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Faculty of Graduate Studies

**Evaluation of Stages, Treatment Protocols
and Outcomes of Colorectal Cancer among
Palestinian Patients**

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Dedication

This work is dedicated to my family for their endless love, support, encouragement, which gave me the strength to face all challenges and bring this research to reality.

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I would like to thank everyone who helped me to accomplish my mission of pursuing master's degree in clinical pharmacy.

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Ibrahim Sawaied

الاقرار

أنا الموقع أدناه، مقدّم الرسالة التي تحمل العنوان:

Evaluation of Stages, Treatment Protocols and Outcomes of Colorectal Cancer among Palestinian Patients

أقر بأن ما اشتملت عليه هذه الأطروحة إنما هو نتاج جهدي الخاص، باستثناء ما تمت الإشارة إليه حيثما ورد. وأن هذه الرسالة كاملة، أو أي جزء منها لم يقدم من قبل لنيل أي درجة أو لقب علمي أو بحثي لدى أي مؤسسة تعليمية أو بحثية أخرى.

Declaration

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

Student's Name:

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List of Abbreviations

ANOVA	Analysis of variance
BMT	Bone marrow transplantation
CI	Confidence interval
CKD	Chronic kidney disease
CRC	Colorectal cancer
CRP	C-reactive protein
CT	Computed tomography
DM	Diabetes mellitus
ESRD	End-stage renal disease
FOLFIRI	5-fluorouracil, leucovorin, irinotecan
FOLFOX	5-fluorouracil, leucovorin, oxaliplatin
HF	Heart failure
HTN	Hypertension
I, II, III, IV	Latin numbers
IHD	Ischemic heart disease
IRB	Institution review board
MAB	Monoclonal antibody
MCV	Mean Corpuscular Volume
MRI	Magnetic resonance imaging
NNU	An-Najah National University
NNUH	An-Najah National University Hospital
PLT	Platelet
SPSS	Statistical package for social sciences
TNM stage	T: tumor size, N: lymph node involvement, M: distant metastases
US	United States
WBC	White blood cells
WHO	World health organization

Evaluation of Stages, Treatment Protocols and Outcomes of Colorectal Cancer among Palestinian Patients

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Abstract

Introduction: In Palestine, the first leading cause of death is cardiovascular diseases, and cancer is ranked as the second leading cause of death. Colorectal cancer is ranked as the second type of cancer among Palestinian patients. Cancer care is improving in Palestinian hospitals with time; however, services like palliative care, targeted therapy, bone-marrow transplantation, and individualized therapy are still limited. The study aims to assess the colorectal cancer stages, treatment protocols, and the survival of patients in Palestine.

Methodology: This is a retrospective study through data collection from medical records in a hospital specialized in cancer patients' care. Patients with confirmed colorectal cancer (stages I, II, III, IV) undergoing surgical or medical treatment were included in the study. Data collection was standardized by using Data Collection Form to gather information from included medical records. The disease outcomes after treatment were categorized into six categories, namely, Death, Cure, Disease Progression, Disease Recurrence, Under-treatment, or Unknown outcomes. Statistical analysis was performed using Statistical Package for Social Sciences (SPSS version 21).

Results: A sample of 252 patients with colorectal cancer from An-Najah National University Hospital (NNUH) was collected, males were 143 (56.7%), their age was between 27 – 86 years with a mean of 60.64 (± 11.4) years. Most of the patients had colon cancer only (183 patient, 72.6%) and (29 patient, 11.5%) had rectal cancer only, while the rest had both rectal and colon cancer (40 patients, 15.9%), most of them were at stage IV (159 patients, 63.1%). Surgery was the most prevailing mode of treatment for colorectal cancer patients (230; 91.3%), on the other hand, in patients who received chemotherapy, FOLFOX (folinic acid, fluorouracil, oxaliplatin) was more prevalent among patients and the physicians tend to choose it compared to FOLFIRI (folinic acid, fluorouracil, irinotecan). The mortality of the disease was high as many patients (41.3%) have died within a short interval between diagnosis and death. Worth mentioning that there was an apparent delay in the diagnosis of the disease as most patients were diagnosed at a later stage which has a poor prognosis. Regression analysis of days between last visit and diagnosis date and the type of treatment received (Chemotherapy, Surgical Treatment, Radiotherapy) ($R^2 = 0.035$) surgical treatment had the longest days between diagnosis and last visit and this was significant ($p = 0.033$). Surgical treatment had a positive impact on increasing the days of survival and it was significant ($p = 0.021$). A Chi-square analysis of the stage at diagnosis and the prognosis of CRC patients using existing data revealed that there is a significant difference ($p < 0.05$) between the stage at diagnosis and the disease outcome. On the other hand, Chi-square analysis for the chemotherapy protocol used among

patients in comparison with disease outcomes, cure rates were highest with the use of FOLFOX (26.7%), death rates were similar between FOLFIRI and FOLFOX patients. These results were significantly different ($p < 0.05$).

