. It includes disorders such as Ulcerative Colitis (UC), Crohn's Disease (CD), and Indeterminate Colitis, each causing significant gastrointestinal distress.⁸ While Crohn's Disease can affect any part of the gastrointestinal tract, Ulcerative Colitis primarily affects the colon but may extend to other digestive organs.¹ IBD is characterized by periods of acute exacerbation and remission, and its symptoms can significantly reduce patients' quality of life.²

Patients with IBD often face psychological challenges due to the chronic, recurring nature of the disease.³ This has been shown to put IBD patients at higher risk for developing mental health disorders, particularly anxiety and depression. Anxiety is characterized by persistent fear, worry, and discomfort, while depression involves sadness and a lack of interest in activities.^{4,5} Studies have shown that the prevalence of anxiety and depression in IBD patients is twice as high compared to the general population, significantly impacting their well-being.⁴

The association between IBD and mental health disorders is thought to be related to the brain-gut axis, which creates a two-way connection between the central nervous system and the gastrointestinal system.⁴ This means that abnormalities in one system, such as mental illness, can negatively affect the other, leading to a vicious cycle that exacerbates both physical and psychological symptoms.⁶ As a result, IBD patients with anxiety or depression often experience more frequent disease flare-ups, worse symptom management, and a higher incidence of complications.⁷

Despite ⁸ the significant impact of anxiety and depression on the lives of IBD patients, these mental health conditions are often underdiagnosed. ⁸ There is limited research on ² the relationship between anxiety, depression, and IBD in Indonesia, making this study particularly important. The research aims to investigate the association between anxiety, depression, and quality of life in IBD patients, highlighting the need for better recognition and treatment of mental health conditions in this population.

METHODS

The research design used was cross-sectional. This research was conducted using primary data through interviews with patients who had been diagnosed with Inflammatory Bowel Disease (IBD) and were undergoing outpatient treatment at the Gastroenterology Polyclinic at Cipto Mangunkusumo National Central General Hospital. It was conducted from 30 October - 11 December 2023.

The research sample is an accessible population that has passed the inclusion criteria: IBD patients who are undergoing outpatient treatment at Cipto Mangunkusumo National Central General Hospital, are in stable condition, namely patients with compos mentis awareness, good vital signs, and can complete ⁴ the Indonesian version of the HADS and IBDQ-9 questionnaires correctly and wholly, aged ≥ 18 years – 60 years, willing to be a respondent and fill out informed consent; and exclusion criteria: unwillingness, moderate/history of psychotic psychiatric disorders, moderate/history of other gastrointestinal disorders (IBS and gastrointestinal malignancies), moderate/history of other malignant disorders outside gastrointestinal malignancies, patients with organic disorders who are unable to complete the HADS and IBDQ-9 questionnaires completely and correctly caused by disturbances in vital signs. Sample calculations use unpaired numerical analytics. There were 172 subjects who met the inclusion criteria and were analyzed.

The research was conducted after passing an ethical review from the FKUI Ethics Committee with number KET-1228/UN2.F1/ETIK/PPM.00.02/2023. This research was also carried out after obtaining a research location permit signed by the Head of the RSCM Innovation and Intellectual Property Management Installation with number YR.02.01/D.IX.2.3/0229/2023

Materials and Equipment

Measurement of Anxiety and Depression

Anxiety and depression were measured using the Hospital Anxiety Depression Scale (HADS), which has been translated into Indonesian and validated. This questionnaire consists of 14 questions, which are divided into 2 subscales, namely HADS-A (anxiety) to assess anxiety in 7 questions and HADS-D (depression) to assess depression in 7 questions as well. Patients also ranked each statement on a 4-rating scale, from 0 (not at all) to 3 (very often). A higher value indicates a problem. Answers are totalled separately, namely assessments for anxiety and assessments for depression, with a minimum and maximum number of 0 and 21 for each scale. From the score results, it is classified if more than 16 is a severe case, 11-15 is a moderate case, 8-10 is a mild case, and less than 7 is not a case of anxiety or depression.^{9,10}

Quality of Life Measurement

Measuring the quality of life of IBD patients uses the Inflammatory Bowel Disease Questionnaire 9 (IBDQ-9), which has been translated into Indonesian and has been tested for reliability and validation. IBDQ-9 consists of nine questions containing abdominal complaints (cramps, bloating, nausea, and abdominal pain), frequency of pain, impact of pain on social life, and perception of feelings of joy.^{11,12}

Data analysis

All the data obtained was recorded in a table using Microsoft Excel software and then processed using the SPSS program on the computer. The basic and clinical characteristics of the research subjects will be presented in tabular form. Numerical data will be displayed in the median (inter-quartile range) if the data is not normally distributed. Categorical data will be displayed in proportion form. Statistical significance testing was carried out on each variable, with a p-value <0.05 considered significant. The data normality test was carried out using the Kolmogorov-Smirnov test. In assessing the relationship between anxiety and depression variables and the quality of life scores of IBD patients, a statistical test was carried out using the Mann-Whitney test ⁷ because the data was not normally distributed. The quality of life variable will be divided into 2 categories, namely good and bad, based on the results of the IBDQ-9 questionnaire. For multivariate analysis, logistic regression analysis is carried out, and for confounding variables, fully adjusted PR (CI 95%) will be displayed.

RESULTS

The population in this study amounted to 172 people, demographic and clinical characteristics are shown in Table 1.

Table 1. Characteristics of IBD Patients

Variable	N=172
IBD type, n (%)	
Crohn's Disease (CD)	88 (51,16)
Ulcerative Colitis (UC)	84 (48,84)
Severity Grade/ Disease Activity	
Remission	114 (66,28)
Mild	40 (23,25)
Moderate	18(10,47)
Gender, n (%)	
Male	66 (38,37)
Female	106 (61,63)
Age	
18 - 39 years	79 (45,93)
40 - 60 years	93 (54,07)
Education	
Elementary School	5 (2,91)
Junior High School	8 (4,65)
Senior High School	73 (42,44)
Diploma/ Bachelor/ Master/ Doctoral	86 (50,0)
Socioeconomic Status, n (%)	
Unemployed	94 (54,65)
Employed	78 (45,35)
Disease Duration	
0 – 5 years	151 (87,79)
6 – 10 years	13 (7,56)
11 – 15 years	6 (3,49)
>15 years	2 (1,16)
Routine IBD Medication	
Mesalazine	82 (47,67)
Sulfasalazine	77 (44,77)
Corticosteroid	15 (8,72)
Immunomodulator	9(5,23)
Laboratory, n (%)	
CRP, n (%) n=132	
Normal	110 (83,33)
Abnormal	22 (16,67)
ESR, n (%), n=128	
Normal	76 (59,38)

