

Factors Associated with Anxiety and Depression in Korean Patients with Inactive Inflammatory Bowel Disease

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See editorial on page 330.

Background/Aims: Psychological distress is highly prevalent in patients with inflammatory bowel disease (IBD). We evaluated the disease characteristics and socioeconomic factors associated with anxiety and depression in Korean patients with quiescent IBD. **Methods:** In total, 142 IBD patients (67 with Crohn's disease [CD] and 75 with ulcerative colitis [UC]) completed self-report questionnaires, including the Hospital Anxiety and Depression Score, the Modified Morisky Adherence Scale-8, the socioeconomic deprivation score, and the Crohn's and Colitis Knowledge Score questionnaires. **Results:** In the CD group, 30 patients (44%) were anxious, and 10 patients (15%) were depressed; in the UC group, 31 patients (41%) were anxious, and 18 patients (24%) were depressed. Using multivariate analysis, in the CD group, socioeconomic deprivation was associated with anxiety ($p=0.03$), whereas disease duration ($p=0.04$) and socioeconomic deprivation ($p=0.013$) were associated with depression. In the UC group, there was no significant independent predictor of anxiety and/or depression; however, low income tended to be associated with depression ($p=0.096$). **Conclusions:** Despite clinical remission, a significant number of IBD patients present with anxiety and depression. IBD patients in remission, particularly those who are socioeconomically deprived, should be provided with appropriate psychological support. (*Gut Liver* 2016;10:399-405)

Key Words: Inflammatory bowel diseases; Anxiety; Depression

INTRODUCTION

Inflammatory bowel disease (IBD), which is comprised of ulcerative colitis (UC) and Crohn's disease (CD), is an idiopathic disease with chronic or recurring immune response and inflammation of the gastrointestinal tract associated with various complications.¹⁻⁴ Intestinal inflammation in IBD can lead to many physical symptoms, such as abdominal pain and diarrhea, which have a direct negative impact on quality of life (QOL).^{5,6} Poorer health-related QOL is known to be associated with higher levels of anxiety and depression.⁷ Previous studies have reported that mood disorders, such as anxiety and depression, are more prevalent in patients with IBD compared to the general population.⁸⁻¹⁰ The prevalence of anxiety and depression in patients with IBD has been reported to be as high as 80% and 60%, respectively, during relapses,¹¹ and these conditions have also been estimated to occur in approximately 29% to 35% of patients during the disease remission state.^{12,13}

Several studies have reported that factors such as socioeconomic deprivation,¹⁴ treatment adherence¹⁴ and patient's knowledge score^{15,16} are related to anxiety and/or depression in patients with IBD. However, most studies on this topic have been conducted exclusively in Western countries. Although a recent study showed that mood disorders, such as anxiety and depression, are common in Korean patients with inactive IBD,¹⁷ no studies have yet investigated the factors associated with anxiety and depression in Korean patients with quiescent IBD.

Therefore, the aim of this study was to evaluate the prevalence of anxiety and depression and identify risk factors for these conditions in Korean patients with IBD during disease remission.

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MATERIALS AND METHODS

1. Subjects

From July 2013 to December 2013, patients with IBD who were regularly evaluated at Kangbuk Samsung Hospital, Seoul, Korea, were enrolled in this study. Diagnoses of CD and UC were confirmed by previously established international criteria based on clinical, endoscopic, histopathological, and radiological findings.¹⁸ Only patients in maintenance of clinical remission over 3 months were included. Clinical remission was defined as a Crohn's Disease Activity Index <150¹⁹ or a Mayo Score <3.²⁰ Patients with less than 6 months of follow-up time were excluded. Informed consent was obtained from each participant. The study protocol was approved by the Institutional Review Board of Kangbuk Samsung Hospital (number: 2013-01-116) and was conformed to the ethical guidelines of the 1975 Declaration of Helsinki.

