An-Najah National University

Faculty of Graduate Studies

EVALUATION OF INFLAMMATORY BOWEL DISEASE SEVERITY, TREATMENT AND OUTCOMES AMONG PALESTINIAN PATIENTS

By

Aya Basem Naser

Supervisor

Prof. Rowa Al Ramahi

This Thesis is Submitted in Partial Fulfillment of the Requirements for the Degree of Master of Pharmacology, Faculty of Graduate Studies, An-Najah National University, Nablus - Palestine.

2024

EVALUATION OF INFLAMMATORY BOWEL DISEASE SEVERITY, TREATMENT AND OUTCOMES AMONG PALESTINIAN PATIENTS

By

Aya Basem Naser

This Thesis was Defended Successfully on 01/02/2024 and approved by

Prof. Rowa' Al Ramahi	
Supervisor	Signature
Prof. Maher Khdour	
External Examiner	Signature
Dr. Suhaib Hattab	
Internal Examiner	Signature

Dedication

I dedicate this work to my husband, who did not stop in his unlimited support, which was always the mentor for me. I am very lucky to have someone like you in my life who supports me.

To my mother and father, it has always been their dream for me to obtain a master's degree, so they were by my side throughout my journey.

To everyone who played a role in supporting me morally.

And to my esteemed doctor, Professor Rowa' Al-Ramahi, who cooperated with me and supported me.

Finally, to my young son Saed, for whom I am trying to create a better future through my development.

Acknowledgments

I would like to thank God Almighty, first and foremost, for the great blessing bestowed upon me.

I appreciate my parents for their trust and support throughout the journey of knowledge. They had the greatest role in my arrival here.

In addition, I appreciate my husband's family for standing with me.

Special thanks to Prof. Rowa Al Ramahi for her efforts in completing my master's thesis.

I also would to express my gratitude to Dr. Qusay Abdo, for his help and cooperation with me in obtaining information to fill out the questionnaires.

My deepest appreciation to An-Najah National University for giving me access to the resources and what I needed to complete the mission and achieve my objectives.

Finally, I would like to thank my husband, my friends, and to everyone else I did not mention.

Declaration

I, the undersigned, declare that I submitted the thesis entitled:

EVALUATION OF INFLAMMATORY BOWEL DISEASE SEVERITY, TREATMENT AND OUTCOMES AMONG PALESTINIAN PATIENTS

I declare that the work provided in this thesis, unless otherwise referenced, is the researcher's own work, and has not been submitted elsewhere for any other degree or qualification.

Student's Name: Aya Basim Naser

Signature: 

Date: 1/2/2024

List of Contents

List of Tables

List of Figures

List of Appendices

EVALUATION OF INFLAMMATORY BOWEL DISEASE SEVERITY, TREATMENT AND OUTCOMES AMONG PALESTINIAN PATIENTS

By

Aya Basem Naser

Supervisor

Prof. Rowa Al Ramahi

Abstract

Background: Inflammatory bowel disease (IBD) is considered a chronic disease, and it has become more widespread recently. Studies related to it in Palestine are limited. The objectives of this study are to evaluate the severity of the disease, its treatment, and its outcomes among Palestinian patients with inflammatory bowel disease to improve its treatment and follow up.

Method: This cross-sectional study was conducted from August 2022 to March 2023 at An-Najah National University Hospital, Nablus, Palestine. A data collection form was used to collect data from patients' files and interviews, it was designed to assess IBD severity, treatment, and outcome. The results were analyzed using the Statistical Package for the Social Sciences (SPSS).

Result: This study included 219 patients 53.4% of them were males and 46.6% were females, the duration of illness 1-38 years, the age ranged between 6-86 years. we found that 47.9% patients suffered from ulcerative colitis and 52.1% from Crohn's disease, regarding severity of the disease which was based on clinical and diagnostic characteristics, patients were diagnosed with mild in 26% cases, while 45.2% had moderate, and 28.8% were diagnosed with severe. Moreover, the most common symptoms were bloody diarrhea 63%. Regarding medications, mesalamine was the most common medication used as a primary medication in patients with IBD, at a rate of 74%. for current medications, mesalamine was used by 46.6%, corticosteroid by 22.8%, azathioprine by 41.1%, and biological therapy by 35.2%.

Conclusion: Many patients have severe stages of the disease which affects their daily life. this study shows number of significant associated factors that should be considered when dealing with IBD. Results of the study may help healthcare providers and strategy

makers to increase knowledge about IBD patients and its treatment, to improve the quality of life of the IBD patient.

Keywords: Inflammatory Bowel disease; treatment; severity; symptoms; factors; AGA; Palestine.

Chapter One

Introduction

1.1 background

The term "inflammatory bowel disease" (IBD) refers to two disorders: Ulcerative colitis (UC) and Crohn's disease (CD), both of which are characterized by chronic gastrointestinal (GI) tract inflammation. Long-lasting inflammation causes GI tract damage(1). CD often affects the ileum and a part of the large intestine. It may affect any part of the GI including the mouth, esophagus, stomach, small intestine, rectum, and anus. UC is found mostly in some parts of the large intestine including the colon and rectum, the small intestine functions normally whereas the large intestine gets inflamed in UC. While CD affects all layers of the intestinal walls, ulcerative colitis mainly affects the innermost region of the colon (2).

Ulcerative colitis is divided into several types based on its spread in the colon, the first of which is Extensive Colitis, or by another name, Pancolitis, which spreads throughout the entire colon from the anus until beyond the splenic flexure, and there is also the second, Left-Sided Colitis, which is spreads from the anus to the splenic flexure, and proctosigmoiditis is considered one of them, as it includes the right part at the top of the anus (Sigmoid) with the anus itself together, and the third is Ulcerative Proctitis, which is limited to less than six inches of the anus, and it is worth noting that here Ulcerative Proctitis is not associated with an increased risk of cancer (3).

However, there are five different types of Crohn's disease based on how they are distributed. The first type is called Ileocolitis and affects both the colon and the terminal ileum. The second type is called Ileitis and affects only the ileum. The third type is called Gastroduodenal Crohn's Disease and affects the stomach and duodenum. The fourth type is called Jejunoileitis and is characterized by patchy areas of inflammation in the upper portion of the small intestine called the jejunum. Finally, there is Granulomatous Colitis, also known as Crohn's Colitis, which affects only the colon (4).

Inflammatory bowel disease affects around 7 million patients worldwide. Over the past 20 years, more patients have been diagnosed even though it is a rare condition (5). People over the age of sixty are involved in 10%-15% of IBD occurrences, compared to 5%-25% in adolescents (6). The rate in the elderly declines with age, with 65 percent of

patients being 60-70 years old, 25 percent being 70-80 years old, and 10 percent being above 80 years old (7). Compared to people without IBD, those with IBD are much more likely to develop other chronic diseases (8).

Intestinal microbes, environmental variables, and aberrant disease susceptibility genes are all implicated in the pathophysiology of IBD, according to recent study findings (9). The most typical symptoms that people with these diseases encounter are vomiting, bloody feces, diarrhea, and stomach discomfort (10).

Disease severity indices, which were based on clinical, laboratory, histological, or endoscopic data, were used to measure the severity of the disease. Different combinations of these indices were applied in scoring systems or scales (11, 12). Due to the high morbidity and mortality rates associated with inflammatory bowel disease (IBD), it is important to carefully evaluate the disease severity to determine the effectiveness of treatment and forecast the course of the illness. As more effective IBD treatments are developed (13-15).

Pharmacological therapies are the initial step used in treating IBD, and their effectiveness is based on the severity of the illness and its underlying phenotype. Medications are typically prescribed by doctors in stages. First, less dangerous medicines are provided; if these prescriptions do not offer the required relief, more drugs are recommended (16, 17).

Although there are several methods and treatment options in cases of IBD, each of which has a specific mechanism of action, as each option has a therapeutic group that is chosen from among them based on several grounds.

A group of corticosteroids that are given exogenously and bind to glucocorticoid receptors, which significantly reduce the production of the initial phase of cytokines and the formation of immunomodulators of cytokines, which produces a significant immunosuppressive effect, and on the other hand, undesirable side effects (18), (19).

Corticosteroids have a first generation, such as prednisolone and methylprednisolone, and a second generation, such as budesonide and beclomethasone dipropionate. budesonide is tolerated by patients more than the first-generation corticosteroids, as it has a higher first-pass metabolism and less systemic bioavailability, In addition, the

therapeutic direction is towards the second generation, which has higher topical effectiveness and lower systemic toxicity, Recently, it has also been included in a drug delivery system that helps it reach the desired location in the best way, such as a Multi-Matrix System (MMX) that controls the release of budesonide orally and up to the intestine, in addition to another system, which is called nanoparticles system (20), (21), (22), (23).

Among the basket of options for patients with IBD, the family, which is considered one of the first designer medications, which comes as a mixture of sulfapyridine and acetylsalicylic acid, which is sulfasalazine, that the origin of aminosalicylates. After digesting sulfasalazine, two compounds mesalamine and sulfapyridine are produced. and a drug was then produced contains only mesalamine because it has fewer side effects and maintains promised effectiveness (24).

Mesalamine or 5-acetylsalicylic acid (5-ASA) has anti-inflammatory properties, and works by negatively regulating lipoxygenase and cyclooxygenase, thus preventing the formation of leukotrienes and prostaglandins, in addition to raising the expression of peroxisome proliferator-activated receptors (PPAR). It comes in two formulations: oral and rectal, but there was a limitation to the effectiveness of mesalamine, as its immediate release form led to its early release and absorption before it effectively reached the target in colon, and therefore it was developed into a controlled release formula in order to ensure that it reaches its target, which is pH-dependent, time-dependent or Multi-Matrix System (25), (26).

Azathioprine is one of the medications in the treatment basket for IBD, and it belongs to the family of antimetabolites, from the subclass of purine analogues.

Since azathioprine is a prodrug, it is converted to 6-marcaptopurine (6-MP), which in turn is converted to one of three forms: either by xanthine oxidase (XO) to 6-thiouric acid, or by thiopurine-S-methyltransferase (TPMT) to 6-Methylmercaptopurine (6-MMP), or by hypoxanthine-guanine phosphoribosyl transferase (HPRT) to 6-thioinosine-5-monophosphate, and the last one in turn turns into 6-methylmercaptopurine ribonucleotide (6-MMP Ribonucleotide), which produces purine, or 6-thioguanine nucleotide (6-TGN), which forms DNA and eventually resulting in immunosuppressing effect. Based on this, we see that there is a direct relationship

between the effectiveness of (TPMT) and (6-MMP), which leads to decrease patient response and increased hepatotoxicity, and the relationship is inverse between (TPMT) and (6- TGN), which increasing of (6-TNG) can potentiate the risk of myelosuppression. We note from the above that azathioprine contributes to immunosuppressive effects, based on a balance between pro-apoptotic and anti-metabolic pathways and the effect depends on gene variation in (TPMT) which differ from patient to patient and affect the response of Azathioprine and tolerability of its adverse events, Azathioprine also inhibits multiple genes linked with intestinal inflammation and leukocyte trafficking to the intestinal tract(26),(27).

Biological monoclonal antibodies (mAbs) are a novelty and development treatment for IBD, which are divided according to their mechanism of action into cytokine blockers and integrin blockers. Integrin is a transmembrane protein that helps white blood cells (WBC) move to adhere to the surrounding environment and helping to stimulate cellular signals, Vedolizumab being an example of the integrin blocker. In addition, cytokine blockers are divided into interleukin blockers, such as Ustekinumab, which is considered the first biological treatment that targets both interleukin 12 and 23, which are secreted by white blood cells and has been approved by FDA for the treatment of Crohn's disease, furthermore to TNF-alpha blockers, which bind to TNF-alpha and thus block the cytokine's binding to its receptor. Examples include Adalimumab, Golimumab, and Infliximab(28),(29),(30, 31).

What's new has come to light recently the biosimilar, is a biological replica of an FDA-approved original medication that exhibits no discernible clinical variations from the reference product, and they are intended to increase competition in the worldwide market and offer the healthcare sector cost-effective options, and the regulation allowing biosimilar products to be approved for all indications of the original product without undergoing testing; this reduces the need for funding extensive clinical trials, among the recently produced and approved biosimilars are Infliximab and Adalimumab(32),(33),(34).

The "nocebo effect" refers to the possibility of a treatment failure when non-medical switching occurs from biologics to biosimilars. In this instance, the variations may result from how each person reacts to the unique molecules in the biosimilars.

Furthermore, 38% of patients who had their original medication changed to a biosimilar did not know they had switched (35).

It is essential to recognize that there are no professionally validated classifications of mild, moderate, or severe IBD before looking into the multitude of scores produced to reflect disease severity.

There are three major areas important to assessing the severity of disease: 1- the disease's influence on the patient (diagnostic symptoms, physician outcomes [PROs], life quality, and incapacity); 2- the inflammatory burden (the degree, position, and severity of intestinal inflammation at any one moment); and 3- the disease progression, including structural damage (36).

Fissures or superficial ulcers taking up more than 10% but less than 30% of the surface area would be considered intermediate endoscopic activity, whereas big ulcers >2 cm would be considered a serious illness (37).

IBD has a significant impact on everyday life, involving education, work, and relationships with others (38). The finding that quality of life can improve over time may be encouraging for people with this lifelong condition. For adults in particular, there was strong confirmation that quality of life deteriorates during active disease and may be reduced for those with Crohn's disease (39).

1.2 Literature review

1.2.1 Overview

This article's objectives are to outline the current Western world IBD epidemiology, compare it to the rise in IBD in recently industrialized nations, and project the effects of IBD worldwide in 2025.IBD is thought to affect over a million people in the United States and Two and a half million in Europe. In addition, the disease has spread to newly industrialized nations in Asia, South America, and the Middle East and is becoming more common across all continents(40).

We could find only one study related to IBD in Palestine. It was conducted to investigate the relationship between disease activity and adherence to medication, as well as the effect on QoL in people with IBD in Palestine. During the research period, 132 patients were questioned at three different hospitals.

It included 77 males (58.3%) and 55 female participants (42%). Fifty-two men in the study had been diagnosed with CD (67.5%), And there are twenty-five with UC (32.5%), with no significant difference between CD and UC based on gender. The sample age varied from 18 to 70 years, with a mean standard deviation of 34 +-13 years. 40% of the patients were university graduates. 51.5% of patients were diagnosed between the ages of 15 and 30. The most common diagnoses were CD 83 (62.9%) and UC 49 (37.1%).

The disease duration was separated into two groups: those who had the disease for less than 5 years compared to those who had the disease for 5 years or more. More than (32%) of the individuals who participated were smokers. IBD was diagnosed in (18.9%) (of individuals' first-degree relatives (mother, father, sister, or brother). During the patient interview, it was discovered that 69%) of them consumed fruits and vegetables, whereas (31%) relied on fast food, ninety patients (68%) avoided specific items such as milk and grains.

Several drugs have been prescribed. Azathioprine (Imuran®) was prescribed to 96 (72.7%), the 5-ASA (Pentasa®) to 68.2% of, and Adalimumab (Humira®) to (26.5%) of patients. During the course of the disease, 16 subjects (12.9%) were subjected to surgical therapy (41).

In another study in the United States, 61 people completed a screening questionnaire, with a mean age of 24.7 (SD = 2.9). (90%) of the participants were female, (64%) had Crohn's disease (n = 39), and (36%) had Ulcerative Colitis (n = 22).

The most common symptoms were fatigue (n = 44, 72.1%), abdominal cramps (n = 42, 68.9%), abdominal pain (n = 39, 63.9%), and diarrhea (n = 38, 62.3%), with fatigue (M = 3.3, SD = 2.6) being the specific symptom that most interfered with daily activities. Medications used in the study were: Amin salicylates (n=22 36.1%), Biological (n=37 60.7%), (n=11 18.0%) Corticosteroids and (n=16, 26.2%) Immunomodulators (42).

This study demonstrated the similarities and differences in symptoms between CD and UC. Fatigue (80.6%) and abdominal pain (80.4%) were the most common presenting symptoms in CD, whereas passage of plasma with bowel movements (BM) (86.6%) and watery BMs (86.5%) were the most common in UC. The five symptoms with the

greatest differences between UC and CD were blood passage with urgent BM (UC 82.5%/CD 63.9%), BM (UC 86.6%/CD 45.3%), and mucus passage with BM (UC 67.7%/CD 36.9%) (43).