Abnormal	52 (40,63)
Variable	N=172
Comorbidity, n (%)	
No	24 (13,95)
Yes	148 (86,05)
Autoimmune	16 (9,30)
Extraintestinal IBD Manifestation	37 (21,51)
Diabetes Mellitus	7 (4,07)
Hypertension	29 (16,86)
Anemia	12 (6,98)
Liver Disease	10 (5,81)
Gastrointestinal Disease	120 (69,77)
Obesity	14 (8,14)
History of Post-Diagnosis IBD Surgery, n (%)	
No	124 (72,09)
Yes	48 (27,91)
Incision, excision and anastomosis of the intestine	26 (15,12)
Colon resection	6 (3,49)
Perianal and rectum surgery	12 (6,98)
Stoma (ileostomy and colostomy)	7 (4,07)
Smoking Status, n=170, n (%)	
Yes	21 (12,35)
No	149(87,65)
HADS Score	
Anxiety median (IQR)	7 (4-10)
Depression median (IQR)	4 (1,5-6)
IBDQ-9 Score	
Quality of Life, median (IQR)	60,68 (56,61-64,07)
Good	161 (93,6)
Bad	11 (6,4)

Table 1. (Continued)

IBD=inflammatory bowel disease; CD=crohn's disease; UC=ulcerative colitis; CRP= C-reactive protein; ESR= Erythrocyte sedimentation rate; HADS= Hospital Anxiety Depression Scale; IBDQ-9= Inflammatory Bowel Disease Questionnaire 9; IQR=interquartile range

Based on Table 1, the type of IBD disease is Crohn's Disease as much as 51.16% and Ulcerative Colitis as much as 48.84%. As many as 66.28% of IBD patients are in the remission phase. Most research subjects were female (61.63%), aged 40 to 60 years (54.07%), diploma/bachelor/master/doctoral education level (50.0%), and not working (54.65%). The majority of IBD patients have a disease duration of 0-5 years (87.79%). Mesalazine is the routine treatment most frequently used by research subjects, namely 47.67%. Most subjects showed CRP and ESR test results within normal limits, 83.33% and 59.38% respectively. Most of the research subjects had comorbidities as much as 86.05%, with gastrointestinal diseases (GERD, H. pylori infection, and cholelithiasis) as the most common comorbidities, reaching 69.77%. Most of the study subjects had no history of surgery related to IBD, reaching 72.09%. Meanwhile, the most common types of surgery related to IBD were incision, excision, and intestinal anastomosis at 15.12%. The majority of patients had non-smoking status (87.65%). The median anxiety score in research subjects was 7 (range 4 – 10), while the median depression score was 4 (range 1.5 – 6). The median quality of life score based on IBDQ-9 was 60.68 (range 56.61-64.07), with the majority of subjects having good quality of life, namely 93.6% of the total research subjects.

In this study, it was found that the prevalence of anxiety and depression was higher in Crohn's disease sufferers at 51.14% in anxiety (the majority was mild anxiety 21.91%) and 23.86% in depression (the majority was mild depression 17.89%) compared to ulcerative colitis. amounted to 34.52% for anxiety (mild and moderate anxiety values were the same at 16.18%) and 17.86% for depression (the majority were mild depression 13.40%).

Table 2. The Association of Anxiety, Depression on the Quality of Life of Inflammatory Bowel Disease (IBD) Patients based on IBDQ-9 and HADS

Variable	Quality of Life		P
	Good	Bad	
Anxiety, Median (IQR)	7 (4 – 10)	12 (7 – 13)	0,004
Depression, Median (IQR)	3 (1 – 6)	7 (4 – 8)	0,009

IQR=interquartile range

Based on Table 2, the analysis using the Mann-Whitney test revealed the association of anxiety, depression on the quality of life of IBD patients based on IBDQ-9 and HADS. The analysis results for anxiety showed a p-value = 0.004 ($p < 0.05$), and for depression, the p-value = 0.009 ($p < 0.05$). This indicates the association of anxiety, depression on the quality of life of IBD patients.

Table 3. The Association of Anxiety, Depression Categories on the Quality of Life of Inflammatory Bowel Disease (IBD) Patients based on IBDQ-9 and HADS

Variable	Quality of Life		PR (CI 95%)	p
	Good	Bad		
Anxiety				
Yes	66 (89,19)	8 (10,81)	3,531 (0,966 – 12,095)	0,056
No	95 (96,94)	3 (3,06)		
Depression				
Yes	31 (86,11)	5 (13,89)	3,148 (1,015 – 9,763)	0,047
No	130 (95,59)	6 (4,41)		

PR=prevalence ratio; CI=confidence interval

Based on Table 3, the results of the analysis using the Chi-Square test revealed that the association of depression on the quality of life of IBD patients is based on IBDQ-9 and HADS, with the analysis results for depression showing a p-value = 0.047 ($p < 0.05$).

However, there was no association of anxiety on the quality of life of IBD patients based on IBDQ-9 and HADS, with the analysis results for anxiety showing a p-value = 0.056. This illustrates the association of depression on the quality of life of IBD patients.

Table 4. The Association of Confounding Variables on the Quality of Life of Inflammatory Bowel Disease (IBD) Patients based on IBDQ-9

Variable	Quality of Life		p
	Good	Bad	
IBD Type			
Crohn's Disease (CD)	82 (93,18)	6 (6,82)	0,817
Ulcerative Colitis (UC)	79 (94,05)	5 (5,95)	
Severity Grade			
Remission	112 (98,25)	2 (1,75)	<0,0001
Mild	34 (85,0)	6 (15,0)	
Moderate	15 (83,33)	3 (16,67)	
Crohn's Disease (CD)			
Remission	71 (97,26)	2 (2,74)	0,001
Mild	7 (63,64)	4 (36,36)	
Moderate	4 (100,0)	0 (0,0)	
Ulcerative Colitis (UC)			
Remission	41 (100,0)	0 (0,0)	<0,0001
Mild	27 (93,10)	2 (6,90)	
Moderate	11 (78,57)	3 (21,43)	
Gender			
Male	61 (92,42)	5 (7,58)	0,619
Female	100 (94,34)	6 (5,66)	
Age			
18-39 years	73 (92,41)	6 (7,59)	0,557
7 40- 60 years	88 (94,62)	5 (5,38)	
Education			
Elementary School	4 (80,0)	1 (20,0)	0,621
Junior High School	7 (87,50)	1 (12,50)	
Senior High School	70 (95,89)	3 (4,11)	
Diploma/ Bachelor/ Master/ Doctoral	80 (93,02)	6 (6,98)	
Socioeconomic Status			
Unemployed	88 (93,62)	6 (6,38)	0,994
Employed	73 (93,59)	5 (6,41)	
Disease Duration			

Variable	Quality of Life		p
	Good	Bad	
0 – 5 years	143 (94,70)	8 (5,30)	0,064
6 – 10 years	11 (84,62)	2 (15,38)	
11 – 15 years	6 (100,0)	0 (0,0)	
>15 years	1 (50,0)	1 (50,0)	
Routine IBD Medication			0,467
Yes	154 (93,90)	10 (6,10)	
No	7 (87,50)	1 (12,50)	
Laboratory			1,000
CRP			
Normal	105 (95,45)	5 (4,55)	
Abnormal	21 (95,45)	1 (4,55)	
ESR			0,635
Normal	73 (96,05)	3 (3,95)	
Abnormal	49 (94,23)	3 (5,77)	
Comorbidity			0,032
Yes	141 (95,27)	7 (4,73)	
No	20 (8,33)	4 (16,67)	
History of Post-Diagnosis IBD Surgery			0,520
Yes	44 (91,67)	4 (8,33)	
No	117 (94,35)	7 (5,65)	
Smoking Status			<0,0001
Yes	21 (100,0)	0 (0,0)	
No	138 (92,62)	11 (7,38)	

IBD=inflammatory bowel disease; CD=crohn's disease; UC=ulcerative colitis; CRP= C-reactive protein; ESR= Erythrocyte sedimentation rate

Based on Table 4, it was found that the association of confounding variables on the quality of life of IBD patients was significant, namely the severity of IBD, $p = <0.0001$ ($p < 0.05$), smoking status, $p = <0.0001$ ($p < 0.05$), and comorbidities, $p = 0.032$ ($p < 0.05$).