2. Demographic and disease characteristics

Patient demographics and clinical information were obtained by reviewing administered questionnaires and electronic medical records. Sociodemographic variables were self-reported by patients and included age, gender, smoking use, body mass index (BMI), family history of IBD, educational level, employment status, income, marital status, and membership in the "IBD Society." All participants also completed questionnaires including the Hospital Anxiety and Depression Scores (HADS),²¹ Modified Morisky Adherence Scale-8 (MMAS-8),²² the Evaluation of Precarity and Inequalities in Health Examination Centers (EPICES) score,²³ and the Crohn's and Colitis Knowledge Score questionnaires.²⁴ We carried out a survey under identical environmental condition. In other words, all of enrolled patients were asked to fill the questionnaires in interview room by clinical research coordinator with direct face to face interview methods. Anxiety and depressive symptoms were evaluated based on the HADS,²¹ which is a self-administered scale consisting of 14 items split across anxiety and depression subscales (seven items for each subscale), each with a four-point ordinal response format giving maximum scores of 21. Higher scores correspond to more severe symptoms: HADS 8 to 10 suggests a possible anxiety disorder and/or depressive disorder and a score ≥ 11 suggests a probable disorder. We used a cutoff score of 8, which has been widely validated and detects anxiety and depressive disorders at an early stage.^{25,26} Treatment adherence was evaluated using the MMAS-8. The MMAS-8 is an eight-question survey and patients are classified as low adherers (<6 points), medium adherers (6 to 7 points), and high adherers (8 points).²² Socioeconomic deprivation, whether it is in working conditions, housing, or income, was assessed with the EPICES score developed in France. The EPICES score is generated from an 11-question survey consisting of marital status (one item), health insurance status (one item), economic status (three items), family support (three items),

and leisure activity (three items). The score divides patients into two subgroups: the less deprived with a score of 30.17 and the more deprived with a score of >30.17.²³ To assess the knowledge score, we used a certified and notarized Korean translation version of Crohn's and Colitis Knowledge Score, which provides a valuable index of overall knowledge. It is a psychometric test consisting of 24 multiple choice questions covering five objectives (eight questions related to general IBD knowledge, five to medication, four to anatomy, five to disease complications, and two related to diet).²⁴

3. Statistical analysis

Analyses were conducted with anxiety and depression as the primary dependent variables. Differences in the variables between the groups were examined with a chi-square test or the Fisher exact test. For comparisons of quantitative variables, a Student t-test was used and the results are presented as mean \pm standard deviation. We constructed multivariate logistic regression models to identify independent factors associated with anxiety and depression. Variables with $p < 0.2$ in univariate analysis were included in a multivariable logistic regression model. Reported p-values were two-tailed, and $p < 0.05$ was considered statistically significant. The statistical analyses were performed using PASW Statistics version 18.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

1. Baseline characteristics of the study population

A total of 142 patients with IBD (67 patients with CD and 75 patients with UC) were enrolled in this study. Sociodemographic and clinical characteristics of study population are shown in Table 1. The mean age at diagnosis was significantly younger in patients with CD than in patients with UC (32.9 vs 44.7, $p < 0.001$). Patients with CD had a higher rate of IBD-related admission, as well as higher use of azathioprine and infliximab than did patients with UC. In the CD group, 15 patients (22%) had stricturing disease and 12 (18%) had penetrating disease. In the UC group, 18 patients (24%) had left-sided disease and 15 (20%) had extensive disease.

In the CD group, 30 patients (44%) were anxious and 10 (15%) were depressed. In the UC group, 31 (41%) were anxious and 18 (24%) were depressed. There were no significant differences in income, education status, socioeconomic deprivation status, knowledge score, and adherence to treatment between the patients in the CD and UC groups.