In the Arab world, we could find a study that assessed the prevalence and/or epidemiological features of IBD in Arab nations, with a total of 1,588 patients with Crohn's disease (CD) and 1,627 patients with ulcerative colitis (UC) included in these studies. A thorough examination. The mean age of diagnosis in adult cases varied from 24.13 to 43.6 years and from 4.5 to 16 years in pediatric cases. The majority of patients in the majority of the included trials were men. UCAS had a compound incidence rate of 2.33 (95% confidence interval [CI] 1.2-3.4) per 100,000 person-years, according to quantitative analysis. Similarly, the Arab world's overall incidence of CD was 1.46 (95% CI 1.03-1.89) per 100,000 person-years. They concluded that IBD is more prevalent in our area (44).

The percentage of tests and procedures requested for the entire population in a Canadian study (n = 210) and the number of tests and procedures refused by these patients are presented in terms of patients' compliance with diagnosis or monitoring. Blood tests were the most frequently requested test/procedure (96.7% of patients), followed by colonoscopy (93.3%), colon biopsy (81.4%), and stool test (67.1%), and medical imaging (58.1%). Some patients choose not to have these tests/procedures performed. The refusal rate for the majority of tests/procedures is similar (2 to 5 refusals), but significantly higher for the blood test, which was declined by 74 patients. As a result, while the blood test is the most frequently requested, it is also the most frequently declined. this is mostly due to pain and cost (45).

Although a minority of studies did not find beneficial effects, the available clinical research showed that some herbal treatment like Chamomile and sage produces clinically significant relief or improvement in patients with mild or moderate IBD that is at least comparable to the effects of drugs already used in the therapy of IBD patients (46).

Exercise may be an important modifiable factor in the development and progression of IBDs. Current self-reported and measured exercise rates differ greatly across IBD patient cohorts. According to the data, exercise rates are inversely associated with

current disease severity. Exercise, in addition to other factors, may play a preventive role in the development of IBDs (47).

Diet has a significant impact on the onset and progression of (IBD). Patients want to know what they should eat to minimize symptoms and attacks, but there are no dietary recommendations. A review of current food-level evidence is required to counsel patients. Limit red meat, other dairy products, and sugar, and avoid legumes, which may aggravate symptoms. Sunflower oil outperformed extra virgin olive oil in terms of disease activity index and proinflammatory cytokine levels (48).

More research is needed to better characterize sleep disturbances in IBD patients. According to a previous study, patients with active IBD (82%) had poorer sleep quality than patients with inactive IBD (51%) (49).

The cigarette smoking protects against the onset and progression of ulcerative colitis (UC), as it is thought to have immune-modulating properties and activates nicotinic receptors, which reduces the production of pro-inflammatory cytokines (50).

Inflammatory bowel disease may lead to a deficiency in vitamins and iron, lack of absorption of vitamin B12 (51) and deficiency in vitamins D which in turn is responsible for increasing calcium absorption, which reduces inflammation in the patient (52).

There are studies that have confirmed the unfavorable effects of IBD on liver and kidney functions (53).

1.2.2 Evaluation of inflammatory bowel severity

In diagnosis the Ulcerative colitis Based on clinical and endoscopic examinations disease activity can be graded as mild, moderate, or severe (54).

Early tools for assessing illness severity focused on symptoms and basic clinical and laboratory tests (Stool tests for fecal pathogens and Clostridium difficile should be undertaken (55) performed at the same time (56).

Truelove and Witts Severity Index is a disease activity measurement technique that includes six variables: number of stools per day, blood in stools, temperature, pulse, hemoglobin, and erythrocyte sedimentation rate (ESR) (57).

- Mild illness: was defined as four or less bowel movements per day with no more than modest quantities of macroscopic blood in stools, no fever, no tachycardia, no severe anemia, and an ESR that did not rise more than 30 mm in one hour.

- Moderately severe: was characterized as being in the middle between severe and moderate.

- Severe disease: was defined as 6 or more bowel movements per day with macroscopic blood in the stools; fever (mean evening temperature greater than 37.5°C [99.5° F]; tachycardia (mean pulse rate greater than 90 beats/min); anemia (hemoglobin 75 percent or less; allowance made for recent transfusion); and ESR more than 30 mm in one hour (56).

The Mayo endoscopic score (MES) is the most extensively used score in clinical trials and daily practice to assess endoscopic activity (58).

The entire Mayo Score assesses the stage of ulcerative colitis using four criteria: feces frequency, rectal bleeding, endoscopy examination, and the physician's overall judgment.

The score's parameters range from zero (regular or inactive illness) to three (severe activity).

Mayo 0: normal epithelial or inactive disease, normal number of stool and no blood seen.
Mayo 1activity: (erythema, reduced vascular pattern, modest friability), 1-2 stool more than normal and streaks of blood with stool less than half the time.
Mayo 2 activity level :(marked erythema, absence of vascular pattern, friability, erosions), 3-4 stool more than normal and obvious blood with stool most the time.

Mayo 3: extreme activity (unpredictable bleeding, extensive ulcerations), 5 or more stool than normal and blood passed alone(59).

Currently, computed tomography (CT) and magnetic resonance imaging (MRI) are used to analyze the gastrointestinal system (60).

CT accurately depicts mucosal abnormalities, bowel thickness, mucosa hyperemia, ulcers, stiffness, vasa recta engorgement, lymph nodes, and mesenteric involvement in individuals suspected of having Crohn's disease.

MRI provides the benefit of viewing the complete thickness of the intestinal wall as well as the perivisceral loose connective tissue, which standard methods do not.

In reality, the approach allows for the detection of mucosal lesions, problems, stenosis evaluation, and its importance in determining bowel-wall thickness (61).

Crohn's disease progresses from low to moderate to severe. The earlier you manage and treat Crohn's disease, the less chance you have of developing severe symptoms.

Mild to moderate: Ambulatory and able to accept oral nutrition without signs of dehydration, systemic toxicity, stomach soreness, uncomfortable mass, intestinal blockage, or weight loss of more than (10%).

Moderate to severe: Those who have not responded to therapies for mild to moderate illness, or those who have more pronounced symptoms such as fever, severe weight loss, stomach pain or soreness, frequent vomiting or nausea or severe anemia.

Severe: Patients presenting with high fevers, recurrent vomiting, indications of intestinal blockage, severe peritoneal signs such as voluntary guarding or rebound soreness, cachexia, or evidence of an abscess (55).

Only an ileocolonoscopy with biopsy can provide a definite diagnosis of UC. In UC patients with acute abdominal symptoms, abdominal computed tomographic (CT) scanning is the first radiographic imaging investigation. The Mayo scoring system is a popular indicator for assessing illness severity and monitoring patients throughout treatment. Treatment is determined on the degree, severity, and progression of the disease. Topical 5-aminosalicylic acid (5-ASA) medications are the first-line treatment for proctitis (62).

The most often utilized first-line radiologic scan in the evaluation of small bowel CD is abdominal computed tomography (CT) enterography (63).

1.2.3 Inflammatory bowel disease treatment and outcome

The American Gastroenterology Association's (AGA) official recommendations for the treatment of mild to moderate ulcerative colitis (UC) Guidelines current evidence supports the use of Mesalamine at the standard dose for remission maintenance and induction in patients with mild to moderate extensive UC (64).

Current evidence supports the use of biologic therapy (infliximab) to induce and maintain remission in patients with moderate to severe UC. Immunotherapy (thiopurine) monotherapy should not be used to induce remission, but may be considered to maintain remission.

Although combination therapy with a biologic agent and an immunomodulator is more effective than either agent alone, patients, particularly those with less severe disease and those who are sensitive to medication side effects, may prefer monotherapy.

Biological agents, with or without an immunomodulator, should be used early rather than gradually in patients with moderate to severe disease activity who are at high risk for colectomy or after 5-ASA has failed to maintain remission (65).

On the other hand, the article elucidates an evidence-based update on Crohn's disease management options. CD disease is resonating on two levels: flare-up and remission, which requires in treatment to induction and maintenance.

Corticosteroids can be used as an option to achieve control of symptoms throughout induction, preferably among them Budesonide, which can be used in mild to moderate cases due to its substantial first-pass metabolism in the liver, which results in decreased systemic absorption.

Maintenance therapy entails taking a lower dose of a Corticosteroid-free medication, including an immunomodulator or a biologic, for the rest of the patient's life in order to keep the patients in remission and prevent disease flares, And to allocate, Immunomodulators (azathioprine) can be used as Crohn's disease maintenance medications, but they tend to be less effective compared with biologic therapies or combination therapies with biologics, in addition to keep in mind here that Corticosteroids are ineffective as maintenance treatments, and it is worth noting that

Mesalamine therapy, which are commonly used to treat ulcerative colitis, are ineffective in the medical treatment of Crohn disease (66).

The medical treatment of moderate to severe CD is addressed also in AGA guideline, they mentioned that with the exception of corticosteroids, most drugs started for induction of remission continue as maintenance therapy, moreover, it recommends biologic drug alone over thiopurine alone for the induction and maintenance of remission, but using them in combination is more effective, and it was against using 5-aminosalicylates for induction or maintenance.

The final and clear message that AGA was advised to take home was encourage to start the biologic option sooner, either with or without an immunomodulator, instead of waiting until 5-aminosalicylates and/or corticosteroids fail (67). As additional CD and UC medicines are licensed for clinical use, more research on predictors of response to therapy and head-to-head studies are needed to guide doctors on how to effectively position therapeutic alternatives for patients with IBD (68).

Corticosteroids are typically used to treat CD flare-ups. In individuals with moderately to highly active CD and UC, conventional corticosteroids are helpful at lowering signs and symptoms and inducing remission.

For mild to moderate illness, oral formulations may be utilized, while systemic corticosteroids are recommended for moderate to severe disease.

Traditional corticosteroids are seldom useful in allowing patients to achieve mucosal healing. They have traditionally been used as a "bridge" medication to treat symptoms until immunomodulators and/or biological medicines become effective and allow mucosal repair.

Although not as effective as traditional oral corticosteroids like prednisolone, controlled ileal release (CIR) budesonide could be useful for short-term alleviation of symptoms in people with mild-to-moderate CD (55).

Corticosteroids are particularly successful in managing acute IBD flare-ups, however (16%) of patients do not react, and (20%-30%) respond just partially (69).

Antimycobacterial (most commonly used metronidazole, ciprofloxacin, or a combination of the two medications) treatment has not been found to be useful in causing or maintaining recovery or mucosal repair in CD patients (55).

The British Society of Gastroenterology (BSG) suggested antibiotics for secondary complications in CD like abscesses and bacterial overgrowth , and the European Crohn's and Colitis Organization (ECCO) guidelines suggest antibiotics in UC patients in the situation of an acute infection or prior to surgery (70).

Biologics therapy may be a successful technique for minimizing long-term Corticosteroid use while still sustaining remission; this may be one of the reasons biologics have seized the majority of the IBD market.

There has been an increasing tendency in recent years toward adopting biologic treatment as first-line therapy for some clinical conditions:

- infliximab was the first anti-TNF medication authorized for IBD is a very effective treatment for moderate to severe IBD, resulting in a reduction in the Mayo score of at least three points and at least 30%, as well as a reduction in the rectal bleeding sub score of at least one, In addition, the frequency of draining fistulas was reduced by 50% from baseline (71).

- The FDA has authorized Ustekinumab for the adult treatment of IBD patients with the moderate-to-severe illness, Ustekinumab has demonstrated efficacy in initiating and sustaining clinical response in active CD and UC patients.

- Preliminary clinical trial data indicated that Risankizumab is well tolerated and capable of mediating lengthy clinical response and endoscopic recovery in active CD patients.

- Natalizumab, was later licensed for the management of CD patients. Natalizumab has shown considerable clinical effectiveness in individuals with moderate-to-severe CD.

Amino salicylates These treatments are tiny compounds that are taken orally or rectally to reduce gut inner wall inflammation. Amino salicylates are the most commonly given IBD medications and the first-line therapeutic choice for UC patients who have mild-to-moderate illness (Some amino salicylates such as balsalazide and mesalamine) (70).

JAK Inhibitors Because of oral administration, early start of action, or absence of immunogenicity, some JAK inhibitors have shown promising outcomes for induction and maintenance of remission in moderate to severe UC or CD (72). Their safety profiles must be verified in larger phase III clinical studies.

Immunomodulator therapy is given to patients intravenously or orally to modify their immune systems and decrease inflammation. Immunomodulators are often helpful in sustaining remission and are administered to patients who aren't responsive to amino salicylates and Corticosteroids, or as an adjuvant therapy to anti-TNF to avoid anti-body development, notably with infliximab (some immunomodulators include azathioprine, cyclosporine, mercaptopurine, methotrexate and tacrolimus (70).

Thiopurine that has been used to treat individuals with (IBD) who have not responded well to mercaptopurine (MP) or azathioprine (AZA). Concerns concerning nodular regenerative hypertrophy (NRH) of the liver have impeded its widespread usage (73). Thiopurine monotherapy is a long-term successful treatment for UC, however it is substantially less effective in CD. In both UC and CD, the combination of thiopurines and infliximab (IFX) is better to either medication alone in producing remission (74).

Dietary Therapies Diets high in fruits and vegetables, low in processed meats and refined carbs, and high in water for hydration were related to a decreased risk of active IBD symptoms, although higher fruit and vegetable intake alone did not lower the likelihood of CD symptoms (75).

Regarding treatment, several biological medicines against tumor necrosis factor (TNF), as well as several biochemical compounds and molecules, have been produced during the last decade for the medical treatment of individuals with inflammatory bowel disease (IBD). However, conventional medicines continue to be the cornerstone of therapy for the vast majority of patients. Newer mesalamine formulations with a smaller tablet size and only one dosage per day are as effective as previous versions. New

corticosteroids maintain the effectiveness of previous corticosteroids while being safer (76).

Anti-interleukin 12 (anti-IL-12)/IL-23 medicines provide novel and effective therapeutic options for CD, whereas oral small molecules now provide an oral alternative for the treatment of moderate-to-severe illness that required subcutaneous injection or intravenous infusion previously. Alternatives to pharmaceutical therapy, like stem-cell transplantation and fecal microbiota transplantation, are also showing promise in the treatment of both CD and UC (77).

Increasing the amount of the anti-inflammatory cytokine interleukin-10 (IL-10) is a potential method for slowing the course of pathogenic inflammation, including inflammatory bowel disease (IBD). Because inhibition of cyclin-dependent kinase 8 (CDK8) can increase the amount of IL-10 in activated myeloid-derived dendritic cells, it is thought to be a useful target for IBD therapy (78).

With a rising respect for mucosal healing, a treat-to-target technique is becoming more popular. An objective measurement of mucosal inflammatory response is critical for verifying treatment success. Clinical symptom measures were formerly employed to assess therapy effectiveness.

Endoscopy, histology, radiography, immunochemical monitoring biomarkers, quality of life evaluation, and other approaches are now available to give more meaningful references for disease activity assessment.

At the moment, the primary therapy for IBD is pharmacological, with amino salicylates, CSs, immunomodulators, and biologics being the most commonly used. However, a significant proportion of patients do not achieve clinical remission during therapy or lose responsiveness over time

1.3 Problem statement

The incidence and prevalence of IBD are increasing with time and in different regions around the world, indicating its emergence as a global disease (44). Symptom severity may hinder patients from enjoying their hobbies and affect their job performance. The main goal of treatment for any chronic disease such as IBD is to improve the patient’s symptoms.

In our country, data about IBD patients is very limited. In general, limited studies have been established to provide sufficient information about the symptom severity, the most commonly used medications and factors that increase or reduce symptoms, to relate all these variables to each other, and to provide a comprehensive overview of understanding and managing symptoms experienced by IBD patients and how they affect the patient's quality of life to contribute to its improvement**.**

1.4 Importance of the study

Studies related to IBD are limited in Palestine. This study will give data on evaluating the severity and stages of the disease, through which we will determine the appropriate treatment, and we will also evaluate the existing treatments on the market for treating the disease and the differences between them. The results may help increase community awareness about disease and avoid factors that could worsen the disease. On the other hand, there are factors that reduce the severity of symptoms, and this may improve treatment outcomes and the quality of life of these Palestinian patients.

1.5 Objectives

1.5.1 General objective

The aims of this study were to assess the severity, treatment, and outcomes of inflammatory bowel disease among Palestinian patients, to assess the effect of socio-demographic and the extent of patients' commitment to following up with the doctor and performing continuous examinations.

1.5.2 Specific objectives

1. To determine the stage and severity of the disease among included patients.
2. To evaluate the most common symptoms of disease among patients.
3. To conduct a comprehensive evaluation of IBD treatment and the most prescribed medications.
4. The most important factors that contribute to the improvement or worsening of the patient's condition.

