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Assessment of Health-Related Quality of Life for Patients with Inflammatory Bowel Diseases in Palestine

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Assessment of health-related quality of life for patients with inflammatory bowel diseases in Palestine

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Dedication

I lovingly dedicate this thesis to my beloved parents, who never stop giving of themselves in countless ways. To my dearest husband, for his endless support and encouragement. To My beloved daughter, Sham, who lighten my life up and give me the power to keep on. Also to my brothers and sisters, who supported me each step of the way and have been my constant source of inspiration. They all have given me the drive and discipline to tackle any task with enthusiasm and determination. Without their unfailing support and help this work would not have been possible.

Tasneem Smerat

Declaration

I certify that the thesis submitted for the degree of master is the result of my own research, except where otherwise acknowledged, and that this thesis (or any part of the same) has not be submitted for a higher degree to any other university or institution.

Signed: ……..

Tasneem Ismail Smerat

Date: May 5, 2018

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{وَمَا تَوْفِيقِي إِلَّا بِاللَّهِ عَلَيْهِ تَوَكَّلْتُ وَإِلَيْهِ أُنِيبُ}هود 88

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List of Abbreviations

5-ASA:	5-aminosalicylic acid
CD:	Crohn's disease
GI:	Gastrointestinal
IBD:	Inflammatory Bowel Disease
IBDQ:	Inflammatory Bowel Disease Questionnaire
MMAS-8:	Modified Morisky Medication Adherence Scale
QoL:	Quality of Life
REC:	Research Ethical Committee
SPSS:	Statistical Package for Social Sciences program
TNF:	Tumor Necrosis Factor
TPMT:	Thiopurine S-methyl Transferase
UC:	Ulcerative Colitis
WHO:	World Health Organization

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Abstract

Background: Measuring patient's quality of life (QoL) in chronic diseases is very important to assess disease outcomes and impact of intervention. Inflammatory bowel disease (IBD) has a large impact on patient's QoL. Disease activity has been suggested as an important indicator for QoL in patients with IBD. Limited studies regarding association between medication adherence and QoL in IBD patients are available worldwide and data was conflicting. Therefore, this study was performed to examine the association between disease activity, medication adherence and its impact on QoL among IBD in Palestine. Also, this study aimed to determine the QoL profile, medication adherence for IBD patients and stated the factors associated with QoL.

Methods: A correlation cross-sectional study was conducted from July 2017 to February 2018 at An-Najah National University Hospital, Nablus, Alia Governmental Hospital, Hebron and Dr. Khalil Suleiman Hospital, Jenin, Palestine. The disease specific tool inflammatory bowel disease questionnaire (IBDQ) was used to examine QoL. Medication adherence was measured using modified Morisky adherence scale8 (MMAS-8). The results were analyzed using Statistical Package for Social Sciences (SPSS) program version 20. Multiple linear regression analysis was performed to determine the most important variables related with QoL in IBD patients.

Results: One hundred and thirty two patients were involved in this study. Of them, about 58.3% are males with a mean ± SD for age of 34 ± 13 years ranged from 18-70 years. Active disease was reported in 81 participants (61.4%) in the previous 6 months. Using MMSA-8 questionnaire, low adherence was reported in 39.4% of the participants. The reported QoL of this study was measured by using the average IBDQ scores, which was 150.72 ± 30.08 and this is indicated a low QoL among Palestinian IBD patients. Emotional and bowel domains are more disrupted than other domains. Active disease was the major significant factor associated with IBD patients QoL in its all dimensional score (*P- value<0.001*). No significant association was found between medication adherence and patients QoL. Diagnosis (Type of disease) didn't affect any IBDQ dimensional score. Regression analysis revealed that: patients with remission (r^2 = 0.436, *p-value <0.001),* with high educational status (r^2 =0.035, *p-value =0.009*) and using Azathioprine drug (r^2 =0.017, *p- value =0.034*) were independently associated with high QoL.

Conclusions: This study shows a low QoL among Palestinian IBD patients compared to other countries and identified a number of significant associated factors that should be considered when dealing with IBD. Results of the study may help healthcare providers to identify patients at risk of low QoL especially those in the relapse status and active symptoms. Attention should be provided by healthcare givers and strategy makers to increase knowledge about IBD, to improve IBD patient's QoL and to identify the importance of treatment adherence**.**

Keywords: *Inflammatory Bowel disease, Inflammatory Bowel disease questionnaire, Active disease, Quality of Life, Palestine*.

Chapter One

Introduction

1. Introduction

1.1 Background

1.1.1 Inflammatory bowel disease

Inflammatory bowel disease (IBD) is an autoimmune disorder, defined as a chronic progressive relapsing inflammation of the intestinal mucosa (Hanauer 2006). It is comprised of Crohn's disease (CD) and ulcerative colitis (UC). IBDs commonly appear in young adults between the ages of fifteen and thirty, but it may occur at any age (Hanauer 2006, Baumgart and Carding 2007).

Crohn's disease is a chronic IBD characterized by inflammation of the digestive or gastrointestinal (GI) tract. In fact, Crohn's can affect any part of the GI tract, from the mouth to the anus, although the terminal part is most commonly involved (the ileum) where it joins the beginning of the large intestine (or colon).

Ulcerative colitis is a chronic relapsing inflammatory disease of the colon. It affects the colon and rectum and typically involves only the innermost lining or mucosa, manifesting as continuous areas of inflammation and ulceration, with no segments of normal tissue (Colitis–Pathophysiology 2003).

The exact reason of IBD occurrence is not clear yet, it considered a result of complex relationship between genetic, infectious triggers, immune related and environmental factors like human gut microbiota, foods, smoke, chemical contamination that combine to contribute to progress of clinical CD (Gaya, Russell et al. 2006). It appears that immune system mistakenly attacks healthy bacteria in the GI tract then the chronic inflammation causes thickening of the intestinal wall, which triggers the symptoms (Khor, Gardet et al. 2011).

Strong evidence suggests a genetic basis for IBD. Nearly 10 to 20% of IBD patients also have a family history of the disease, with the greater risk among first-degree relatives (mother,

father, sister, or brother). Relatives of affected individuals have at least a 10-fold increased risk for IBD (Orholm, Munkholm et al. 1991, Scott 2000).

Inflammatory bowel disease is more common in developed countries (Bernstein, Fried et al. 2010, Molodecky, Soon et al. 2012). However in recent years its rate in industrialized countries has been stabilized while the number of patients with CD is rising up in developing countries (Baumgart and Sandborn 2012) with significant increase within Asian countries (Economou, Zambeli et al. 2009) .

The diagnosis is made based on clinical features, endoscopic findings, histology, radiology and in some cases serology (Nikolaus and Schreiber 2007, Bernstein, Fried et al. 2010). Diagnosis is based on the presence of architectural distortion (e.g., trans-mural or superficial patchy granulomatous in filtration) and/or acute inflammatory cells with an inability to down regulate the inflammatory immune response once activated (Hanauer 2006, Bernstein, Fried et al. 2010).

The predominant symptoms of IBD are diarrhea (with blood or/and mucus), GI bleeding, abdominal pain, weight loss, nausea and vomiting. Extra intestinal involvement includes skin lesions, arthritis, and iritis. Also, patients may develop abscesses and ulcers in the area of the anus in case of CD. Symptoms like joint pain, skin lesions, fatigue, and night sweats may also occur (FARMER 1974, Casati and Toner 2000, De Rooy, Toner et al. 2001).

Use of effective treatment regimens aiming to maintain patients in remission is of great importance. In treatment approaches, they can be either "step-up," which starts with milder drugs first, or “top-down," which gives people stronger drugs earlier in the treatment process. Many pharmaceutical preparations can be used to treat IBD. Although medical treatment of IBD is individualized to each patient, anti-inflammatory drugs are often the first step in the treatment of IBD. They include drugs such as Aminosalicylates.

Aminosalicylates are one of the oldest drugs currently used in the treatment of IBD. Salazopyrin is the prototype drug in this family, however Mesalazine (5-aminosalicylic acid [5-ASA]) (Pentasa®) is the main Aminosalicylates used in IBD treatment today. These are safe drugs that can be administered orally or rectally to reduce inflammation localized to different regions of the GI. 5-ASA is highly effective in mild to moderate UC that is considered the drug of choice for approximately 90% of patients with UC at first diagnosis (Langholz, Munkholm et al. 1991). In CD,5-ASA is still a therapeutic option in conjunction with other therapies to adequately control inflammation with CD confined to the colon. However, current European Crohn's and Colitis Organization (ECCO) discourages the use of 5-ASA drugs in both ileac and colonic disease, even if mild (Travis, Stange et al. 2006). Aminosalicylates are associated with a number of side effects, including digestive distress and headache.

Corticosteroids as anti-inflammatory are usually reserved for moderate to severe UC or CD patients that do not respond to other treatments. But it is associated with numerous side effects, including a puffy face, night sweats, excessive facial hair, insomnia and hyperactivity. More-serious side effects include high blood pressure, diabetes, osteoporosis, bone fractures, cataracts, glaucoma and increased chance of infection. They are not usually given for long term (Waljee, Wiitala et al. 2016).

Immunomodulators suppress the immune response from releasing inflammation-inducing chemicals in the intestinal lining. The most widely used immunomodulator for treatment of IBD is Azathioprine (Imuran®). Close follow-up with doctor is required to check for side effects especially on the liver and pancreas. Additional side effects include lowered resistance to infection and a rare chance of developing cancers such as lymphoma and skin cancers. Severe leucopenia, thrombocytopenia, anemia including macrocytic anemia, and/or pancytopenia may occur in patients being treated with Azathioprine. Severe bone marrow

suppression may also occur depending on patients with intermediate thiopurine S-methyl transferase (TPMT).

Cyclosporine is also considered an option but reserved for people who have not responded well to other medications. Its use is generally limited to UC with potential for serious side effects such as: kidney and liver damage, seizures and fatal infections and is not for long-term use.

Tumor necrosis factor (TNF)-alpha inhibitors, or "biologics," such as infliximab (Remicade®), adalimumab (Humira®) and golimumab (Simponi®) which work by neutralizing a protein produced by immune system. Methotrexate (Rheumatrex®) is sometimes used for people with CD who do not respond well to other medications. Care should be taken due to its side effects.

Natalizumab (Tysabri®) and vedolizumab (Entyvio®) work by stopping certain immune cell molecules (integrins) from binding to other cells in the intestinal lining. Natalizumab is associated with a rare but serious risk of progressive multifocal leuko-encephalopathy. Vedolizumab was recently approved for CD; it works like Natalizumab but appears not to have a risk of brain infection. Ustekinumab (Stelara®) a drug used to treat psoriasis can be useful in treating Crohn's. Also antibiotic can be used to reduce the amount of drainage and sometimes heal fistulas and abscesses in people with CD, commonly prescribed antibiotics are Metronidazole (Flagyl®) and Ciprofloxacin (Cipro®) (Mowat, Cole et al. 2011).

Generally, diet and nutrition are one of the important interesting topics for patients with IBD. Patients try to use a dietary modification to manage their underlying symptoms; they may reduce or totally avoid nutritionally important foods, as this may place them at increased risk for developing nutritional deficiencies. A low residue diet is commonly recommended for IBD by health professionals (Brown, Rampertab et al. 2011). Pre-illness studies and intervention trials in IBD provide an evidence recommendation that a plant-based diet,

increased consumption of fruit and vegetables and reduced red meat intake could be optional to patients with IBD in remission (Hou, Abraham et al. 2011). Dietary risk factors for IBD development includes: an excessive consumption of sugar, animal fat and linoleic acid, while a citrus fruit and high fiber diet may play a protective role.

1.1.2 Quality of life in IBD patients

Health related Quality of Life (QoL) studies are an important aspect in clinical trials especially for chronic diseases. The concept measures the functional impact of a disease and its therapy on the patient's daily life (Irvine 2008). As World Health Organization (WHO) defines health as *not merely the absence of disease or infirmity, but a state of complete psychical, mental and social well-being(Organization 1995)*, QoL encompasses several dimensions in addition to physical functioning, including social, cognitive, emotional functioning, and participation in daily activities (Rubin, Hungin et al. 2004).

All dimensions are related to each other, and they are affected by the patient's socio-demographic and clinical characteristics (Wilson and Cleary 1995).

In the past 10 years, there has been an increasing awareness of the importance of QoL issues related to IBD. Several studies indicate that QoL in IBD patients have been impaired in relative to healthy individual (Casellas, López-Vivancos et al. 2001, Nordin, Påhlman et al. 2002). Patients with IBD need life-long medical treatments and GI specialist's observation. Despite medical therapy reduces intestinal inflammation and ameliorates symptoms; curative therapy does not exist yet. Every drug has side effects that affect patient's life one way or another. Also despite therapeutic advances, approximately 20% of patients will require intestinal re-sectional surgery during their lifetime (Colitis–Pathophysiology 2003, Cima and Pemberton 2005, Peyrin-Biroulet, Harmsen et al. 2012).

Both UC and CD can be characterized as following a course of exacerbations followed by periods of remission; between 25% and 50% of patients will relapse within a year (Riley, Mani et al. 1990, Borley, Mortensen et al. 1997, Sewitch, Abrahamowicz et al. 2001, Husain and Triadafilopoulos 2004). All factors mentioned above have significant physical and

psychosocial impact on the patient's QoL (Ghosh and Mitchell 2007). The disease itself limits patient's lifestyle and daily activities.

Many socio-demographic variables such as gender, age, or educational level directly affect IBD patients QoL (Irvine, Feagan et al. 1994, Han, James et al. 1999, Hjortswang, Järnerot et al. 2003). Clinical variables such as type of intervention (medical treatment or surgery), therapy effectiveness, the occurrence of extra intestinal symptoms, annual rate of flare-ups, their severity, or the need for hospitalization have an impact on IBD patients' QoL (Casellas, López-Vivancos et al. 2000).

Generally in any chronic disease, treatment non-adherence is a common problem, averaging 50% in developed countries and is even poorer in developing countries (Sabaté 2003). Association between medication adherence in IBD patients and their QoL is not clear and data available are differing from research to another.

Adherence has been defined as cooperation of the patients in taking prescribed drugs, which includes timing, dosage and frequency (San Roman, Bermejo et al. 2005). It can be measured using different tools that were tested in clinical and research settings (e.g., circulating drug or metabolites levels, pharmacy refill, patient questionnaires, interviews, and diaries), no tool is considered a standard compared to others but self-report subjective measures appeared to be more reliable than the objective ones (Farmer 1999). One of the questionnaires that have been used to measure therapy adherence is the Modified Morisky Medication Adherence Scale (MMAS-8), a self-administered questionnaire, initially validated in patients on antihypertensive medications and then tested and validated also in IBD (Krousel-Wood, Islam et al. 2009, Kane, Becker et al. 2012, Goodhand, Kamperidis et al. 2013).

