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DEPRESSION AND ANXIETY DISORDERS IN SURGICALLY MANAGED PATIENTS WITH INFLAMMATORY BOWEL DISEASE

By
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Abstract

Inflammatory bowel diseases are mainly treated medically, especially with the availability of biological agents, but surgery is recommended when medical treatment fails, as in ulcerative colitis, or when complications occur, as in Crohn's disease. Although IBD patients who underwent surgery had a better quality of life, they also had a higher risk of depression and anxiety than the general population. This study compared psychiatric morbidities regarding anxiety and depression in surgically managed IBD patients to non-surgically managed patients.

The anxiety and depression prevalence were determined in 105 IBD patients, including seven who underwent surgery, by performing a psychiatric interview using SCID I and assessing depression and anxiety severity using the Hamilton Depression Scale (HAM-D) and the Hamilton Anxiety Scale (HAM-A), respectively. Similarity in surgically and non-surgically managed IBD patients might be due to small number of surgical patients.

Keywords: Patients, IBD, Depression, Anxiety, HAM-D, HAM-A.

Introduction

Inflammatory bowel diseases are chronic inflammatory conditions with frequent remission on and exacerbation affecting the patient's quality of life in addition to increased morbidity and mortality in comparison with the normal population (Bewtra *et al*, 2013). UC is distinguished by continuous mucosal affection started from the anal verge to the more proximal colon, almost limited to colon and sometimes ileum or backwash ileitis (Ordás *et al*, 2012), whereas in CD, pathogenesis is transmural, encompassing the entire gastrointestinal tract, from the mouth to the anus. Because of its transmural nature fistulas, abscesses and strictures may complicate treatment (Ott and Schölmerich, 2013).

The inflammatory bowel diseases are treated medically especially with biological agents and anti-TNF are readily available (Guasch *et al*, 2020). However, the immunomodulatory drugs have decreased the necessity for surgery, 12% of CD patients and 6% of UC ones still undergone IBD-related surgery within one year of diagnosis (Vind *et al*, 2006). Surgery was recommended in failure of medical treatment as in ulcerative colitis or in complicated ones as in Crohn's disease (Guasch, *et al*, 2020). Although surgery improved the physical well-being, but still doing an ostomy changes the patient's life, particularly in UC ones who have restorative proctocolectomy and a temporary ostomy (Scardillo et al, 2016).

The CD patients require repeated surgery (intestinal resection) due to the recurrent disease nature and permanent stoma. But, in chronic active perianal disease or extensive colonic involvement, permanent stoma could influence the psychological well-being leading to depression and anxiety, or even suicidal atempts (Hwang and Yu, 2019).

Inflammatory bowel disease patients' experience more postoperative problems than those who have had other types of colon surgery, due to bad general condition, anemia, malnutrition, and immunosuppressant and anti-TNF

use just before surgery. This might led to poor wound healing, leakage, and anastomotic stricture (Li and Zhu, 2018).

A narrative review assessed the psychological impact of surgery on IBD patients and showed that although when compared with the general population, there was an improvement in life quality, yet also a greater incidence of depression and anxiety (Spinelli *et al,* 2014**)**.

The postoperative CD patients were more liable to depression because of their need for recurrent surgeries, but UC patients were more liable to anxiety because of the curative nature of surgery and worries of stoma still present (Zangenberg and El-Hussuna, 2017).

The study aimed to assess the evidence as to psychiatric morbidities in surgically managed IBD patients compared to non-surgically managed ones; to detect patient features linked to an increased risk of psychiatric diseases.

Patients and Methods

Ethical consideration: The study was done according to regulations of the Research Ethical Committee, Faculty of Medicine, Ain Shams University, with the approval number of FMASU R 107/2021 (26/4/2021). These regulations went with Helsinki guidelines (2008). Written informed consent for study acceptance was obtained collected from all patients after explaining the study aim and their freedom to with-drawn anytime.

Study design: The study was observational and cross-sectional. Seven IBD patients treated surgery were selected among 105 patients attended the IBD clinic of Ain Shams University Hospitals from October 2021 to the end of December 2021.

Eligibility criteria: 1- Disease duration of less than 3 years, 2- Patients with neither any history of other psychiatric disorders, nor any serious chronic conditions, such as chronic heart failure, chronic obstructive pulmonary disease, other immunological disorders, and cancer.

All patients who met the criteria were assessed by a consultant psychiatrist using the Arabic version of the structured clinical interview for DSM IV axis diagnosis (SCID I) for the presence of a major depressive disorder or generalized anxiety disorder. The Hamilton depression scale (HAM-D) and the Hamilton anxiety scale (HAM-A) were used to assess the severity of depression and anxiety in them (Hamilton, 1959; 1960).