Chapter Two

Methods

2.1 Study design and setting

This cross-sectional study was conducted from August 2022 to March 2023 using a data collection form (appendices A and B) to collect data from patients' files and interviews. (It was arranged with Dr. Qusay Abdo to include all patients of An-Najah National University Hospital), as the number of patients included in the study were from various northern governorates in the West Bank.

2.2 Population

Patients from the northern areas of the West Bank with inflammatory bowel disease undergoing medical treatment for any stage of the disease (mild, moderate and severe).

2.3 Inclusion criteria and exclusion criteria

- **Inclusions criteria will be as follows:**

1. Male and female
2. Confirmed diagnosis of inflammatory bowel disease
3. Patients who received treatment
4. Patients in the northern areas of the West Bank

- **Exclusion criteria will be as follows**:

1. Pregnant women
2. Patients who did not have confirmed diagnosis of inflammatory bowel disease

2.4 Sample size

In a previous study from the West Bank, the lists of IBD patients from 3 hospitals included 200 patients, so their sample was 132 (18). The expected number of IBD patients is in hundreds. For example, if the patients are around 400, the Raosoft sample size calculator (an automated software program):

http://www.raosoft.com/samplesize.html) suggests a sample of 197 patients. The goal was to include around 200 patients.

2.5 Ethical Considerations

This study protocol was conducted authorized by An-Najah National University Institutional Review Board (IRB) Reference number: Mas.Nov.2022/27 (Appendix C) and An-Najah National University Hospital before the initiation of this study.

All information obtained from the questionnaire was kept confidential and only summarized data was presented in reports or publications.

Maintenance of high-level objectivity in discussion and analysis throughout the research was assured.

2.6 Data Collection

The data collection form was a questionnaire prepared after a literature review of previous studies (41), (48), (47), (46).The data collection tool is a questionnaire divided into three sections: social, demographic, and clinical information. The data collection form is presented in Appendix A. The first section collects data about the patient's age, sex, factors influencing the disease including food, exercise and herbs respectively. the second section is the residence and the third section duration of the disease, age at first diagnosis of the disease (age of onset), questions about the method of treatment (medical or surgical), the type of medication used depends on the severity of the disease, tests performed (45), questions about the first appearance of symptoms, most common symptoms (43) and other questions through which we can reach results to achieve the objectives of the study.

A pilot study was conducted on a small number of patients to evaluate the questionnaire, and the results were not included in the final analysis.

2.7 Statistical Analysis Methods

The Statistical Package for Social Sciences (SPSS version 21) was used for statistical analysis. For continuous data, the means ± standard deviation were determined. For categorical variables, frequencies and percentages were computed. To evaluate the significant association between variables (categorical variables), cross-tabulation with Chi-square test was used. A p value of < 0.05 was considered as significant association.

Chapter Three

Results

3.1 Sociodemographic and clinical characteristics of the patients

This study included 219 patients with Inflammatory Bowel Disease (IBD), their percentage in terms of gander was: (53.4% men and 46.6% women), sixty six men in the study had been diagnosed with the CD (56.4%), others with UC (43.6%) (n=51) and eighty four women diagnosed with CD (47.1%), other with UC (52.9%) (n=54) and regarding their history of smoking (25.6% were smokers, 57.5% were non-smokers and 16.9% were former smokers), there were (28.8%) (n=63) of patients who had a family history of IBD and the remaining (71.2%) (n=156) did no, the duration of illness in our sample was (1-38 years; median 4 years) and we find that about two-thirds of the sample (64.8%) were diagnosed during the last five years. Details are shown in Table (3.1), in terms of age it ranged between 6-86 years with a mean 33.58±14.8 years and patients' weight was between 16-120 kg and a mean 68.15±16.4 kg.

Table 3.1

Sociodemographic and clinical characteristics of the patients

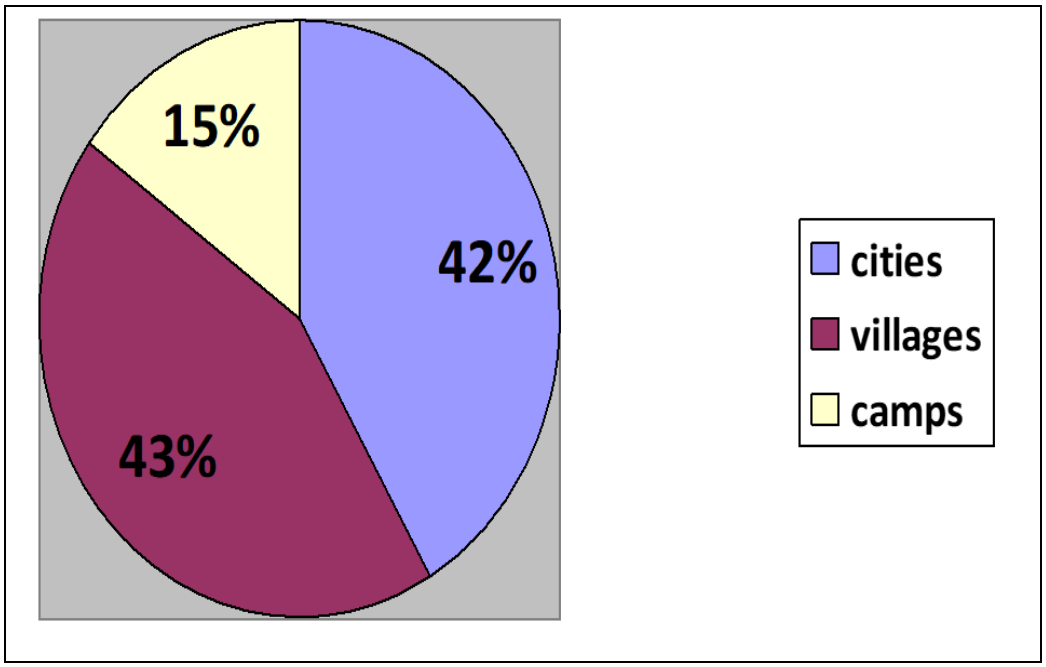
	Frequency	Percentage
Gender		
Male	117	53.4%
Female	102	46.6%
Residency		
Cities	91	41.6%
Villages	95	43.4%
Camps	33	15.1%
Educational Level		
Illiterate	1	0.5%
Middle-school	30	13.7%
High-school	50	22.8%
Diploma	20	9.1%
Undergraduate	109	49.8%
Postgraduate	9	4.1%
History of smoking		
Smokers	56	25.6%
Non-Smokers	126	57.5%
Former-Smokers	37	16.9%
UC		
Smoker	25	23.8%
Non-smoker	64	60.9%
I was smoking	16	15.2%
CD		
Smoker	31	27.2%
Non-smoker	62	54.4%
I was smoking	21	18.4%
Family History		
Yes	63	28.8%
No	156	71.2%

UC: Ulcerative Colitis, CD: Crohn's Disease

distributed in terms of residence (41.6%) (n=91) in the cities,(43.4%) (n=95) in the villages, and (15.1%) (n=33) in the camps, by educational level (0.5%) (n=1) illiterate, (13.7%) (n=30) reached to middle-school, (22.8%) (n=50) reached to high-school, (9.1%) (n=20) obtained diploma, (49.8%) (n=109) undergraduate, and (4.1%) (n=9) postgraduate.

Figure 3.1

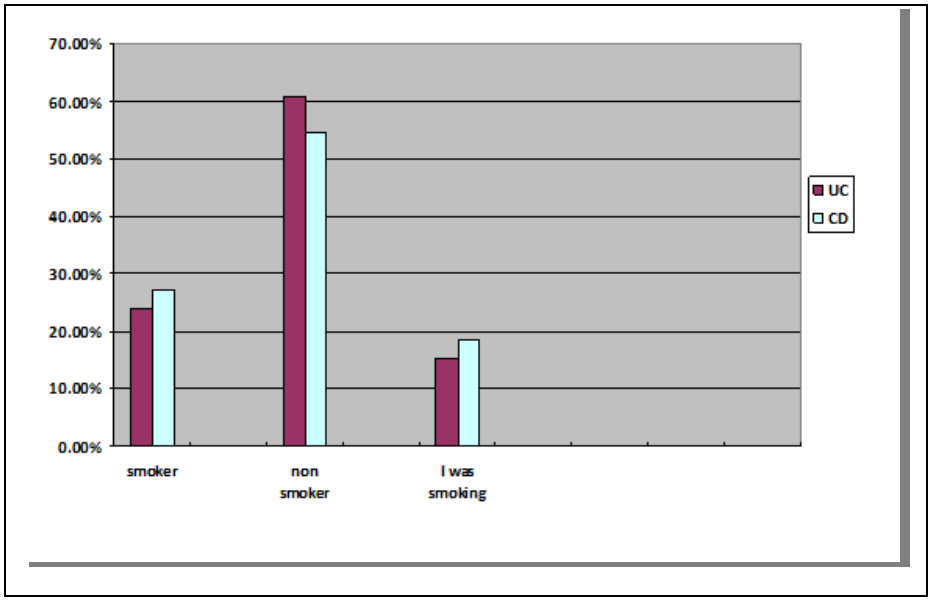
Percentage of residency among IBD patients



Regarding their history of smoking of UC Smoker (n= 25) (23.8%) Non-smoker (n=64) (60.9%) I was smoking (n=16) (15.2) and for CD smoker (n= 31) (27.2%) Non-smoking (n=62) (54.4%) i was smoking (n=21) (18.4%)

Figure 3.2

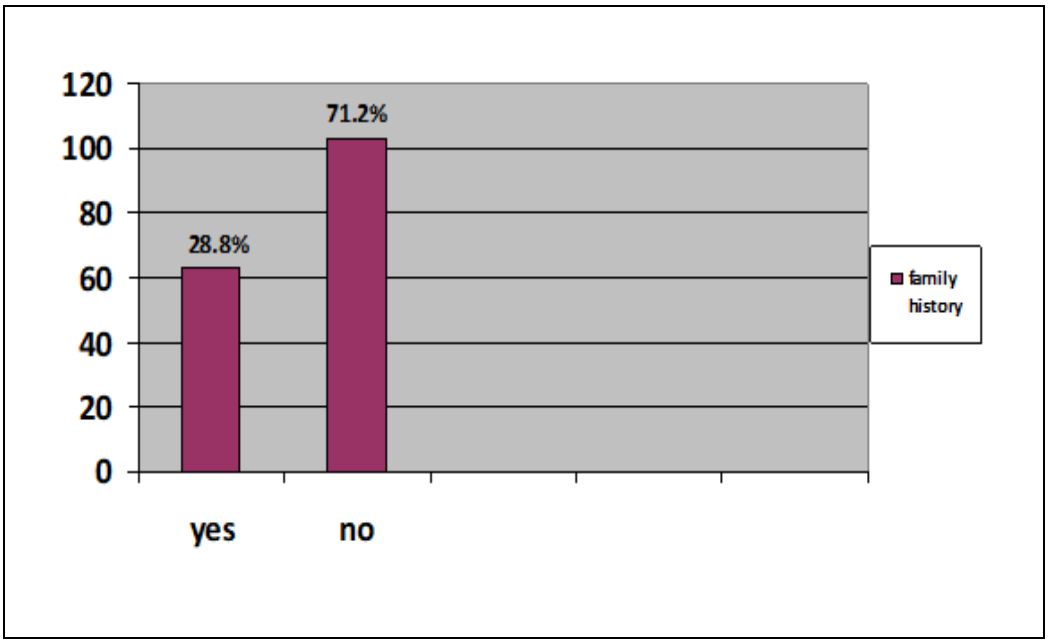
Smoking vs diagnosis



There were (28.8%) (n=63) of patients who had a family history of IBD and the remaining (71.2%) (n=156) did not

Figure 3.3

Family history of IBD patients

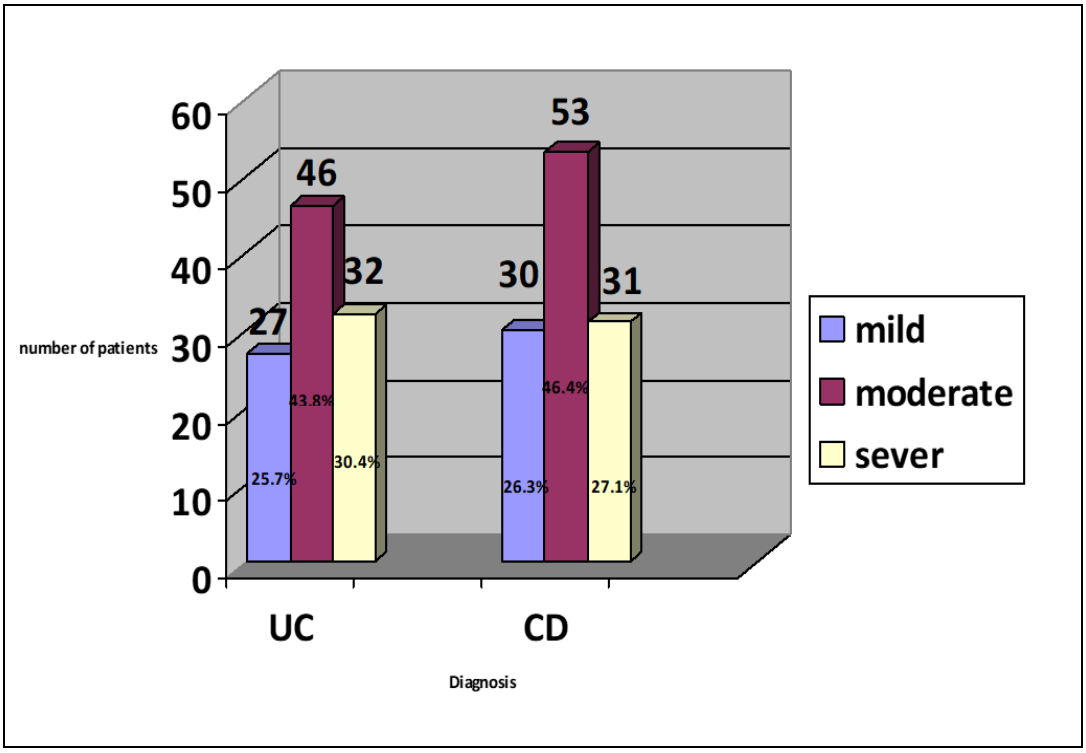


3.2 Evaluation the severity of the disease

In this study we found that (47.9%) (n=105) patients suffered from ulcerative colitis (UC) and (52.1%) (n=114) from Crohn's disease, regarding severity of the disease which was based on clinical and diagnostic characteristics, patients were diagnosed with mild stage in 57 (26%) cases, while 99 (45.2%) had moderate disease, and 63 (28.8%) were diagnosed with severe disease .

Figure 3.4

Distribution of IBD patient severity



We created a questionnaire for our patients to obtain more accurate information, including whether gastrointestinal operations were performed during their IBD, such as bowel resection. The percentage of patients who underwent operations was (16%) (n=35), the mean duration of disease among patients who needed surgery was 9.3±8.6 years while it was 5.4±5.7 years among those who did not have surgery (p-value = 0.001) (table 3.4). Moreover, the disease affected their quality of sleep by (64.4%) (n=141), and some types of foods had negatively affected IBD patients by (67.6%) (n=148). (See the figure 3.5 and Table 3.2). There were signs in a positive direction, such as the effect of herbs on IBD patients, which reduced symptoms in (47.5%) (n=104) of patients and greatest improvement was among patients with moderate disease severity and less extent with equality in mild and severe patients according to (table 3.3), and a portion of patients felt better when they exercised their percentage was (12.8%), on the other hand, (26.5%) did not feel better even though they had exercise and the rest of patients who are the largest population, did not have exercise with (60.7%) and UC patients felt an improvement in symptoms by (12%) when they exercised ,CD patients an improvement of (16%) (Table 3.4).