Non- adherence of IBD patients to their medication is a significant problem which may lead to several adverse clinical outcomes including an increase in disease activity, relapse (Kane,

Huo et al. 2003, Khan, Abbas et al. 2012), loss of response to anti-TNF agents (van der Have, Oldenburg et al. 2016), increased health costs(Kane and Shaya 2008), disability and possibly poor QoL(Hommel, Davis et al. 2008) that lead to higher morbidity and mortality (e.g., with colorectal cancer) .

A comprehensive knowledge about how the disease process, symptoms, complications, management itself as well as medication adherence affect the patients' QoL is needed.

During assessment of IBD patients QoL several instruments that have generally reflected a physician's perspective of disease activity were used. However QoL studies have suggested that functional status from the patient's viewpoint may be more indicative of health care utilization than the physicians' (Drossman, Patrick et al. 1989) and that patients are less likely to volunteer information regarding psychosocial impairment (Mitchell, Guyatt et al. 1988). Thus objections were raised to the inclusion of subjective instrument to assess patients QoL. Inflammatory Bowel Disease Questioner (IBDQ) a disease specific tool, the most common used questionnaire to assess the health related QoL in IBD patients worldwide. The IBDQ (Guyatt, Deyo et al. 1989, Irvine, Feagan et al. 1994) possesses both reliability and validity in several domains (digestive symptoms, emotional status, social function and systematic symptoms).

1.2 Statement of problem and study rational

The incidence and prevalence of IBD are increasing with time and in different regions around the world, indicating its emergence as a global disease (Molodecky, Soon et al. 2012).The main goal of the treatment in any chronic disease such as IBD is to improve the patient's symptoms and health related QoL. Many patients with IBD have concerns regarding symptoms, medication side effects, risk of cancer, and the need for surgery (Drossman, Patrick et al. 1989). All of these aspects can contribute to psychological distress and undermine QoL. Symptoms severity may hinder patients from enjoying their hobbies and affect their job performance. Health related QoL has received little scientific attention in gastroenterology, possibly because it's difficult to conceptualize and measure. However, recent studies indicate that people are able to categorize certain dimensions such as systemic, bowel, social and emotional status. Many studies indicate a lack of communication between the patients and their physicians when it comes to QoL.

Few studies on the association between drug adherence and health-related QoL in IBD patients are available and the data are conflicting(Chan, Chen et al. 2017).

1.3 Significance of the study

It is important to have baseline data about IBD patients QoL and to use the quantitative assessment of health perception and ability to functioning the physical, social and emotional domains to evaluate the natural history of the disease, catalogue the needs of IBD patients, focus the direction of research and allocation of resources towards patient suffering and assess outcome in clinical studies.

Measuring health related QoL, identifying the variables affecting it and evaluating whether health related QoL influences medication adherence and vice versa in IBD patients, is important to guide professionals towards intervention strategies implemented to improving patients QoL.To the best of our knowledge; this is the first study in the Palestinian West Bank to evaluate IBD patients QoL, the medications used and their medication adherence.

1.4 Objectives

1.4.1 Main objectives

The aims of this study were to evaluate our Palestinian IBD patients' QoL and to assess the effect of socio-demographic, clinical variables and adherence to medication on the health related QoL and to identify its predictors.

1.4.2 Specific objectives

- To obtain information about personal experiences of patients with IBD and the impact of symptom flare-ups on patients' QoL.
- To identify the most commonly prescribed drug in the treatment of IBD both CD and UC in Palestinian patients.
- To find the relationship between socio-demographic factors and the patient QoL
- To find if smoking is considered as a predisposing factor for impaired QoL or no.
- To find the effect of some clinical variables (disease duration, age at first diagnosis of the disease (age of onset), method of treatment (medical or surgical) on health related QoL.
- To assess medication adherence among IBD Palestinian patients.
- To find the relationship between medication adherence and patient QoL.

Chapter Two

Literature Review

2. Literature Review

Measuring patients QoL in chronic diseases is very important to assess disease outcomes and impact of its intervention (Moreno-Jiménez, Blanco et al. 2007). In this study we assessed Palestinian IBD patients QoL and established the relationship between socio-demographic, clinical factors with a health related QoL. This association has been investigated in other countries (Badia, Fernandez et al. 1995, Hjortswang, Järnerot et al. 2003, Han, McColl et al. 2005). Several studies have indicated the importance of age, educational level (Drossman, Leserman et al. 1991, Badia, Fernandez et al. 1995, Hjortswang, Järnerot et al. 2003) or sex with regard to QoL in IBD processes. The duration of IBD, the effects of treatments, and the consequences of its complications also affect the daily lives of these patients and impair their QoL (Drossman, Leserman et al. 1991). A study conducted in Saudi Arabia showed that patients aged 20 years to less than 30 years and patients with higher education levels had significantly better social QoL scores, also the longer disease duration (5 years or more) was associated with significantly lower systemic QoL scores than shorter duration (Mahalli and Alharthi 2017).

Also a study conducted by Blanco, Moreno-Jimenez *et al.* 2005found that men showed higher QoL scores in systemic, bowel, emotional and social symptoms and global IBDQ, and the differences between males and females were significant (Blanco, Moreno-Jimenez et al. 2005).

Many clinical variables such as type of treatment (medical treatment or surgery), occurrence of extra intestinal symptoms, presence of flare-ups and symptoms, their severity or the need for hospitalization have a great impact on IBD patients' QoL (Casellas, López-Vivancos et al. 2000, Blanco, Moreno-Jimenez et al. 2005). Moreover, Blanco *et al*. (Blanco, Moreno-Jimenez et al. 2005) showed patients undergoing surgery had lower QoL scores in comparison to those who received medical treatment only.

As the disease activity is one of the most important predictors for decreased QoL (Larsson, Lööf et al. 2008). Active disease has been found to contribute to poor QoL for IBD patients (Blondel-Kucharski, Chircop et al. 2001, Casellas, López-Vivancos et al. 2002, Janke, Raible et al. 2004, Saibeni, Cortinovis et al. 2004, Casellas, Arenas et al. 2005). IBD patients in remission scored significantly higher QoL scores for all domains using Short Form-36 (SF-36)(Zhou, Ren et al. 2010). Usually the patients who had relapse had an increased symptoms severity , stress, anxiety and lower QoL score compared to those who had inactive disease (Graff, Walker et al. 2006). In a Spanish study, they found that as disease severity worsened, a corresponding worsening in QoL occurs, regardless of disease subtype either CD or UC (Casellas, Arenas et al. 2005).

Symptoms severity hindered IBD patients from enjoying their hobbies and affected their job performance. A survey conducted by De Rooy *et al.,* for IBD outpatients found that concerns regarding loss of bowel control, producing unpleasant odors, achieving their full potential in the workplace, feeling dirty or smelly, and issues with sexual problems, ranked highly for both UC and CD (De Rooy, Toner et al. 2001). While there is some controversy in the field of evidence, Many studies indicate that patients with CD are more affected by their disease in terms of QoL than are patients with UC (Drossman, Leserman et al. 1991, Farmer, Easley et al. 1991, Irvine 1997).

This study assessed patients QoL using IBDQ as a subjective tool to indicate the impact of disease on patient's QoL. The IBDQ total score in health related QoL assessment studies in countries such as Netherlands, England, and Greece and Saudi Arabia has been calculated (de Boer, Wijker et al. 1995, Han, McColl et al. 1998, Pallis, Vlachonikolis et al. 2002). In some studies, IBD had more impact on patients' social and systemic symptoms when compared to the emotional and bowel symptoms (de Boer, Wijker et al. 1995, Han, McColl et al. 1998, Pallis, Vlachonikolis et al. 2002).

The link between IBD and smoking was reported in many studies. Smoking is known to affect disease activity in IBD (Russel, Nieman et al. 1996), in a cross sectional study conducted by Russel *et.al.,* on 1105 patients with IBD, they concluded a relationship between smoking and patients QoL in both UC and CD as smoking females had a lower QoL than non-smoking females in all dimensions of the IBDQ. In this study, we tried to find if smoking is considered as a predisposing factor for impaired QoL or not (Russel, Nieman et al. 1996).

Dietary factors in IBD development seem to play an underestimated role in the clinical course of the disease. On the other hand, data about food and IBD is not clear yet. Appropriate nutrition in both disease period (relapse and remission) may help prolonging remissions and thus improve the QoL for patients. Up to 71% of patients with IBD believe that diet affects their clinical course of disease and symptoms, with 90% of CD patients and 71% of UC patients employing diet restriction while in remission (Owczarek, Rodacki et al. 2016, Holt, Strauss et al. 2017). In a case-control study conducted by Guerreiro *et.al.,* a significantly lower mean daily intakes of several dietary groups were found in IBD patients due to patients exclusion of dairy products, vegetables and fruit (Guerreiro, Cravo et al. 2007).

Appropriate medication adherence is an important issue for successful IBD therapy. It seems reasonable that a good adherence to therapy results in a better QoL. But in IBD patient's data regarding association between drug adherence and health-related QoL in IBD patients was limited and controversial. In this study, we will try to evaluate whether health related QoL influences medication adherence in IBD patients and vice versa or not. In Hommel *et al* (Hommel, Davis et al. 2008) study the relationship between medication adherence and QoL in 36 young people with IBD was significant. Non-adherence to 6-mercaptopurine /Azathioprine was significantly associated with lower physical health QoL in patients. On the other hand, a study conducted by Horvath *et al*. (Horváth, Farkas et al. 2012)enrolled 592

IBD patients to evaluate whether QoL influences medication adherence and vice versa using Short Form-36 (SF-36) questionnaire and a medication adherence report scale. Their study concluded that no association between the sums of health related QoL and different sub-scores and non-adherence. They demonstrated that IBD is related to low QoL, which is not affected by drug therapy. Forgetting to take the medication' was the main reason for non-adherence in 67.6% of the cases. Medication adherence was significantly higher among non-smoker patients, and in the case of immunomodulator therapy. In some studies, the term of disability which seems to be more objective in measuring the effects of non-adherence on IBD patients than QoL, was found to be significantly higher in non-adherers than adherent patients (Horváth, Farkas et al. 2012).

In Jackson *et.al*., review (Jackson, Clatworthy et al. 2010) of 17 studies with 4,322 adult IBD subjects found that oral medications non-adherence in IBD ranging from 7% to 72%. But the rate in Asian IBD patients ranged between 20% and 30% (Kawakami, Tanaka et al. 2013). Many studies concluded that adherence rate with biological therapy is higher than other medications (Selinger, Robinson et al. 2011, Lopez, Billioud et al. 2013).

Poor medication adherence has several clinical outcomes, for example Kane, Huo et al demonstrated that non-adherent IBD patients had more than a fivefold greater risk of recurrence than adherent patients (Kane, Huo et al. 2003). Also non-adherence to anti-TNF therapy may result in immunogenicity thus decrease response to treatment.

In a study conducted by Van der Have *et al.* on 128 IBD patients who were on either infliximab or adalimumab, adherence was negatively associated with loss of response to anti-TNF agent (van der Have, Oldenburg et al. 2016).

A study conducted in 2017 (Bucci, Zingone et al. 2017) to assess factors predicting adherence to therapy in Italian IBD, 151 patients filled MMAS-8 questionnaire. Almost 30% of IBD

patients reported low compliance to therapy. According to the scale, they showed a 62.5% medium to high adherence to oral 5-ASA, a 72% medium to high adherence to Immunomodulators, and a 60% medium to high adherence to oral steroids and 94.9% adherence to biologics. Younger patients tend to be less compliant to their therapy. The main reasons for the low adherence to therapy were the “hassle of sticking to the medication plan” and “their feeling better”.

Chapter Three

Methodology

3. Methodology

This section describes the population and the subjects of the study, sample size, data collection instrument, and data analysis method.

3.1 Study design

This cross-sectional study was conducted by using standardized and validated assessment tools with IBD patients from July 2017 to February 2018.

3.2 Study setting

This study was conducted in Al-Najah National University hospital (Dr. Qusay clinic) the main referral hospitals for the northern Palestine, Nablus, Dr. Khalil Suleiman Hospital, Jenin and Hebron governmental hospital; Hebron. These hospitals serve as the major referral hospitals for the northern and southern districts of West Bank-Palestine and receive most cases of IBD patients from all northern and southern West Bank districts.

3.3 Study population

The medical records of all hospitals in 2017 showed that the number of IBD patients in hospitals was 200 patients during the study period (the numbers were taken from the hospital medical records and medication sheets). Each studied hospital gave us a list with the names of IBD patients in order to assess their comfort for this study.

3.4 Sampling procedure and sample size calculation

The Raosoft sample size calculator (an automated software program: http://www.raosoft.com/samplesize.html) was used for sample size calculation. We used a 5% margin of error at a 95% confidence interval as recommended; the required sample size was calculated to be 132 patients. Convenience sampling was used to recruit participants.

3.5 Inclusion and exclusion criteria

Patients aged 18 years and above who had UC or CD and were under the treatment for the disease, and who agreed to be participants in this study were included. Pregnant women were excluded.

3.6 Data collection

Data collection form (Appendix 1) was a questionnaire prepared after literature review of previous studies. Standard demographic questions were used to assess age, sex, and other background and clinical variables: disease duration, age at first diagnosis of the disease (age of onset), and disease activity (remission or relapse), method of treatment (medical or surgical), etc. Disease activity was determined based on patient report of symptom persistence for the previous 6 months, using a 6-level response format from (a – f). Active disease was defined as experiencing symptoms constantly to occasionally in the last six months and represented by (one of responses a– d), and inactive disease was defined as experiencing infrequent symptoms or feeling well (responses e or f).

Modified Morisky Medication Adherence Scale (MMAS-8), a self-administered questionnaire, initially validated in patients on antihypertensive medications and then tested and in IBD patients (Krousel-Wood, Islam et al. 2009, Kane, Becker et al. 2012, Goodhand, Kamperidis et al. 2013). In 2011, Trindade et al. validated this questionnaire in IBD, concluding that it could identify patients with poor adherence better than physicians (Trindade, Ehrlich et al. 2011) . Response categories are dichotomous with yes/no for the first 7 items and a 5-point Likert response for the last item. The scale is scored by assigning a single point to each question answered "no" in questions 1-4 and 6-7. A point is given in question 5 for an answer of "yes."