2. Factors associated with anxiety and depression in CD

In the univariate analysis, socioeconomic deprivation (odds ratio [OR], 3.75; 95% confidence interval [CI], 1.25 to 11.17; $p = 0.018$) was associated with anxiety in patients with CD. Family history of IBD (OR, 4.37; 95% CI, 0.81 to 23.53; $p = 0.086$)

Table 1. Baseline Characteristics of the Study Population

Characteristic	CD (n=67)	UC (n=75)	p-value
Age at diagnosis, yr	32.9±10.7	44.7±11.6	<0.001
Male sex	48 (71.6)	48 (64.0)	0.331
Disease duration, yr	5.1±3.7	6.2±4.4	0.108
BMI, kg/m ²	21.7±2.1	22.7±2.4	0.011
Smoking use, current	29 (43.3)	34 (45.3)	0.806
Family history of IBD	8 (11.9)	7 (9.3)	0.614
Anxiety	30 (44.8)	31 (41.3)	0.679
Depression	10 (14.9)	18 (24.0)	0.175
Montreal classification of CD			
L1 (isolated ileal disease)	12 (17.9)	NA	NA
L2 (isolated colonic disease)	23 (34.3)	NA	NA
L3 (ileocolonic disease)	32 (47.8)	NA	NA
L4 (concomitant UGI disease)	12 (17.9)	NA	NA
P (concomitant perianal disease)	20 (29.9)	NA	NA
B1 (nonstricturing, nonpenetrating)	40 (59.7)	NA	NA
B2 (stricturing)	15 (22.4)	NA	NA
B3 (penetrating)	12 (17.9)	NA	NA
Montreal classification of UC			
E1 (ulcerative proctitis)	NA	42 (56.0)	NA
E2 (left-sided UC)	NA	18 (24.0)	NA
E3 (extensive UC)	NA	15 (20.0)	NA
IBD-related surgery*	5 (7.5)	2 (2.7)	0.188
IBD-related admission [†]	32 (47.8)	20 (26.7)	0.014
Medication			
5-Aminosalicylate	54 (80.6)	74 (98.7)	<0.001
Steroid	6 (9.0)	10 (13.3)	0.410
Azathioprine	34 (50.7)	17 (22.7)	<0.001
Infliximab	26 (38.8)	8 (10.7)	<0.001
Income, <3 million won	30 (44.8)	27 (36.0)	0.287
Education status, university graduation or high	63 (94.0)	68 (90.7)	0.454
Employment status, working	38 (56.7)	51 (68.0)	0.165
Married	24 (35.8)	53 (70.7)	<0.001
Membership of the "IBD Society"	12 (17.9)	19 (25.3)	0.285
Socioeconomic deprivation	21 (31.3)	19 (25.3)	0.427
Knowledge score	9.0±4.3	8.2±4.1	0.296
Adherence to treatment, low	32 (49.3)	36 (48.0)	0.881

Data are presented as mean±SD or number (%).

CD, Crohn's disease; UC, ulcerative colitis; BMI, body mass index; IBD, inflammatory bowel disease; NA, not applicable; UGI, upper gastrointestinal.

*Excluded anal fistula-related surgery; [†]Excluded infliximab-related admissions.

and low treatment adherence (OR, 2.20; 95% CI, 0.82 to 5.87; $p=0.116$) tended to be associated with anxiety; however, this association was not statistically significant. In a multivariate analysis that included the variables with $p<0.2$ from the univariate analysis, socioeconomic deprivation (OR, 3.95; 95% CI, 1.14 to 13.67; $p=0.03$) was identified as an independent factor associated with anxiety (Table 2). Multivariate analysis also

showed that disease duration (OR, 1.24; 95% CI, 1.01 to 1.53; $p=0.04$) and socioeconomic deprivation (OR, 8.22; 95% CI, 1.57 to 43.03; $p=0.013$) were associated with depression in patients with CD (Table 2).

