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The Prevalence of Depression and Its Association with Prior Opioid Use Among Patients in an Outpatient IBD Program

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1. Abstract

1.1. Background: Depression is a common comorbidity in chronic medical conditions including inflammatory bowel disease (IBD) and is a major determinant of health-related quality of life (HR-QOL). IBD patients often also experience chronic pain, and hence this population has significant opioid use. The aim of this study is to determine the prevalence of depression in patients with IBD, and to study the relationship between depression in IBD patients and opioid use.

1.2. Methods: We performed a retrospective review of 792 patients in an IBD program at a tertiary academic center. Patients were defined as depressed if they had documented depression diagnosis by any clinical provider during time of study. Prior opioid exposure was also studied in this cohort of patients. Studied outcomes included the prevalence of depression among opioid tolerant patients, defined as patients with prolonged opioid use.

1.3. Results: The prevalence of depression among IBD patients at this tertiary academic center was 16% (95% CI: 13.8% - 19%). There is a statistically significant association between depression and opioid exposure with 80% of depressed patients and 65% of non-depressed patients having been prescribed opioids ($p < 0.006$).

1.4. Conclusion: About 1 in 6 IBD patients at this single tertiary academic center experienced depression at some point during their disease course. In this study, depressed patients were shown to be significantly more likely to have opioid exposure than non-depressed patients.

2. Summary

Depression is a common comorbidity in inflammatory bowel disease (IBD) and a major determinant of quality of life. Looking at 792 patients within one IBD center showed a statistically significant association between depression and opioid exposure within this patient cohort.

3. Introduction

Depression is the most common mental illness in the world with a lifetime prevalence of about 17%. An estimated 16 million people are afflicted by this disease in the United States [1, 2]. Depression is a common comorbidity of chronic illnesses including as diabetes, Chronic Obstructive Lung Disease (COPD), heart disease. It is also shown to have an increased prevalence in Inflammatory Bowel Disease (IBD), though the exact pathophysiological link still remains unclear [3].

It is estimated that 38% of patients with IBD will have depression at some point in their disease course [4]. It has been shown that there is an increased psychological morbidity in IBD, and that anxiety/depression can trigger IBD flares and worsen overall disease control [5, 6]. Studies have shown that patients with active IBD have higher rates of depression when compared to patients in remission [7]. In fact, the presence and severity of depression is a better predictor of health-related quality of life (HR-QOL) for IBD patients than dis-

ease activity. Patients have been shown to have improved QOL and disease activity scores with depression treatment [8].

There is an increasing cohort of patients in the primary care setting who present with opioid use/abuse, depression, and IBD [8, 9]. Up to 20% of IBD patients experience chronic abdominal pain despite control of their disease [8]. It has also been estimated that up to 13% of IBD patients are on chronic opioids [10]. Furthermore, patients with depression and chronic pain develop maladaptive coping mechanisms that can increase their risk for opioid use disorder [11]. Previous studies have shown that depression more prevalent in patients who use opioids than in the opioid naïve population [12, 13].

The aim of this study is to determine the prevalence of depression among patients in the Yale IBD program and to study the association between depression and opioid use within this population. We hypothesized that depression is more prevalent in the IBD population when compared to the general public, and that there is a significant association between opioid use and depression within this cohort of patients.

4. Methods

Data from Yale's IBD Program were obtained by the Joint Data Analytics Team (JDAT) at Yale University and Yale-New Haven Hospital via an automated data extraction using EPIC, an electronic medical record. The data extraction was performed by collecting all patients who had at least one outpatient clinical encounter at the Yale Digestive Diseases IBD Center from April 2011 to April 2015 and an ICD-9 code for either Ulcerative Colitis or Crohn's Disease. Total of 792 patients were studied within this cohort. Medication lists of these patients were queried for antidepressants (including SSRI, SNRIs, TCAs and MAOIs) or opioids (any medications that contained codeine, morphine, meperidine, oxycodone, hydrocodone, hydromorphone) between April 2011 and April 2015. A manual chart review of all patients was then performed. Patients were considered depressed if they had a diagnosis of documented depression in their clinical record by any provider either in the problem list or clinical notes. If there was documentation that they were using an antidepressant for other indications, such as chronic pain or peripheral neuropathy they were excluded from this study. A patient prescribed opioids for any condition, not just for IBD related pain, was considered to have prior opioid exposure.

The rate of depression with a 95% CI was calculated with GraphPad Prism (version 7.0a, GraphPad Software Inc, San Diego, CA) using the Clopper and Pearson exact test. The association between depression and opioids was calculated using the Fisher's exact test. The prevalence of depression in the general population came from a large survey of

mental illness conducted by the World Health Organization [1]. This study was exempt from formal IRB review after submission to the institutional Human Investigation Committee.