Figure 3.5

Foods cause pain and diarrhea with IBD patients

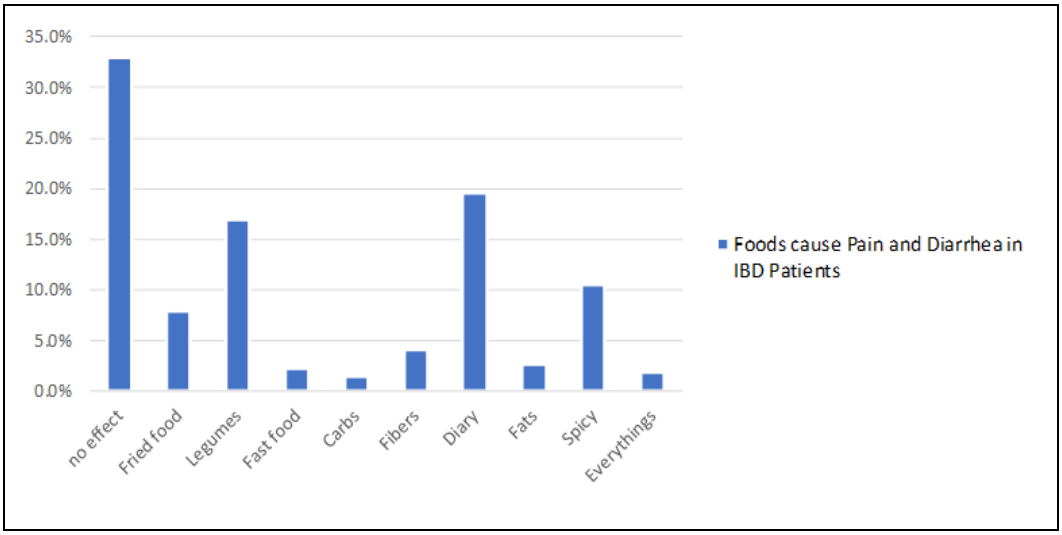


Table 3.2

Questions related severity of symptoms in patients with IBD

QUESTIONS	Frequency	Percentage
Have you previously performed operations on the digestive system, such as cutting the intestines?		
Yes	35	16%
No	184	84%
Do the symptoms affect your daily activity?		
Yes	149	68%
no	70	32%
Does the disease affect your sleep?		
Yes	141	64.4%
no	78	35.6%
Do you think that the disease has anything to do with the nature of your food?		
Yes	148	67.6%
no	71	32.4%
Do you think that herbs have a role in alleviating symptoms?		
Yes	104	47.5%
no	115	52.5%
Do you exercise and feel better?		
I don't exercise	133	60.7%
I exercise and don't feel better	58	26.5%
I exercise and feel better	28	12.8%

Table 3.3

The number of patients whose symptoms improved with herbs according to the stage of their disease

	Herbs have alleviating Symptoms	Herbs have no alleviating Symptoms
Mild	31	26
Moderate	43	56
Sever	30	33

Table 3.4

Some differences between UC and CD patients

	UC		CD		
Socio- demographic factor	Percentage	Frequency	Percentage	Frequency	p.value
I don't exercise	62.8%	66	58.7%	67	
I exercise and don't feel better	21.9%	23	30.7%	35	
I exercise and feel better	15.2%	16	10.5%	12	0.948160
Number of patients	14.2%	15	17.5%	20	0.148395
who had bowel resection	85.7%	90	82.4%	94	
Yes					
no					

CD: Crohn's disease, UC: ulcerative colitis

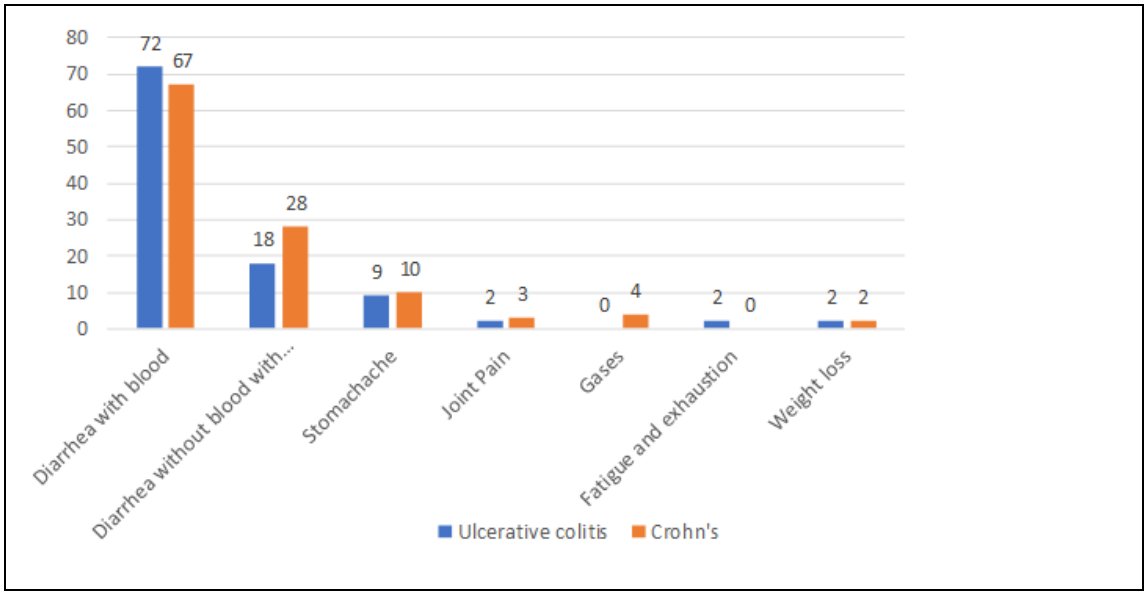
3.3 Symptoms experienced by the patients

When the patients were asked about the first symptoms, they felt that made them visit a healthcare professional, the most common symptoms were bloody diarrhea (63%), then mucous diarrhea (21%), then abdominal pain (8.7%), and there were symptoms such as joint pain, gases, fatigue, and weight loss, but to a lesser extent: (2.3%, 1.8%, 0.9%, and 1.8%), respectively.

To elucidate which of the first symptoms were prevalent in either Crohn's or UC patients, the results are also presented in the following (Figure 3.6).

Figure 3.6

First symptoms in crohn's and ulcerative colitis patients



We followed up on the symptoms they felt and which they continued to feel as a result of the disease such as diarrhea (75.3%), abdominal pain (66.6%), gases (58.9%), bulges (34.7%), joint pain (45.2%), rash (13.2%), abdominal mass (10.0%), hemorrhoids (23.7%), fistula (16.8%) weight loss (41.0%), fatigue (49.3%), constipation (26.9%), stomachache (30.1%), vomiting (30.5%), dry skin (15.9%), night sweat (17.8%), anorexia (36.1%), inflammation eye, joint, skin (11.8%) and delayed growth (3.6%) . There was a statistically significant difference between UC and CD patients in abdominal pain which was more common in CD patients (84 out of 114 (73.7%)) vs UC patients (62 out of 105 (59.0%)), p- value = 0.022, and in abdominal mass which was more common in UC patients (16 out of 105 (15.2%)) vs CD patients (6 out 114 (5.3%)), p-value = 0.014.

3.4 Evaluation of IBD medications prescribed for the patients

For newly diagnosed IBD patients, the healthcare professional determines the stage of their disease as mild, moderate, or severe to provide appropriate treatment based on the type of disease, whether it is ulcerative colitis or Crohn's.

In our study, we had 114 Crohn's patients, (26.3%) (n=30) of whom were mild cases, (46.5%) (n=53) were moderate, and (27.2%) (n=31) were severe cases.

In the other arm there were 105 patients with ulcerative colitis, (25.7%) (n=27) of them were mild cases, (43.8%) (n=46) were moderate and (30.5%) (n=32) were severe.

First medication with IBD patients

There are 4 treatment options that can be considered as first medication for patients with IBD: mesalamine, azathioprine, corticosteroids, or biological therapy. Then it is possible to adjust therapeutic doses or change the medication according to the patient's response.

- **Mesalamine First Medication**

Mesalamine is considered the most common for use as first medication in patients with inflammatory bowel disease, (74%) (n=162) of patients used it as the first medication, especially when the disease was diagnosed as a moderate stage (44.4%) (n=72). (The results were listed in the below table (3.5).

Table 3.5

Use Mesalamine as first medication with IBD Patients

	frequency	percentage
Mild		
CD	14	12.2%
UC	23	21.9%
Moderate		
CD	35	30.7%
UC	37	35.2%
Sever		
CD	25	21.9%
UC	28	26.6%

- **Corticosteroids First Medication**

Corticosteroids is considered the second most common medication for use as the first medication in patients with inflammatory bowel disease, (15%) (n=33) of patients used it as the first medication, especially with Crohn's patients in Mild stage (57.9%) (n=11). (The results were listed in the below table (3.6))

Table 3.6

Use corticosteroid as first medication with IBD patients

	Frequency	Percentage
Mild		
CD	11	33.3%
UC	3	9.1%
Moderate		
CD	5	15.2%
UC	7	21.2%
Sever		
CD	3	9.1%
UC	4	12.1%

- **Azathioprine First Medication**

Azathioprine used usually as first medication in patients with Crohn's disease, especially in Moderate stage with (65%) (n=13). (The results were listed in the below table (3.7))

Table 3.7

Use azathioprine as first medication with IBD patients

	Frequency	Percentage
Mild		
CD	5	21.7%
UC	1	4.3%
Moderate		
CD	13	56.5%
UC	2	8.6%
Severe		
CD	2	8.6%
UC	0	0

- **Biological treatment First Medication**

It is worth noting that biological treatment is rarely used as a first medication in cases of IBD, and it is used only in severe cases, in our study only one patient 0.0045% was prescribed it as first treatment.

3.5 Current medications with IBD patients

- **Mesalamine Current Medication**

The number of patients using Mesalamine as their current medication for IBD decreased from (74%) (n=162) to (46.6%) (n=102), and (61.9%) (n=65) of total ulcerative colitis patients were using Mesalamine as current medication and (32.5%) (n=37) of total Crohn's patients too. (Figure (3.7) and Figure (3.8) elucidate the number of patients according to stages for each disease).

Figure 3.7

Current user of mesalamine in different stages of crohn's disease

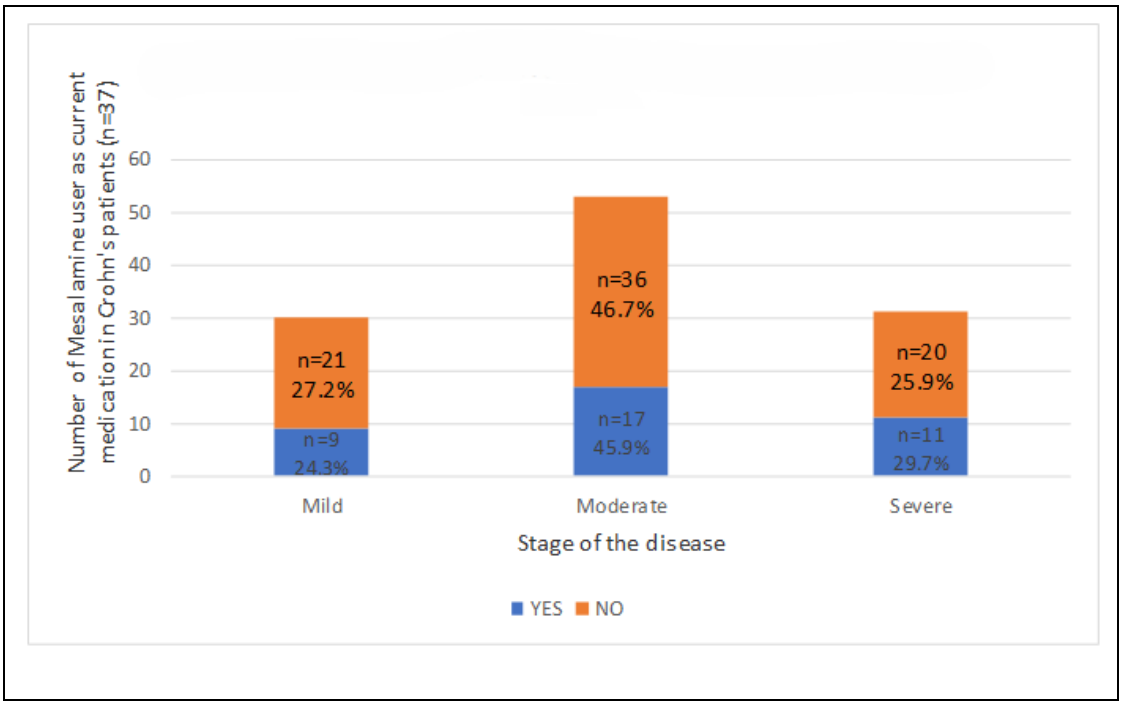
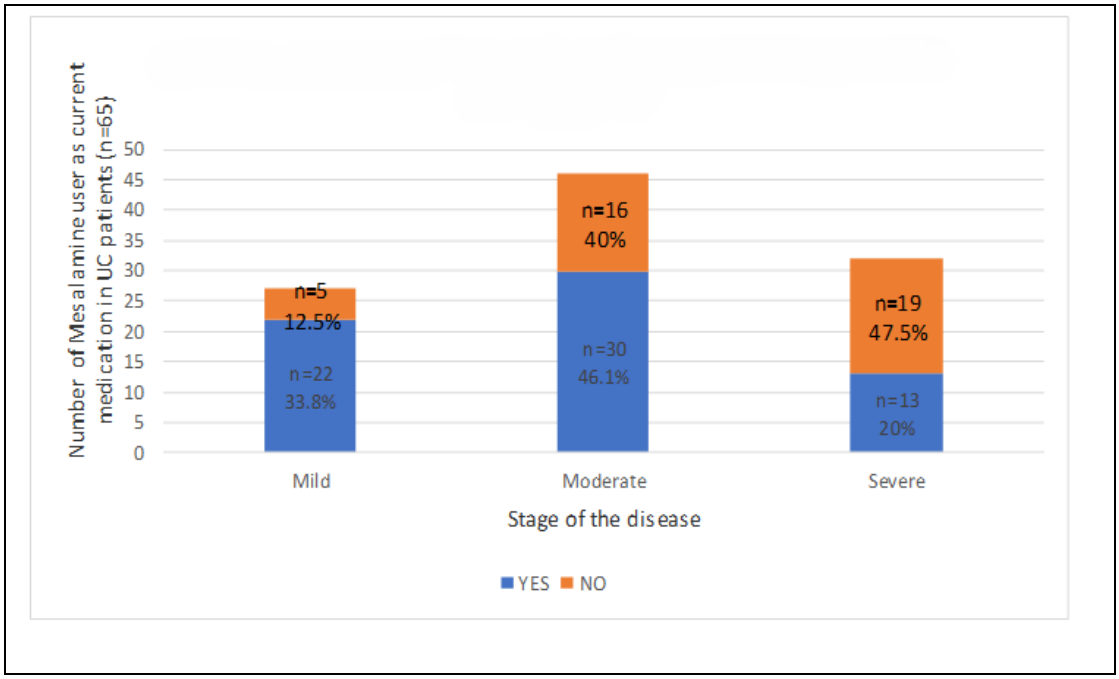


Figure 3.8

Current user of mesalamine in different stages of ulcerative colitis disease



- **Corticosteroids Current Medication**

Patients with IBD currently using Corticosteroids were (22.8%) (n=50), (21%) (n=22) of total ulcerative colitis patients were using corticosteroids as current medication and (24.6%) (n=28) of total Crohn's patients too. (Figure (3.9) and Figure (3.10) elucidate the number of patients according to stages for each disease).