3. Factors associated with anxiety and depression in UC

Among the various variables, we found no significant predic-

Table 2. Factors Associated with Anxiety and Depression in Crohn's Disease

Factor	Anxiety						Depression					
	Univariate analysis			Multivariate analysis			Univariate analysis			Multivariate analysis		
	OR	95% CI	P-value	OR	95% CI	P-value	OR	95% CI	P-value	OR	95% CI	P-value
Age at diagnosis	0.98	0.94–1.03	0.519	-	-	-	0.98	0.92–1.05	0.700	-	-	-
Male sex	0.86	0.29–2.50	0.788	-	-	-	4.15	0.48–35.31	0.192	2.88	0.30–27.17	0.356
Disease duration	1.09	0.95–1.25	0.181	1.12	0.96–1.31	0.146	1.18	0.99–1.41	0.056	1.24	1.01–1.53	0.040
BMI	1.04	0.83–1.30	0.692	-	-	-	0.80	0.54–1.19	0.284	-	-	-
Smoking use, current	0.47	0.17–1.28	0.141	0.38	0.11–1.22	0.105	1.37	0.35–5.28	0.643	-	-	-
Family history of IBD	4.37	0.81–23.53	0.086	4.17	0.60–28.78	0.148	2.12	0.36–12.41	0.403	-	-	-
Disease distribution												
Ileocolonic	1.50	0.57–3.95	0.412	-	-	-	1.78	0.45–7.02	0.405	-	-	-
UGI	0.55	0.15–2.07	0.383	-	-	-	0.46	0.05–4.06	0.488	-	-	-
Perianal disease	0.56	0.19–1.65	0.297	-	-	-	1.00	0.23–4.37	0.990	-	-	-
Disease behavior												
Strictureing or penetrating	0.72	0.21–2.50	0.611	-	-	-	0.41	0.04–3.62	0.427	-	-	-
IBD-related surgery*	1.94	0.30–12.46	0.483	-	-	-	1.47	0.14–14.72	0.742	-	-	-
IBD-related admission [†]	1.50	0.57–3.95	0.412	-	-	-	0.69	0.17–2.71	0.596	-	-	-
Medication												
5-Aminosalicyalte	1.37	0.40–4.76	0.611	-	-	-	0.49	0.10–2.25	0.365	-	-	-
Steroid	1.25	0.23–6.74	0.788	-	-	-	3.31	0.51–21.13	0.205	-	-	-
Azathioprine	0.45	0.17–1.21	0.116	0.34	0.11–1.11	0.075	0.96	0.25–3.70	0.959	-	-	-
Infliximab	0.84	0.31–2.28	0.746	-	-	-	1.06	0.26–4.18	0.933	-	-	-
Income, <3 million won	1.88	0.70–4.99	0.207	-	-	-	2.06	0.52–8.11	0.300	-	-	-
Education status, university graduation or high	1.11	0.42–2.93	0.831	-	-	-	1.25	0.32–4.94	0.742	-	-	-
Employment status, working	0.78	0.29–2.08	0.625	-	-	-	1.27	0.48–3.38	0.625	-	-	-
Married	1.38	0.50–3.78	0.521	-	-	-	1.38	0.50–3.78	0.521	-	-	-
Membership of the "IBD Society"	1.29	0.37–4.51	0.688	-	-	-	1.29	0.37–4.51	0.688	-	-	-
Socioeconomic deprivation	3.75	1.25–11.17	0.018	3.95	1.14–13.67	0.030	3.75	1.25–11.17	0.018	8.22	1.57–43.03	0.013
Knowledge score	1.06	0.94–1.18	0.316	-	-	-	1.06	0.94–1.18	0.316	-	-	-
Adherence to treatment, low	2.20	0.82–5.87	0.116	2.63	0.83–8.34	0.099	1.66	0.42–6.54	0.464	-	-	-

OR, odds ratio; CI, confidence interval; BMI, body mass index; IBD, inflammatory bowel disease; UGI, upper gastrointestinal.

*Excluded anal fistula-related surgery; [†]Excluded infliximab-related admissions.

tor of anxiety in patients with UC (Table 3). In the multivariate analysis, low income tended to be associated with depression (OR, 2.78; 95% CI, 0.83 to 9.32; $p=0.096$), although it was not statistically significant (Table 3).