Health related QoL was assessed by using a disease specific questionnaire IBDQ. IBDQ was validated and translated into Arabic language previously. IBDQ have an adequate validity

and reliability in different languages and cultures. We obtained the Arabic-translated version form McMaster University (Guyatt, Mitchell et al. 1989).The IBDQ contains 32 questions that are classified into four main domains: bowel symptoms (10 questions), social impairment (5 questions), emotional function (12 questions) and systemic symptoms (5 questions) (Irvine 1993). The options for each question are graded from 1 to 7, where 1 indicates the worst symptoms and 7as the best symptoms. The total score ranges from 32 to 224 the higher score indicates a better QoL.

Academic experts in clinical pharmacists and academic researcher in statistical analysis reviewed and evaluated measurement items for content validity and clinical accuracy. Data collection forms were completed by interviewing participants.

3.7 Statistical analysis

All data was coded, entered and analyzed using SPSS windows version 20. Descriptive statistics were carried out for all variables. Mean ± standard deviation or median (Q1-Q3) were computed for domains. Frequencies (percentages) were calculated for socio-demographic variables. Categorical variables were compared using Chi-square. Independent student t-test or Mann Whitney tests used to compare means for two groups. One way ANOVA was used to compare groups of more than two; Kolmogorov–Smirnov test was used for normality. The comparison between UC and CD was made by chi-squared test and t-test. The comparison between the two groups depended on the total of the IBDQ scores and the four domains of the IBDQ where a P-value ≤ 0.05 was considered as significant result. Multiple linear regression tests were used to examine the factors affecting IBDQ score.

3.8 Ethical consideration

Approval from Research Ethical Committee (REC) at Al-Quds University (Appendix 2) and Palestinian Ministry of Health was taken before the study initiation (Appendix 3). All patients were interviewed after receiving consent form that confirms their willing to participate (Appendix 4).

Chapter Four

Results

4. Results

4.1 Socio-demographic and clinical characteristics of the patients

One hundred and thirty-two patients were interviewed during the study period in three different hospitals; 78 (59%) patients from Al-Najah National University Hospital -the major center in southern Palestine-, Nablus, 35(27%) patients from Alia Governmental Hospital, Hebron and 19 (14%) patients from Dr. Khalil Suleiman Hospital, Jenin (Figure **4.1**).

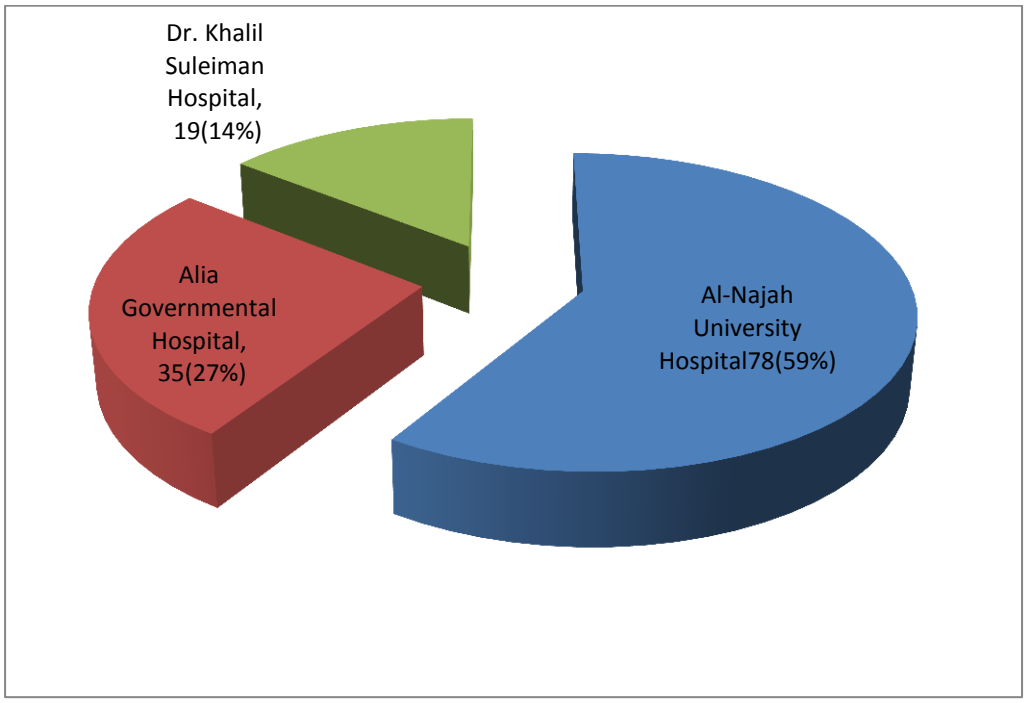

Figure 4.1: Number of participants interviewed from hospitals included in the study

Seventy-seven participants (58.3%) were males (Figure **4.2**). Mean ± standard division of the sample age equals to 34 ± 13 years ranged from 18-70 years.

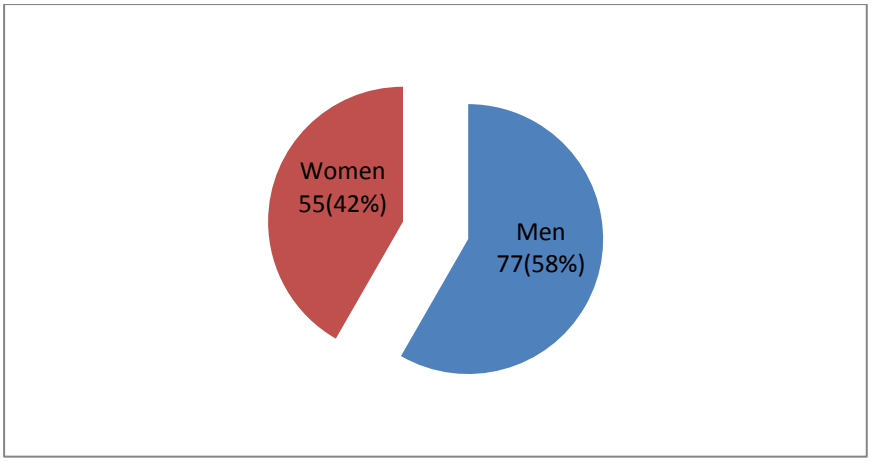

Figure4.2: Gender distribution of patients participating in the study

Eighty-six (65.2%) participants were married. More than 52% of the participants were employed and 56 (42.4%) participants with a moderate monthly income level. 40% of the patients had a university educational level. 51.5% of patients were diagnosed at the age between fifteen to thirty years. The duration of disease was divided into two groups: a group included those who had the disease for less than 5 years, the other group who had the disease for 5 years and more. More than 32% of participants were smokers. 18.9% of participants had a first-degree relative (mother, father, sister, or brother) diagnosed with IBD. 29.5% had a stress related condition before a short time of disease diagnosis. All patients received medical treatment during study period. Sixteen participants (12.9%) exposed to surgical treatment during the disease life (Table **4.1**).

Table4.1: Socio-demographic and clinical data of the study participants

Socio-demographic factors		Frequency	Percentages(N =132)
Marital status	Single, never married	46	34.8%
	Married or domestic partnership	86	65.2%
Current status	Student	22	16.7%
	Employed	69	52.3%
	Unemployed	41	31.1%
Income	Less than ₪3000	48	36.4%
	₪3000-₪4000	56	42.4%
	More than ₪4000	28	21.2%
Level of education	University or college or equivalent	54	40.9%
	Intermediate between secondary level and University	15	11.4%
	Secondary school	40	30.3%
	Primary school only (or less)	23	17.4%
Age at 1st diagnosis	Less than 15 years	14	10.6%
	15 to 30 years	68	51.5%
	More than 30 years	50	37.9%
Disease duration	Less than 5 years	83	62.9%
	5 years and more	49	37.1%
First degree relative	No	107	81.1%
	Yes	25	18.9%
Stress related condition	No	93	70.5%
	Yes	39	29.5%
Smoking habits	No	89	67.4%
	Yes	43	32.6%
Method of Treatment	Drugs	115	87.1%
	Both surgical and drugs	16	12.9%

6.2Type of food and dietary restriction

During the patient's interview, around 69% of them were found to include fruits and vegetables in their diet and 31% relied on fast food (Figure 4.3).

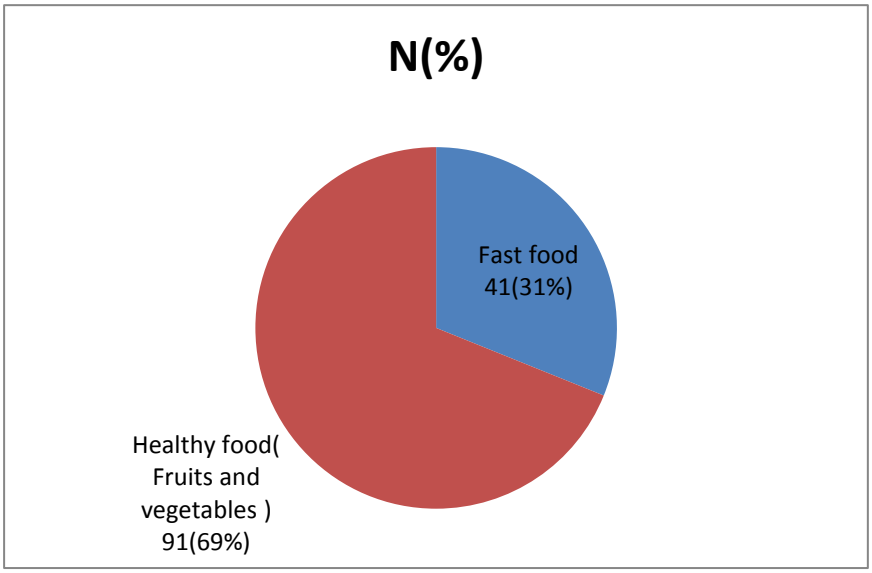

Figure 4.3: Type of food that patients generally eat

Ninety patients (68%) avoided certain types of foods such as milk, cereals and others (figure **4.4**).

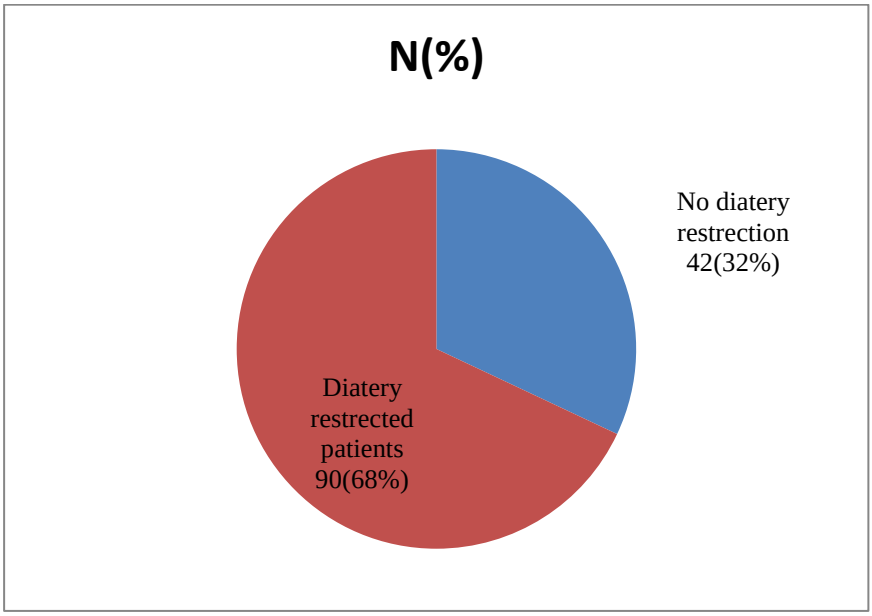

Figure4.4: Percentage of dietary restriction among IBD patients

4.3. Medications prescribed for IBD patients

4.3.1. Medications prescribed to treat IBD

Several types of medications have been prescribed. The most common medications prescribed were Azathioprine (Imuran®) in 96 patients (72.7%), 5-ASA (Pentasa®) in 68.2% of patients and Adalimumab (Humira®) in 26.5% of patients as shown in Figure **4.5**.

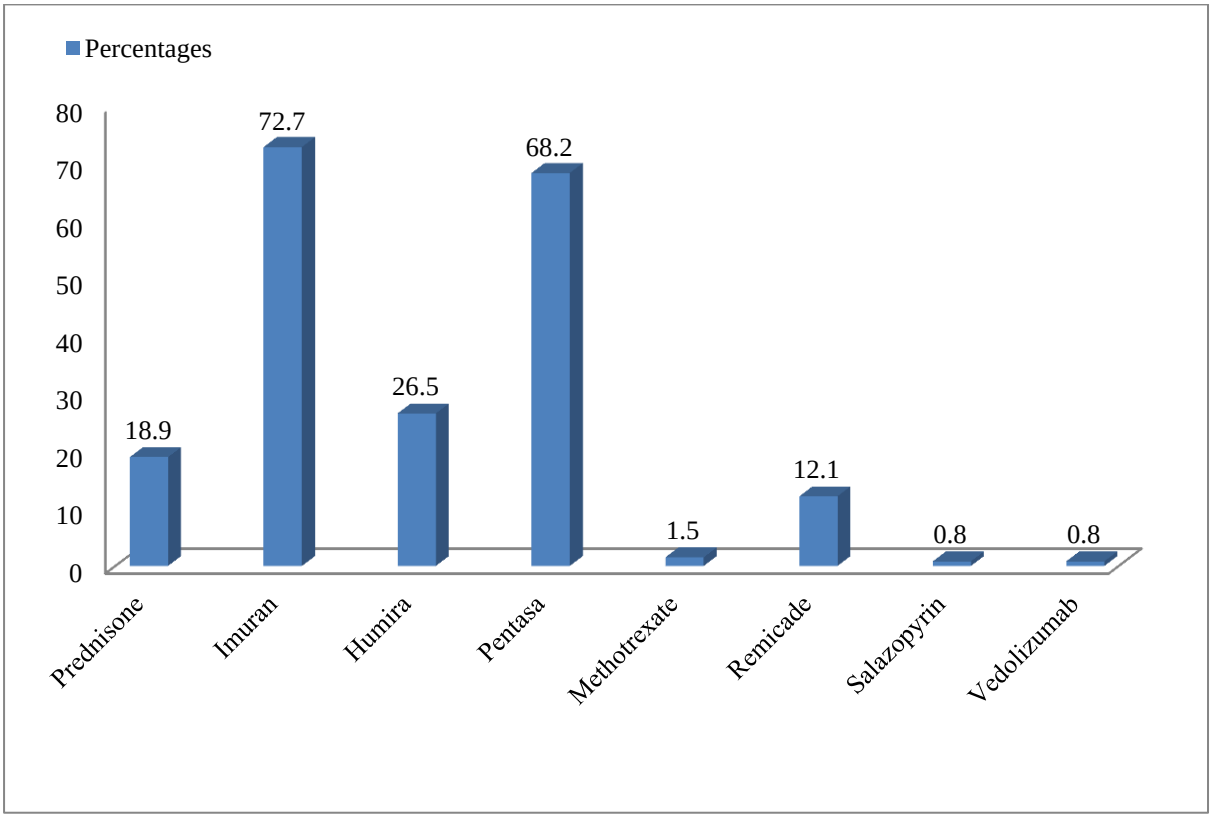

Figure4.5: Medications prescribed to treat IBD

4.3.2 Antibiotic prescribed to IBD patients.

One hundred and seventeen patients (88.6%) were not prescribed antibiotic during the study period, others were prescribed Ciprofloxacin, Metronidazole or both with the following percentages 1.5%, 6.1% and 3.8% respectively as shown in table **4.2**.