Figure 3.9

Current user of corticosteroid in different stages of crohn's disease

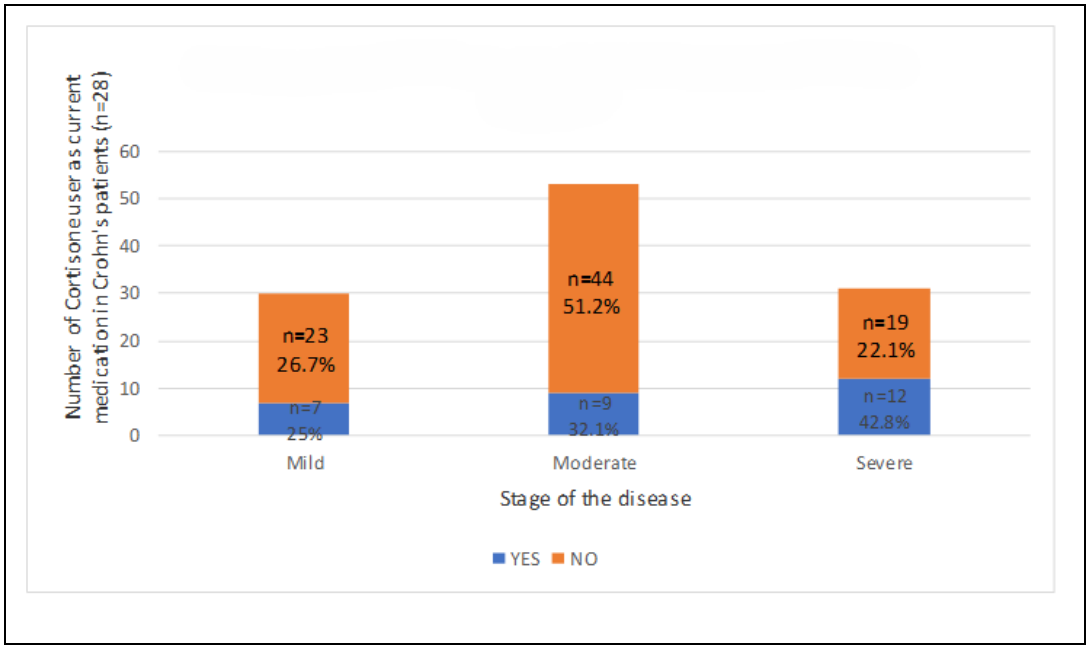
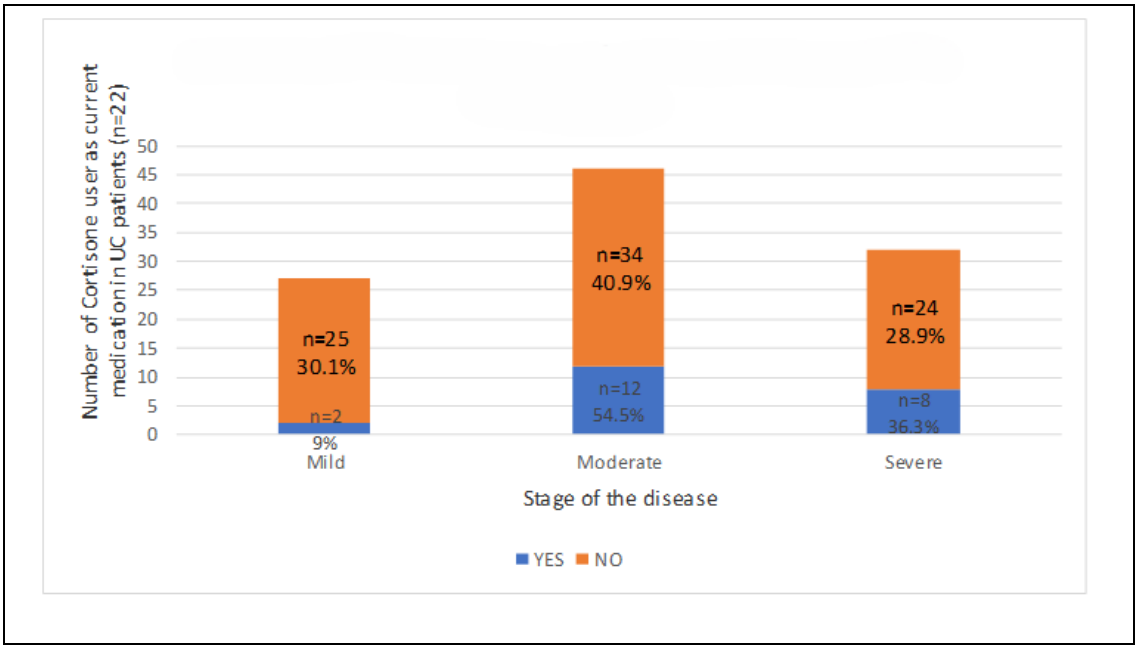


Figure 3.10

Current user of corticosteroid in different stages of ulcerative colitis disease



- **Azathioprine Current Medication**

The number of patients using Azathioprine as their current medication for IBD increased from (10.5% to 41.1%, 37.1%) of total ulcerative colitis patients were using Azathioprine as current medication and (44.7%) of total Crohn's patients too.

Biological treatment Current Medication

The number of patients using biological treatment (infliximab) as their current medication for IBD increased from one patient (0.45%) to 77 (35.2%), Its use has increased in all stages of the disease, especially in the severe stage, as it was used in 12 (21.1%) with mild stage, and in 31 (31.3% with moderate stage and in 34 (54.0%) with severe stage. There was a statistically significant association between the severity and the use of biological agents; (p-value < 0.001).

3.6 Tests performed by the patients

The majority of patients (88.6%) in the study performed periodic examinations, including iron test (45.7%), vitamin B12 (25.1%), vitamin D (23.3%), blood test(81.3%), urine test (62.6%), kidney function (34.2%), liver function (34.2%), gastrointestinal endoscopy (27.4%), abdominal CT (15.5%), fluids and blood clotting factor (7.8%), calprotectin (17.4%), and inflammation factor (42.5%) (Table 3.8).

It is worth noting that the most common tests performed by the patient and requested by the healthcare professional were blood and stool test.

Table 3.8

Frequencies and percentages of IBD Patient who performed different tests

IBD Patient tests	Frequency	Percentage
Blood test		
Yes	178	81.3%
No	41	18.7%
Stool examination		
Yes	137	62.6%
No	82	37.4%
Iron level		
Yes	100	45.7%
No	119	54.3%
B12		
Yes	55	25.1%
No	164	74.9%
Vitamin D		
Yes	51	23.3%
No	168	76.7%
Liver function		
Yes	75	34.2
No	144	65.8
Kidney function		
Yes	75	34.2%
No	144	65.8%
Inflammation factor		
Yes	93	42.5%
No	126	57.5%
Gastrointestinal Endoscopy		
Yes	60	27.4%
No	159	72.6%
CT scan of abdomen		
Yes	34	15.5%
No	185	84.5%
Fluidity and coagulation of blood		
Yes	17	7.8%
No	202	92.2%
Calprotectin test		
Yes	38	17.4%
No	181	82.6%

Chapter Four

Discussions and Conclusions

4.1 Sociodemographic and clinical characteristics of the patients

The percentage of men with inflammatory bowel disease in this study was (53.4%) while women were (46.6%). This was similar to a previous study from Palestine (41), where the percentage of IBD patients among men was higher (58.3%), while women were (41.7%), and a study from the Arab world, where the percentage of men with IBD was more than women also (44). On the other hand, in a study from the United States (42), the percentage of women in the sample was (90%), and women tended to suffer from Crohn's disease more.

What we can explain in this context is that the genes in Palestine are different, the female-to-female transmission pattern, or "female imprinting," is caused by sex-determined epigenetic factors that may affect the relative risk for females. This phenomenon has been found to be especially common in familial CD. Females with polymorphisms in the promoter of interleukin (IL)-10 are at a higher risk of developing ulcerative colitis (UC) at younger ages. This effect may be amplified by estrogens, which block the production of IL-10 and other anti-inflammatory cytokines. While women who carry an IL-23 receptor variant are generally protected against CD and IBD, they are especially protected against UC by another genetic variant of the same receptor (79).

It is worth noting that when comparing our study with another study in Palestine(41), in which there were more patients with Crohn's disease than patients with Ulcerative Colitis, versus the study in the Arab world (44), in which there were more patients with ulcerative colitis than patients with Crohn's disease, the sample was large and random, so that 2.33 per 100000 had ulcerative colitis, and 1.46 per 100000 had Crohn’s disease. It is possible that the reason for this difference in results can be attributed to cultures, genetics, health insurance, interest in discovering the disease and follow-ups.

We note in terms of education level that many of the patients were university graduates: 49.8% of our sample were university graduates, and also (40%) in a previous study (41), our society currently has a relatively large number of people completing their education to university, and the secret behind this increase of their numbers in the sample will

often be due to the awareness of educated patients about the disease and moving towards discovering it, or at least reading about the reasons behind the symptoms that they have.

It is interesting to note in our study that the prevalence of ulcerative colitis was lower in patients who were smokers and former smokers, but the prevalence of Crohn's disease was not affected by smoking. and as mentioned earlier (50) cigarette smoking protects against the onset and progression of ulcerative colitis (UC), which related to the presence of nicotine and its benefit in patients with ulcerative colitis, as it is considered to have immune-modulating properties and activates nicotinic receptors, which in turn reduces the production of pro-inflammatory cytokines, However, due to the side effects of smoking and its long-term harms, it has not been considered an effective focus of attention as a treatment.

Having a relative with IBD, increases the risk of developing the disease and this was seen in this study as (28.8%) of patients had relatives with the disease. This was also indicated in a previous study from our country (41), where the percentage of those who had IBD and had first-degree relatives with it was (18.9%).

In general, IBD can affect patients at any age, whether children, adolescents, adults, or the elderly, as in our sample the ages range from 6 to 86 years, but the age distribution varies, as the largest number of patients is among adults, and accordingly, our mean age was 33.58 years. The results were similar in study (41), where the mean age was 34 years and more than half of the sample was between the ages of 15-30 years, meaning they were adults, it is expected that behind this controversy, people's eating and life habits begin to change and fluctuate. For example, they may start smoking at this stage and go to different eating habits, and perhaps also their hormonal fluctuations will be influential, and life stress may also be higher.

When reviewing our sample in terms of the duration of the disease among the patients who were diagnosed, we find that about two-thirds of the sample (64.8%) were diagnosed during the last five years, and this is also close to the result of the study (41), as their percentage reached (62.9%), and this indicates that the diagnosis of IBD has increased dramatically in Palestine recently.

This also has certain implications. This is attributed to the fact that the diagnosis of IBD has become through the interest in performing diagnostic examinations and colonoscopy for a larger number of patients and the interest in diagnosing it early through random samples to diagnose or screening for other diseases such as colorectal cancer patients in people genetically predisposed, as the percentage of patients diagnosed in the last year only is (35.2%) of those diagnosed in the last 5 years in IBD, and perhaps the reason for this could be due to psychological or genetic reasons or certain behaviors and foods that have recently entered our life-style.

4.2 Evaluation the severity of the disease

Patients are distributed according to the severity of IBD. The mild stage occurred in 57 (26%) of the cases, while 99 (45.2%) were in the moderate stage, and 63 (28.8%) were in the severe stage, meaning that a large proportion of patients had difficult symptoms. This affects their quality of life and requires stronger and more stringent treatment options. When talking about the impact on life, education, work, and social relationships, the disease impact was felt by about two-thirds of the sample, similar to a previous study (38) which confirmed this as well.

As expected, the disease affects the quality of sleep with IBD patients, as we have in our sample (64.4%) of patients whose sleep quality was affected whether the disease was active or not, as was clear according to study (49), in which (82%) of the patients suffering from active inflammatory bowel disease had poorer sleep quality. However, there is something that can explain this in a different way, as when patients with inflammatory bowel disease are in the active stage, their treatment basket includes corticosteroids, which affect melatonin levels and thus we enter the steroid-induced sleep disturbance stage and thus we go to insomnia and delirium, and this could be the direct explanation for this, not the severity of the disease alone (80),(81).

As for the effect of food on IBD, it is clear that avoiding certain foods for a massive number of patients is able to reduce the development of the disease and its severity. We find in our study that (67.6%) of the patients were affected by the type of foods, especially dairy, legumes, fast food, and spicy food. This is similar to the results of previous studies where (68%) of patients avoided specific foods such as milk and grains (41), so patients are advised to reduce red meat, dairy products, and sugar, and avoid legumes (48). Suitable counselling about diet is highly recommended to improve

outcomes, and good to know that the patients with IBD can get a good overview of the Groningen anti-inflammatory diet (GrAID), which was created and compared to other IBD diets on a food level. This thorough analysis concentrates on the anti-inflammatory properties of food, giving IBD patients the best information on what foods to eat or stay away from in order to minimize flare-ups. The GrAID was created utilizing this (48).

We found that for patients who had bowel resections due to IBD, in our study the rate was (16%), the mean duration of disease among patients who needed surgery was 9.3±8.6 years while it was 5.4±5.7 years among those who did not have surgery (p-value = 0.001), so it seems that the risk increases significantly as the duration of the disease increase, it is expected that the bowel resection in patients with inflammatory bowel disease will decrease in the era of biological treatment (82).

Regarding herbs, we found that less than half of the sample, (47.5%), improved when using herbs, and the greatest improvement was among patients with moderate disease severity. they were useful in patients with mild and moderate disease severity (46), so recommending patients to use certain herbs may be useful. Theoretically, there are various ways that herbal remedies work to promote healing, such as immunological regulation, antioxidant activity, blocking leukotriene B4 and nuclear factor-kappa B (46).

Since we are elucidating a complete lifestyle for patients in our study, we must mention the role of exercise and its effect on IBD patients, as in our study the result was that (32.6%) of patients who exercise felt an improvement in their disease severity, and the rest did not feel any improvement even though they were exercising. In a previous study (47), the result was an inverse relationship between the severity of the disease and exercise. Therefore, we recommend to conduct other studies and determine whether there are specific exercises capable of improving IBD, and to counsel patients about exercises that are beneficial for their disease.

4.3 Symptoms experienced by the patients

The pathophysiology of diarrhea associated with inflammatory bowel disease is complex and primarily results from mucosal damage brought on by ongoing inflammation. This damage leads to dysregulated intestinal ion transport, compromised epithelial barrier function, and increased pathogen accessibility to the intestinal mucosa.

The primary reason of water buildup and electrolyte retention in the intestinal lumen that results in diarrhea in individuals with inflammatory bowel disease is altered expression and/or function of epithelial ion transporters and channels. Erroneous barrier function exacerbates diarrhea by means of the leak-flux mechanism. Enteric infections that penetrate the mucosa induce dysbiosis and worsen the immune system, which prolongs the tissue damage and diarrhea associated with IBD (83).

In our study, the first symptom in patients with IBD was diarrhea (84.5%) in all stages of severity, and most of them has bloody diarrhea (75.1%). When we examined the differences in the first symptom, bloody diarrhea in patients with Crohn's disease and ulcerative colitis was (48.1% and 51.9%) respectively, but regarding to the mucous diarrhea, Crohn's patients suffered more than ulcerative colitis patients, especially in mild and severe stages.

When we also followed the symptoms of the disease that remained with the patients after their diagnosis, the results were a slight decrease in patients suffering from diarrhea to (75.3%), and equally among patients with Crohn's disease and ulcerative colitis, but that the major improvement was in patients suffering from bloody diarrhea that decreased to (44.8%) in patients with inflammatory bowel disease in general, and in patients with Crohn’s disease to a greater extent than in patients with ulcerative colitis but not significant (p=0.063), based on what was explained previously, preserving mucosal membrane and reducing inflammation will have this role in reducing diarrhea.

When we compared the number of patients who had diarrhea from inflammatory bowel disease in our study (75.3%) and in a previous study which was (63.9%) (42), the results in the two studies confirm that this symptom is very common among patients. In this study one of the most common symptoms was abdominal pain at a rate of 66.6%; (57.8%) of them were Crohn's patients, and this was similar in a previous study where (80.4%) Crohn's patients suffered from abdominal pain more than ulcerative colitis patients (43).

One of the symptoms suffered by approximately half of the patients with inflammatory bowel disease in our sample is fatigue and exhaustion. The results were also similar in our study and a previous study (43) in terms of the distribution of the percentage between patients with Crohn's disease and ulcerative colitis, and with a slight increase

in symptoms in the two studies with Crohn's patients, and fatigue and exhaustion are expected due to sleep problems, in addition to problems absorbing vitamins and minerals those necessary for the body.

Gases was also common symptoms in our sample, as it was the third symptom with (58.9%) of cases, and it was equally present in patients with Crohn's and ulcerative colitis, but in study (43) it was slightly more common in patients with ulcerative colitis.

There may be other symptoms that were present in patients, but they were less common, some of which were higher in Crohn's disease or ulcerative colitis patients, and there were similar percentage of symptoms among them in our study, as follows: anorexia (55.7%), night sweats (53.8%), vomiting (61.2%), constipation (62.7%), weight loss (56.6%), fistula (56.8%), rash (58.6%), joint pain (53.3%), so they were higher in Crohn's patients with these percentages. The percentages were highest among patients with ulcerative colitis as follows: inflammation of the eyes, skin, and joints 53.8%, hemorrhoid (53.8%), abdominal mass (72.7%), and bulges (53.9%). There were symptoms that were equal in both sides, such as stomachache, dry skin, and delayed growth, we believe that delayed growth is likely caused by a lack of absorption of vitamins and minerals in young age patients with inflammatory bowel disease.

4.4 First medications prescribed for patients

Mesalamine is considered one of the medications most prescribed as the first medication for cases of inflammatory bowel disease in general (74%), and when we sub-analyze our sample, we found that it is also the first medication in cases of mild-stage ulcerative colitis in particular with (62.2%) compared to Crohn's disease (37.3%), and they attribute its use largely to the fact that it is one of the first medication option when inflammatory bowel disease is in the active state. And also tend to be used higher with moderate and severe stages of ulcerative colitis patients.