For the multivariate analysis ¹ of anxiety, depression on the quality of life of IBD patients, based on Table 4 (The Association of Confounding Variables ² on the Quality of Life of Inflammatory Bowel Disease (IBD) Patients based on IBDQ-9), the confounding variables that have $p < 0.250$ are the degree of severity, smoking status, comorbidities and disease

duration, are entered one by one starting from the smallest p-value and then look at the change in delta PR, if >10% then it is proven to be a confounding variable.

Table 5. Multivariate Analysis of Anxiety on Quality of Life in Inflammatory Bowel

Disease (IBD) Patients

Variable	Crude PR (CI 95%)	p	Delta PR
Crude			
Anxiety	3,531 (0,966 – 12,905)	0,056	
Adjusted	Adjusted PR (CI 95%)		
+ Severity Grade	3,694 (1,052 – 12,969)	0,041	4,6
+ Smoking Status	3,407 (0,992 – 11,702)	0,052	7,7
+ Comorbidity	3,943 (1,413 – 11,005)	0,009	15,7
+ Disease Duration	4,241 (1,292 – 13,924)	0,017	7,5

1 PR=prevalence ratio; CI=confidence interval

Based on Table 4, it is proven that comorbid variables are confounding variables in anxiety on the quality of life of IBD patients because it has a delta PR change of >10%. Based on the results of the multivariate analysis, after controlling for confounding variables, the fully adjusted PR for anxiety was 4.241 (CI 1.292 – 13.924) with p-value = 0.017. From the results of the multivariate analysis above, it can be inferred that there is an association of anxiety on the quality of life of Inflammatory Bowel Disease (IBD) patients.

Table 6. Multivariate Analysis of Depression on the Quality of Life of Inflammatory Bowel Disease (IBD) Patients

Variable	Crude PR (CI 95%)	p	Delta PR
Crude			
Depression	3,148 (1,015 – 9,763)	0,047	
Adjusted	Adjusted PR (CI 95%)		
+ Severity Grade	2,404 (0,719 – 8,034)	0,154	23,6
+ Smoking Status	2,978 (0,962 – 9,318)	0,061	23,9
+ Comorbidity	2,882 (1,057 – 7,855)	0,039	3,2
+ Disease Duration	3,276 (1,033 – 10,387)	0,044	13,7

PR=prevalence ratio; CI=confidence interval

Based on Table 6, it is evident that the variables Severity of Disease, Smoking Status, and Disease Duration are confounding variables in depression towards the quality of life of IBD patients as they have a delta PR change >10%. ⁷ Based on the results of the multivariate analysis, after controlling with confounding variables, the fully adjusted PR depression is 3.276 (CI 1.033-10.387) with $p = 0.044$. From the multivariate analysis results above, it can be inferred that there is an association of depression on the quality of life of Inflammatory Bowel Disease (IBD) patients.

DISCUSSION

Characteristics of IBD Patients

In the research results, it was found that the most common types of IBD were Crohn's Disease with 51.16% and Ulcerative Colitis with 48.84%. This research data is in accordance with IBD prevalence data from RSUP Prof. Dr. R D Kandou in 2017-2018 in Manado, North Sulawesi, there was more Crohn's Disease (59.6%) than Ulcerative Colitis (40.4%).¹³ Research by Panara et al. in the United States in 2014 stated that 69% of research respondents were diagnosed ⁵ with Crohn's disease, while around 31% had Ulcerative Colitis.¹⁴ The increasing incidence of Crohn's Disease is related to the impact of industrialization and concomitant environmental and lifestyle changes.¹⁵

In this study, the majority of IBD patients experienced a remission phase, amounting to 66.28% of the total respondents. Research by Brink et al. in the Netherlands in 2018 stated that 75.4% of the total respondents experienced a remission phase.¹⁶ Research by Mitropoulo et al. in Greece in 2022 stated that 69.1% of the total respondents were in remission.¹⁷ Quality of life can be a factor for patients to achieve remission. This is in accordance with research conducted by Iglesias et al. and Van Der Have et al., which stated that improving the quality of life related to health can be achieved by reducing disease activity or achieving remission. However, there are still a large number of IBD patients who have a low quality of life even though they are in remission.^{18,19}

The research results showed ⁷ that the majority of respondents were female with 61.63% of the total respondents. This is in accordance with research by Navabi et al. in Pennsylvania, USA where the majority of respondents were women, with 59.4% of the total respondents.⁴ Research by Mitropoulou et al. in Greece, namely the number of female respondents was

66.2% of the total respondents.¹⁷ Research according to Rolston et al., found that many women had sensitive hormonal symptoms related to hormonal changes, which appeared as significant changes in IBD symptoms related to variations in hormonal fluctuations.²⁰

In the research results, it was found that the maximum age was 40-60 years as much as 54.07% of the total respondents. Research by Panara et al. in Florida, USA in 2014, stated that the average age of IBD patients was 43 years.¹⁴ Research by Rolston et al. in Los Angeles in 2018 stated that the average age of IBD patients was 43 years.²⁰ The aging process is associated with several physiological changes, including changes in the composition and function of the gut microbiota, namely dysbiosis associated with IBD.²¹

In this study, it was found that the characteristics of respondents who had a higher level of diploma/bachelor's/master's/doctoral education were 50.0% of the total respondents who experienced IBD, compared to other levels of education. The results of this research data are in accordance with research by Stroie et al. in Switzerland in 2022 which stated that the majority of patients had a high level of education, 49.5%.²² Research by McDermott et al. in Ireland in 2018 stated that most IBD patients had a high level of education, 53%.²³

In this study, it was found that the socioeconomic level of respondents was dominated by 54.65% of respondents who did not have a job. This research is in line with research by Zaltman et al. in 2021 in Brazil which found that 62.1% of research subjects were unemployed.²⁴ This can happen because, most IBD patients at work experience difficulties such as impaired concentration, having to work more slowly than usual, having to isolate themselves from colleagues, and delays in work production.²⁵ Apart from that, IBD patients also often complain of weakness and stress at work, making patients prioritize these complaints over work, thus indirectly affecting ⁵ the patient's quality of life.²⁶

Based on this research, the maximum duration of IBD disease is in the range of 0-5 years (87.79%). Research by Matos R et al. in Portugal in 2021 stated that the average duration of illness for IBD patients was around 164 months or around 5.5 years.²⁷ The disease duration is significantly shorter and usually tends to have symptoms of anxiety/depression. This may happen because ² patients with a longer illness duration have more time to adapt and implement coping mechanisms for the illness they suffer from.¹⁶

Based on the research results, it was found that the most frequently used routine IBD drug was mesalazine (47.67%). This is in line with research by Panara et al., which stated that as many as 52.6% of IBD patients received the routine medication mesalazine.¹⁴ Based on meta-analysis research by Coward et al. stated that high doses of mesalamine could be the main choice for maintaining the patient's remission phase compared to patients who are taking steroids in Crohn's Disease with moderate to severe severity.²⁸

From the research results, it was stated that the majority of patients had normal ESR values of 59.38% (76 patients) and normal CRP of 83.33% (110 patients). This is different from research by Yang et al. in Korea in 2015, which found 22% of patients with normal CRP laboratory results and 78% with abnormal results.²⁹ Research by Alper A et al. in America in 2017 found that 72% of patients had abnormal ESR and CRP values for Crohn's Disease and 48% for Ulcerative Colitis.³⁰ Elevated CRP levels help differentiate between active and inactive IBD. CRP levels <10 mg/l indicate a remission stage in IBD.³¹ In this study, it was found that 82.95% of the research subjects were mostly in the remission phase, so that in this study the ESR and CRP results for the majority of the research subjects had normal values.