DISCUSSION

This is the first study to investigate the predictive factors related to anxiety and depression in patients with inactive IBD in Korea using validated and detailed scores. Our study showed that in patients with CD, the factor associated with anxiety was socioeconomic deprivation and the factors associated with depression were related to disease duration and socioeconomic

deprivation. In patients with UC, there was no significant independent predictor of anxiety and depression, but, low income tended to be associated with depression.

In our study, a significant number of patients with IBD had anxiety (44% in CD, 41% in UC) or depressive symptoms (15% in CD, 24% in UC) despite clinical remission. Our results are similar to those of other studies that evaluated the prevalence of mood disorders in IBD patients (anxiety, 26% to 43%; depression, 15% to 89%).^{17,27,28} Although we could not directly compare our study group with healthy matched controls, we were able to indirectly identify that the prevalence of mood disorders in quiescent IBD patients was higher than that of general population (anxiety, 25% and depression, 8.4%).^{29,30} Our

Table 3. Factors Associated with Anxiety and Depression in Ulcerative Colitis

Factor	Anxiety			Depression					
	Univariate analysis			Univariate analysis			Multivariate analysis		
	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
Age at diagnosis	1.03	0.99–1.07	0.133	1.05	1.00–1.10	0.043	1.05	0.99–1.11	0.065
Male sex	1.32	0.50–3.47	0.571	1.16	0.38–3.56	0.787	-	-	-
Disease duration	1.05	0.94–1.16	0.337	1.03	0.91–1.15	0.612	-	-	-
BMI	0.98	0.81–1.18	0.847	1.16	0.93–1.43	0.173	1.05	0.81–1.35	0.698
Smoking use, current	1.54	0.61–3.88	0.360	0.95	0.32–2.76	0.931	-	-	-
Family history of IBD	1.07	0.22–5.16	0.931	1.30	0.23–7.35	0.767	-	-	-
Disease extent									
Extensive UC	1.83	0.58–5.74	0.295	1.19	0.32–4.34	0.787	-	-	-
IBD-related surgery*	1.43	0.08–23.82	0.802	3.29	0.19–55.51	0.408	-	-	-
IBD-related admission [†]	1.61	0.57–4.54	0.360	1.07	0.32–3.53	0.903	-	-	-
Medication									
5-Aminosalicyalte	0.89	0.23–3.43	0.866	1.01	0.32–3.06	0.994	-	-	-
Steroid	1.50	0.39–5.70	0.552	1.42	0.32–6.21	0.634	-	-	-
Azathioprine	1.35	0.45–4.01	0.586	1.44	0.42–4.84	0.554	-	-	-
Infliximab	0.43	0.08–2.32	0.331	2.08	0.44–9.72	0.352	-	-	-
Income, <3 million won	1.22	0.47–3.17	0.682	2.94	0.99–8.74	0.052	2.78	0.83–9.32	0.096
Education status, university graduation or high	0.61	0.23–1.55	0.299	0.46	0.15–1.36	0.164	0.82	0.23–2.85	0.758
Employment status, working	1.02	0.38–2.73	0.968	0.98	0.36–2.62	0.968	-	-	-
Married	1.02	0.37–2.81	0.960	1.02	0.37–2.81	0.962	-	-	-
Membership of the “IBD Society”	0.77	0.26–2.27	0.640	0.77	0.26–2.27	0.646	-	-	-
Socioeconomic deprivation	1.85	0.64–5.29	0.250	1.85	0.64–5.29	0.250	-	-	-
Knowledge score	1.03	0.92–1.15	0.540	1.03	0.92–1.15	0.540	-	-	-
Adherence to treatment, low	1.59	0.63–4.03	0.321	0.82	0.28–2.40	0.729	-	-	-

OR, odds ratio; CI, confidence interval; BMI, body mass index; IBD, inflammatory bowel disease; UC, ulcerative colitis.

*Excluded anal fistula-related surgery; [†]Excluded infliximab-related admissions.

results showed similar trends to those described by Kim *et al.*,¹⁷ who observed that Korean IBD patients in remission are likely to have higher rates of anxiety or depression compare with the general population.

