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Online Survey of Important Symptoms, Side Manifestations, and the Use of Biological Treatments in Patients of Inflammatory Bowel Disease

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Abstract

Crohn's disease (CD) and ulcerative colitis (UC), are two chronic and relapsing conditions that cause inflammation of the gastrointestinal system, examples of inflammatory bowel diseases (IBDs). Online surveys may offer a valuable shared space for IBD patients to seek and provide information about their symptoms, extraintestinal manifestations, and management ways. We amid to acquire knowledge about IBD by using social media to encounter the disease and prevent delays in diagnosis which has been linked to poor input. A survey was conducted for patients with IBD, internet-based questionnaires by using Google Forms targeted members of patients who accessed the internet in March and April 2023. A total of 333 patients with IBD, 160 CD, and 173 UC accessed the survey. The respondents of females with IBD was higher than males (53.45% versus 46.54%). In addition, the two subtypes (CD and UC) had a greater impact on younger ages, especially the groups between thirty and fifty years old, causing many disturbing symptoms, the common one was diarrhea and blood with stool, but constipation may sometimes occur, especially in CD patients with 20%. These diseases cause many extraintestinal manifestations such as arthritis and eye infections. 60% of patients used biological treatment as an effective management and the majority of them agreed that the disease is not inheritable but may occur among members of the same family. Furthermore, there is a delay in diagnosis that may reach more than one year. IBD patients showed an interest in using social networks to assist in their education. The use was more common in younger women patients, this information can help clinical populations, promote health self-management, and ultimately improve health outcomes.

Keywords: Internet survey, IBD, Symptoms, Extraintestinal symptoms, Biological treatments

أستطلاع الكتروني لأهم الاعراض والاعراض الجانبية وأهمية العلاج البايلوجي عند مرضى التهاب الامعاء

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الخلاصة

مرض كرون (CD) والتهاب القولون التقرحي(UC) ، أمثلة على أمراض الأمعاء الالتهابية(IBDs) وهما حالتان مرضيتان مزمنتان تسببان التهاب الجهاز الهضمي، أن أجراء استطلاع الكتروني يوفر مساحة قيمة يشارك من خلالها مرضى التهاب الأمعاء معلومات حول أهم ألاعراض التي يعانون منها وألاعراض المرضية خارج معوية وطرق السيطرة عليها من خلال استعمال العلاج المناسب. أن الهدف من هذا الاستطلاع هو العمل على اكتساب المعرفة حول مرض التهاب الأمعاء (IBD) من خلال استخدام وسائل التواصل الاجتماعي لمنع التأخير في التشخيص والذي يرتبط بضعف المعلومات المتوفرة . تم إجراء دراسة استقصائية الكترونية للمرضى الذين يعانون من مرض التهاب الأمعاء (IBD)، باستخدام نماذج Google للاستبيان التي استهدفت أعضاء من المرضى الذين استخدموا وسائل التواضل الاجتماعي خلال شهري مارس وأبريل 2022.وكان عدد الاشخاص الذين دخلوا إلى

الاستطلاع ما مجموعه 333 مريضًا يعانون من التهاب امعاء مزمن ، (160 مرضى كرونز، و173التهاب قولون تقرح.). وكانت نسبة الإناث المصابات بهذا المرض أعلى من الذكور (53.45% مقابل 46.54%). بالإضافة إلى ذلك، فإن كلا المرضين (CD و UC)كان لهما تأثير كبير على الأعمار الشابة، خاصة الفئات التي تتراوح أعمارهم بين الثلاثين ووالخمسين عامًا، مسببا العديد من الأعراض المرضية اهمها الإسهال مع او بدون دم ، ولكن قد يحدث الإمساك في بعض الأحيان، وخاصة في مرضى كرونز بنسبة 20%. هذه الامراض تسبب العديد من الاعراض الخارج معوية مثل التهاب المفاصل واصابات العيون. وقد لوحظ ان 60% من المرضى قد استعملوا العلاج البايلوجي كعلاج فعال للسيطرة على المرض وان اكثر المشاركين قد ايدوا ان المرض غير وراثي لكن قد يحدث بين اعضاء الاسرة الواحدة كذلك فان هناك تأخيرا في تشخيص المرض قد يصل الى اكثر من سنه. من هذه النتائج نستدل على ان مرضى التهاب القولون لديهم اهتمام كبير في استعمال وسائل التواصل الاحتماعي للحصول على معرفة اكثر حول المرض وان اكثر المشاركين من النساء الشابات حيث ان مشاركة هذه المعلومات بين المرضى لها دور في تعزيز الصحة الذاتية وتطوير المعلومات الصحية.