Although corticosteroid medication is the second drug in terms of use as first medication in cases of IBD (15%), it was observed in our sample that most of its use was in cases of mild-stage in patients with Crohn's disease (78.6%) and ulcerative colitis (21.4%), but it is used in cases of moderate and severe stages of ulcerative colitis with tend to be higher as a first medication than Crohn's cases.

When we talk about immunomodulatory medication, azathioprine will come as the third first medication used in patients with IBD (10.5%), and the majority of its users at all stages of severity were Crohn's patients with (87%).

We can say that biological treatment is rarely used as a first medication when trying all other initial options due to its price and the difficulty of taking the dose that in most cases needs to be taken in the hospital, so only one patient used it as a first treatment.

4.5 Current medications prescribed for patients

Mesalamine was used by (46.6%) (n=102) of our inflammatory bowel disease patients, (36.3%) (n=37) of Crohn's disease patients and the order of severity of them is mild (24.3%,) moderate 45.9%, and severe 29.7%, and according to ulcerative colitis patients (63.7%) (n=65) the distribution of severity of them is mild (33.8%), moderate (46.2%), and severe (20%).

Corticosteroid was used by (22.8%) (n=50) of our inflammatory bowel disease patients, with (56%) (n=28) having Crohn's disease and the order of severity of them is mild (25%), moderate (32.1%), and severe (42.9%), and on the other side (44%) (n=22) having ulcerative colitis dispensed by severity into mild (9.1%), moderate (54.5%), severe (36.4%).

Azathioprine was used by (41.1%) (n=90) of our inflammatory bowel disease patients, with (56.7%) (n=51) having Crohn's disease and their severity divided by percentage into mild (31.4%), moderate (39.2%, severe 29.4%, and 43.3%) (n=39) having ulcerative colitis their percentage of severity stages mild (23.1%, moderate 43.6%, severe 33.3%).

Biological treatment was used by (35.2%) (n=77) of our inflammatory bowel disease patients, with Crohn's disease accounting for (52.3%) (n=48) they are distributed to (mild 16.7%, moderate 58.1%, severe 31.3%), and ulcerative colitis accounting for 37.7% (n=29) distributed by severity into (mild 13.8%, moderate 20.7%, severe 65.5%).

Crohn's disease patients in the mild severity stage, 30% use mesalamine, (23%) use corticosteroid, (53%) use azathioprine, and (27%) use biological therapy. Most patients take azathioprine in the mild stage of treatment, and it is considered one of the effective treatments at this stage.

And for Crohn's patients with moderate severity stage, (32.1%) use mesalamine, (17%) use corticosteroid, (37.3%) use azathioprine, and (47.2%) use biological therapy. We noticed a reasonable decrease in the use of corticosteroid and azathioprine as well, in exchange for an increase in the use of biological treatment compared to the low-severity stage. This decrease in the use of corticosteroid indicates that patients in moderate severity are exposed to flares less frequently, and that the early use of biological treatment is as recommended internationally in the early stages (67).

For Crohn's patients in the severe stage, (35.5%) used mesalamine, (38.7%) used corticosteroid, (48.4%) used azathioprine, and (48.4%) used biological therapy. The escalating in azathioprine and corticosteroid user, as the use of azathioprine in a very similar manner to biological treatment may be an indication of the use of combination therapy, which is more effective than the mono therapy of either of them.

For ulcerative colitis patients in the mild stage, (81.5%) used mesalamine, (7.4%) used corticosteroid, (33.3%) used azathioprine, and (14.8%) used biological therapy. As it is known, the most recommended treatment for ulcerative colitis in simple cases is mesalamine, and this explains that most patients take it. There is also a portion that can be observed that does not take mesalamine, (18.5%) (n=5), and this may be because there are patients who are allergic to the drug, or have possible drug-drug interaction that prevent them from taking it, and perhaps side effects that do not suit them, or they have no response to it. We also noticed that a good portion of patients are on azathioprine, perhaps for considerations of increased effectiveness or, as we mentioned, for certain limitations on mesalamine, there is a slight use of corticosteroid, which indicates the lack of relapses in current treatment plans. There are patients who have been resorted to biological treatment and they certainly have certain considerations.

And for Ulcerative Colitis patients with moderate stage, (65.2%) used mesalamine, (26.1%) used corticosteroid, (37%) used azathioprine, and (13%) used biological therapy. we noticed a decline in the percentage of mesalamine users in the moderate severity stage in patients with ulcerative colitis. This may be due to some of the reasons we mentioned previously, including side effects or lack of response. We noticed a decrease in its use as a percentage and, moreover, an increase in corticosteroid users, an indication that relapses being more frequent. We do not have a clear reason behind these flares, and it is preferable that this be studied carefully in the future to determine the

reasons behind this to elucidate and evaluate, it is suggested that the use of biological treatment be increased further at this stage.

The results for Ulcerative Colitis patients in the severe stage showed that 40.6% used mesalamine, (25%) used corticosteroid, (40.6%) used azathioprine, and (59.4%) used biological therapy. the use of mesalamine has decreased to a greater extent, but on the other hand, the use of biological treatment has increased massively at this stage. However, there is high use of corticosteroid and also at a rate that makes us look more into the available biological treatment options, and comparing treatments to each other with different combination therapies.

By comparing our results to a previous study from Palestine, the most commonly prescribed medication for Crohn's patients was Azathioprine in both studies, in our study their percentage was (44.7%) of total Crohn's patients, and in (41) they were (77.1%) of total Crohn's patients. This is good evidence of the cost-effectiveness of Azathioprine for Crohn's patients in Palestine in both studies, It is expected that the explanation for the decrease in its use compared to the study (41) is that AGA guideline tends to start with biological treatment or mixed with azathioprine (67), in addition to that in our study patients with moderate to severe Crohn's disease constitute the largest part.

The use of biological therapy (infliximab) in patients with Crohn's disease in our sample and study (41) were, (42.1%) and (44.6%), respectively, which is a good indicator, according to the recommendations of the AGA, it is recommended to start biological treatment in patients with Crohn's disease as early as possible (67), due to its proven effectiveness for both induction or maintenance cases, certainly, comparing biological therapies and studying their different types, their impact, and affordability on Palestinian populations require further studies.

As for Mesalamine, its use among Crohn's patients in our study and study (41) were, (32.5%) and (59%), respectively, and the attribute of difference in both studies to the fact that recent recommendations are against its use in patients with Crohn's disease in both induction and maintenance therapy (67), but it is expected that some patients will continue to use it, might for special cases in which Crohn's disease is present in the end of the GI tract.

The least used option as a current treatment for patients with Crohn's disease was corticosteroid, but it was used more in our study than study (41), (24.6%) and (18.1%), respectively. This is expected to happen due to greater flares-up of Crohn's patients. Because according to the recommendations, it is recommended to give corticosteroid to Crohn's patients in the induction of remission and not in the maintenance of remission, which encourages the use of biological treatments more and more to maintain the remission as long as possible, and there may be differences in the results because there is no clear distinction in the study (41) about the treatments offered at each severity stage of the disease in Crohn's patients, as we have in our sample, so that we can evaluate it more precisely and in detail, as we did previously in our study.

As for patients with ulcerative colitis, there is a difference in the number of patients between the two samples, and there are no clear severity stages of the disease in the patients, but we can take this in the form of percentages as an indication.

Whereas the number of mesalamine users among ulcerative colitis patients in study (41) was (83.7%) and ours is (61.9%), this is considered a fairly large percentage of ulcerative colitis patients in our study who do not use it as a treatment, this reason may be logical, as the distribution of our ulcerative colitis patients shows that (74.3%) of UC patients have moderate and severe disease severity, and indicating that they have not benefited from it in advanced stages, or perhaps they have limitations to use it, even though it is usually considered as first-line of treatment for induction and maintenance of remission in mild and moderate stage, and this may lead us to choose another therapeutic options, such as Biological therapy at different stages, or combined treatment options ,or giving Mesalamine in different pharmaceutical forms in combination with each other, on the other hand, as we mentioned earlier, study (41) did not contain a disease severity distribution, and this reduces our ability to compare.

As for azathioprine, the percentage of its users among ulcerative colitis patients in study (41) was (65.3%), while in our study it was (37.1%), although it is not considered one of the preferred options in cases of flares, but its uses are in the stage of maintenance remission, the percentage of its use in combination with other medications or as an alternative to mesalamine is possible, and it is clearly more present in the study (41) as a percentage, Even if it is used with biological treatment, which is the preferred approach

in terms of effectiveness, its side effects remain, which reduces its use in patients who complain about this or who prefer fewer medications.

Regarding Biological therapy, the percentage of its users among ulcerative colitis patients in study (41) was (28.6%), while in our study it was (27.6%), The rate of its use is close, even though the patients in our study had high advanced cases and it was expected that the use of biological treatment in our sample would be greater than that, due to recommendations related to its use for induction and maintenance of remission, but there remain limitation of its use, including expensiveness and the doses for biological treatment are not usually taken easily as they often require a hospital to take them, and there are less chances of patient compliance, however, guidelines (65) currently recommend using biological treatment at the earliest convenience and not gradually, and the presence of biosimilars that make of biological medicines more affordable and there are promising methods of administration for biological therapy to be more comply

For corticosteroid, its use in a previous study (41) among patients with ulcerative colitis was (20.4%), compared to (21%) in our study. It is expected that the use of corticosteroid will be less in general due to its side effects and its limited use in flares-up cases in particular, but we hope that the escalation use of biological treatment more widely in the future can reduce its use and also avoid patients' disease triggers, such as those we are studying.

4.6 Tests performed by the patients

Regarding examinations, the patient with inflammatory bowel disease should comply to having them performed periodically. These tests include vitamin D, iron, and B12, which are among the vitamins that have important roles in patient health, as their deficiency may worsen the patient's health (52). Maintaining them in the normal range reduces the symptoms that may appear due to their deficiency, in addition to their role in alleviating the symptoms of IBD, so it is necessary to adhere to tests and take vitamins in case of a deficiency.

Other tests include checking the functions of the liver and kidneys, because they may be affected by the IBD (53), in addition, there are some medications for treating IBD that may affect liver and kidney functions as well.

The results of our study of tests related to the disease showed that (34.2%) of patients undergo periodic tests for both liver and kidney functions.

As for the periodic tests for the levels of iron, B12, and vitamin D, they were (45.7%), (25.1%), and (23.3%) respectively. Given the importance of these tests and their impact on patient, we advise all IBD patients to perform these tests on regular basis.

As for the rest of the tests, their importance goes back to diagnosing the disease, and through some of these tests we can know the affected part, and thus health care professional can determine whether it is Crohn's or UC, such as a Gastrointestinal Endoscopy examination. There are tests through which we can know the stage of the disease and thus it is treated in the appropriate way when the type and stage are known.

The most frequent test performed by patients was the blood test, at a rate of (81.3%). In a previous study (45), the blood test had a rate of (78.7%), and it is one of the most requested tests due to its comprehensiveness.

4.7 Strength and Limitations

The strength of this study is in providing base line data about severity and treatment of IBD in our country as the studies related to these patients in Palestine are very limited. The study has several limitations, as it was conducted in only one hospital in the West Bank, Palestine, and thus the results may not be generalizable. Lastly, collecting study data through patient interviews may be detrimental because this may affect participants' responses, leading to less reliable data.

4.8 Conclusion

Many patients have severe stages of the disease which affects their daily life. Different types of foods and herbs may affect symptoms in patients with IBD. The most common symptoms were diarrhea, whether bloody or containing mucus, fatigue, and gases. The pattern of treatment for patients with ulcerative colitis prescribed as a first and current medications was consistent with what was mentioned in the AGA, except for the necessity to increase the use of biological therapy as first medication in moderate and severe cases early and not gradually.

When we review the treatments for patients with Crohn's disease, we find that mesalamine is widely used as a first and current medication despite recommendations not to use it due to lack of effectiveness, moreover, we support the AGA recommendation on the early use of biological therapy as a first medication for patients with Crohn's disease in induction and remission phase.

4.9 Recommendations

The findings of this study provide some information of IBD patients in Palestine, as well as an assessment of their medications, disease severity, outcomes, and the most important factor affecting patients. Our findings also highlight some critical issues that must be addressed in the future, which include the following:

- Conduct additional studies to determine whether certain exercises can improve IBD, as well as advise patients on which exercises are beneficial for their disease.

- Investigate the prevalence of IBD in Palestine, population-based on a larger scale study are required**.**

- Awareness sessions for patients with inflammatory bowel disease to emphasize the importance of adhering to their medications and the types of foods that are recommended or should be avoided in order to maintain the remission.

- In the future, we hope to conduct studies to differentiate between the results of biological medications individually among patients with inflammatory bowel disease in Palestine, in order to make a comprehensive comparison about the results of each of them, in addition to study the effectiveness of biosimilars and their new pharmaceutical forms and the extent of their impact on treatment outcomes in Palestine, and studying the effectiveness of new therapeutic options such as JAK inhibitors.

- We hope that biological treatments will be used more widely and earlier, in addition to reducing the use of mesalamine in patients with Crohn's disease, in accordance with international recommendations update.

List of Abbreviations

Abbreviation	Meaning
5-ASA	5-aminosalicylic acid
AGA	American Gastroenterology Association's
CD	Crohn's disease
CT	Computed tomographic
GI	Gastrointestinal
IBD	Inflammatory Bowel Disease
MRI	Magnetic resonance imaging
QoL	Quality of life
REC	Research Ethical Committee
SPSS	Statistical Package for Social Sciences program
TNF	Tumor Necrosis Factor
TPMT	Thiopurine S-methyl T
UC	Ulcerative colitis

References

1. Prevention CfDCa. What Is Inflammatory Bowel Disease (IBD)? 2022.
2. Seyedian SS, Nokhostin F, Malamir MD. A review of the diagnosis, prevention, and treatment methods of inflammatory bowel disease. J Med Life. 2019;12(2):113-22.
3. Foundation CsC. Types of Ulcerative Colitis. 2024.
4. Foundation CsC. Overview of Crohn's Disease. 2024.
5. prevention cfdca. World IBD Day– May 19, 2022 2022 [
6. Nimmons D, Limdi JK. Elderly patients and inflammatory bowel disease. World J Gastrointest Pharmacol Ther. 2016;7(1):51-65.
7. Charpentier C, Salleron J, Savoye G, Fumery M, Merle V, Laberenne J-E, et al. Natural history of elderly-onset inflammatory bowel disease: a population-based cohort study. Gut. 2014;63(3):423-32.
8. prevention cfdca. People with IBD Have More Chronic Diseases 2022 [
9. Nakase H, Uchino M, Shinzaki S, Matsuura M, Matsuoka K, Kobayashi T, et al. Evidence-based clinical practice guidelines for inflammatory bowel disease 2020. Journal of Gastroenterology. 2021;56(6):489-526.
10. Fakhoury M, Negrulj R, Mooranian A, Al-Salami H. Inflammatory bowel disease: Clinical aspects and treatments. Journal of inflammation research. 2014;7:113-20.
11. Sandborn WJ, Feagan BG, Hanauer SB, Lochs H, Löfberg R, Modigliani R, et al. A review of activity indices and efficacy endpoints for clinical trials of medical therapy in adults with Crohn's disease. Gastroenterology. 2002;122(2):512-30.
12. D'Haens G, Sandborn WJ, Feagan BG, Geboes K, Hanauer SB, Irvine EJ, et al. A review of activity indices and efficacy end points for clinical trials of medical therapy in adults with ulcerative colitis. Gastroenterology. 2007;132(2):763-86.
13. Danese S. New therapies for inflammatory bowel disease: from the bench to the bedside. Gut. 2012;61(6):918-32.

14. Denmark VK, Mayer L. Current status of monoclonal antibody therapy for the treatment of inflammatory bowel disease: an update. Expert Rev Clin Immunol. 2013;9(1):77-92.

15. Monteleone G, Pallone F, MacDonald TT. Emerging immunological targets in inflammatory bowel disease. Curr Opin Pharmacol. 2011;11(6):640-5.

16. Andrews J, Travis SP, Gibson PR, Gasche C. Systematic review: does concurrent therapy with 5-ASA and immunomodulators in inflammatory bowel disease improve outcomes? Alimentary pharmacology & therapeutics. 2009;29(5):459-69.

17. Kruis W, Kiudelis G, Racz I, Gorelov IA, Pokrotnieks J, Horynski M, et al. Once daily versus three times daily mesalazine granules in active ulcerative colitis: a double-blind, double-dummy, randomised, non-inferiority trial. Gut. 2009;58(2):233-40.