Based on the research results, it was said that as many as 86.05% had comorbidities. The type of comorbidity that most patients had was gastrointestinal disease (GERD, H. Pylori

infection, and cholelithiasis) as much as 69.77%. Research by Vadstrup et al. in Denmark in 2020 stated that the most common comorbidities in Crohn's Disease and Ulcerative Colitis were gastrointestinal diseases at 15.5% and 8.7%.³² Research by Mitropoulou et al. in Greece in 2022 stated that as many as 85.3% of IBD patients had comorbidities.¹⁷ Based on research by Barrat et al. in England in 2011, it was stated that patients with Crohn's Disease were associated with impaired intestinal motility in the upper digestive tract and delayed gastric emptying.³³ The **cause of the increased prevalence of gallstones in patients with Crohn's Disease is** related to reduced bile acid absorption in individuals with extensive terminal ileal involvement or after ileal resection.³⁴ Absorption of bile acids in the terminal ileum and colon is an important component of enterohepatic circulation. This process can be disrupted during IBD.³⁵

Based on the research results, it was found that the majority of research subjects did not have a history of surgery after IBD diagnosis (72.09%), only 15.12% of patients had a history of surgery after IBD diagnosis in the form of incision, excision, and intestinal anastomosis. Research by Xin Gao et al. China in 2021 stated that as many as 65.7% of patients had no history of surgery after IBD.⁷ Research by Mitropoulo et al. stated that as many as 85.3% of patients had no history of surgery after IBD and as many as 13.2% of patients had a history of surgery after IBD.¹⁷ IBD-related surgery was defined as patients undergoing surgery for current or previous IBD-related strictures, fistulas, perforations, or cancer.⁷ Crohn's Disease patients with a history of surgery are reported to have more active disease compared with those who have not had surgery, with 45% suffering from IBD symptoms every week.³⁶ A history of appendectomy surgery causes anxiety and depression disorders. The appendix

plays a vital role in maintaining and regulating homeostasis in the intestinal microbiota, which increases immunity.³⁷

The results of this study showed that the majority of respondents had a history of not smoking, namely 87.65% of the total respondents (PC= 51.16%, KU= 48.84%, n= 172). Research by Cheng Chen et al. in Taiwan in 2022 stated that the number of ulcerative colitis patients who did not smoke was 79.1%. Meanwhile, 80.2%⁵ of Crohn's disease patients do not smoke.³⁸ Research by Abdallah et al. in Qatar in 2023 stated that the number of ulcerative colitis patients who had never smoked was 72.7%. Patients with Crohn's disease who never smoked were 79%.³⁹ The earliest described environmental factor consistently⁵ associated with Crohn's Disease was smoking. Active smokers have twice the⁵ risk of Crohn's disease compared to those who have never used tobacco products. On the other hand, active smokers are protected from the risk of Ulcerative Colitis. However, quitting smoking significantly increases the risk of Ulcerative Colitis. The mechanism by which smoking impacts IBD remains unclear. Likewise, the mechanism by which smoking provides protection⁵ in ulcerative colitis but adversely affects Crohn's Disease. One of the components of cigarette smoke that is thought to be responsible for this is nicotine, and animal clinical trials have found that administration of nicotine causes improvement in ulcerative colitis. Several studies show that the effects of smoking trigger oxidative stress.⁴⁰

In this study, the median anxiety score in research subjects was 7 (range 4 – 10), while the median depression score was 4 (range 1.5 – 6). This research is in accordance with Avinir's research, where the median anxiety score for IBD patients was 8 ± 8 and the depression score was 3 ± 5 .⁴¹ In research conducted by Navabi et al., it was found that 44% of IBD patients

had anxiety and depression scores that were the same. As many as 39.4% of patients had symptoms of anxiety and 25% of patients had symptoms of depression.⁴

In this study, the median quality of life score was 60.08 (with a range of 56.61-64.07), with the majority of subjects having a good quality of life, 93.6% (Table 1) of the total research subjects. Most of the patients in this study experienced an IBD remission phase of 98.25% (Table 4), this illustrates that the majority of IBD patients in the remission phase have a good quality of life. Based on research by Castillo et al. in Spain in 2013, the median IBDQ-9 score was 67.5 (with a range of 58-73.6) for the total respondents. The median IBDQ-9 score in remission patients was 68.5 (with a range of 60.98-73.6).⁴² Health-related quality of life in IBD patients is associationd by disease-related factors, psychosocial factors, and demographic factors, although controversial.^{43,44} In a study by Garcia et al., it was found that people with Crohn's disease and Ulcerative Colitis had the same quality of life scores, both had poor scores during acute exacerbations and good scores during remission.⁴⁵

2 **Prevalence of Anxiety and Depression in Inflammatory Bowel Disease (IBD) Patients Based on HADS**

Based on Figure 5.1 in this study, it was found that the prevalence of anxiety and depression was higher in people with Crohn's Disease at 51.14% and 23.86%. Meanwhile, Ulcerative Colitis was 34.52% for anxiety and 17.86% for depression. This is in accordance with research by Garcia-Alanis et al. in 2020, of 104 IBD sufferers, the prevalence of mental disorders was found to be around 56%. The most common mental illness is generalized anxiety disorder at around 44.2%, followed by mood disorders such as depression at 27.9%.⁴⁵

Based on research by Ali et al. in the United States in 2022, it is stated that Crohn's Disease

has a stronger relationship with anxiety compared to Ulcerative Colitis. This occurs because patients with Crohn's Disease have a longer hospital stay and higher inpatient costs compared to Ulcerative Colitis patients.⁴⁶

The Association ¹ of Anxiety, Depression on the Quality of Life of Inflammatory Bowel Disease (IBD) Patients based on IBDQ-9 and HADS

In this study, it was found that there was a relationship between anxiety and the quality of life of Inflammatory Bowel Disease (IBD) patients based on IBDQ-9 and HADS with a p-value = 0.004 ($p < 0.05$). In line with research by Yamamoto et al. in 2021 in Mexico, it was stated that there was an association of anxiety on the patient's quality of life ($p < 0.001$).⁴⁷ Apart from that, in this study, it was also found that there was an association of depression on the quality of life of Inflammatory Bowel Disease (IBD) patients based on IBDQ-9 and HADS with a p-value = 0.009 ($p < 0.05$). This is in line with research by Farbod et al. in Canada in 2021, which states that depression can reduce the quality of life of IBD patients ($p < 0.001$).⁴⁸