Table 4.2: Antibiotic prescribed to IBD patients

Antibiotic usage	**Frequency**	**Percentages**
Patients were not prescribed Antibiotic	117	88.6%
Patients were prescribed Ciprofloxacin	2	1.5%
Patients were prescribed Metronidazole	8	6.1%
Patients were prescribed Both (Ciprofloxacin and Metronidazole)	5	3.8%

4.4 Assessment of disease activity status in IBD patients:

Active disease or relapse was reported in 81 participants (61.4%) in the previous 6 months.

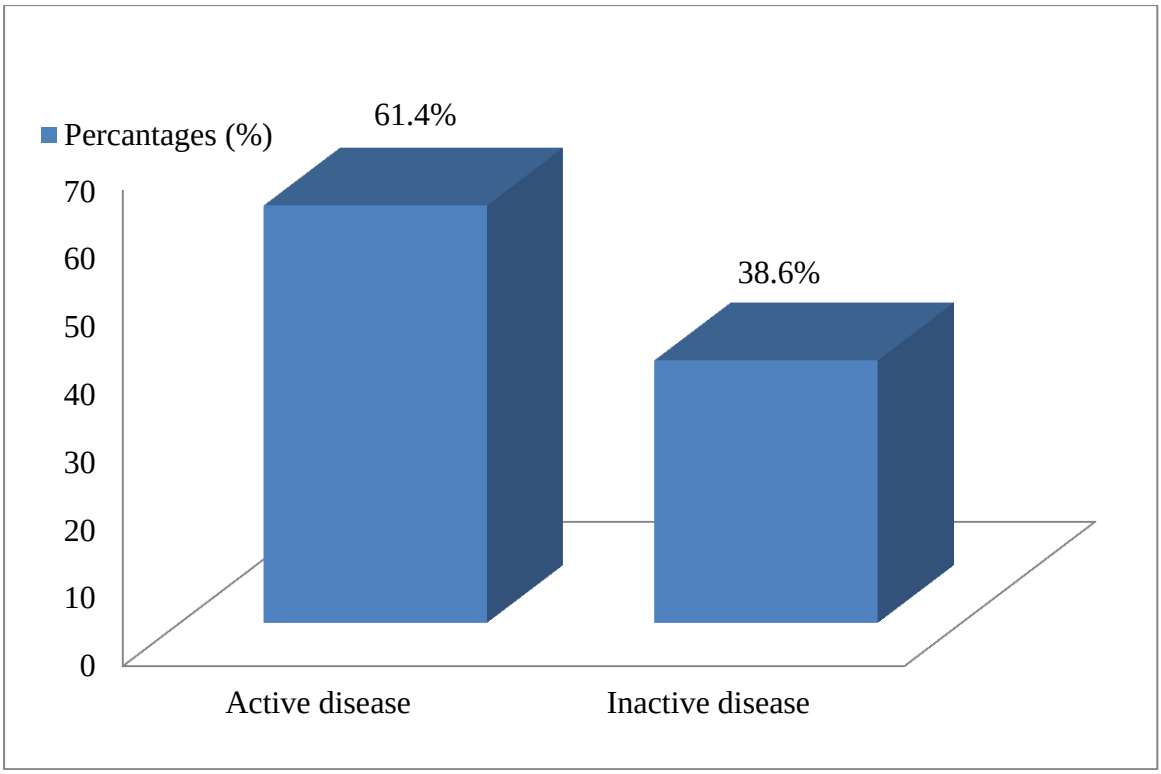

Figure 4.5: Disease activity measurement

4.5 Assessment of Medication adherence among IBD patients:

Based on MMAS-8, 52 (39.4%) of patients had a low adherence, 54 (40.9%) had a medium adherence and 26 (19.7%) had a high medication adherence. The average adherence score is 5.70 ±1.86 for the study sample generally indicates low rate of adherence among Palestinian IBD patients.

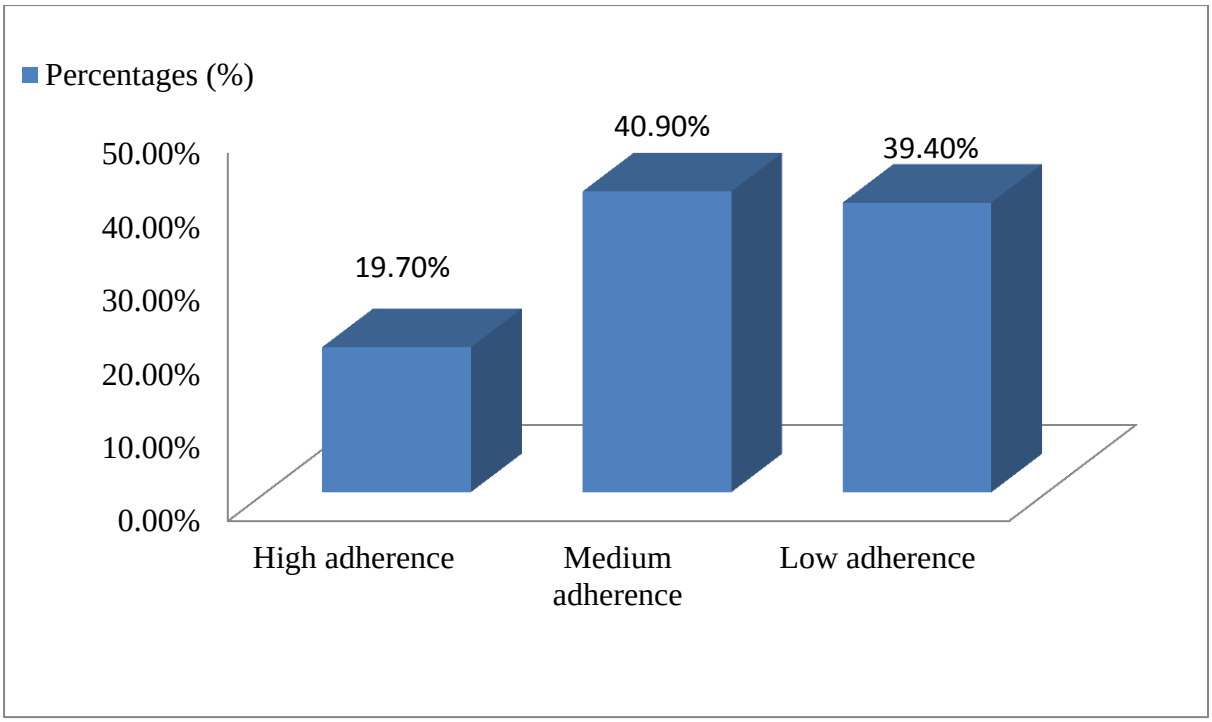

Figure 4.6: Medication adherence among IBD patients.

4.6 Type of Disease

The majority of patients were diagnosed with CD 83(62.9%) with a mean age of (32.73 ±12.71), while others with UC 49(37.1%) with higher mean age (34.94±12.69) as shown in (Figure **4.7**).

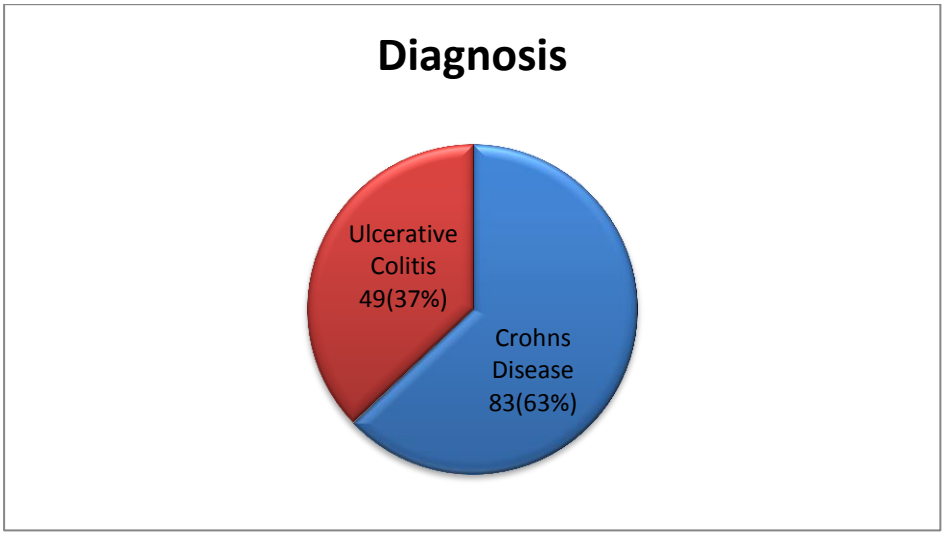

Figure 4.7: Type of disease according to physician's data.

Of males, fifty two participants were diagnosed with CD (67.5%), others with UC (32.5%), no significant difference between CD and UC according to their gender. In both diseases the majority of patients are those of highly educated level and diagnosed between (15 -30) years. As forty three participants were smokers, nearly 70% of them were diagnosed with CD, others with UC; however the difference was not significant.

According to clinical characteristics of the participants, around 94% of patients who undergo a surgery during their disease life were CD patients, while others were UC patients and the difference was significant (P-value=0.017). Drugs prescribed to treat both diseases are similar, on the other hand the use of Pentasa® and Remicade® had a statistically significant difference between the two groups (CD and UC)as P-value = (0.003, 0.006); respectively. As

Active disease was reported in 81 participants (61.4%) in the previous 6 months, 60.5% of them were CD while others were UC patients (39.5%).

The majority of CD patients showed a medium adherence to their drug medication (42.16%), while the majority of UC (42.85%) showed low adherence to their medication. All data was shown in Table **4.3**.

Table 4.3: Demographics according to the type of disease (CD vs. UC) identified, P-value.

Socio- demographic factor	**Sub classification**	**CD**	**UC**	***P- value***
		Frequency (%)	**Frequency (%)**	
Gender	Male	52(67.5%)	25(32.5%)	*0.190*
	Female	31(56.4%)	24(43.6%)	
Level of education	University or college	35(64.8%)	19(35.2%)	*0.723*
	Intermediate school	11(73.3%)	4(26.7%)	
	Secondary school	23(57.5%)	17(42.5%)	
	Primary school or less	14(60.9%)	9(39.1%)	
Age_1st_diagnosis	Less than 15	10 (71.4%)	4(28.6%)	*0.569*
	15_30	40 (58.8%)	28(41.2%)	
	More than 30	33 (66.0%)	17(34.0%)	
Stress related condition	No	56 (60.2%)	37 (39.8%)	*0.328*
	Yes	27(69.2%)	12 (30.8%)	
First degree relatives	No	70(65.4%)	37 (34.6%)	*0.211*
	Yes	13(52.0%)	12 (48.0%)	
Smoking habit	No	53 (59.6%)	36 (40.4%)	*0.255*
	Yes	30(69.8%)	13(30.2%)	
Method of treatment	Drugs	67 (58.3%)	48(41.7%)	*0.017*
	Surgical and drugs	16 (94.1%)	1(6.3%)	
Prednisone users		15(60.0%)	10(40.0%)	*0.741*
Imuran users		64(66.7%)	32(33.3%)	*0.141*
Humira users		22 (62.9%)	13(37.1%)	*0.998*
Pentasa users		49 (54.4%)	41 (45.6%)	*0.003**
Remicade users		15 (93.8%)	1 (6.3%)	*0.006**
Disease activity	Active disease	49 (60.5%)	32 (39.5%)	*0.475*
	Inactive disease	34 (66.7%)	17 (33.3%)	
Medication adherence	High adherence	17 (65.4%)	9 (34.6%)	*0.821*
	Medium adherence	35 (64.8%)	19(35.2%)	
	Low adherence	31 (59.6%)	21(40.4%)	

*******P value ≤0.05*

4.7 Assessment of health related QoL in IBD patients

The mean score of IBDQ in total sample of patients was (150.72 ± 30.08) ranged from 48.96 to 208.96. The mean total score is less than 157 and represents low QoL in Palestinian IBD patients (Irvine 1993).

In the comparison of the four domains of the IBDQ, it was found that social and systemic domains had higher score than other domains with mean per item± SD equal to (24.75±6.6), (23.7±6.45), respectively.

Table 4.4: Assessment of health related QoL in IBD patients (N=132).

IBDQ domains	Range	IBDQ Scores± SD	Median
Bowel functioning	10–70	46.1±12.2	47
Emotional functioning	12–84	54.48±13.56	58
Systemic domain	5–35	23.7±6.45	26
Social domain	5–35	24.75±6.6	25
Total IBDQ score	**32–224**	**150.72±30.08**	**151**

4.8. Relationships between IBD patients QoL with other independent variables

4.8.1. Association of QoL with socio-demographic and clinical variables of the patients

Total IBDQ score was not affected by socio-demographic factors such as: gender, material status, occupation, level of education and smoking, however, the disease activity status had a statistically significant effect at the level of significant $\alpha \leq 0.05$, the mean IBDQ scores and all its domains showed that patients in remission (inactive disease stage) had better QoL scores than those in relapse (P value =0.000). In the comparison of IBDQ scores between CD and UC no significant difference had been detected (P value=0.882).

Clinical variables such as: disease duration, age at disease onset and treatment options didn't affect any IBDQ dimensional score. The mean bowel domain of IBDQ scores showed a significance differences depending on the presence of first degree relatives in family while the mean systematic domain had a nearly significant difference among Adalimumab users and non-users (P-value=0.047) as shown in Table **4.5**.