18. Ramamoorthy S, Cidlowski JA. Corticosteroids: mechanisms of action in health and disease. Rheumatic Disease Clinics. 2016;42(1):15-31.

19. Brattsand R, Linden M. Cytokine modulation by glucocorticoids: mechanisms and actions in cellular studies. Alimentary pharmacology & therapeutics. 1996;10(Sup2):81-90.

20. Bruscoli S, Febo M, Riccardi C, Migliorati G. Glucocorticoid Therapy in Inflammatory Bowel Disease: Mechanisms and Clinical Practice. Front Immunol. 2021;12:691480.

21. Rutgeerts P, Lofberg R, Malchow H, Lamers C, Olaison G, Jewell D, et al. A comparison of budesonide with prednisolone for active Crohn's disease. New England Journal of Medicine. 1994;331(13):842-5.

22. Löfberg R, Danielsson Å, Suhr O, Nilsson Å, Schiöler R, Nyberg A, et al. Oral budesonide versus prednisolone in patients with extensive and left sided ulcerative colitis. Gastroenterology. 1996;110(6):1713-8.

23. Edsbäcker S, Andersson T. Pharmacokinetics of budesonide (Entocort™ EC) capsules for Crohn’s disease. Clinical pharmacokinetics. 2004;43:803-21.

24. Campregher C, Gasche C. Aminosalicylates. Best Practice & Research Clinical Gastroenterology. 2011;25(4):535-46.

25. Abinusawa A, Tenjarla S. Release of 5-Aminosalicylic Acid (5-ASA) from Mesalamine Formulations at Various pH Levels. Advances in Therapy. 2015;32(5):477-84.

26. Deissler H, Krammer H, Gillessen A. pH-dependent vs. constant release of mesalazine in the treatment of ulcerative colitis: Do drug delivery concepts determine therapeutic efficacy? (Review). Biomed Rep. 2021;15(5):96.

27. Díaz-Villamarín X, Fernández-Varón E, Rojas Romero MC, Callejas-Rubio JL, Cabeza-Barrera J, Rodríguez-Nogales A, et al. Azathioprine dose tailoring based on pharmacogenetic information: Insights of clinical implementation. Biomedicine & Pharmacotherapy. 2023;168:115706.

28. Neurath MF. Current and emerging therapeutic targets for IBD. Nat Rev Gastroenterol Hepatol. 2017;14(5):269-78.

29. Simon EG, Ghosh S, Iacucci M, Moran GW. Ustekinumab for the treatment of Crohn's disease: can it find its niche? Therap Adv Gastroenterol. 2016;9(1):26-36.

30. Feagan BG, Sandborn WJ, Gasink C, Jacobstein D, Lang Y, Friedman JR, et al. Ustekinumab as Induction and Maintenance Therapy for Crohn's Disease. N Engl J Med. 2016;375(20):1946-60.

31. Cherry LN, Yunker NS, Lambert ER, Vaughan D, Lowe DK. Vedolizumab: an α4β7 integrin antagonist for ulcerative colitis and Crohn's disease. Ther Adv Chronic Dis. 2015;6(5):224-33.

32. Rawla P, Sunkara T, Raj JP. Role of biologics and biosimilars in inflammatory bowel disease: current trends and future perspectives. J Inflamm Res. 2018;11:215-26.

33. Rudrapatna VA, Velayos F. Biosimilars for the Treatment of Inflammatory Bowel Disease. Pract Gastroenterol. 2019;43(4):84-91.

34. Solitano V, D'Amico F, Fiorino G, Peyrin-Biroulet L, Danese S. Biosimilar switching in inflammatory bowel disease: from evidence to clinical practice. Expert Rev Clin Immunol. 2020;16(10):1019-28.

35. Fleischmann R, Jairath V, Mysler E, Nicholls D, Declerck P. Nonmedical Switching From Originators to Biosimilars: Does the Nocebo Effect Explain

Treatment Failures and Adverse Events in Rheumatology and Gastroenterology? Rheumatol Ther. 2020;7(1):35-64.

36. D'haens G, Sandborn WJ, Feagan BG, Geboes K, Hanauer SB, Irvine EJ, et al. A review of activity indices and efficacy end points for clinical trials of medical therapy in adults with ulcerative colitis. Gastroenterology. 2007;132(2):763-86.

37. Koutroumpakis E, Katsanos KH. Implementation of the simple endoscopic activity score in crohn's disease. Saudi J Gastroenterol. 2016;22(3):183-91.

38. Kim YS, Jung SA, Lee KM, Park SJ, Kim TO, Choi CH, et al. Impact of inflammatory bowel disease on daily life: an online survey by the Korean Association for the Study of Intestinal Diseases. Intest Res. 2017;15(3):338-44.

39. Knowles SR, Keefer L, Wilding H, Hewitt C, Graff LA, Mikocka-Walus A. Quality of Life in Inflammatory Bowel Disease: A Systematic Review and Meta-analyses—Part II. Inflammatory Bowel Diseases. 2018;24(5):966-76.

40. Kaplan GG. The global burden of IBD: from 2015 to 2025. Nat Rev Gastroenterol Hepatol. 2015;12(12):720-7.

41. Smerat T, Khdour M, Abdoh Q, Hallak H. Assessment of health-related quality of life in patients with inflammatory bowel disease in occupied Palestinian territory: a correlation cross-sectional study. Lancet. 2021;398 Suppl 1:S48.

42. Kamp K, Dudley-Brown S, Heitkemper M, Wyatt G, Given B. Symptoms among emerging adults with inflammatory bowel disease: a descriptive study. Res Nurs Health. 2020;43(1):48-55.

43. Perler BK, Ungaro R, Baird G, Mallette M, Bright R, Shah S, et al. Presenting symptoms in inflammatory bowel disease: descriptive analysis of a community-based inception cohort. BMC Gastroenterology. 2019;19(1):47.

44. Mosli M, Alawadhi S, Hasan F, Abou Rached A, Sanai F, Danese S. Incidence, Prevalence, and Clinical Epidemiology of Inflammatory Bowel Disease in the Arab World: A Systematic Review and Meta-Analysis. Inflamm Intest Dis. 2021;6(3):123-31.

45. Noiseux I, Veilleux S, Bitton A, Kohen R, Vachon L, White Guay B, et al. Inflammatory bowel disease patient perceptions of diagnostic and monitoring tests and procedures. BMC Gastroenterol. 2019;19(1):30.

46. Triantafyllidi A, Xanthos T, Papalois A, Triantafillidis JK. Herbal and plant therapy in patients with inflammatory bowel disease. Ann Gastroenterol. 2015;28(2): 210-20.

47. Engels M, Cross RK, Long MD. Exercise in patients with inflammatory bowel diseases: current perspectives. Clin Exp Gastroenterol. 2018;11:1-11.

48. Campmans-Kuijpers MJE, Dijkstra G. Food and Food Groups in Inflammatory Bowel Disease (IBD): The Design of the Groningen Anti-Inflammatory Diet (GrAID). Nutrients. 2021;13(4).

49. Kinnucan JA, Rubin DT, Ali T. Sleep and inflammatory bowel disease: exploring the relationship between sleep disturbances and inflammation. Gastroenterol Hepatol (N Y). 2013;9(11):718-27.

50. Berkowitz L, Schultz BM, Salazar GA, Pardo-Roa C, Sebastián VP, Álvarez-Lobos MM, et al. Impact of Cigarette Smoking on the Gastrointestinal Tract Inflammation: Opposing Effects in Crohn's Disease and Ulcerative Colitis. Frontiers in Immunology. 2018;9.

51. Yakut M, Üstün Y, Kabaçam G, Soykan I. Serum vitamin B12 and folate status in patients with inflammatory bowel diseases. European Journal of Internal Medicine. 2010;21(4):320-3.

52. Ananthakrishnan AN. Vitamin D and Inflammatory Bowel Disease. Gastroenterol Hepatol (N Y). 2016;12(8):513-5.

53. Gaspar R, Branco CC, Macedo G. Liver manifestations and complications in inflammatory bowel disease: A review. World J Hepatol. 2021;13(12):1956-67.

54. Mohammed Vashist N, Samaan M, Mosli MH, Parker CE, MacDonald JK, Nelson SA, et al. Endoscopic scoring indices for evaluation of disease activity in ulcerative colitis. Cochrane Database Syst Rev. 2018;1(1):Cd011450.

55. Lichtenstein GR, Loftus EV, Isaacs KL, Regueiro MD, Gerson LB, Sands BE. ACG Clinical Guideline: Management of Crohn's Disease in Adults. Official journal of the American College of Gastroenterology | ACG. 2018;113(4).

56. Pabla BS, Schwartz DA. Assessing Severity of Disease in Patients with Ulcerative Colitis. Gastroenterology Clinics of North America. 2020;49(4):671-88.

57. D’Haens G, Sandborn WJ, Feagan BG, Geboes K, Hanauer SB, Irvine EJ, et al. A Review of Activity Indices and Efficacy End Points for Clinical Trials of Medical Therapy in Adults With Ulcerative Colitis. Gastroenterology. 2007;132(2):763-86.

58. Viscido A, Valvano M, Stefanelli G, Capannolo A, Castellini C, Onori E, et al. Systematic review and meta-analysis: the advantage of endoscopic Mayo score 0 over 1 in patients with ulcerative colitis. BMC Gastroenterology. 2022;22(1):92.

59. Paine ER. Colonoscopic evaluation in ulcerative colitis. Gastroenterology Report. 2014;2(3):161-8.

60. Schiavone C, Romano M. Diagnosis and management of Crohn's disease. J Ultrasound. 2015;18(1):1-2.

61. Gatta G, Di Grezia G, Di Mizio V, Landolfi C, Mansi L, De Sio I, et al. Crohn's disease imaging: a review. Gastroenterol Res Pract. 2012;2012:816920.

62. Gajendran M, Loganathan P, Jimenez G, Catinella AP, Ng N, Umapathy C, et al. A comprehensive review and update on ulcerative colitis(). Dis Mon. 2019;65(12):100851.

63. Gajendran M, Loganathan P, Catinella AP, Hashash JG. A comprehensive review and update on Crohn's disease. Dis Mon. 2018;64(2):20-57.

64. Ko CW, Singh S, Feuerstein JD, Falck-Ytter C, Falck-Ytter Y, Cross RK, et al. AGA Clinical Practice Guidelines on the Management of Mild-to-Moderate Ulcerative Colitis. Gastroenterology. 2019;156(3):748-64.

65. Feuerstein JD, Isaacs KL, Schneider Y, Siddique SM, Falck-Ytter Y, Singh S, et al. AGA Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis. Gastroenterology. 2020;158(5):1450-61.

66. Cushing K, Higgins PDR. Management of Crohn Disease: A Review. Jama. 2021;325(1):69-80.

67. Feuerstein JD, Ho EY, Shmidt E, Singh H, Falck-Ytter Y, Sultan S, et al. AGA Clinical Practice Guidelines on the Medical Management of Moderate to Severe Luminal and Perianal Fistulizing Crohn’s Disease. Gastroenterology. 2021;160(7):2496-508.

68. Grossberg LB, Papamichael K, Cheifetz AS. Review article: emerging drug therapies in inflammatory bowel disease. Aliment Pharmacol Ther. 2022;55(7):789-804.

69. Martínez-Montiel MP, Casis-Herce B, Gómez-Gómez GJ, Masedo-González A, Yela-San Bernardino C, Piedracoba C, et al. Pharmacologic therapy for inflammatory bowel disease refractory to steroids. Clin Exp Gastroenterol. 2015;8:257-69.

70. Elhag DA, Kumar M, Saadaoui M, Akobeng AK, Al-Mudahka F, Elawad M, et al. Inflammatory Bowel Disease Treatments and Predictive Biomarkers of Therapeutic Response. International Journal of Molecular Sciences. 2022;23(13).

71. Fakhoury M, Negrulj R, Mooranian A, Al-Salami H. Inflammatory bowel disease: clinical aspects and treatments. J Inflamm Res. 2014;7:113-20.

72. Dudek P, Fabisiak A, Zatorski H, Malecka-Wojciesko E, Talar-Wojnarowska R. Efficacy, Safety and Future Perspectives of JAK Inhibitors in the IBD Treatment. J Clin Med. 2021;10(23).

73. Bayoumy AB, Van Liere ELSA, Simsek M, Warner B, Loganayagam A, Sanderson JD, et al. Efficacy, safety and drug survival of thioguanine as maintenance treatment for inflammatory bowel disease: A retrospective multi-centre study in the United Kingdom. BMC Gastroenterology. 2020;20(1).

74. Singh A, Mahajan R, Kedia S, Dutta AK, Anand A, Bernstein CN, et al. Use of thiopurines in inflammatory bowel disease: an update. Intest Res. 2022;20(1):11-30.

75. Limketkai BN, Hamideh M, Shah R, Sauk JS, Jaffe N. Dietary Patterns and Their Association With Symptoms Activity in Inflammatory Bowel Diseases. Inflamm Bowel Dis. 2022.

76. Triantafillidis JK, Merikas E, Georgopoulos F. Current and emerging drugs for the treatment of inflammatory bowel disease. Drug Des Devel Ther. 2011;5:185-210.

77. Hazel K, O'Connor A. Emerging treatments for inflammatory bowel disease. Therapeutic Advances in Chronic Disease. 2020;11:2040622319899297.

78. Yan Y, Xing C, Xiao Y, Shen X, Zhang Z, He C, et al. Discovery and Anti-Inflammatory Activity Evaluation of a Novel CDK8 Inhibitor through Upregulation

of IL-10 for the Treatment of Inflammatory Bowel Disease In Vivo. Journal of Medicinal Chemistry. 2022;65(10):7334-62.

79. Lungaro L, Costanzini A, Manza F, Barbalinardo M, Gentili D, Guarino M, et al. Impact of Female Gender in Inflammatory Bowel Diseases: A Narrative Review. J Pers Med. 2023;13(2).

80. Cole JL. Steroid-Induced Sleep Disturbance and Delirium: A Focused Review for Critically Ill Patients. Fed Pract. 2020;37(6):260-7.

81. Dokoohaki S, Ghareghani M, Ghanbari A, Farhadi N, Zibara K, Sadeghi H. Corticosteroid therapy exacerbates the reduction of melatonin in multiple sclerosis. Steroids. 2017;128:32-6.

82. Lowe SC, Sauk JS, Limketkai BN, Kwaan MR. Declining Rates of Surgery for Inflammatory Bowel Disease in the Era of Biologic Therapy. Journal of Gastrointestinal Surgery. 2021;25(1):211-9.

83. Anbazhagan AN, Priyamvada S, Alrefai WA, Dudeja PK. Pathophysiology of IBD associated diarrhea. Tissue Barriers. 2018;6(2):e1463897.