Research by Gao et al. China in 2021, stated that untreated anxiety and depression in IBD patients can worsen the course of the disease. In addition, IBD patients who had depressive symptoms tended to show ² lower quality of life scores than patients without depressive symptoms ($p < 0.0001$).⁷ In IBD with mental disorders, it will cause ² changes in the quality of life that are more disturbing for sufferers, such as the tendency to isolate themselves from social interactions, more difficult economic conditions due to more medication, as well as disturbances in the sufferer's self-adjustment or coping mechanisms which cause The

symptoms and course of IBD become increasingly uncontrolled and increase the risk of surgery.^{49,50}

The Association of Anxiety, Depression Categories on the Quality of Life of Inflammatory Bowel Disease (IBD) Patients based on IBDQ-9 and HADS

Based on the research findings, there was no categorical association of anxiety on the quality of life of IBD patients based on IBDQ-9 and HADS, as determined by the Chi-Square test. However, concerning the depression variable, a significant association on the quality of life of IBD patients was observed, as indicated by the Chi-Square test. In this study a p-value=0.047 ($p < 0.05$) was obtained, signifying a categorical association of depression on the quality of life of IBD patients based on IBDQ-9 and HADS.

This aligns with a study by Gao et al. in China in 2021, which stated that untreated depression in IBD patients can worsen the course of the disease. Additionally, IBD patients with depressive symptoms tend to exhibit lower quality of life scores compared to patients without depressive symptoms ($p < 0.0001$).⁷ Similarly, a study by Mitropoulou et al. in Greece in 2022 indicated that depression tends to result in decreased quality of life in emotional symptoms ($p < 0.001$).¹⁷ Another study by Farbod et al. in Canada in 2021 stated that depression can decrease the quality of life of IBD patients ($p < 0.001$).⁴⁸

IBD patients experiencing depression also encounter many disease-related complications, which naturally affect their productivity. Moreover, they require more treatments with various side effects. Patients with IBD and depression typically exhibit extraintestinal

manifestations of IBD and experience more severe symptoms.⁴ These factors undoubtedly lead to more disruptive changes in the quality of life for patients, such as a tendency to isolate themselves from social interactions, financial difficulties due to increased medication expenses, and disturbances in the adaptation or coping mechanisms of patients, leading to exacerbated symptoms and disease progression in IBD, ultimately increasing the risk of undergoing surgery.^{49,50}

The Association of Confounding Variables ² on the Quality of Life of Inflammatory Bowel Disease (IBD) patients based on IBDQ-9

In this study, confounding variables were found for the quality of life of IBD patients, namely the severity of IBD ($p = <0.0001$), smoking status ($p = <0.0001$), and comorbidities ($p = 0.032$).

In this study, it was found that the remission phase that had the most good quality of life was Ulcerative Colitis at 100%. Meanwhile, Crohn's Disease is 97.26%. In Garcia et al.'s research, it was found that people with Crohn's Disease and Ulcerative Colitis had the same quality of life scores, both had poor scores during acute exacerbations and good scores during remission.⁴⁵ More severe degrees of IBD disease are associated with lower quality of life. This is related to the use of health facilities as well as increased costs and disruption to daily work productivity.⁵¹

Comorbidities can cause a significant reduction in the physical component of quality of life. This is also reported in other IBD studies showing that IBD patients with extraintestinal manifestations experience a greater degree of limitation in their daily life due to greater symptom burden, high medication consumption, and decreased life satisfaction. Research by

Min Ho et al. in Singapore in 2019 stated that IBD patients with comorbidities had a low quality of life.⁵²

Research by Rezaei et al. shows that there is a negative relationship between nicotine dependence and quality of life and mental disorders.⁵³ Smoking is associated with higher costs of living and lower quality of life in IBD patients.⁵⁴ In addition, nicotine use can also affect several neurochemical systems, including the acetylcholine and catecholamine systems, which play a role in causing depression.⁵⁵

Multivariate Analysis¹ of Anxiety, Depression on Quality of Life in Inflammatory Bowel Disease Patients

In multivariate analysis, comorbid variables were confounding variables in anxiety and quality of life in IBD patients because they had delta PR changes >10%. Based on the results of the multivariate analysis, after controlling for confounding variables, the fully adjusted PR for anxiety was 4.241 (CI 1.292 – 13.924) with p-value = 0.017. From the results of the multivariate analysis above, it is clear that there is an association of anxiety on the quality of life of Inflammatory Bowel Disease (IBD) patients.

Research by Bahler et al. in Switzerland in 2017 showed that as many as 78% of IBD sufferers had at least one comorbid disease. IBD has been³ shown to be associated with various chronic comorbidities, with it being assumed³ that IBD shares pathogenic pathways with other immune-mediated inflammatory diseases. In line with this assumption, several studies have found an increased likelihood of immune-mediated disease in IBD patients. IBD is associated with a wide variety of extraintestinal manifestations. The reported frequency varies from 14% to 47% and accounts for the majority of comorbidities in IBD. Additionally, it has been shown

that IBD is ³ associated with an increased likelihood of mental disorders such as generalized anxiety, depression, and other mood disorders compared to the general population. Concomitant chronic comorbid conditions, especially ³ psychological disorders, have a strong negative impact on the quality of life in IBD patients.⁵⁶ Research by Garcia-Alanis et al. and Tomazoni El and Benvegno DM. said that anxiety affects the quality of life of patients with Crohn's Disease and Ulcerative Colitis based on IBDQ-32 ($p < 0.001$).^{57,58} Based on the results of this study, it was found that 86.05% of patients had comorbidities. The type of comorbidity that most patients had was Gastrointestinal Disease (GERD, H. Pylori Infection, and Cholelithiasis) as many as 120 patients (69.77%).

In this study, the variables severity grade, smoking status, and disease duration were confounding variables for ¹ depression on the quality of life of IBD patients because they had a delta PR change of $> 10\%$. Based on the results of the multivariate analysis, after controlling for all confounding variables, the fully adjusted PR for depression was 3.276 (CI 1.033 – 10.387) with $p\text{-value} = 0.044$. From the results of the multivariate analysis above, it is clear that there is an association of depression on the quality of life of Inflammatory Bowel Disease (IBD) patients.