1. Introduction

Internet provides a mechanism for conducting survey research in a timely and effective manner and the traditional methods are becoming more difficult to use [1]. There is a growing interest in using social media to manage chronic diseases [2]. The benefits include lower costs, greater number of participants, faster study completion time, and fewer facilities than conventional methods, nearly half of all IBD patients are already searching the internet for information about their disease [3].

There are many studies about using internet surveys in IBD management such as a survey by Coulson [4]**.** found that 249 IBD patients, shared their online support community life experience, including reasons for joining, patterns of use, and how involvement has impacted their disease experience. Frohlich *et al*. [5]. investigated online communities to understand how IBD patients use social media to develop their meanings of chronic illness living. Becker *et al*.[6] demonstrated that respondents with IBD expressed a strong desire to learn more about disease progression, particularly extraintestinal manifestations through a survey of 281 IBD patients and 32 family members**.**

Both UC and CD diseases are chronic IBDs that cause digestive problems and inflammation. The reason for their occurrence is still unknown. The prevalence of CD and UC can be attributed to a variety of factors, such as geographical location, poor diet, genetics, and an ineffective immune response. Both diseases are more common in cities than in rural areas, and each has its own set of difficulties and side effects. Given the prevalence of this disease at younger ages and the fact that it disrupts half of the patient's life, it will become a major health issue shortly, even in developing countries [7].

IBD has a significant impact on daily life, such as work, education, and social relationships. [8]. With high-frequency social media users, nearly one-third of patients thought social media could be useful in the management of their IBD. The majority of patients wanted to get IBD-related information from their gastroenterologist via social media. The primary limitations to social media use were privacy and confidentiality issues and some patients were suspicious of the value of IBD information available online [2].

2. Methods

2.1 Study design and study population

A cross-sectional study was conducted for individuals living with IBD in many countries. The survey content was developed for groups in an Internet application (Facebook).
The research was carried out between March and April 2022. The electronic survey was in Arabic language, uploaded online. A proposed questionnaire is as follows:

The questioner paper	6. Delayed in diagnosis
1. **Type of IBD disease** ○ Crohn disease ○ Ulcerative colitis	less than six months ○ more than six months ○ 1-2 years
2. Gender ○ male ○ female	**7. Taking the biological treatment** yes no
3. Age ○ 1-10 ○ 11-20 ○ 21-30 ○ 31-40 ○ 41-50 ○ 51-60 ○ 61-70	**8. smoking** yes no **9. sport** yes no 10. weight ○ **If there is another member in the family with the same symptoms** ○ yes no
4. Symptoms of disease ○ diarrhea ○ constipation ○ blood with stool ○ nausea	
5. Extraintestinal symptoms ○ arthritis ○ eye infection ○ liver infection ○ skin infection ○ fistula	

2.2 Statistical analysis

Data analysis was performed using SPSS version 26. The Chi-square test was used to compare between different groups. P- A value less than or equal to 0.05 is considered statistically significant for all analyses**.**

3. Results

3.1 Sex distribution of IBD respondents

There were 333 respondents in the survey Table 1. The majority were female at percentage 53.45% while males at 46.54%. P- value <0.05 there was a significant statistical relationship between sex and the type of disease.

Table 1- gender distribution of inflammatory bowel disease (IBD) respondents

Gender	Crohn's disease	Ulcerative colitis	Total
Males	65 (19.51%)	90 (27.02%)	155(46.54%)
Females	95 (28.52%)	83 (24.92%)	178(53.45%)
total	160 (48.03%)	173 (51.94%)	333(100%)
p-value	0.037		

3.2 Age distribution in patients with IBD respondents

Table 2 shows that high prevalence of disease in the young ages especially in the age groups (31-40) and (41-50) years old.

Table 2- Age distribution in IBD patients

Ages(years)	CD	UC	Total
1-10	6 (1.80%)	4(1.20%)	10(3.00%)
11-20	25 (7.50%)	19(5.71%)	44(13.21%)
21-30	34 (10.22%)	37 (11.11%)	71(21.32%)
31-40	42(12.61%)	40 (12.01%)	82(24.63%)
41-50	38(11.41%)	39 (11.71%)	77(23.12%)
51-60	12(3.60%)	20(6.01%)	32(9.61%)
61-70	3(0.90%)	14(4.20%)	17(5.11%)
Total	160(48.04%)	173(51.95%)	333(100%)
p-value	0.123		

3.3 symptoms in patients with IBD:

when we look at Figure 1 we notice that diarrhea was the most common symptom in both CD and UC respectively. 40% of UC respondents had blood with stool while constipation may occur especially in Crohn's patients with 20%.