5. Results

792 patients were included in this study. 421 (53%) of patients were female and 605 (76%) were white/Caucasian. The average age was 44.5 years-old with a standard deviation of 15.9 (Table 1). 285 (36%) of patients had a diagnosis of Ulcerative Colitis while 507 (64%) had a diagnosis of Crohn's disease. The prevalence of depression among our center's IBD Program patients was 16% (95% CI: 13.8% - 19%). There was no statistically significant difference between the depression rate at our center and that of the general population without IBD's (17%).

67% (95% CI: 63% - 69.7%) of Yale's IBD patients had previously been prescribed opioids. Patients who are depressed were significantly more likely to have had opioid exposure than not (81% vs 19%, $p<0.0006$). Depressed patients were also statistically significantly more likely to have had opioid exposure than non-depressed patients (81% vs 65%, $p = 0.0001$) (Figure 1).

Table 1: Patient Characteristics

Total Patients		792 (100%)
Female n (%)		421 (53%)
Age mean (std dev)		44.5 (15.9)
Race n (%)		
	Caucasian	605 (76%)
	African American	81 (10%)
	Asian	20 (3%)
	Other	58 (7%)
	Refused	28 (4%)
IBD diagnosis n (%)		
	Ulcerative Colitis	285 (36%)
	Crohn's Disease	507 (64%)
Depression n (%)		128 (16%)
Opioid exposure n (%)		536 (68%)

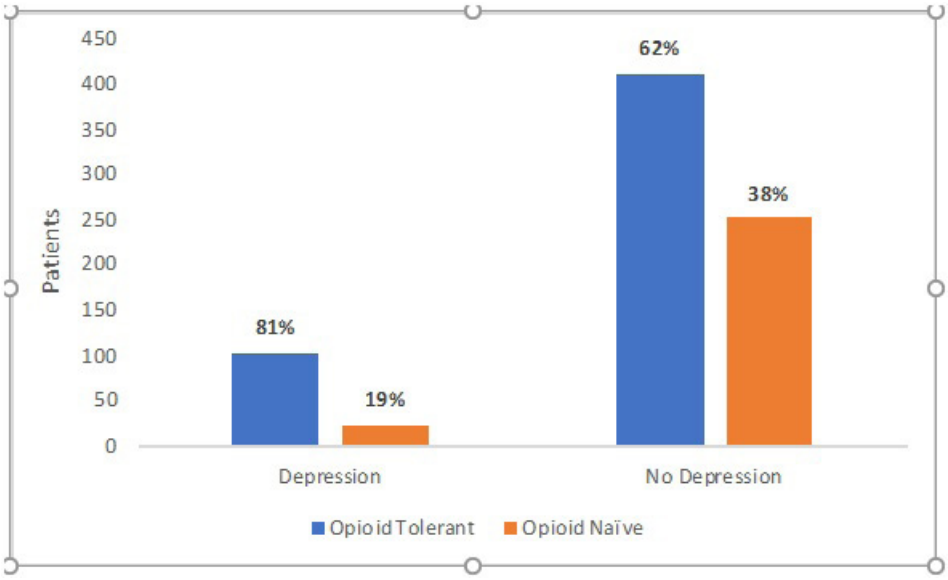

Figure 1: Title: Opioid Use Association with Depression.
Opioid exposure for patients with and without depression. Percentages represent the proportion of patients within that group with prior opioid use or opioid naïve. Total number of patients demonstrated on Y axis.

6. Discussion

The patients in this tertiary academic center IBD program had similar rates of depression when compared to the general non-IBD population. The majority of IBD patients (67%) within this center had also been prescribed opioids in the past. There is a statistically significant association between opioid use and depression among this cohort of patients. The prevalence of depression is almost twice as high in patients with prior opioid exposure when compared to opioid naïve patients. This study adds to the growing literature stating that depression is a cofactor associated with opioid use in chronic illnesses. Our study also highlights the high prevalence of opioid exposure (67%) within the IBD population, and the association between depression and opioid exposure within this disease.

The strengths of this study were its large sample size, follow-up time, and utility of objective measures for opioid usage. The limitations of our study include the retrospective observational study design that relied on accurate documentation to determine the prevalence of depression and opioid use. It is unclear what proportion of opioid prescriptions were short-term vs. chronic prescriptions. The limited data set also prevented evaluating for additional patient characteristics confounders such as other psychiatric disorders, prior IBD surgeries, and severity of IBD disease. Furthermore, all patients were from a single tertiary center study which limits the generalizability of our findings. Despite these limitations, our study does demonstrate the significant comorbid relationship of opioid exposure and depression in patients with IBD.

There are several areas open for future investigation. The role of pharmacological treatment of depression in IBD and its effect on HR-QOL should be further explored. Additionally, the effect of opioid usage on the HR-QOL should be further studied since they are largely prescribed to patients to improve HR-QOL.

In conclusion, the prevalence of depression was similar in the Yale IBD program when compared to the general population within the United States. There is a significant association between depression and opioid use within the IBD patient, which should caution the physician regarding chronic opioid use within this patient population.

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