Socioeconomic deprivation is known to as factor associated with high psychiatric morbidity, disability and mood disorder in many chronic diseases.^{31–33} In the present study, the factor associated with anxiety and depression in patients with CD was socioeconomic deprivation. Additionally, low income in patients with UC tended to be associated with depression. Similar to our results, a recent study conducted in France demonstrated that socioeconomic deprivation was an independent predictor of anxiety (OR, 1.99) and depression (OR, 4.5) in IBD patients.¹⁴ Other studies have reported that lower socioeconomic status is related to anxiety³⁴ and depression³⁵ in patients with CD. As observed in a previous study, psychiatric evaluation and treatment in IBD patients may be effective in improving health related QOL.³⁶ Our study suggests that the socioeconomic deprivation factor should be evaluated, even in IBD patients in remission,

and appropriate psychological support should be provided for particularly deprived patients.

The present study also identified disease duration (OR, 1.24) as a risk factor for depression in patients with CD. This association is in agreement with the finding that the longer a perianal CD patient suffers from the illness, the more likely the patient is to have depressive symptoms.³⁷ Consequently, attention should be paid to patients with long standing CD in order to provide adequate psychological support.

Previous studies have reported that steroid treatment was likely to increase psychiatric adverse effects,^{38,39} and that surgery history might be related to improving QOL in patients with CD⁴⁰ and decreasing anxiety in patients with IBD.¹⁴ Contrary to these results, our study revealed that steroid treatment and IBD-related surgery were not significantly associated with anxiety and depression. One of the reasons for this discrepancy may be the low proportion of IBD-related surgeries (7.5% in CD, 2.7% in UC) and steroid treatment (9.0% in CD, 13.3% in UC) in our study participants, due to the fact that our study included only

patients in clinical remission.

Previous studies have shown mixed results regarding the possible association of anxiety and depression with knowledge level. Similar to our result, several studies have reported that education does not cause anxiety in patients with IBD.^{15,16} On the other hand, some studies have reported that increased patient knowledge is associated with higher anxiety levels.^{41,42} Consequently, it is still controversial whether disease knowledge level affects anxiety in patients with IBD. Further studies will be needed to clarify these issues. The reasons for the discrepancies between studies may be attributed to differences in the sociodemographic and clinical characteristics of IBD depending upon the geographic area and ethnicity of the population.^{43,44}

Several studies conducted in Western countries found additional risk factors relating to anxiety and depression in patients with IBD which we did not examine. One cross-sectional study demonstrated that in patients with UC, anxiety was associated with perceived stress and a new diagnosis of IBD, while depression was associated with stress, inpatient status, and active disease. Furthermore, in patients with CD, anxiety was associated with stress and abdominal pain, while depression was associated with stress and increasing age.³⁴ Further studies will be needed to identify whether the factors discussed as above are consistently associated with Korean patients with quiescent IBD.

Our study has some limitations. First, the study subjects were recruited from a single university-based clinic, which could lead selection bias. Further large-scale, multicenter studies will be needed to provide reliable confirmation of the predictors for anxiety and/or depression. Second, we were unable to directly compare our study cohort with healthy matched controls. Third, we were unable to evaluate the correlation between disease activity and the level of anxiety/depression. Previous studies have reported that anxiety and depression were more frequent during flares or when patients had more severe disease.^{10,45,46} However, in order to more accurately evaluate the factors associated with anxiety and depression, we included only patients who were in clinical remission because disease activity *per se* may affect mood states.

In conclusion, a significant number of patients with IBD present with anxiety and/or depressive symptoms, despite being in clinical remission. In patients with CD, the risk factor associated with anxiety was socioeconomic deprivation, while the factors associated with depression were disease duration and socioeconomic deprivation. In patients with UC, low income tended to be associated with depression. We recommend that the socioeconomic deprivation factors be routinely evaluated in patients with IBD, including those IBD patients in remission, and that the appropriate psychological support should be provided for particularly deprived patients.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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