The study focused on the prevalence of depression and anxiety in the surgically managed IBD patients and their relation to clinical characteristics, as well as a comparison of the depression and anxiety in surgically and non-surgically managed IBD patients.

Surgical intervention with general anesthesia was carried out using the suitable type of colectomy operations; total-colectomy, partial, hemi, or procto. This usually required other procedures to reattach the digestive system remaining portions and permit waste to leave body (Moletta *et al,* 2020)

Statistical analysis: Data were collected, coded, tabulated, and introduced to Pc using the statistical package of social sciences (SPSS 25). Continuous variables were expressed as mean or median, while binary variables were expressed as numbers and percentages. Paired samples were compared by either paired t-test; or Wilcoxon signed-rank test. Fisher's exact test examined the relationship between two qualitative variables. P-value <0.05 was considered significant.

Results

Clinical features: Among 105 IBD patients, seven had IBD-related surgeries, five females (54%) and two males (46%) and four were single (about 51%). Three of the seven surgically managed IBD patients had UC and four had Crohn's disease. Two patients received a combination of Adalimumab and azathioprine, three patients received Infliximab and azathioprine, and the last two neither received biological nor AZA therapy.

Depression and anxiety in surgically-managed IBD patients: Among them, four (57.1%) had depression and two (28.6%) had anxiety.

Depression and clinical features of surgically-managed IBD patients were without significant differences neither in ages nor in sexes, or marital status, or diagnosis, or even medical treatment outcome. Also, there was neither significant difference in ages of both groups with or without anxiety nor in sexes, or marital status, or diagnosis, or even medical treatment outcome. The majority of IBD-related surgeries didn't show significant difference in anxiety or depression prevalence rates. Nevertheless, the suicide attempts were not reported among the surgically managed IBD patients as compared to 15 ones (15.3%) of non-surgically managed who had suicidal thoughts and attempts.

Details were given in tables (1, 2, 3, 4, 5, 6, 7, 8 & 9) and figures (1, 2 & 3).

Table 1: Patients medical history and clinical characters

Type of surgery	Age	Sex	Marital status	Diagnosis	Severity score	Concomitant treatment
Total colectomy	48	Female	Single	Ulcerative colitis	10	Adalimumab & AZA
Total colectomy	35	Female	Married	Ulcerative colitis	5	No
Total colectomy	30	Female	Single	Ulcerative colitis	12	No
Right hemicolectomy	35	Male	Single	Crohn's	258	Adalimumab & AZA
Limited Right hemicolectomy	25	Female	Single	Crohn's	275	Infliximab & AZA
Limited Right hemicolectomy	32	Male	Married	Crohn's	163	Infliximab & AZA
Limited Right hemicolectomy	42	Female	Married	Crohn's	228	Infliximab & AZA

Table 2: Prevalence of depression and anxiety in surgically managed IBD patients:

Item	Depression		Anxiety	
	Yes	No	Yes	No
No.	4	3	2	5
%	57.1%	42.9%	28.6%	71.4%

Table 3: Correlation between depression and age in surgically managed IBD patients:

Item	No depression	Depression	t- test		
	Mean ±SD	Mean ±SD	t	P value	sig.
Age	34.0 ±8.5	36.3±8.1	-0.353	0.741	NS

Table 4: Correlation between depression and clinical characters of surgically managed IBD patients:

Variations		No depression		Depression		Fisher exact test	
		No.	%	No.	%	P value	Sig.
Sex	Female	2	50.0%	2	50.0%	1	NS
	Male	1	33.3%	2	66.7%		
Marital status	Single	1	25.0%	3	75.0%	0.486	NS
	Married	2	66.7%	1	33.3%		
IBD diagnosis	UC	1	33.3%	2	66.7%	1	NS
	Crohn's	2	50.0%	2	50.0%		
Azathioprine	No	1	50.0%	1	50.0%	1	NS
	Yes	2	40.0%	3	60.0%		
Biological Therapy	No	1	50.0%	1	50.0%	1	NS
	Yes	2	40.0%	3	60.0%		

Table 5: Correlation between anxiety and age in surgically managed IBD patients:

Item	No anxiety	Anxiety	t-test		
	Mean ±SD	Mean ±SD	t	P value	Sig.
Age	33.4±6.35	40.0±11.31	-1.04	0.347	NS

Table 6: Correlation between anxiety and clinical characters of surgically managed IBD patients:

Variations		No anxiety		Anxiety		Fisher exact test	
		No.	%	No.	%	P value	Sig.
Sex	Female	3	75.0%	1	25.0%	1	NS
	Male	2	66.7%	1	33.3%		
Marital status	Single	3	75.0%	1	25.0%	1	NS
	Married	2	66.7%	1	33.3%		
IBD	UC	2	66.7%	1	33.3%	1	NS
	Crohn's	3	75.0%	1	25.0%		
Azathioprine	No	2	100.0%	0	0.0%	1	NS
	Yes	3	60.0%	2	40.0%		
Biological Therapy	No	2	100.0%	0	0.0%	1	NS
	Yes	3	60.0%	2	40.0%		

Table 7: Prevalence of depression among surgically and non-surgically managed IBD patients:

Variations	No (N=46) %	Yes (N=59) %	OR (CI 95%)	Significance test	
				P value	Sig.
Non-surgically IBD patients	43 (93.48%)	55 (93.22%)	1.04 (0.22±4.91)	1.00(F)	NS
Surgically IBD patients	3 (6.52%)	4 (6.78%)			

(F) Monte-Carlo Fisher's exact test of significance.

Table 8: Prevalence of anxiety among surgical and non-surgical managed IBD patients:

Variations	No (N=66)	Yes (N=39)	OR (CI 95%)	Significance test	
	No. (%)	No. (%)		P value	Sig.
Non-surgical IBD patients	61 (92.42%)	37 (94.87%)	0.66 (0.12±3.57)	1.00(F)	NS
Surgical IBD patients	5 (7.58%)	2 (5.13%)			

(F) Monte-Carlo Fisher's exact test of significance.

Table 9: Suicidal attempts among surgical and non-surgical managed IBD patients:

Variations	No Suicidal attempts		Suicidal attempts	
	No.	%	No.	%
Surgically managed IBD pts	7	100%	0	0%
Non-surgically managed IBD pts	83	84.7%	15	15.3%

Discussion

Previous studies have shown that patients with inflammatory bowel disease (IBD) have an increased risk of anxiety and mood disorders as compared to the normal community ones (Kurina *et al,* 2001; Fuller-Thomson and Sulman, 2006). Walker *et al.* (2008) reported that the rates of depression and panic disorders were significantly more in the IBD patients than in matched community ones (27% versus 12% & 8% versus 4.7% respectively). Rates of anxiety and depressive disorders were higher in IBD patients as compared to patients with other chronic diseases, such as colorectal cancer and irritable bowel syndrome (Filipovic *et al,* 2007; Kunzendorf *et al,* 2007). Surgery proved to be important event in IBD patient lifetime (Zang enberg and El-Hussuna, 2017). IBD patients showed (56.2%) depression and (37.1%) anxiety (Askar *et al,* 2021). In the present study, about 20% of ulcerative colitis patients needed surgery, but Crohn's disease ones needed surgical intervention during life. This agreed with Carter *et al.* (2004).

Total proctocolectomy with ileoanal pouch anastomosis is an operation of choice for UC patients who required surgical intervention, as may cause a permanent cure. But, for CD pat ients, surgical intervention is not always a definitive cure. Intestinal resection is indicated for patients who develop severe complications such as intestinal obstruction, recurrent subacute intestinal obstructions and intra-abdominal abscesses. Most commonly, ileo-cecal resection and primary reanastomosis was done (Sica and Biancone, 2013). But in some cases, bowel resection and created ostomy that may be another factor increasing psychological burden over patients with UC or CD (Nahon *et al,* 2012). Although surgery may give some good effects for patients by improving general condition and decreasing frequency of bowel motions, but the ostomy is distressing making their lifestyle much more different than before (Scardillo *et al,* 2016). Thus, multiple studies were done anxiety and depression in IBD patients that experienced surgical management for their diseases, involving 4340 patients, and compared post-surgical IBD patients to those who had surgery for other diseases such as diverticulitis, inguinal hernia, and post-surgical IBD patients to non-operated IBD ones (Zangenberg and El-Hussuna, 2017).