Intestinal inflammation can affect the composition and function of the intestinal microbiota. The microbiota in the gastrointestinal system has the ability to produce neurotransmitters (γ -aminobutyric acid (GABA), noradrenaline, dopamine, and serotonin (5-hydroxytryptamine (5-HT))), amino acids (tyramine and tryptophan), and microbial metabolites (acid short-chain fats and 4-ethylphenylsulfate).⁵⁹ An imbalance in the gut microbiota due to when the disease is active will affect the brain-gut axis. As a result of inflammation in the intestine, it will result in the release of pro-inflammatory cytokines, which are triggered by psychological

stress, potentially causing changes in the gut microbiota axis in the brain and causing damage to the intestinal mucosa and microbiota. So these changes cause the number of neurotransmitters and neuromodulators to be unbalanced and can cause the development of mental disorders such as depression.⁶

In this study, based on the severity/activity of the disease, the majority of IBD patients experienced a remission phase, amounting to 66.28% of the total respondents. Improved quality of life can be achieved by reducing disease activity or achieving remission. However, there are still a large number of IBD patients who have a low quality of life even though they are in remission.^{60,61}

Smoking has a particularly strong association with ² symptoms of depression and anxiety because it is associated with mood-elevating effects associated with feelings of isolation and dissatisfaction with life.⁶² Nicotine use can increase the incidence of depression due to its effect on several neurochemical systems, including the acetylcholine and catecholamine systems which play a role in causing depression.⁵⁵ Research by Mitropoulo et al., states that the higher the level of depression, the lower their quality of life in terms of emotional function.¹⁷

This study shows that more patients who do not smoke, 87.65%, is associated with ² the prevalence of anxiety and depression in IBD patients in this study, illustrating that the prevalence of IBD patients with depression is lower than the prevalence of IBD patients with anxiety. Furthermore, related to quality of life in this study, the majority of patients had a good quality of life, amounting to 93.6%.

Research from Brink et al. in England in 2018, stated that the duration of the disease was significantly related to the presence of symptoms of anxiety and depression. It was found that

patients with a shorter duration of IBD had moderate to severe symptoms of anxiety and depression. This indicates ² that patients with a longer duration of IBD disease have had time to adapt and implement coping mechanisms.¹⁶ Disease duration can also be a predictor of quality of life. Patients with longer duration had a higher quality of life. Meanwhile, patients who have a shorter duration of IBD are more likely to experience symptoms of anxiety and depression, which means it certainly has an impact on the patient's quality of life. With a longer duration of illness, patients will appreciate and be able to have a more positive attitude towards their bodies.²⁷

Based on this research, it was found that the highest duration of IBD disease was in the range of 0-5 years (87.79%). However, more patients in this range did not experience depression, amounting to 77.48%. This is related to the results of research, which found that the majority of IBD patients in this study were in the remission phase, amounting to 66.28%. Furthermore, related to quality of life in this study, the majority of patients had a good quality of life amounting to 93.6%, because the majority of patients were in the remission phase.

CONCLUSION AND SUGGESTION

Conclusion

In this study, it was concluded that there was an association of ⁸anxiety and depression on the quality of life of IBD patients based on the Indonesian version of IBDQ-9 after controlling for confounding variables.

Suggestion

From the results of this study, early detection ²is needed to determine the presence of anxiety and depression in IBD patients; early detection of the quality of life of IBD patients using the Indonesian version of the IBDQ-9 questionnaire, and identification of risk factors, as an effort to prevent IBD complications; a holistic approach and management is carried out in IBD patients with anxiety and depression, where patients require multidisciplinary management involving professionals in their fields to control and manage anxiety and depression; control the severity/activity of the disease to maintain the remission phase and prevent repeated relapses by educating patients to increase patient compliance in taking medication and regular control, preparing guidelines regarding the management of IBD with anxiety and depression disorders; and the need to develop further research on IBD patients to obtain a comprehensive picture of the usefulness of ⁴the Indonesian version of IBDQ-9 by considering research design and population variations.

Acknowledgement

⁴
I would like to thank all the staff of the Department of Internal Medicine, especially the Divisions of Pancreatobiliary Gastroenterology and Gastrointestinal Endoscopy at the Faculty of Medicine, University of Indonesia and Cipto Mangunkusumo National Central General Hospital, for all their support in this study

REFERENCES

1. Pasternak G, Aebisher D, Filip R, Bartusik-Aebisher D. Inflammatory bowel disease: clinical aspects. *European Journal of Clinical and Experimental Medicine*. 2019;16(4):341–5.
2. Burisch J, Jess T, Martinato M, Lakatos PL. The burden of inflammatory bowel disease in Europe. *Journal of Crohn's and Colitis*. 2013;7(4):322-37.
3. Bannaga AS, Selinger CP. Inflammatory bowel disease and anxiety: Links, risks, and challenges faced. *Clinical and Experimental Gastroenterology*. 2015:111–7.
4. Navabi S, Gorrepati VS, Yadav S, Chintanaboina J, Maher S, Demuth P, et al. Influences and impact of Anxiety and Depression in the setting of inflammatory bowel disease. *Inflamm Bowel Dis*. 2018 Nov 1;24(11):2303–8.
5. World Health Organization (WHO). Depression and Other Common Mental Disorders Global Health Estimates. 2017.
6. Zhang B, Wang HHE, Bai YM, Tsai SJ, Su TP, Chen TJ, et al. Bidirectional association between inflammatory bowel disease and depression among patients and their unaffected siblings. *Journal of Gastroenterology and Hepatology*. 2022 Jul 1;37(7):1307–15.
7. Gao X, Tang Y, Lei N, Luo Y, Chen P, Liang C, et al. Symptoms of anxiety/depression is associated with more aggressive inflammatory bowel disease. *Sci Rep*. 2021 Dec 1;11(1).
8. Peppas S, Pansieri C, Piovani D, Danese S, Peyrin-Biroulet L, Tsantes AG, et al. The brain-gut axis: Psychological functioning and inflammatory bowel diseases. *Journal of Clinical Medicine*. 2021;10(3):1–22.

9. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. *Acta psychiatrica scandinavica*. 1983;67(6), 361-70.
10. Rudy M, Widyadharma IPE, Adnyana IMO. Reliability indonesian version of the hospital anxiety and depression scale (hads) of stroke patients in sanglah general hospital denpasar. *ResearchGate*. 2015;2:1-23.
11. Casellas F, Alcalá MJ, Prieto L, Miró JRA, Malagelada JR. Assessment of the Influence of Disease Activity on the Quality of Life of Patients with Inflammatory Bowel Disease Using a Short Questionnaire. *American Journal of Gastroenterology*. 2004 Mar;99(3):457–61.
12. Esa DF, Shatri H, Rumende CM, Susilo A, Maulahela H, Fauzi A, et al. Validity and reliability of the Indonesian version of the 9-item Inflammatory Bowel Disease Questionnaire (IBDQ-9). *Medical Journal of Indonesia*. 2023 Des 1;32(3):168–72.
13. Makmun D, Fauzi A, Maulahela H, Pribadi RR. *Konsensus Nasional Penatalaksanaan Inflammatory Bowel Disease (IBD) di Indonesia*. Jakarta: PIP Interna; 2019.
14. Panara AJ, Yarur AJ, Rieders B, Proksell S, Deshpande AR, Abreu MT, et al. The incidence and risk factors for developing depression after being diagnosed with inflammatory bowel disease: A cohort study. *Aliment Pharmacol Ther*. 2014;39(8):802–10.
15. Salgado VCL, Luiz RR, Boechat N, Schorr BC, Leão IS, Nunes T, et al. Crohn's disease environmental factors in the developing world: A case-control study in a statewide catchment area in Brazil. *World J Gastroenterol*. 2017 Aug 14;23(30):5549–56.
16. van den Brink G, Stapersma L, Vlug LE, Rizopolous D, Bodelier AG, van Wering H, et al. Clinical disease activity is associated with anxiety and depressive symptoms in

adolescents and young adults with inflammatory bowel disease. *Aliment Pharmacol Ther.* 2018 Aug 1;48(3):358–69.