Although there is no significance correlation at the level of significant $\alpha \leq 0.05$ between age and the IBDQ (R= 0.065, P-value= 0.232), there is a positive correlation between age and emotional domain (R= 0. 0.174, P-value= 0. 0.24) as shown in Table **4.6**.

Table 4.5: Association between QoL and socio-demographic and clinical variables of the patients.

Socio-demographic and clinical variables	Sub-classification	Systemic Mean rank per item	Social Mean rank per item	Bowel Mean rank per item	Emotional Mean rank per item	IBDQ Mean ± SD
Type of disease	Crohn's disease	4.80±1.25	4.95±1.27	4.64 ± 1.21	4.50±1.12	4.71±0.93
	Ulcerative colitis	4.64±1.37	4.94±1.40	4.57 ± 1.24	4.59±1.15	4.70±0.97
	P- value	*0.307*	*0.860*	*0.818*	*0.882*	*0.943*
Gender	Male	4.80±1.22	5.01±1.14	4.57 ± 1.13	4.51±1.07	4.72±0.81
	Female	4.65±1.38	4.85±1.54	4.6 ± 1.33	4.57±1.22	4.68±1.11
	P- value	*0.299*	*0.795*	*0.921*	*0.409*	*0.998*
Marital Status	Single	4.73±1.21	4.99±0.22	4.52 ± 1.28	4.34±1.09	4.72±0.12
	Married	4.74±1.34	4.92±1.63	4.66 ± 1.19	4.64±1.14	4.70±1.17
	P- value	*0.881*	*0.651*	*0.647*	*0.442*	*0.783*
Current Status	Student	4.52±1.21	4.99±0.22	4.47 ± 1.22	4.20±1.03	4.70±0.02
	Employed	4.82±1.28	5.01±1.32	4.72 ± 1.05	4.66±1.05	4.75±0.91
	Unemployed	4.70±1.36	4.80±1.63	4.51 ± 1.46	4.50±1.46	4.63±1.22
	P- value	*0.152*	*0.600*	*0.400*	*0.387*	*0.689*
Income	Low	4.40±1.40	4.67±1.35	4.39 ± 1.37	4.17±1.27	4.52±1.02
	Moderate	4.91±1.09	4.99±1.35	4.63 ± 1.14	4.71±0.96	4.77±0.90
	High	4.95±1.39	5.31±1.12	4.97 ± 1.02	4.81±1.06	4.90±0.85
	P- value	*0.347*	*0.336*	*0.993*	*0.464*	*0.632*
Level of education	University or college	4.80±1.27	5.22±1.10	4.88 ± 1.04	4.79±1.05	4.92±0.73
	Intermediate	4.76±1.46	4.82±1.49	4.80 ± 1.43	4.63±1.29	4.72±1.15
	Secondary school	4.71±1.17	4.73±1.36	4.36 ± 1.24	4.21±1.10	4.50±0.97

	Primary school only (or less)		4.62±1.50	4.75±1.54	4.30 ±1.32	4.42±1.15	4.56±1.13
	P- value		*0.215*	*0.586*	*0.231*	*0.155*	*0.193*
History of smoking	No		4.80±1.28	5.00±1.32	4.69 ± 1.27	4.61±1.19	4.77±0.92
	Yes		4.62±1.31	4.82±1.32	4.46 ± 1.09	4.39±0.99	4.58±0.94
	P- value		*0.079*	*0.613*	*0.578*	*0.108*	*0.704*
Stress related condition	No		4.75±1.25	4.99±1.34	4.58 ± 1.22	4.59±1.09	4.77±0.94
	Yes		4.70±1.39	4.83±1.26	4.70 ± 1.22	4.42±1.22	4.56±0.98
	P- value		*0.114*	*0.567*	*0.754*	*0.290*	*0.400*
1st degree relatives	No		4.73±1.28	4.94±1.33	4.64±1.23*	4.50±1.12	4.69±0.91
	Yes		4.62±1.31	4.99±1.30	4.49 ± 1.17	4.71±1.19	4.76±0.69
	P- value		*0.320*	*0.099*	*0.031**	*0.486*	*0.228*
Method of Treatment	Drugs		4.71±1.32	4.96±1.37	4.63 ± 1.21	4.59±1.14	4.72±0.99
	Both surgical and drugs		4.87±1.08	4.82±0.92	4.41 ±1.34	4.14±0.99	4.58±0.54
	P- value		*0.676*	*0.769*	*0.058*	*0.774*	*0.749*
Drugs used to treat IBD	Prednisone	No	5.02±1.04	5.20±1.05	4.85 ± 1.00	4.75±0.96	4.89±0.73
		Yes	3.54±1.56	3.85±1.75	3.56 ± 1.54	3.64±1.37	3.91±1.28
	P- valve		*0.889*	*0.899*	*0.702*	*0.493*	*0.762*
	Imuran	No	4.67±1.52	4.70±1.61	4.73± 1.31	4.65±1.34	4.57±1.25
		Yes	4.76±1.20	5.04±1.18	4.57 ± 1.18	4.49±1.04	4.76±0.80
	P- value		*0.262*	*0.887*	*0.860*	*0.615*	*0.696*
	Humira	No	4.93±1.15	5.11±1.25	4.73 ±1.11	4.70±1.00	4.82±0.85
		Yes	4.19±1.53	4.49±1.40	4.29 ± 1.45	4.08±1.33	4.38±1.10
	P-value		*0.047**	*0.074*	*0.849*	*0.513*	*0.065*
	Pentasa	No	4.62±1.34	4.98±1.16	4.65 ± 1.35	4.36±1.16	4.72±0.94
		Yes	4.79±1.27	4.93±1.39	4.60 ± 1.16	4.62±1.11	4.70±0.93
	P-value		*0.423*	*0.062*	*0.229*	*0.575*	*0.217*

	Methotrexate	No	4.73±1.30	4.95±1.33	4.61 ± 1.22	4.52± 1.13	4.72±0.94
		Yes	5.20±0.28	4.95±0.00	4.90 ± 0.85	5.25 ±0.59	4.70±0.93
	P-value		*0.874*	*0.716*	*0.709*	*0.120*	*0.687*
	Remicade	No	4.74±1.32	4.93±1.34	3.63 ± 1.21	4.55± 1.16	4.71±0.95
		Yes	4.69±1.12	5.06±1.15	4.49 ± 1.29	4.46± 0.89	4.71±0.00
	P-value		*0.420*	*0.642*	*0.440*	*0.852*	*0.671*
	Salazopyrin	No	4.74±1.29	4.95±1.32	4.62± 1.22	4.54± 1.13	4.70±0.98
		Yes	4.80±0.00	5.4±0.00	4.30± 0.00	4.42± 0.00	4.78±0.58
	P-value		*0.050**	*0.170*	*0.661*	*0.687*	*0.331*
	Vedolizumab	No	4.73±1.29	4.95±1.32	4.61±1.22	4..53±1.13	4.71±0.94
		Yes	5.2±0.00	4.95±0.00	5.50±0.00	5.50±0.00	4.59±0.00
	P-value		*0.941*	*0.890*	*0.551*	*0.341*	*0.998*
Antibiotic used	No		4.84±1.16	5.08±1.17	4.73 ± 1.10	4.64±1.00	4.80±0.82
	Ciprofloxacin		4.80±0.57	4.70±0.71	4.35 ± 0.35	4.75±1.06	4.63±0.53
	Metronidazole		4.46±2.17	4.24±1.90	4.23 ± 1.98	4.17±1.75	4.34±1.29
	Both Ciprofloxacin & Metronidazole		2.60±1.21	2.94±1.90	2.68 ± 1.08	5.65±1.45	3.04±1.58
	P-value		*0.779*	*0.790*	*0.622*	*0.991*	*0.836*
Type of food	Fast food		4.77±1.20	5.07±0.90	4.83± 1.08	4.60±1.10	4.77±0.68
	Fruits and vegetables		4.72±1.34	4.89±1.47	4.52 ± 1.27	4.51±1.14	4.68±1.04
	P-value		*0.318*	*0.530*	*0.542*	*0.318*	*0.474*
Dietary restriction	Yes		5.04±1.24	4.86±1.31	4.45± 1.24	4.48±1.14	4.62±0.92
	No		4.62±1.29	5.19±1.27	4.99 ±1.08	4.72±1.05	4.94±0.92

	P-value	*0.422*	*0.317*	*0.763*	*0.267*	*0.568*
Disease activity	Active Disease	4.22±1.33	4.45±1.37	4.11±1.24	4.09±1.15	4.31±0.94
	Inactive disease	5.55±0.65	5.73±0.69	5.40±0.60	5.24±0.63	5.32±0.53
	P-value	*0.000**	*0.000**	*0.000**	*0.000**	*0.000**

P value ≤0.05

Table 4.6: Correlation between age and IBDQ scores using* Pearson *correlation coefficient

QoL scores	**Age**	
	R	**Sig**
Bowel domain	0.085	*0.169*
Emotional domain	0.174	*0.024 **
Systemic domain	0.042	*0.317*
Social domain	0.027	*0.380*
IBDQ	0.065	*0.232*

P value ≤0.05

4.8.2 Association of QoL with medication adherence

There was no association between the sum of health related QoL and different sub-scores of health related QoL and non-adherence.

Table 4.7: Association between medication adherence and patients QoL

	Medication adherence	Mean± SD	P-value
Bowl domain	high adherence	4.4962± 1.39871	0.749
	medium adherence	4.5815± 1.29339	
	low adherence	4.7078± 1.03862	
Emotion domain	high adherence	4.4199± 1.33051	0.818
	medium adherence	4.5355± 1.14291	
	low adherence	4.5929± 1.01790	
Systemic domain	high adherence	4.4769± 1.59105	0.101
	medium adherence	4.5815± 1.38142	
	low adherence	5.0353± 0.94124	
Social domain	high adherence	4.6197± 1.75347	0.355
	medium adherence	4.9864± 1.26827	
	low adherence	5.0669± 1.09381	
IBDQ	high adherence	4.4042± 1.16688	0.149
	medium adherence	4.7172± 0.95365	
	low adherence	4.8450± 0.77261	

***P value ≤0.05*

4.9 Predictors of QoL domains

Regression analysis, using QoL score as a dependent variable and other factors as independent variables found that patients in remission status (r^2 = 0.436,*p-value <0.001*), patients with high educational levels (r^2 =0.035, *p-value=0.009*) and those using Azathioprine (r^2 =0.017, *p-value=0.034*) were independently associated with high QoL. The factors significantly associated with QoL according to stepwise regression analyses are summarized in Table 4.8.

Stepwise regression analysis explained 54.1% of variation in QoL with these independent variables (disease status, level of education, using corticosteroid, Antibiotics and Azathioprine. The factor that affects IBDQ the most is **disease status** where it interprets 43.6% of the variation in the IBDQ. Furthermore it is the factor that affects bowel, systemic, social and emotional domain the most where it interprets 41.1%, 41.2%, 37.7% and 40.7% of the variation in each domain respectively.

As a change in disease activity from remission to relapse statues was significantly negatively associated with change in QoL score. Relapse results in a decrease in IBDQ and all domains score. Highly educational level considered a positive predictor for IBDQ scores, bowel, emotional and social domains and using Azathioprine (Imuran®) drug also considered a positive predictor for IBDQ scores and social domain. While taking corticosteroid medication was negatively associated with IBDQ scores and the four domains (social, emotional, bowel and systematic domains) as shown in Table **4.8**.

Table4.8: Stepwise regression models testing for the predictors of QoL of IBD patients in Palestine (2017).

Model	Variable	R	R Square	R Square Change	B	Sig.
Bowel domain	Disease activity status	0.641	0.411	0.411	-0.462	0.000 *
	Level of education	0.673	0.453	0.042	0.209	0.002 *
	Corticosteroid Drug	0.700	0.490	0.037	-0.617	0.003 *
	Disease duration	0.716	0.513	0.024	-0.370	0.015 *
	Stress related condition	0.728	0.530	0.017	-0.353	0.035 *
Systematic domain	Disease activity status	0.642	0.412	0.412	-0.432	0.000*
	Corticosteroid Drug	0.678	0.459	0.047	-0.739	0.005*
	Adalimumab Drug	0.696	0.484	0.025	-0.502	0.008*
Social domain	Disease activity status	0s.614	0.377	0.377	-0.443	0.000*
	Azathioprine Drug	0.640	0.409	0.032	0.459	0.009*
	Corticosteroid Drug	0.666	0.444	0.034	-0.681	0.006*
	Level Of Education	0.683	0.466	0.023	0.179	0.022*
	Antibiotics	0.696	0.485	0.019	-0.258	0.034*
Emotional domain	Disease activity status	0.638	0.407	0.407	-0.426	0.000*
	Level of education	0.666	0.443	0.036	0.198	0.005*
	5-ASA	0.688	0.474	0.030	0.312	0.008*
	Corticosteroid Drug	0.703	0.495	0.021	-0.461	0.023*
	Adalimumab Drug	0.716	0.512	0.017	-0.350	0.036*
IBDQ	Disease activity status	0.660	0.436	0.436	-0.347	0.000*
	Level of education	0.686	0.471	0.035	0.148	0.009*
	Corticosteroid Drug	0.709	0.503	0.031	-0.460	0.006*
	Antibiotics	0.724	0.525	0.022	-0.184	0.022*
	Azathioprine Drug	0.736	0.541	0.017	0.276	0.034*

*****P value ≤0.05

R: regression coefficient, **B**: standardized coefficient, **Sig.:** significance

Chapter Five

Discussion

5. Discussion

This study is the first of its type in Palestine to assess IBD patients QoL, demographic and clinical characteristics of the patients, their medication adherence and factors affecting their health related QoL.

This study provides health care professionals with information concerning IBD patients QoL in Palestine, and to assess the extent to which different socio-demographic factors (age, gender, etc.), clinical variables and medication adherence impact on the QoL of IBD patients.

Recently the importance of QoL studies has been largely recognized especially for chronic diseases. IBD affects not only patients' well-being, but also social implications which was largely affected either by disease itself, its complication, need for hospitalization, frequent physician visits and the side effects of treatment(Casellas, López-Vivancos et al. 2002).