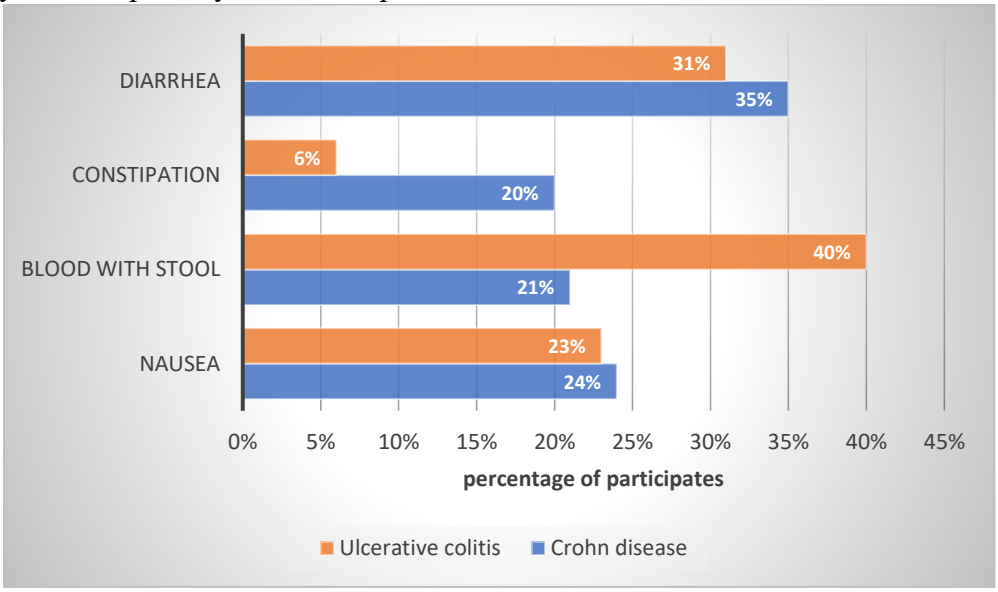

Figure -1 The important symptoms of IBD patients' respondents

3.4 The extra-intestinal manifestations

In Figure 2 arthritis was the common extraintestinal in UC and CD, the second manifestation was an eye infection, in which fistula was the third common symptom.

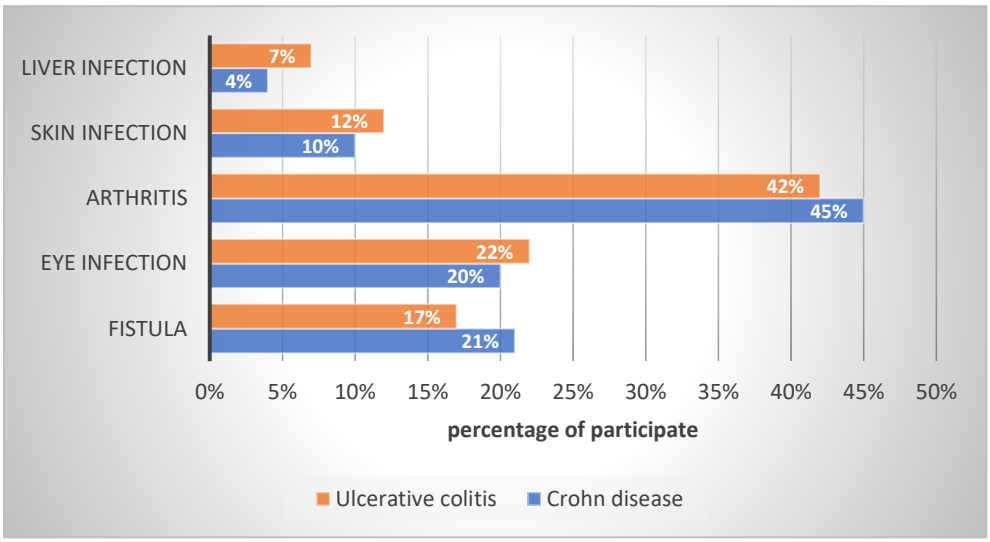

Figure -2 The important extra-intestinal symptoms in IBD patients

3.5 The delayed diagnosis

We can see in Table 3 that there was a delay in diagnosis of the disease for more than 6 months and may be reached for more than one year. There was a significant relationship between the type of disease and the delay in diagnosis P-value < 0.05, this delay was clear in Crohn's disease more than in ulcerative