17. Mitropoulou MA, Fradelos EC, Lee KY, Malli F, Tsaras K, Christodoulou NG, et al. Quality of Life in Patients With Inflammatory Bowel Disease: Importance of Psychological Symptoms. *Cureus.* 2022 Aug 28;14(8)
18. Van der Have M, van der Aalst KS, Kaptein AA, Leenders M, Siersema PD, Oldenburg B, et al. Determinants of health-related quality of life in Crohn's disease: A systematic review and meta-analysis. Vol. 8, *Journal of Crohn's and Colitis.* 2014. p. 93–106.
19. Iglesias M, Vázquez I, De Barreiro Acosta M, Figueiras A, Nieto L, Piñeiro M, et al. Calidad de vida en pacientes con enfermedad de Crohn en remisión. *Revista Espanola de Enfermedades Digestivas.* 2010;102(11):624–30.
20. Rolston VS, Boroujerdi L, Long MD, McGovern DPB, Chen W, Martin CF, et al. The Influence of Hormonal Fluctuation on Inflammatory Bowel Disease Symptom Severity - A Cross-Sectional Cohort Study. *Inflamm Bowel Dis.* 2018 Jan 18;24(2):387–93.
21. Nishida A, Inoue R, Inatomi O, Bamba S, Naito Y, Andoh A. Gut microbiota in the pathogenesis of inflammatory bowel disease. *Clinical Journal of Gastroenterology.* 2018;11(1):1–10.
22. Stroie T, Preda C, Meianu C, Croitoru A, Gheorghe L, Gheorghe C, et al. Health-Related Quality of Life in Patients with Inflammatory Bowel Disease in Clinical Remission: What Should We Look For? *Medicina (Lithuania).* 2022 Apr 1;58(4).
23. McDermott E, Healy G, Mullen G, Keegan D, Byrne K, Guerandel A, et al. Patient education in inflammatory bowel disease: A patient-centred, mixed methodology study. *J Crohns Colitis.* 2018 Apr 1;12(4):419–24.

24. Zaltman C, Parra RS, Sassaki LY, Santana GO, Ferrari MD, Miszputen SJ, et al. Real-world disease activity and sociodemographic, clinical and treatment characteristics of moderate-to-severe inflammatory bowel disease in Brazil. *World Journal of Gastroenterology*. 2021 Jan 1;27(2):208-23.
25. De Boer AGEM, Evertsz FB, Stokkers PC, Bockting CL, Sanderman R, Hommes DW, et al. Employment status, difficulties at work and quality of life in inflammatory bowel disease patients. *Eur J Gastroenterol Hepatol*. 2016;28(10):1130–6.
26. Le Berre C, Loy L, Lönnfors S, Avedano L, Piovani D. Patients' perspectives on smoking and inflammatory bowel disease: An online survey in collaboration with European Federation of Crohn's and Ulcerative Colitis Associations. *World J Gastroenterol*. 2020 Aug 7;26(29):4343–55.
27. Matos R, Lencastre L, Rocha V, Torres S, Vieira F, Barbosa MR, et al. Quality of life in patients with inflammatory bowel disease: the role of positive psychological factors. *Health Psychol Behav Med*. 2021;9(1):989–1005.
28. Coward S, Kuenzig ME, Hazlewood G, Clement F, McBrien K, Holmes R, et al. Comparative Effectiveness of Mesalamine, Sulfasalazine, Corticosteroids, and Budesonide for the Induction of Remission in Crohn's Disease: A Bayesian Network Meta-Analysis. *Inflamm Bowel Dis*. 2017;23(3):461–72.
29. Yang DH, Yang SK, Park SH, Lee HS, Boo SJ, Park JH, et al. Usefulness of C-reactive protein as a disease activity marker in Crohn's disease according to the location of disease. *Gut Liver*. 2015 Jan 1;9(1):80–6.

30. Alper A, Zhang L, Pashankar DS. Correlation of Erythrocyte Sedimentation Rate and C-Reactive Protein with Pediatric Inflammatory Bowel Disease Activity. *J Pediatr Gastroenterol Nutr.* 2017 Aug 1;65(2):e25–7.
31. Chen P, Zhou G, Lin J, Li L, Zeng Z, Chen M, et al. Serum Biomarkers for Inflammatory Bowel Disease. *Front Med (Lausanne).* 2020 Apr 22;7(23).
32. Vadstrup K, Alulis S, Borsi A, Jørgensen TR, Nielsen A, Munkholm P, et al. Extraintestinal Manifestations and Other Comorbidities in Ulcerative Colitis and Crohn Disease: A Danish Nationwide Registry Study 2003–2016. *Crohn's and Colitis* 360. 2020, 2(3):1–10.
33. Barratt SM, Leeds JS, Sanders DS. Quality of life in Coeliac Disease is determined by perceived degree of difficulty adhering to a gluten-free diet, not the level of dietary adherence ultimately achieved. *J Gastrointest Liver Dis [Internet].* 2011;20(3):241–5.
34. Scott C, Patel A, Maka N, MacDonald JC. Crohn's disease of the gallbladder. *BMJ Case Rep.* 2021 Sep 22;14(9):e243579.
35. Fitzpatrick LR, Jenabzadeh P. IBD and Bile Acid Absorption: Focus on Pre-clinical and Clinical Observations. *Front Physiol.* 2020 Jun 12;11.
36. Haapamäki J, Turunen U, Roine RP, Färkkilä MA, Arkkila PET. Impact of demographic factors, medication and symptoms on disease-specific quality of life in inflammatory bowel disease. *Quality of Life Research.* 2009;18(8):961–9.
37. Ekström LD, Ekström H, Dal H, Kosidou K, Gustafsson UO. Childhood appendectomy and adult mental disorders: A population-based cohort study. *Depress Anxiety.* 2020 Nov 1;37(11):1108–17.

38. Chen BC, Weng MT, Chang CH, Huang LY, Wei SC. Effect of smoking on the development and outcomes of inflammatory bowel disease in Taiwan: a hospital-based cohort study. *Sci Rep*. 2022 Dec 1;12(1).
39. Abdallah B, Arif M, Al-Malki M, Hourani R, Al-Maadeed T, Khodr N, et al. The Association Between Inflammatory Bowel Disease and Exposure to Tobacco Smoking: A Case-Control Study in Qatar. *Int J Gen Med*. 2023;16:233–42.
40. Ananthakrishnan AN. Environmental triggers for inflammatory bowel disease. *Curr Gastroenterol Rep*. 2013 Jan 1;15(1).
41. Avinir A, Dar S, Taler M, Taler M, Haj O, Gothelf D, Kopylov U, Horin SB, Domachevsky EM. Keeping it simple: mental health assessment in the Gastroenterology Departement - Using the Hospital Anxiety and Depression Scale (HADS) for IBD pastients in Israel. *Therapeutic Advances in Gastroenterology*. 2022;15:1-8
42. Castillo-Cejas MD, Robles V, Borruel N, Torrejón A, Navarro E, Peláez A, et al. Questionnaires for measuring fatigue and its impact on health perception in inflammatory bowel disease. *Revista Española de Enfermedades Digestivas*. 2013 Mar;105(3):144–53.
43. Bastida G, Herrera-de Guise C, Algaba A, Ber Nieto Y, Soares JM, Robles V, et al. Sucrosomial Iron Supplementation for the Treatment of Iron Deficiency Anemia in Inflammatory Bowel Disease Patients Refractory to Oral Iron Treatment. *Nutrients*. 2021 May 22;13(6):1770.
44. Zheng K, Zhang S, Wang C, Zhao W, Shen H. Health-Related Quality of Life in Chinese Patients with Mild and Moderately Active Ulcerative Colitis. *PLoS One*. 2015 Apr 27;10(4)