Appendices

Appendix A

Questionnaire English Version

Data Collection Form

<u>Patient demographic characteristics</u>

- **Gender**
  - Male
  - female

- **Residence**
  - City
  - village
  - camp

- **Age** _____

- **Weight** _____

- **Education level**
  - No studying
  - primary school
  - middle school high school
  - diploma
  - under graduate
  - Post graduate

- **Smoking**
  - Smoker
  - non-smoker
  - I was smoking

- **Diagnosis**
  - Crohn’s
  - ulcerative colitis

- **Duration illness** _____

- **Stage of disease**
  - mild
  - moderate
  - sever

- **Have you previously performed operations on the digestive system, such as cutting the intestines?**
  - Yes
  - no

- **Family history**
  - Yes
  - no

- **Do the symptoms affect your daily activity?**
  - yes
  - no

- **Does the disease affect your sleep?**
  - Yes
  - no
- **Do you think that the disease has anything to do with the nature of your food?**
  - Yes
  - no

- **What foods cause pain and diarrhea?**
  - no-thing
  - fried food
  - legumes
  - fats
  - fast food
  - carb
  - fibers
  - dairy
  - spicy
  - everything

- **Do you think that herbs have a role in alleviating symptoms?**
  - Yes
  - no

- **Do you exercise and feel better?**
  - I don’t exercise
  - I exercise and don’t feel better
  - I exercise and feel better

- **What was the first symptom you experienced?**
  - Diarrhea with blood
  - diarrhea without blood
  - and mucus
  - stomach ache
  - gases
  - fatigue
  - weight loss

What did you experience from these symptoms?

diarrhea	Yes	no
Abdominal pain	yes	no
Gases	yes	no
Bulges	yes	no
Joint pain	yes	no
Rash	yes	no
Abdominal mass	yes	no
Hemorrhoids	yes	no
Fistula	yes	no
Weight loss	yes	no
Fatigue and exhaustion	yes	no
Constipation	yes	no
Stomachache	yes	no
Vomiting	yes	no
Dry skin	yes	no
Blood coming out with the stool	yes	no
Night sweats	yes	no
Anorexia	yes	no
Inflammation of the skin, eyes and joints	yes	no
Delayed growth	yes	no

- **The first medication I used**
  - Mesalamine
  - azathioprine
  - corticosteroid
  - biology

- **Current medications**

mesalamine	yes	no
Azathioprine	yes	no
Corticosteroid	yes	no
Biology	yes	no

- **Do you perform regular checks?**
  - Yes
  - no
  - **If yes, what tests do you do periodically:**

blood test	yes	no
Stool examination	yes	no
Iron level	yes	no
B12	yes	no
vit D	yes	no
Liver functions	yes	no
kidney functions	yes	no
Inflammation factor	yes	no
Gastrointestinal Endoscopy	yes	no
CT scan of the abdomen	yes	no
Fluidity and coagulation of blood	yes	no
Calprotectin test	yes	no

Appendix B

Questionnaire Arabic Version

الجنس:

- **ذكر**
- **انثى**

الإقامة:

- **مدينة**
- **قرية**
- **مخيم**

العمر: _____

الوزن: _____

- **غير دارس**
- **ابتدائي**
- **اعدادي**
- **ثانوية عامة**
- **دبلوم(كلية)**
- **جامعي (بكالوريوس)**
- **دراسات عليا**

التدخين:

- **مدخن**
- **كنت مدخن وتركت التدخين**
- **غير مدخن**

التشخيص:

- **كرون**
- **قولون تقرحي**

مدة المرض: ----------_____

دورة المرض:

- **بسيط**
- **معتدل**
- **شديد**

هل قمت في اجراء عمليات سابقا في الجهاز الهضمي مثل قص الامعاء (ضع x في حال لا يوجد):

- **نعم**
- **لا**

تاريخ عائلي لنفس المرض:

- **يوجد**
- **لا يوجد**

هل تؤثر الاعراض على نشاطك اليومي؟

- **نعم**
- **لا**

هل يؤثر المرض على نومك؟

- **لا يؤثر**
- **يؤثر**

هل تعتقد ان المرض له علاقة في طبيعة الطعام؟

- **نعم**
- **لا**

في حال كان جوابك نعم ما هي الأطعمة التي تثير الوجع والاسهال؟

_____

هل تعتقد ان للأعشاب دور في تخفيف الاعراض؟

- **نعم**
- **لا**

هل تمارس الرياضة وتشعر بتحسن؟

- **لا امارس**
- **امارس ولا اشعر بتحسن**
- **امارس واشعر بتحسن**

ما هو اول عرض عانيت منه:

- **اسهال مع دم**
- **اسهال بدون دم مع مخاط**
- **وجع بطن**
- **وجع مفاصل**
- **تعب وارهاق**
- **غازات**
- **نقص بالوزن**

ماذا عانيت من هذه الاعراض:

- **اسهال**
- **الم في البطن**
- **غازات**
- **انتفاخات**
- **وجع مفاصل**
- **طفح جلدي**
- **كتلة في البطن**
- **بواسير**
- **نواصير**

- **نقصان في الوزن**
- **تعب وارهاق**
- **امساك**
- **وجع في المعدة**
- **تقيئ**
- **جفاف في الجلد**
- **خروج دم مع البراز**
- **تعرق ليلي**
- **فقدان الشهية**
- **التهاب الجلد، العيون والمفاصل**
- **تأخر في النمو**

اول دواء استخدمته:

- **ميسالامين (بنتازا، رافاسال)**
- **ازاثيوبرين (اميوران)**
- **كورتيزون**
- **بيولوجي (هيوميرا, ريمسيما, ريميكيد)**
- **غير ذلك**

إذا كان الجواب غير ذلك الرجاء كتابة اسم الدواء

_____

الادوية الحالية:

- **ميسالامين (بنتازا، رافاسال)**
- **ازاثيوبرين (اميوران)**
- **كورتيزون**
- **بيولوجي (هيوميرا, ريمسيما, ريميكيد)**
- **غير ذلك**

إذا كان الجواب غير ذلك الرجاء كتابة اسم الدواء_____

هل تقوم بفحوصات دورية:

- **نعم**
- **لا**

ما هي الفحوصات التي تقوم بها دورياً:

- **فحص دم**
- **فحص براز**
- **منسوب الحديد**
- **معامل الالتهاب**
- **وظائف الكبد**
- **وظائف الكلى**
- **فيتامين دال**
- **فيتامين بي 12**
- **منظار**
- **صورة طبقية للبطن**
- **ميوعة وتخثر الدم**
- **فحص كالبر وتكتين البرازي**

Appendix C

IRB Approval

An-Najah National
University
Faculty of Medicine &
Health Sciences
Institutional Review Board

جامعة النجاح الوطنية
كلية الطب وعلوم الصحة
لجنة اخلاقيات البحث العلمي

Ref:. **Mas. Nov. 2022/27**

IRB Approval Letter

Title of Research:
Evaluation of inflammatory bowel disease severity, treatment, and outcomes among Palestinian patients

Submitted by :
Aya Basim Naser

Supervisor :
Rowa Al Ramahi

Approved:
28th Nov. 2022.

Your Study Title "**Evaluation of inflammatory bowel disease severity, treatment, and outcomes among Palestinian patients.**" reviewed by An-Najah National University IRB committee and was approved on 28th Nov. 2022.

Hasan Fitian, MD
IRB Committee Chairman

IRB
Institutional Review Board

Nablus - P.O Box :7 or 707 | Tel (970) (09) 2342902/4/7/8/14 | Faximile (970) (09) 2342910| E-mail : IRB@najah.edu

Appendix D

Tables of Study

Table D1

The results of the symptoms the patients felt

	frequency		percentage		
	yes	no	yes	no	p.value
Diarrhea					
UC	82	23	78.1%	21.9%	0.365
CD	83	31	72.8%	27.2%	
Abdominal pain					
UC	62	43	59.1%	40.9%	0.022
CD	84	30	73.6%	26.3%	
Gases					
UC	65	40	61.9%	38.1%	0.387
CD	64	50	56.1%	43.8%	
Bulges					
UC	41	64	39%	60.9%	0.196
CD	35	79	30.7%	69.2%	
Joint pain					
UC	46	59	43.8%	56.2%	0.691
CD	53	61	46.5%	53.5%	
Rash					
UC	12	93	11.4%	88.5%	0.448
CD	17	97	14.9%	85.1%	
Abdominal mass					
UC	16	89	15.2%	84.7%	0.014
CD	6	108	5.2%	94.7%	
Hemorrhoids					
UC	28	77	26.6%	73.3%	0.330
CD	24	90	21.1%	78.9%	
Fistula					
UC	16	89	15.2%	84.7%	0.531
CD	21	93	18.4%	81.5%	
Weight loss					
UC	39	66	37.1%	62.8%	0.255
CD	51	63	44.7%	55.2%	
Fatigue					
UC	53	52	50.4%	49.5%	0.742
CD	55	59	48.2%	51.7%	

Constipation					
UC	22	83	20.9%	79%	0.056
CD	37	77	32.4%	67.5%	
Stomachache					
UC	32	73	30.4%	69.5%	0.917
CD	34	80	29.8%	70.2%	
Vomiting					
UC	26	79	24.7%	75.2%	1
CD	41	73	35.9%	64%	
Dry skin					
UC	17	88	16.2%	83.8%	0.936
CD	18	96	15.7%	84.2%	
Blood with stool					
UC	42	63	40%	60%	0.063
CD	32	82	28.1%	71.9%	
Night sweat					
UC	18	87	17.1%	82.8%	0.805
CD	21	93	18.4%	81.5%	
Anorexia					
UC	35	70	33.3%	66.6%	0.419
CD	44	70	38.5%	61.4%	
Inflammation Skin, eye, joint					
UC	14	91	13.3%	86.6%	0.522
CD	12	102	10.5%	89.4%	
Delayed growth					
UC	4	101	3.8%	96.2%	0.906
CD	4	110	3.5%	96.5%	

UC: ulcerative colitis, CD: crohn’s disease

Appendix E

Figure of Study

Figure E1

Current user of azathioprine in different stages of crohn's disease

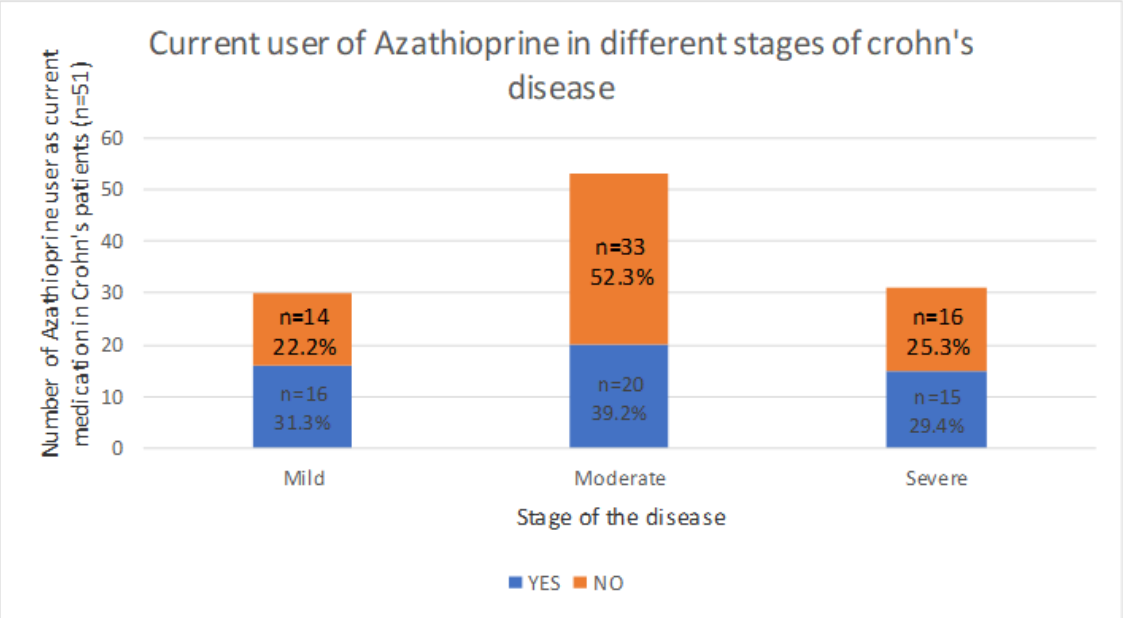
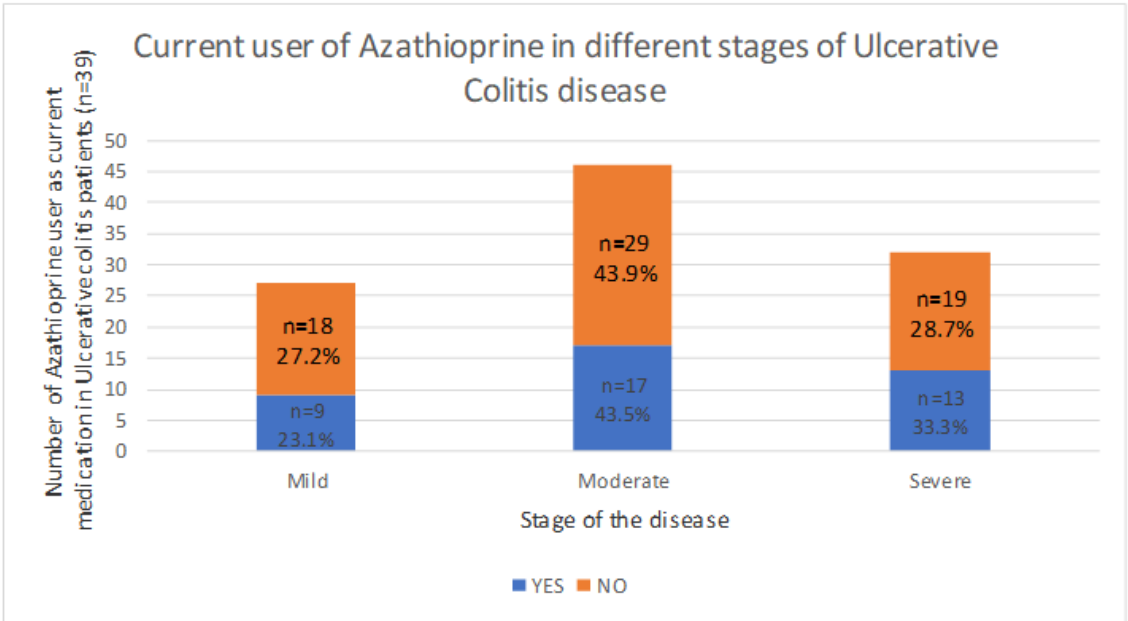


Figure E2

Current user of azathioprine in different stages of ulcerative colitis disease



جـامعـــة النجاح الوطنية
كليـــة الدراســـات العليـــا

تقييم شدة مرض التهاب الأمعاء وعلاجه ونتائجه بين المرضى الفلسطينيين

إعداد

آيه باسم ناصر

إشراف

أ. د. رواء الرمحي

قدمت هذه الرسالة استكمالا لمتطلبات الحصول على درجة الماجستير في علم الأدوية، من كلية الدراسات العليا، في جامعة النجاح الوطنية، نابلس– فلسطين.

2024

تقييم شدة مرض التهاب الأمعاء وعلاجه ونتائجه بين المرضى الفلسطينيين

إعداد

آيه باسم ناصر

إشراف

أ. د. رواء الرمحي

الملخص

الخلفية والاهداف: يعتبر مرض التهاب الأمعاء من الأمراض المزمنة، وقد أصبح أكثر انتشارًا في الآونة الأخيرة. الدراسات المتعلقة به في فلسطين محدودة. تهدف هذه الدراسة إلى تقييم مدى خطورة المرض وعلاجه ونتائجه بين المرضى الفلسطينيين المصابين بمرض التهاب الأمعاء لتحسين علاجه ومتابعته.

منهجية الدراسة: اجريت هذه الدراسة المقطعية في الفترة من أغسطس 2022 إلى مارس 2023 في مستشفى النجاح الجامعي الوطني، نابلس، فلسطين. تم استخدام نموذج جمع البيانات لجمع البيانات من ملفات المرضى والمقابلات، وقد تم تصميمه لتقييم شدة مرض التهاب الأمعاء وعلاجه ونتائجه. شارك في الدراسة ما مجموعه 219 مريضا. وتم تحليل النتائج باستخدام الحزمة الإحصائية للعلوم الاجتماعية (SPSS).

النتائج: شملت هذه الدراسة 219 مريضاً، 53.4% منهم ذكور و46.6% إناث، مدة المرض 1–38 سنة، وتراوحت أعمارهم بين 6–86 سنة. وجدنا أن 47.9% من المرضى يعانون من التهاب القولون التقرحي و52.1% من مرض كرون، وفيما يتعلق بخطورة المرض التي اعتمدت على الخصائص السريرية والتشخيصية، تم تشخيص المرضى بالخفيف في 26% من الحالات، في حين أن 45.2% كانوا معتدلين، و28.8%. تم تشخيصهم بحالة شديدة. علاوة على ذلك فإن الأعراض الأكثر شيوعاً كانت الإسهال الدموي بنسبة 63%. فيما يتعلق بالأدوية، كان الميزالامين هو الدواء الأكثر شيوعًا المستخدم

كدواء أولي لدى مرضى التهاب الأمعاء، بنسبة 74%. أما بالنسبة للأدوية الحالية فقد تم استخدام الميسلامين بنسبة 46.6%، والكورتيزون بنسبة 22.8%، والآزوثيوبرين بنسبة 41.1%، والعلاج البيولوجي بنسبة 35.2%.

الاستنتاج: يعاني العديد من المرضى من مراحل حادة من المرض مما يؤثر على حياتهم اليومية. توضح هذه الدراسة عددًا من العوامل المرتبطة المهمة التي يجب أخذها في الاعتبار عند التعامل مع مرض التهاب الأمعاء. قد تساعد نتائج الدراسة مقدمي الرعاية الصحية وواضعي الاستراتيجيات على زيادة المعرفة حول مرضى التهاب الأمعاء الالتهابي وعلاجه، لتحسين نوعية حياة مريض التهاب الأمعاء الالتهابي.

الكلمات المفتاحية: مرض التهاب الأمعاء، العلاج، الشدة، الأعراض، العوامل، فلسطين AGA.