Table 3- The delay in diagnosis of the disease

The delay in diagnosis	Crohn's disease	Ulcerative colitis	Total
Diagnosed less than 6 months	50(15.02%)	80(24.02%)	130(39.04 %)
Diagnosed more than 6 months	79(23.72%)	65(19.52%)	144(43.24%)
Diagnosed in 1 -2 years	31(9.31%)	28(8.41%)	59(17.72%)
total	160(48.05%)	173(51.95%)	333(100%)
p-value		0.019	

3.6 The effect of biological treatment

In Figure 3 there were 60% of respondents took biological treatments whereas 40% did not.

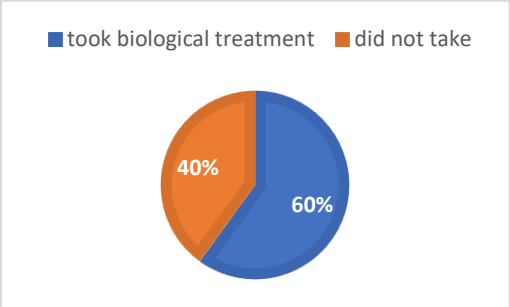

Figure- 3 the percentage of patients that took biologic treatment

3.7 The influence of some environmental factors:

Sport, smoking, and weight did not affect the occurrence or progression of the disease. There was no genetic transmission from parents to their children but 20% of participants have the same symptoms between the members of their family.

4. Discussion

Patients with IBD expressed strong attention to the use of social media to help them with the management of the disease. Because these chronic conditions are frequently self-managed [9]. The use was more common among younger patients, and females, especially with active disease. The number of women with IBD is usually greater than men whether in the on line participants or reality according to many studies. In a global internet survey for gastrointestinal disorders, women are more respondents [10]. An internet survey in Saudi Arabia shows a high percentage of respondents females in both CD and UC [11]. A study by Brant and Nguyen [12]. showed that gender distribution in Crohn's disease or ulcerative colitis is affected by the disease subtype, females have a higher prevalence. The data from Betteridge *et al*.,[13]. where females are more prevalent than males (417 versus 284 per 100,000) In general, the etiology of observed sex disparities in IBD is multifactorial and complex.

It was reported that sex differences in IBD have been identified for epidemiology, illness presentation, disease course, and complications [14]. There are two possible reasons for this result which are attributed to genetic susceptibility, hormonal differences, or both. Genetic susceptibility to IBD is linked to the X chromosome [15]. Many loci on the X chromosome are related to IBD such as *CD40LG- ARHGEF6* locus [16].

In an animal model, the loss of one allele of the X-linked gene that encodes for a chaperon, involved in the sex-specific risk of CD and UC was found only in female mice [17]. Estrogens, on the other hand, hormone is known to influence the pathology and course of IBD [18]. There are Multiple studies, including a meta-analysis by Cornish *et al*. [19]. found that females who use oral contraceptives have a higher incidence of both CD and UC.

This disease affects people of all ages. According to this study, most respondents in young ages. IBD is more common in younger people and disrupts half of the patient's life [7] An internet survey by Meeralam *et al*. [20]. came by this study which found that high prevalence of people with IBD aged between 31 and 40.

It was reported that CD tends to affect patients slightly earlier in life, at an average age of 15 to 25, whereas UC is more likely to set in between 25 and 35 years of age [21].

Genetic susceptibility and change in lifestyle with more dependence on fast food and lack of movement in young people and children may be among the important factors that affect the composition of the microbiome and lead to intestinal problems [22]. Compared with younger IBD patients, genetics contribute less to the pathogenesis of older-onset IBD, with dysbiosis and dysregulation of the immune system playing a significant role in the development of IBD. These results came following a study from 9 European countries which showed that CD hospitalization was age-distributed, with a large peak in younger patients followed by a small peak in older patients while a small peak in younger patients was followed by a large peak in older patients for UC hospitalization [23].