In the present study, three patients had ulcerative colitis and four had Crohn's disease. Others estimated that 10-30% with UC and 38-70% with CD patients underwent surgery in the first 10 & 20 years, respectively (Cosnes *et al*, 2011; Solberg *et al,* 2007). Alexander *et al.* (2009) in USA reported that many surgeons preferred conservative management of stricturing CD than stricturoplasty to avoid high postoperative recurrences. They added that both number of strictures (NSX) and strictureplasties (NSXP) were associated with CD recurrence and may be used as prognostic indica-

tors for CD. Kim e*t al.* (2013) in Korea average age of surgically treated IBD patients' ranged from 30 to 48 years, and age was a risk factor in IBD patients with mood disorders, being 40 years or more was an indicator of poor life quality. They concluded that suitable management must be administered according to age of patients and presence of concomitant functional gastrointestinal disorders and mood disorders to improve their health-related quality of life. Esmat *et al.* (2014) in Egypt reported that some tertiary centers were evolved for treatment of IBD with precise patient registry. Gionchetti *et al*. (2017) in Italy reported that European guidelines considered that previous intestinal resection a risk factor for postoperative recurrence. Anyane-Yeboa *et al.* (2018) in USA reported that postoperative treatment with anti-TNF agents could reduce the risk of postoperative recurrence. Chen *et al.* (2019) in China reported that diagnostic age, disease behavior, preoperative use of anti-TNF and complication with perianal lesions were independent risk factors for postoperative recurrence in Crohn's disease.

Kamel *et al.* (2021) in Egypt reported that patient's age at diagnosis and at operation; ileal location of Crohn's disease can significantly predict postoperative recurrence. They added that the postoperative biological therapy significantly decreased the incidence of postoperative recurrence. Rowan *et al.* (2021) in Ireland mentioned that obesity is now considered an inflammatory state. They concluded that visceral adiposity increased in Crohn's disease with some evidence associated with more complex disease phenotypes. They added that also a signal that post-operative recurrence rates were affected by increasing mesenteric adiposity. But, there was a lack of data on UC patients and more high-quality studies are indicated to elucidate the relationship between visceral adiposity and IBD and the implications for patient outcomes.

Gu *et al.* (2022) in USA concluded that the visceral adipose tissue (VAT) volume was associated with anti-TNF treatment response in a non-dose dependent manner, and that the visceral:subcutaneous adipose tissue ratio (VFI) indicated the risk of surgery after anti-TNF initiation. If confirmed by prospective studies, VAT volumetrics were potentially useful biomarkers to inform IBD treatment decisions.

In the present study, females were more of surgically managed patients, 71% than males 29%. This agreed with Askar *et al.* (2021) who found that female sex was an increased risk of anxiety and more prone to depression in IBD ones. There were two females and two males, two CD cases and two UC ones. Before surgery, three on AZA as biological treatment. Another study among patients underwent IBD surgery had a higher 5-year postoperative risk of depression than those underwent diverticulitis or inguinal hernia surgery, with significant increase in risk of depression in CD patients treated surgically compared to those not surgically treated (Ananthakrishnan *et al*, 2013). Depression post-surgery measured (HADS-score $\geq$ 11) with prate of 4%-16% (Knowles *et al,* 2013). This controversy may be due to the fact that Crohn's disease patients were more likely to experience depression after stoma surgery than UC ones (Nordin *et al*, 2002). But, in the present results, both IBD types had equal ratios and chances of postoperative depression in 2 cases of each of CD & UC.

Abdul-Baki *et al.* (2007) in Lebanon reported that the psychosocial burden of IBD in was significant. Knowles *et al* (2013) in Australia assessed the psychological impact of surgery on patients with IBD. They found improvement in quality of life, but also increased risk of depression and anxiety in those patients compared with the general population. They concluded that in psychological interventions, to focus on identifying and working with illness perceptions was a must.

In the present study, average age of anxiety was 40 years old, only 2/7 surgically managed patients developed an anxiety disorder, comp-

ared to 37/98 medically managed ones. Also, the present study showed that most IBD-related surgeries didn't show any significant anxiety and depression disorders rates, as only one UC patient suffered from post-surgical anxiety and another one had CD. This disagreed with Zangenberg and El-Hussuna (2017), who reported that CD patients were highly depressed & UC ones had higher anxiety risk. They added that multiple surgeries in the CD versus curative nature of UC surgery, led to anxiety.

Conclusion

Surgery is considered an important event in the lifetime of an IBD patient. No differences were detected among surgically and non-surgically managed IBD patients, may probably due to a limited number of patients. IBD-related surgeries didn't significantly affect the rates of anxiety and depression disorders.

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Authors' declaration: They declared that there neither have conflict of interest nor received fund.

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Explanation of figures

Fig.1: Covering ileostomy after total proctocolectomy with pouchoanal anastomosis
Fig. 2: Multiple small intestinal strictures in patient with Crohn's disease
Fig. 3: Total proctocolectomy for UC after failure of medical treatment