5.1Assessment of QoL in IBD patients

In our study, IBDQ instrument was applied to measure IBD patients QoL. IBDQ was also used to assess QoL among IBD patients in different countries (de Boer, Wijker et al. 1995, Han, McColl et al. 1998, Pallis, Vlachonikolis et al. 2002, Alowais, Alferayan et al. 2016) . The total score for IBDQ of IBD patients was (150.72 ± 30.4), indicating that our population had a relatively lower QoL than other populations such as Netherlands, England and Grecian, Saudi Arabia. Our population total score was lower than Han *et al*,Athansions G *et al.* and Alowais *et al*. as they scored (173.7 ± 33.1),(178.1 ± 36.9) and (160.3 ± 42.7) respectively and was higher compared to De Boer *et al* study (N=271*)* which had a total QoL scores (119.1 ± 22.0) (de Boer, Wijker et al. 1995, Han, McColl et al. 1998, Pallis, Vlachonikolis et al. 2002, Alowais, Alferayan et al. 2016).

These variations in QoL may be due to several factors, firstly: the differences in methodology such as different patient population .Secondly: differences in cultural understanding, attitudes

towards the disease aspects and the degree of social support between different populations also seem as factor. Thirdly: ethnicity and genetic factors may contribute to disease behavior and patients response to treatment thus affecting patients QoL. And finally, these differences might be due to inclusion of patients with severe symptoms who seek the medical advice, generally patients in developing countries do not seek medical advice until debilitating symptoms or complications appeared, so a delay in treatment that results in a reduction in patient's QoL occur.

Comparison between IBDQ dimensions, emotional and bowel dimensions in our sample (54.48±13.56) and (46.1±12.2); respectively were more disturbed than systemic and social once (23.7±6.45) (24.75±6.6) respectively); this indicated that patients with IBD suffer from significant psychological stress that affects patients QoL due to their chronic disease and symptoms.

Social domain had a higher score in our population and this is similar to a study conducted by Horváth *et al*. in 2012, that used SF-36 questionnaire to measure QoL in their sample, they showed that QoL impairment are less in social functions than other domains (Horváth, Farkas et al. 2012). The data also differs from studies that showed IBD had more impact on patients' social and systemic symptoms when compared to the emotional and bowel symptoms (de Boer, Wijker et al. 1995, Han, McColl et al. 1998, Pallis, Vlachonikolis et al. 2002).

Social domain is the least affected in our sample and this finding could be explained by differences in socio-demographic characteristics of the participants as a high proportion of our sample (52.3%) were of employed category and 16.7% were students either in a university or a secondary school and almost both categories have daily working activity which enhances the social communication of them.

5.2Association between IBD patients QoL and socio-demographic and clinical factors

According to relationships between socio-demographic factors and patients QoL, gender didn't affect any QoL domain in our population, this result is in agreement with Zahn *et al*. study that concluded demographic parameters did not significantly affect IBDQ scores (Zahn, Hinz et al. 2006).While several literatures indicated that female gender was associated with a lower QoL than male (Hjortswang, Järnerot et al. 2003, Moradkhani, Beckman et al. 2013). This is maybe due to differences in socio-demographic and clinical characteristics of the both genders in the study.

The importance of age variable in patients QoL have been indicated in several studies (Badia, Fernandez et al. 1995, Han, James et al. 1999, Hjortswang, Järnerot et al. 2003). In this study, similarly to other reports (Graff, Walker et al. 2006, Haapamäki, Turunen et al. 2009, Moser 2009) age variable was not found to affect QoL in IBD patients, this result also in line with Moradkhani *et al.* study conclusions (Moradkhani, Beckman et al. 2013). While increasing age increases the emotional domain score in our study and this may be related to increasing patient's ability to cope with the disease, relapse symptoms, or complications of therapy as the age increases.

Disease duration, treatment options and prescribing medication also had no impact on patient's health related QoL. No statistical difference due to their disease duration either less than five years or more, this is in agreement with Kalafateli *et al*. who didn't find differences in patients with either short or long history of IBD regarding their QoL (Kalafateli, Triantos et al. 2013) and comparable with Jäghult *et al*. study as patients with short disease duration had lower QoL scores compared with patients with long disease duration (Jäghult, Saboonchi et al. 2011).

Imuran® (Azathioprine) and Pentasa® (5-ASA) were the two most commonly used medication by Palestinian patient population (72.7% and 68.2% respectively). Prednisone was prescribed to 18.6% of the sample; this is consistent with general practice. Prednisone can be used during flare up and two biological may be utilized: Humira® and Remicade®(Mowat, Cole et al. 2011, Waljee, Wiitala et al. 2016) .

The information concerning the impact of different treatments on QoL in previous studies was conflicting (Bernklev, Jahnsen et al. 2005, Haapamäki, Turunen et al. 2009, Romberg-Camps, Bol et al. 2010). In this study, no significant difference was found among users and non-users of corticosteroids, 5-ASA, and immunosuppressive therapy except for Adalimumab (p-value=0.047). Although, this may be due to the small number of patients included.

Despite our data showed no significant association between IBDQ scores and method of treatment ,Blanco *et al.*, 2005 study showed that patients undergoing a surgery during their disease life had a lower IBDQ scores in compared to those who received medical treatment only and the difference was significant (Blanco, Moreno-Jimenez et al. 2005).

Smoking is a well-known factor in the clinical course of IBD. However, the influence of cigarette smoking on QoL is less well known. Our data showed no significant difference between smokers and non-smokers regarding QoL this result supports what Casellas *et al.* concluded in 354 patients with IBD were interviewed in Spain (Casellas, Lopez-Vivancos et al. 2002).

As 68% of our patients had dietary restriction based on patients opinion and this is around the percentage reported in a systematic review that approximately 70% of IBD patients are known to employ elimination diets to prolong their remission status (Holt, Strauss et al. 2017). However, no significant association regarding their QoL had been detected.

5.3Association between patients QoL and disease activity

Patients in active disease status (Relapse) had statistically lower IBDQ scores than those in remission (Table 4.5). This is conducted in several literatures (Casellas, López-Vivancos et al. 2001, Mnif, Mzid et al. 2010, Romberg-Camps, Bol et al. 2010, Zhou, Ren et al. 2010). As disease activity is one of the most important independent variable responsible for IBDQ scores and patients QoL (Larsson, Lööf et al. 2008). This may be due to the active disease symptoms in comparable to those in clinical remission who suffers from fewer symptoms and less complications (Hjortswang, Ström et al. 1998). Relapse symptoms such as GI and extra intestinal symptoms and their complications have a large effect on patient's health, worries and increase anxiety, depression and reducing patients QoL (Graff, Walker et al. 2006).

5.4 Association between patients QoL and type of disease

In this study we didn't find significant difference regarding QoL between CD and UC patients, this finding is in line with other studies where diagnosis (CD vs. UC) was not related to bowel symptoms, emotional function, social impairment and systematic impairment, suggesting that diagnosis is not a key determinant of QoL in IBD (Badia, Fernandez et al. 1995, Mussell, Böcker et al. 2004, Blanco, Moreno-Jimenez et al. 2005, Zhou, Ren et al. 2010) on the other hand several studies indicated that CD patients have more impact on patients psychosocial function, patients well-being, as well as lower QOL scores in comparison to UC patients (Drossman, Leserman et al. 1991, Mnif, Mzid et al. 2010, Romberg-Camps, Bol et al. 2010), it may be due to the severity of CD which is variable in different areas of the world.

5.5 Assessment of medication adherence and its relationship to patients QoL

This study is the first of its type in Palestine and Arab world that assess medication adherence in IBD patients and examined the health related QoL simultaneously in the same population. Low medication adherence was reported in about 39.4% of IBD patients, this lies in the limit of non-adherence to oral medications that was reported in Jackson *et.al*., review (Jackson, Clatworthy et al. 2010) ranging from 7% to 72% but higher than what was reported for Asian IBD patients that ranged from 20%to 30% (Kawakami, Tanaka et al. 2013). Also higher than study conducted in Italia 2017 (Bucci, Zingone et al. 2017) to assess medication adherence in 151 IBD patients using MMAS questionnaire and reported 30% of IBD patients had low compliance to their medication.

The results of our study showed that medication adherence did not have impact on patients' QoL, this is in line with Horvath *et al*. study that included a relatively large number of IBD patients and didn't find any association between medication adherence and patients QoL (Horváth, Farkas et al. 2012).Although our results differ from Hommel *et al.*, study (Hommel, Davis et al. 2008) as the relation between medication adherence and QoL in 36 young people with IBD was significant. However there are some limitations in Hommel *et al* study including the types of the different surgeries, small number of patients (N=36).

It seems that QoL in IBD patients is mainly influenced by the disease itself; the presence of chronic relapsing symptoms that affects patient's life.

5.6 Predictors of IBD patients QoL

Identify predictors of IBD patients QoL may help to make interventions that improve patient's health and overall management (Moradkhani, Beckman et al. 2013). Several literature publications indicate that the most important variable for predicting health related QoL is disease activity statues, such as the presence of relapse (Mnif, Mzid et al. 2010, Zhou, Ren et al. 2010, Alowais, Alferayan et al. 2016). The present study found that relapse was a significant predictor for the systemic, social, bowel and emotional domains, as well as IBDQ. Relapse or the active disease resulted in a decrease of QoL scores (Table 4.8).

Level of education was a significant predictor for bowel, social and IBDQ scores where patients with higher education levels led to increase in QoL scores (Table 4.8). Generally, the relationship between education and QoL in chronic diseases is well known and presented in the literature (Wang, Beyer et al. 2008, Mielck, Reitmeir et al. 2012, Saleem, Hassali et al. 2014). As Moradkhani *et al*. concluded that education may improve the way by which patients deal with chronic diseases (Moradkhani, Kerwin et al. 2011). Highly educated patients have a higher chance to read about their disease, symptoms and learn how to deal with frequent relapses so improvement in QoL scores has been detected. Also their knowledge makes them less worried and anxious regarding symptoms. This is relevant for patients with IBD because depression is considered a one of the good predictors for subjective impairment in QoL(Cuntz, Welt et al. 1999) .

Differences in IBDQ score in patients receiving different medications may be explained by differences in disease activity status from relapse to remission. Using Corticosteroid medication was negatively associated with patient's bowel, systematic, emotional and social as well as IBDQ score as shown in Table 4.8. As corticosteroids are the core of "rescue" therapy for patients who are experiencing a flare(Waljee, Wiitala et al. 2016), the reduction in

patients QoL may be related to disease activity status rather than drug itself. However a study conducted by Vivan *et al*. concluded that patients who were taking prednisone had better QoL (Vivan, Santos et al. 2017) although a small number of patients were included in their sample (N=58). Azathioprine (Imuran®) drug was considered a positive predictor for increasing QoL in both social domain and IBDQ scores, and 5-ASA (Pentasa®) for emotional domain. 5-ASA is highly effective in mild to moderate UC, and can be used in conjugation with other therapies in clinical remission of CD.

Chapter Six

Conclusions and Recommendations

6. Conclusions and Recommendations

6.1 Strengths and limitations

Major strengths of this study include: This is the first study about health related QoL among IBD patients conducted at West Bank in Palestine;specifically in North and South Palestine. It provides baseline data about Palestinian IBD patients QoL, their most commonly used medications, their medication adherence, also tried to identify a number of significant associated factors that should be considered when dealing with IBD patients. This study is the first of its type in Palestine and Arab world that assess medication adherence in IBD patients, and examined the health related QoL and the adherence simultaneously in the same population. Only a few studies examined the impact of medical adherence on QoL in IBD patients. The current study measured QoL and medication adherence by using the global instruments: MMSA-8 and IBDQ scales.

Study Limitations

The study has several limitations, first, it was conducted in only three hospitals in the West Bank, Palestine, and thus the results may not be generalized. Second, although a convenience sample of patients in hospitals was selected, some positive selection bias is still possible. Also, the cross-sectional type of this study may prevent us from developing a good cause effect relationship to be identified especially between post-treatment improvement and QoL regarding medication. Lastly, gathering study data via patient's interview may have a negative outcome as the researchers can influence participant's answers, leading to less reliable data.

6.2 Conclusions

This study shows a low QoL among Palestinian IBD patients compared to other countries and identifies a number of significant associated factors that should be considered when dealing with IBD. Results of the study may help healthcare providers to identify patients at risk of low QoL especially those in the relapse status and active symptoms. Attention should be provided by healthcare givers and strategy makers to increase knowledge about IBD, to improve IBD patient's QoL and to clarify the importance of treatment adherence.

6.3 Recommendations

Results of this study give an idea about the status of IBD patients QoL in Palestine and provide some assessment of their medications, disease activity, medication adherence, and the predictors of disease. Our findings also point out some important issues that need to be addressed in future, and these include the followings:

- ✓ Population-based studies are needed to investigate the incidence of IBD in Palestine.
- ✓ The use of IBDQ questionnaire should be implemented for regular follow up in the clinic to evaluate the response to management
- ✓ Attention should be provided by healthcare providers and strategy makers, doctors and health educators to low level QoL. Patients with high risk of low QoL are more likely to have relapsed and active symptoms that interfere with daily living.
- ✓ Awareness sessions for IBD patients to clarify the importance of adherence to their medication and the type of food recommended or food that needs to be avoided in order to maintain remission.
- ✓ Finally, we recommend making periodic studies on larger population and longer duration with patients follow up to confirm the findings of this study.

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Appendix 1

العوامل الاجتماعيه والاقتصاديه

***العمر.....**

***الجنس** ☐ ذكر ☐ انثى

***المدينه.....**

***ما هو نوع مرضك** ☐ **Crohn's disease** ☐ **Ulcerative Colitis**

***مكان تلقي العلاج:**

☐ عياده امراض هضميه خارجيه(OPC)

☐ داخل المستشفى

اذا كان جوابك المستشفى . فما اسمه.....

***الحاله الزوجيه :ما هي حالتك الزوجيه؟**

☐ أعزب/عزباء. لم اتزوج من قبل

☐ متزوج/ة او على علاقه دائمه

☐ أرمل/ة

☐ مطلق/ة

***ما هي طبيعه عملك الحالية؟**

☐ طالب

☐ موظف

☐ غير عامل

***الى أي فئة ينتمي دخلك الأسري الشهري؟**

☐ أقل من3000

☐ 3000-4000

☐ أكثرمن4000

***ما هو المستوى التعليمي الذي وصلت اليه ؟**

☐ كلية او جامعه او ما يعادلهم

☐ تعليم متوسط او مدرسه خاصه

☐ مدرسة ثانويه

☐ تعليم ابتدائي فقط

العمر الذي تم تشخيص المرض ☐ اقل من 15سنه ☐ 15 –30 ☐ اكثر من 30

مده الاصابه بالمرض ☐ اقل من 5 سنه ☐ 5سنوات واكثر

هل تعرضت لضغط نفسي قبل تعرضك للمرض ☐ نعم ☐ لا

هل لديك قريب من الدرجه الاولى مصاب بنفس المرض ☐ نعم ☐ لا

هل انت/ي مدخن حاليا او سابقا ☐ نعم ☐ لا

ما هي طريقه تلقيك للعلاج ☐ جراحيا ☐ غير جراحي (دوائي)

اذا كان تلقيك للعلاج غير جراحي فما هي الادوية التي تستخدمها ?