Another study from Iraq reported that the mean age for UC patients was 46.36 years old in the elderly stage (> 45 years of age) making the highest proportion of UC patients [24]. Similar age distribution has been reported in Asia, where the median age of diagnosis in patients with CD and UC was 34 and 42 years, respectively [25].

The symptoms of inflammatory bowel disease vary depending on the severity of the inflammation and where it occurs. The severity of the symptoms can range from mild to severe. Periods of active illness are followed by periods of remission. Diarrhea, fatigue, abdominal pain and cramping, Blood in stool, reduced appetite, and Unintended weight loss

are all signs and symptoms of Crohn's disease and ulcerative colitis. We also note that among the other most common symptoms is blood with the stool, especially in ulcer patients [26]. A survey by ALOtaibi [11] found that diarrhea and blood with stool in UC patients are the most common symptoms with 63.3% and 33.3% respectively. However, the differential diagnosis between CD and UC patients depending on clinical symptoms alone is difficult because the two subtypes are similar in most symptoms. Therefore, clinicians should also consider besides symptoms and laboratory tests, pathological, radiological, and endoscopic findings [27].

Extraintestinal manifestation most frequently affects joints, skin, and eyes, and can also less frequently involve other organs such as the liver, lungs, and pancreas [28]. According to a Swiss IBD cohort research, 25% of individuals with IBD had several EIMs, (in some cases up to five separate EIMs) and these disorders can arise before the diagnosis of IBD in 25.8% of cases [29]. There are many mechanisms by which gut microbiota drive the pathogenesis of EIMs such as the translocation of luminal bacteria across a leaky intestinal barrier which disrupts immune responses at extraintestinal locations due to common epitopes, or by soluble microbial-derived factors, e.g. Lipopolysaccharide (LPS), may be released into the circulation and promote inflammation at extraintestinal sites, or through the microbiota-derived metabolites, e.g. from the metabolism of bile acids or the generation of short-chain fatty acids, both of which could alter immune signaling [30].

A study by Mendoza *et al*., [31]. which came consistent with this study indicated that the most common EIMs is arthritis which was 51.5% in UC and 42.2% in CD. EIMs have a direct relationship with the activity of bowel diseases, the most common types include pauciarticular arthritis, oral aphthous ulcers, erythema nodosum, and episcleritis [32]. Cutaneous disorders may precede or occur at the same time, or follow a diagnosis of IBD; they occur in 22–75 % of CD and 5–11 % of UC patients. The visual system, in another hand, is one of the most frequently affected in IBD patients, and Crohn himself described the first case of ocular involvement in IBD patients [33]. The prevalence of ocular manifestations varies from 0.3 % to 13 % in IBD patients, and it is more frequent in CD patients than in UC patients [33]. Fistulae represent an important complication in patients suffering from IBD and about one-third of CD patients suffer from fistulae formation. Fistulae originate from an epithelial defect due to destructive inflammation. Tan *et al*., [34]. showed that fistulas are common in CD and less in UC in which this result is similar to this study.

It is important to differentiate between extraintestinal manifestations and complications of IBD, the latest ones include iron-deficiency anemia and osteoporosis are consequences of disease-specific treatment and intestinal obstruction. However, extraintestinal manifestations and complications strongly influence the quality of life of IBD patients [35].

Biologic therapies are widely regarded as the most significant therapeutic advance in the treatment of inflammatory bowel disease (IBD) to date, allowing for highly specific treatments directed at molecules shown to play critical roles in disease pathogenesis, with advantages in potency and selectivity[36]. An across-sectional study of IBD patients in Arabic countries found that 41% of patients received biological treatments [37].

In our study, 60 % of participants took biologic therapy this percentage will increase in the future because of its availability and low cost.

Between 2010 and 2016, the proportion of people starting biologics increased from 17% to 33% for CD and from 7% to 13% for UC.[38]. A delay in diagnosis was linked to poor

outcomes, such as an increased risk of intestinal surgery in patients with CD and UC.[39]. Because symptoms were not specific or consistent over time, and diagnostic study findings overlapped with those of other diseases such as tuberculosis and connective tissue disease, the diagnosis is frequently established after a significant delay[40].

Indeed, in the Swiss IBD cohort study, the median duration of the diagnostic delay period in CD patients was 24 months compared to 12 months for UC [40]. A diagnostic delay was associated with poor clinical outcomes in patients with CD, such as an increased risk of bowel stenosis, fistula, abscess formation, and intestinal surgery [41].

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