45. García-Alanís M, Quiroz-Casian L, Castañeda-González H, Arguelles-Castro P, Toapanta-Yanchapaxi L, Chiquete-Anaya E, et al. Prevalence of mental disorder and impact on quality of life in inflammatory bowel disease. *Gastroenterol Hepatol*. 2021 Mar 1;44(3):206–13.
46. Ali H, Pamarthy R, Bolick NL, Lambert K, Naseer M. Relation between inflammatory bowel disease, depression, and inpatient outcomes in the United States. *Bayl Univ Med Cent Proc*. 2022 May 4;35(3):278–83.
47. Yamamoto-Furusho JK, Bozada Gutiérrez KE, Sarmiento-Aguilar A, Fresán-Orellana A, Arguelles-Castro P, García-Alanís M. Depression and Anxiety Disorders Impact in the Quality of Life of Patients with Inflammatory Bowel Disease. *Psychiatry J*. 2021 Oct 27;2021:1–7.
48. Farbod Y, Popov J, Armstrong D, Halder S, Marshall JK, Tse F, et al. Reduction in Anxiety and Depression Scores Associated with Improvement in Quality of Life in Patients with Inflammatory Bowel Disease. *J Can Assoc Gastroenterol*. 2022 Feb 1;5(1):12–7.
49. Hu S, Chen Y, Chen Y, Wang C. Depression and Anxiety Disorders in Patients With Inflammatory Bowel Disease. Vol. 12, *Frontiers in Psychiatry*. Frontiers Media S.A.; 2021.
50. Park SC, Jeon YT. The mental health state of quiescent inflammatory bowel disease patients. *Gut and Liver*. 2016;10(3):330–1.
51. Slomp FM, Bara TS, Picharski GL, Cordeiro ML. Association of cigarette smoking with anxiety, depression, and suicidal ideation among Brazilian adolescents. *Neuropsychiatr Dis Treat*. 2019;15:2799–808.

52. Ho PYM, Hu W, Lee YY, Gao C, Tan YZ, Cheen HH, et al. Health-related quality of life of patients with inflammatory bowel disease in Singapore. *Intest Res*. 2019 Jan 1;17(1):107–18.
53. Rezaei S, Matin BK, Karyani AK, Woldemichael A, Khosravi F, Khosravipour M, Rezaeian S. Impact of Smoking on Health-Related Quality of Life : A General Population Survey in West Iran. *Asian Pacific Journal of Cancer Prevention*. 2017;18(11):3179-3185
54. Severs M, Mangen MJJ, van der Valk ME, Fidder HH, Dijkstra G, van der Have M, et al. Smoking is Associated with Higher Disease-related Costs and Lower Health-related Quality of Life in Inflammatory Bowel Disease. *J Crohns Colitis*. 2016 Sep 19;11(3):342–52
55. Flensburg-Madsen T, Bay Von Scholten M, Flachs EM, Mortensen EL, Prescott E, Tolstrup JS. Tobacco smoking as a risk factor for depression. A 26-year population-based follow-up study. *J Psychiatr Res*. 2011 Feb;45(2):143–9.
56. Bähler C, Schoepfer AM, Vavricka SR, Brüngger B, Reich O. Chronic comorbidities associated with inflammatory bowel disease: prevalence and impact on healthcare costs in Switzerland. *Eur J Gastroenterol Hepatol*. 2017;29(8):916–25
57. García-Alanis M, Toapanta-Yanchapaxi L, Reyes-Velásquez A, Mancilla F, Pérez-Mayo I, Yamamoto-Furusho JK. The interrelation between anxiety and quality of life among patients with ulcerative colitis in remission. *Gastroenterol Hepatol [Internet]*. 2023;46(10):747–53. Available from: <https://www.sciencedirect.com/science/article/pii/S0210570523000055>

58. Tomazoni EI, Benvegnú DM. Symptoms of anxiety and depression, and quality of life of patients with Crohn's disease. *Arq Gastroenterol*. 2018 Apr 1;55(2):148–53.
59. Morais LH, Schreiber IV HL, Mazmanian SK. The gut microbiota–brain axis in behaviour and brain disorders. *Nature Reviews Microbiology*. 2021; 19(4): 241-55
60. Van der Have M, van der Aalst KS, Kaptein AA, Leenders M, Siersema PD, Oldenburg B, et al. Determinants of health-related quality of life in Crohn's disease: A systematic review and meta-analysis. *Journal of Crohn's and Colitis*. 2014;8(2):93–106.
61. Iglesias M, Vázquez I, De Barreiro Acosta M, Figueiras A, Nieto L, Piñeiro M, et al. Calidad de vida en pacientes con enfermedad de Crohn en remisión. *Revista Española de Enfermedades Digestivas*. 2010;102(11):624–30.
62. Suls J, Green PA, Boyd CM. Multimorbidity: Implications and directions for health psychology and behavioral medicine. *Health Psychology*. 2019 Sep;38(9):772–82.

THE ASSOCIATION OF ANXIETY, DEPRESSION ON THE QUALITY OF LIFE OF INFLAMMATORY BOWEL DISEASE PATIENTS .docx

ORIGINALITY REPORT

7%

SIMILARITY INDEX

6%

INTERNET SOURCES

10%

PUBLICATIONS

3%

STUDENT PAPERS

PRIMARY SOURCES

1	Raiza Lima Silva, Francisca Isabelle da Silva e Sousa, Gabriel Lucas Ferreira da Silva, Victória Danielly Rabelo Almeida et al. "The impact of anxiety and depression on quality of life in a cohort of inflammatory bowel disease patients from Northeastern of Brazil", <i>Gastroenterología y Hepatología</i> , 2024 Publication	2%
2	repub.eur.nl Internet Source	1%
3	Caroline Bähler, Alain M. Schoepfer, Stephan R. Vavricka, Beat Brüngger, Oliver Reich. "Chronic comorbidities associated with inflammatory bowel disease", <i>European Journal of Gastroenterology & Hepatology</i> , 2017 Publication	1%
4	mji.ui.ac.id Internet Source	1%

5	Cosimo Prantera, Burton Korelitz. "Crohn's Disease", CRC Press, 2019 Publication	1 %
6	Arneil Sitepu, Bahagia Loebis, M. Surya Husada. "Correlation between Indonesian Version of Montreal Cognitive Assessment Score and Hospital Anxiety and Depression Scale Scores for Post-Stroke Patients", Open Access Macedonian Journal of Medical Sciences, 2022 Publication	1 %
7	perpustakaan.poltekkes-malang.ac.id Internet Source	1 %
8	Submitted to Australian Catholic University Student Paper	1 %

Exclude quotes Off

Exclude matches < 1%

Exclude bibliography On