☐ ***5-ASA 5-aminosalicalic acid(rafassal^{R})***

☐ ***Azathioprine(immuran^{R})***

☐ ***Adalimumab amp (humira^{R})***

☐ ***Prednisone***

☐ ***Methotrexate***

☐ ***Mycophenolate mofetil (cellcept^{R})***

☐ ***Mycophenolate sodium (Myfortic®)***

اذا كانت غير المذكور فما هي ……

- **ما نوع المضاد الحيوي الذي تستخدمه ?**
-

☐ **Metronidazole** ☐ **Ciprofloxacin** ☐ **If other, Please name ……..**

- **ما هو نوع الغذاء الذي تكثر من تناوله ?**

☐ **Fast food** ☐ **Fruits and vegetables**

* **هل هنالك اي قيود على استخدامك للغذاء ?بسبب المرض** ☐ **نعم** ☐ **لا**

هل بامكانك التوضيح……

**** في خلال ال 6 شهور الماضيه مرضك كان:***

(a)كان المرض فعالا جدا. بحيث هنالك اعراض يوميه
(b) غالبا فعال. فأعراضي تأتي يوم بعد يوم او أكثر بقليل
(c) فعال بشكل محدود. حيث ان الاعراض تاتي فقط بشكل قليل بالاسبوع (من مره الى اثنتين بالاسبوع)
(d) قليله الفعاليه.حيث أن الأعراض تأتي فقط مره او اثنتين بالشهر الواحد
(e) نادر جدا أن يكون فعال .الاعراض نادرا ما اتت خلال ال 6 شهور الماضية
(f)لم أعاني من أي أعراض مضت خلال ال 6 شهور السابقة

***مواظبتك على أخذ الدواء :**

1 هل تنسى أحيانا تناول الدواء؟

☐ نعم ☐ لا

2 يفقد الناس أحيانا أدويتهم لأسباب أخرى غير النسيان. بالتفكير خلال الأسبوعين الماضيين، هل كانت هناك أي أيام لم تتناول فيها الدواء؟

☐ نعم ☐ لا

3 هل سبق لك أن قطعت أو توقفت عن تناول الدواء دون إخبار طبيبك لأنك شعرت أنك أسوأ عندما تناولته ؟

☐ نعم ☐ لا

4عند السفر أو مغادرة المنزل، هل ننسى أحيانا جلب الدواء الخاص بك؟

☐ نعم ☐ لا

5 هل تناولت كل أدويتك بالأمس؟

☐ نعم ☐ لا

6 عندما تشعر بأن أعراضك تحت السيطرة، هل تتوقف أحيانا عن تناول الدواء؟

☐ نعم ☐ لا

7 أخذ الدواء كل يوم هو إزعاج حقيقي لبعض الناس. هل تشعر بالانزعاج أثناء متابعتك للخطة العلاجيه الخاصه بك ؟

☐ نعم ☐ لا

8 كم مرة واجهت صعوبة في تذكر تناول أدويتك ؟
A. أبدا / نادرا
B. مرة واحدة خلال مده قصيره
C. أحيانا
D. عادة
E .طوال الوقت

تعليمات لأجل تعبئة المشارك للـ IBDQ

صُمِّمَ هذا الاستبيان لقياس تأثيرات التهاب الأمعاء على أداء وظائفك اليومية ونوعية حياتك. سوف توجه لك أسئلة حول أعراض كنت تعاني منها ناتجة عن مرض معوي و كيف كان شعورك العام و كيف كان مزاجك.

يوجد نسختين من هذا الاستبيان:ألـ IBDQ والـ IBDQ-Stoma. إذا كنت تعاني من الكولوستومي (فتحة في البطن التي من خلالها يُخرج المعي الاكبر السوائل) أو الالوستومي (فتحة في البطن التي من خلالها يُخرج المعي الدقيق السوائل), ينبغي عليك أن تملأ/ي الـ IBDQ –Stoma فقط . الأسئلة1،5،17،22،24 و 26 تختلف بشكل طفيف في كلّ نسخة. تأكّد من حصولك على الاستبيان الصّحيح.

في هذا الاستبيان يوجد 32 سؤالاً. لكلّ سؤال يوجد إجابات متدرّجة من 1 حتّى 7. الرجاء اقرأ/ي بحذر كل سؤال وأجب على الرّقم الّذي يصف بأفضل صورة شعورك خلال الأسبوعين الأخيرين.

مثال

كم من الوقت شعرت بأنّك لست على ما يرام نتيجة لمشكلة الأمعاء لديك في الأسبوعين الماضيين؟

1 كلّ الوقت
2 معظم الوقت
3 جزء لا بأس به من الوقت
4 بعض الوقت
5 قليل من الوقت
6 بالكاد في أي وقت
7 ولا في أي وقت

إذا كان لديك مشكلة في فهم سؤال، **توقف/ي** للحظة ! فكر/ي فيما يعنيه السؤال بالنسبة لك. كيف يتأثّر بمشكلة الأمعاء الّتي تعاني منها؟ ثم اجب/ أجيبي عن السؤال بأفضل طريقة ممكنة. ستكون لديك فرصة لتسأل الممرضة أسئلة بعد الانتهاء من الاستبيان. يتطلّب ذلك بضع دقائق فقط لإكماله.

استبيان جودة الحياة مع مرض التهاب الأمعاء (IBDQ)

صُمِّمَ هذا الاستبيان لمعرفة كيف كان شعورك خلال الأسبوعين الماضيين. سوف تُسأل عن أعراض مررت بها نتيجة لمرض التهاب الأمعاء لديك، كيف كان شعورك العام و كيف كان مزاجك.

1. كم من الوقت تكرر الخروج خلال الأسبوعين الأخيرين؟ الرجاء الإشارة إلى مدى تكرار الخروج خلال الأسبوعين الأخيرين وذلك بإختيار إحدى الاجابات التالية:

1 تكرر الخروج هو بأسوأ صورة كان عليها
2 متكرّر بشدة
3 متكرّر كثيراً
4 زيادة متوسطة في تكراريّة الخروج
5 بعض الزيادة في تكراريّة الخروج
6 زيادة طفيفة في تكراريّة الخروج
7 طبيعيّ، لم تطرأ أيّ زيادة على تكراريّة الخروج

2. كم من الوقت شكّل الإحساس بالتّعب أو الإرهاق والإنهاك مشكلةً بالنّسبة لك خلال الأسبوعين الأخيرين؟ الرجاء أشر/أشيري إلى كمية الوقت الّتي شكّل فيها الإحساس بالتّعب والإرهاق مشكلةً بالنّسبة لك خلال الأسبوعين الأخيرين وذلك بإختيار إحدى الاجابات التالية:

1 كلّ الوقت
2 معظم الوقت
3 جزء لا بأس به من الوقت
4 بعض الوقت
5 قليل من الوقت
6 بالكاد في أي وقت
7 ولا في أي وقت

3. كم من الوقت، خلال الأسبوعين الأخيرين، شعرت بالإحباط، نفاذ الصّبر، أو العصبية؟ الرجاء اختيار إجابة واحدة من

1 كلّ الوقت
2 معظم الوقت
3 جزء لا بأس به من الوقت
4 بعض الوقت
5 قليل من الوقت
6 بالكاد في أي وقت
7 ولا في أي وقت

4. كم من الوقت خلال الأسبوعين الأخيرين لم يكن باستطاعتك الذّهاب إلى المدرسة أو مزاولة عملك بسبب مشكلتك بالأمعاء؟ الرجاء اختيار إجابة واحدة من

1 كلّ الوقت
2 معظم الوقت
3 جزء لا بأس به من الوقت
4 بعض الوقت
5 قليل من الوقت
6 بالكاد في أي وقت
7 ولا في أي وقت

5. كم من الوقت خلال الأسبوعين الأخيرين كان الخروج لديك سائلي؟ الرجاء اختيار إجابة واحدة من

1 كلّ الوقت
2 معظم الوقت
3 جزء لا بأس به من الوقت
4 بعض الوقت
5 قليل من الوقت
6 بالكاد في أي وقت
7 ولا في أي وقت

6. كم من الطاقة كان لديك خلال الأسبوعيين الأخيرين؟ الرجاء اختيار إجابة واحدة من

1 لم تكن عندي طاقة إطلاقاً
2 القليل جداً من الطّاقة
3 القليل من الطّاقة
4 بعض الطّاقة
5 كمية متوسّطة من الطاقة
6 الكثير من الطّاقة
7 طاقة كاملة

7. كم من الوقت شعرت خلال الأسبوعين الأخيرين بقلق حول إمكانيّة الاحتياج إلى عمليّة جراحيّة بسبب مشكلة الأمعاء لديك؟ الرجاء اختيار إجابة واحدة من

1 كلّ الوقت
2 معظم الوقت
3 جزء لا بأس به من الوقت
4 بعض الوقت
5 قليل من الوقت
6 بالكاد في أي وقت
7 ولا في أي وقت

8. كم من الوقت خلال الأسبوعين الأخيرين كنت مضطرا/ة لتأجيل أو إلغاء ارتباط اجتماعي بسبب مشكلة أمعائك؟ الرجاء اختيار إجابة واحدة من

1 كلّ الوقت
2 معظم الوقت
3 جزء لا بأس به من الوقت
4 بعض الوقت
5 قليل من الوقت
6 بالكاد في أي وقت
7 ولا في أي وقت

9. كم من الوقت خلال الأسبوعين الأخيرين عانيت من مشاكل مغص في البطن ؟ الرجاء اختيار إجابة واحدة من

1 كلّ الوقت
2 معظم الوقت
3 جزء لا بأس به من الوقت
4 بعض الوقت
5 قليل من الوقت
6 بالكاد في أي وقت
7 ولا في أي وقت

10. كم من الوقت خلال الأسبوعين الماضيين شعرت بأنك لست بخير بشكل عام ؟ الرجاء اختيار إجابة واحدة من

1 كلّ الوقت
2 معظم الوقت
3 جزء لا بأس به من الوقت
4 بعض الوقت
5 قليل من الوقت
6 بالكاد في أي وقت
7 ولا في أي وقت

11. كم من الوقت خلال الأسبوعين الأخيرين إنزعجت بسبب خوفك من عدم إيجاد مرحاض؟ الرجاء اختيار إجابة واحدة من

1 كلّ الوقت
2 معظم الوقت
3 جزء لا بأس به من الوقت
4 بعض الوقت
5 قليل من الوقت
6 بالكاد في أي وقت
7 ولا في أي وقت

12. كم من الصّعوبة، واجَهَت نتيجةً لمشاكل أمعائك بممارسة فعاليات الرفاهية، أو فعاليّات رياضيّة، والتي كنت قد تحبّ ممارستها خلال الأسبوعين الأخيرين؟ الرجاء اختيار إجابة واحدة من

1 صعوبات عظيمة تجعل القيام بالفعاليات أمراً مستحيلاً
2 الكثير من الصعوبات
3 كمية صعوبات لا بأس بها
4 بعض الصعوبات
5 قليل من الصعوبات
6 بالكاد واجهت صعوبة
7 ليست هناك أية صعوبة؛ مشاكل الأمعاء لم تحد من الفعاليّات الرياضيّة أو فعاليّات الرفاهية

13. كم من الوقت خلال الأسبوعين الأخيرين عانيت من ألم في البطن؟ الرجاء اختيار إجابة واحدة من

1 كلّ الوقت
2 معظم الوقت
3 جزء لا بأس به من الوقت
4 بعض الوقت
5 قليل من الوقت
6 بالكاد في أي وقت
7 ولا في أي وقت

14. كم من الوقت خلال الأسبوعين الأخيرين واجهت مشاكل في الحصول على نوم جيد في الليل، أو عانيت من الاستيقاظ أثناء الليل؟ الرجاء اختيار إجابة واحدة من

1 كلّ الوقت
2 معظم الوقت
3 جزء لا بأس به من الوقت
4 بعض الوقت
5 قليل من الوقت
6 بالكاد في أي وقت
7 ولا في أي وقت

15. كم من الوقت خلال الأسبوعين الأخيرين شعرت باكتئاب أو بإنْباط لعزيمتك؟ الرجاء اختيار إجابة واحدة من

1 كلّ الوقت
2 معظم الوقت
3 جزء لا بأس به من الوقت
4 بعض الوقت
5 قليل من الوقت
6 بالكاد في أي وقت
7 ولا في أي وقت

16. كم من الوقت خلال الأسبوعين الأخيرين اضطررت إلى تجنّب المشاركة في أحداث لأنه لم يكن هناك مراحيض قريبة؟ الرجاء اختيار إجابة واحدة من

1 كلّ الوقت
2 معظم الوقت
3 جزء لا بأس به من الوقت
4 بعض الوقت
5 قليل من الوقت
6 بالكاد في أي وقت
7 ولا في أي وقت

17. بشكل عام، في الأسبوعين الأخيرين، الى أي حد واجهت مشكلة في إخراج كميّات كبيرة من الغازات؟ الرجاء اختيار إجابة واحدة من

1 مشكلة رئيسيّة
2 مشكلة كبيرة
3 مشكلة بارزة
4 مشكلة إلى حد ما
5 مشكلة صغيرة
6 بالكاد تكون مشكلة
7 لا مشكلة

18. بشكل عام، في الأسبوعين الأخيرين، كم كان حجم مشكلتك في الحفاظ أو الوصول إلى الوزن الذي تريد/ين؟ الرجاء اختيار إجابة واحدة من

1 مشكلة رئيسيّة
2 مشكلة كبيرة
3 مشكلة بارزة
4 مشكلة إلى حد ما
5 مشكلة صغيرة
6 بالكاد تكون مشكلة
7 لا مشكلة

19. الكثير من المرضى المصابين بمشاكل الأمعاء يشعرون بالعصبية وبمشاعر قلق تتعلّق بمرضهم. تشمل هذه المشاعر القلق من الإصابة بالسّرطان، قلق من عدم الشعور بأي تحسن أبداً، وقلق من الإصابة بنكسات. بشكل عام، كم من الوقت خلال الأسبوعين الأخيرين، شعرت بقلق أو اضطراب؟ الرجاء اختيار إجابة واحدة من

1 كلّ الوقت
2 معظم الوقت
3 جزء لا بأس به من الوقت
4 بعض الوقت
5 قليل من الوقت
6 بالكاد في أي وقت
7 ولا في أي وقت

20. كم من الوقت خلال الأسبوعين الأخيرين إنزعجت بسبب انتفاخ في البطن؟ الرجاء اختيار إجابة واحدة من

1 كلّ الوقت
2 معظم الوقت
3 جزء لا بأس به من الوقت
4 بعض الوقت
5 قليل من الوقت
6 بالكاد في أي وقت
7 ولا في أي وقت

21. كم من الوقت خلال الأسبوعين الأخيرين شعرت بأنك مسترخي وليس لديك أي توتر؟ الرجاء اختيار إجابة واحدة من

1 ولا في أي وقت
2 قليل من الوقت
3 بعض الوقت
4 جزء لا بأس به من الوقت
5 معظم الوقت
6 تقريبا كلّ الوقت
7 كلّ الوقت

22. كم من الوقت خلال الأسبوعين الأخيرين عانيت من نزيف في فتحة الشّرج مرافق لعملية الخروج؟
الرجاء اختيار إجابة واحدة من

1 كلّ الوقت
2 معظم الوقت
3 جزء لا بأس به من الوقت
4 بعض الوقت
5 قليل من الوقت
6 بالكاد في أي وقت
7 ولا في أي وقت

23. كم من الوقت خلال الأسبوعين الأخيرين شعرت بالحرج نتيجةً لمشاكل أمعائك؟ الرجاء اختيار إجابة واحدة من

1 كلّ الوقت
2 معظم الوقت
3 جزء لا بأس به من الوقت
4 بعض الوقت
5 قليل من الوقت
6 بالكاد في أي وقت
7 ولا في أي وقت

24. كم من الوقت خلال الأسبوعين الأخيرين إنزعجت من الشعور بضرورة الذهاب إلى المرحاض بالرغم من أن أمعائك كانت فارغة؟ الرجاء اختيار إجابة واحدة من

1 كلّ الوقت
2 معظم الوقت
3 جزء لا بأس به من الوقت
4 بعض الوقت
5 قليل من الوقت
6 بالكاد في أي وقت
7 ولا في أي وقت

25. كم من الوقت خلال الأسبوعين الأخيرين شعرت برغبة في البكاء أو بالانزعاج؟ الرجاء اختيار إجابة واحدة من

1 كلّ الوقت
2 معظم الوقت
3 جزء لا بأس به من الوقت
4 بعض الوقت
5 قليل من الوقت
6 بالكاد في أي وقت
7 ولا في أي وقت

26. كم من الوقت خلال الأسبوعين الأخيرين إنزعجت من ابتلال لإراديّ لملابسك الداخلية بالغائط؟ الرجاء اختيار إجابة واحدة من

1 كلّ الوقت
2 معظم الوقت
3 جزء لا بأس به من الوقت
4 بعض الوقت
5 قليل من الوقت
6 بالكاد في أي وقت
7 ولا في أي وقت

27. كم من الوقت خلال الأسبوعين الأخيرين شعرتَ بغضب نتيجة لمشكلة الأمعاء لديك؟ الرجاء اختيار إجابة واحدة من

1 كلّ الوقت
2 معظم الوقت
3 جزء لا بأس به من الوقت
4 بعض الوقت
5 قليل من الوقت
6 بالكاد في أي وقت
7 ولا في أي وقت

28. إلى أيّ مدى حدّت مشكلة الأمعاء لديك من نشاطك الجنسيّ خلال الأسبوعين الأخيرين؟ الرجاء اختيار إجابة واحدة من

1 لا يوجد أيّ نشاط جنسيّ نتيجة لمرض الأمعاء
2 تقييد كبير نتيجة لمرض الأمعاء
3 تقييد متوسّط نتيجة لمرض الأمعاء
4 بعض التّقييد نتيجة لمرض الأمعاء
5 التقييد قليل نتيجة لمرض الأمعاء
6 بالكاد كان هناك تقييد نتيجة لمرض الأمعاء
7 لم يكن هناك تقييد نتيجة لمرض الأمعاء

29. كم من الوقت خلال الأسبوعين الأخيرين، إنزعجت من الغثيان أو الشعور باضطراب في معدتك؟
الرجاء اختيار إجابة واحدة من

1 كلّ الوقت
2 معظم الوقت
3 جزء لا بأس به من الوقت
4 بعض الوقت
5 قليل من الوقت
6 بالكاد في أي وقت
7 ولا في أي وقت

30. كم من الوقت خلال الأسبوعين الأخيرين شعرت بأنك كنت تنزعج بسهولة؟ الرجاء اختيار إجابة واحدة من

1 كلّ الوقت
2 معظم الوقت
3 جزء لا بأس به من الوقت
4 بعض الوقت
5 قليل من الوقت
6 بالكاد في أي وقت
7 ولا في أي وقت

31. كم من الوقت خلال الأسبوعين الأخيرين شعرت بعدم فهم من قبل الآخرين لك؟ الرجاء اختيار إجابة واحدة من

1 كلّ الوقت
2 معظم الوقت
3 جزء لا بأس به من الوقت
4 بعض الوقت
5 قليل من الوقت
6 بالكاد في أي وقت
7 ولا في أي وقت

32. ما مدى رضاك، سعادتك، أو سرورك عن حياتك الشخصية خلال الأسبوعين الأخيرين؟ الرجاء اختيار إجابة واحدة من

1 غير راضٍ كثيراً، غير سعيد معظم الوقت
2 غير راض بشكل عام وغير سعيد
3 إلى حدّ ما غير راضي، غير سعيد
4 راضٍ بشكل عام، مسرور
5 راضٍ معظم الوقت، سعيد
6 راضٍ كثيراً معظم الوقت، سعيد
7 راض بشدة، لا يمكن أن أكون أكثر سروراً أو سعادة

Appendix 2

Al-Quds University
Jerusalem
Deanship of Scientific Research

بسم الله الرحمن الرحيم

جامعة القدس
القدس
عمادة البحث العلمي

Research Ethics Committee
Committee's Decision Letter

Date: 24/2/2018
Ref No: 34/REC/2018

Dear Ms. Tasneem Smerat, Dr. Maher Khdour,

Thank you for submitting your application for research ethics approval. After reviewing your application entitled "Assessment of health-related quality of life for patients with inflammatory bowel diseases in Palestine" the Research Ethics Committee (REC) confirms that your application is in accordance with the research ethics guidelines at Al-Quds University.
We would appreciate receiving a copy of your final research report/ publication.

Thank you again and wish you a productive research that serves the best interests of your subjects.

Dr. Dina M. Bitar
Research Ethics Committee Chair

Cc. Prof. Imad Abu Kishek - President
Cc. Members of the committee
Cc. file

Abu-Dies, Jerusalem P.O.Box 20002
Tel-Fax: #970-02-2791293
research@admin.alquds.edu
ابوديس، القدس ص.ب. 20002
تلفاكس: #970-02-2791293

Appendix 3

Ministry of Health - Nablus
General Directorate of Education in Health

وزارة الصحة – نابلس
الإدارة العامة للتعليم الصحي

Ref.: ....
Date: ....

الرقم:
التاريخ:

الأخ مدير عام الادارة العامة للمستشفيات المحترم،،،
الأخ مدير مجمع فلسطين الطبي المحترم،،،
تحية واحتراماً...

الموضوع: تسهيل مهمة

تماشياً مع سياسة وزارة الصحة المتعلقة بتعزيز التعاون مع الجامعات والمؤسسات الأكاديمية بإتاحة فرص التدريب أمام الطلبة والخريجين والباحثين في المؤسسات الوطنية وإسهاماً في تنمية قدراتهم.

يرجى تسهيل مهمة الطالبة: تسنيم اسماعيل اسميرات – ماجستير علوم صيدلانية– جامعة القدس، في عمل بحث التخرج بعنوان: ' Assessment of Health-Related Quality of Life for Patients with Inflammatory Bowel Diseases in Palestine'، لذا يرجى تسهيل مهمتها في الحصول على المعلومات اللازمة من خلال مقابلة مرضى لتعبئة استبانة الدراسة (بعد اخذ موافقتهم على المشاركة في البحث) وذلك في:

– مستشفى جنين – مستشفى طولكرم– مستشفى قلقيلية– مستشفى سلفيت – – مستشفى عاليه –
مستشفى يطا – مجمع فلسطين الطبي

وذلك في خلال الفترة من 2017/6/4–2017/12/4، علما بأنه سيتم الالتزام بمعايير البحث العلمي والحفاظ على سرية المعلومات.

البحث تحت اشراف د. ماهر الخضور.

مدير عام التعليم الصحي

نسخة: د. ماهر الخضور المحترم/ جامعة القدس

P.O .Box: 14
TelFax: 09-2333901

ص.ب. 14
تلفاكس: 09-2333901

Appendix 4

PARTICIPANT CONSENT FORM

استمارة موافقة مشارك

أنا المريض .....أوافق على المشاركه بهذا البحث العلمي الذي تم شرح أهدافه وغايته لي من قبل الشخص المقابل والذي يهدف لتقييم كفاءه الحياه لدي, وبذلك أوافق على مقابلة من يجري البحث وهي الطالبه تسنيم اسماعيل سميرات التي تحمل هاتف رقم 0597836405 وهي تجري بحث لمشروع التخرج من جامعه القدس بتخصص علوم صيدلانية ويهدف البحث الى قياس مدى كفاءه الحياه لدي ولدى المرضى الذين يعانون من نفس المرض ومقارنتها بعوامل مختلفة ترتبط بالمرض . ادرك ان المقابله التابعه لهذا البحث ستجرى بالطريقه التي تم وصفها لي .وأعلم أن معلوماتي ستبقى طي الكتمان وأنه بكامل حريتي أستطيع أن أغير أية ملاحظات أو أنسحب من المقابلة في أي وقت ..

التوقيع .....

تقييم جودة الحياة المتعلقة بالصحة للمرضى المصابين بأمراض التهاب الأمعاء في فلسطين

اعداد الطالبة : تسنيم اسماعيل ابراهيم سميرات

باشراف : الدكتور ماهر الخضور, الدكتور حسين الحلاق و الدكتور الاستشاري قصي عبده

الملخص

المقدمه : قياس جودة حياة المريض المصاب بمرض من الأمراض المزمنة هو أمر مهم للغاية لتقييم نتائج المرض وتأثير تداخلاته. يعد مرض الأمعاء الالتهابي ذو تأثير كبير على جودة حياة المرضى. وقد اقترحت الدراسات السابقة أن نشاط المرض هو مؤشر مهم لجوده حياة المرضى المصابين بهذا المرض. هناك عدد محدود من الدراسات في جميع أنحاء العالم تبين علاقة الالتزام بالأدوية بجودة حياة مرضى الالتهاب الامعائي ونتائجها متضاربة . لذلك تم إجراء هذه الدراسة لفحص الارتباط بين نشاط المرض ,الالتزام بالوصفة الدوائية وأثرهما على جودة حياة مرضى التهاب الأمعاء في فلسطين . أيضا ، هدفت هذه الدراسة لتحديد جودة حياة المرضى , الالتزام الدوائي لديهم وأيضا لكشف العوامل المرتبطة بجودة حياتهم وتؤثر عليها.

الأساليب :أجريت دراسة مستعرضة من تموز / يوليو 2017 إلى شباط / فبراير 2018 في مستشفى جامعة النجاح الوطنية، نابلس، مستشفى عالية الحكومي، الخليل، وفي مستشفى الدكتور خليل سليمان ، جنين ، فلسطين. تم استخدام أداة مخصصة لهذا المرض وهي استبيان مرضى التهاب الأمعاء التقرحي (IBDQ) لدراسة جودة حياتهم . تم قياس مدى الالتزام بالأدوية باستخدام مقياس مورسكي المعدل للالتزام بالدواء (8-MMAS). وقد تم تحليل النتائج باستخدام برنامج الحزمة الإحصائية للعلوم الاجتماعية (SPSS). تم إجراء تحليل الانحدار الخطي المتعدد لتحديد أهم المتغيرات المتعلقة بـ جودة حياة هؤلاء المرضى.

النتائج: شارك مئة واثنان وثلاثون مريضا في هذه الدراسة. من بينهم حوالي 58.3 ٪ من الذكور. متوسط أعمار من شاركوا بالدراسة حوالي 34 ± 13 سنة و تراوحت أعمارهم بين 18-70 سنة. 81

مشارك منهم (61.4 ٪) بالدراسة كان مرضهم نشط خلال الستة شهور الماضية.باستخدام مقياس مورسكي المعدل للالتزام، كان حوالي39.4 ٪ من المشاركين لديهم التزام متدني للأدوية. متوسط جودة حياة المرضى باستخدام استبيان مرضى التهاب الأمعاء التقرحي سجل 150.79 درجات. كانت الناحية العاطفية, وأعراض التهاب الأمعاء هما الأكثر تأثرا بالمقارنة مع النواحي الأخرى. ووجدنا أن نشاط المرض هو العامل الرئيسي المرتبط بجودة حياة المرضى (قيمةP<0.001). لم تكن هنالك علاقة بين مدى الالتزام بالدواء وجودة حياة المريض . لم يؤثر التشخيص(نوع المرض) على أي ناحية من نواحي جودة حياة المريض. كشف تحليل المخاطر أن المرضى الذين يعانون من مرحلة شفاء للمرض (r^2 = ,0.436قيمة P<0.001)، والمرضى الذين لديهم مستوى تعليمي عالي (r^2 =0.035 ,قيمة P =0.034)، والذين يستخدمون دواء Azathioprineقيمة P = ,(r^2 =0.017قيمة P =) 0.009ارتبطوا وبشكل مستقل بجودة حياة أفضل.

الاستنتاج:هذه الدراسة تعرض انخفاض جودة حياة المرضى الفلسطينيين المصابين بمرض التهاب الأمعاء بالمقارنة مع الدول الأخرى . وتحدد عددًا من العوامل ذات الصلة الهامة التي يجب أخذها في عين الاعتبار عند التعامل مع مرض التهاب الامعاء.نتائج هذه الدراسة قد تساعد مقدمي الرعاية الصحية لتحديد المرضى المعرضين لخطر انخفاض جودة الحياة ولا سيما الذين هم في حالة انتكاسة أو أعراض نشطة .يجب توفير الاهتمام من قبل مقدمي الرعاية الصحية وصانعي الاستراتيجية لزيادة المعرفة حول مرض التهاب الأمعاء ،ولتحسين جودة حياة المريض ولتوضيح أهمية الالتزام الدوائي لدى المرضى .