Conclusions: A high percentage of patients were diagnosed in advanced disease stages. The modes of treatment generally were adopted from international guidelines, however, the cure rates and good disease prognosis were not high, the disease mortality rate was high. More studies need to be undertaken to investigate the actual application of chemotherapy protocols and involve clinical pharmacists in the chemotherapy protocol choice, dosing, frequency, follow-up. As a result, the present analysis of Palestine's colorectal cancer pattern advocates for a wide range of treatments to lower the disease's burden. These include investments in public awareness campaigns aimed at the general public and primary care professionals, intending to increase understanding of colorectal cancer symptoms and risk factors, as well as the merits of screening, and promotion of healthy lifestyles in order to avoid this serious illness. In order to diagnose the disease much earlier which makes health care providers intervene earlier to promote a better prognosis.

Chapter One

Introduction

1.1 Overview of Colorectal Cancer

Cancer is one of the primary causes of high death rates throughout the world, according to the World Health Organization (WHO), which predicted that 84 million people will die of cancer between 2005 and 2015 and that this number would double between 2000 and 2020, and nearly threefold by 2030. (Beaver et al., 2011). Their expectations were true, colorectal cancer (CRC) was one of the most prevalent forms of cancer; for example, colorectal cancer (CRC) was the third most prevalent cancer globally in 2000, behind breast and lung cancers, with 945,000 new cases diagnosed each year (9.4% of cases) and 492,000 cancer deaths (7.9 percent deaths) (Parkin, Bray, & Devesa, 2001). The incidence rates of CRC for both males and females were significantly increased from 1983-1987 to 1998-2000 for 27 of 51 cancer registries in the world (Zhivotovskiy et al., 2012).

Colorectal cancer was the second most prevalent cause of cancer mortality among men and women globally in 2007, according to the World Gastroenterology Organization/International Digestive Cancer Alliance, with an annual incidence of roughly 1 million cases and more than 500,000 deaths. (Winawer, 2007). In 2008, more than 1 million new cases were diagnosed, including 664,000 new cases in men and 571,000 new cases in women, making CRC Europe's second most prevalent cause of cancer

mortality behind lung cancer. (Jacques Ferlay et al., 2010). CRC was uncommon in Africa and many Asian nations, with males being more affected than females. (Rasool, Kadla, Rasool, & Ganai, 2013). CRC was most common in high-income and industrialized nations like North America and Western Europe, as well as some Asian countries including Japan, Singapore, and North Korea, which are undergoing nutritional revolutions. (Ferlay, Parkin, & Steliarova-Foucher, 2010).

Colorectal cancer (CRC) is a global issue, with an annual incidence of about one million cases and a death rate of more than 500,000 people globally. Colorectal cancer is the fourth most prevalent malignant tumor and the second major cause of mortality in the United States and other Western countries. The prevalence of colorectal cancer has risen dramatically across Asia during the last several decades. Furthermore, data from this region indicates that this prevalence has already approached that of the West, particularly among the more wealthy inhabitants. (Marley & Nan, 2016).

1.2 Risk factors

Until now, the actual causes of colorectal cancer are not well understood. However, it is thought that many factors are involved in developing CRC over a long period. The risks for colorectal cancer vary from country to country and even within countries it varies among individuals based on several factors such as diet, lifestyle, and hereditary factors.

Some studies found that one or two generations of immigrants relocating from low-incidence colorectal cancer nations to high-incidence host nations had a greater colorectal cancer burden (Johnson et al., 2013). It was found that acquired environmental and lifestyle variables such as a low-fiber, high-fat diet, red meat and alcohol, sedentary work, and cigarette smoking might be the key modifiable etiologic causes.

Age over 50, a family history of colorectal cancer, a personal history of colorectal cancer, adenoma, a genetic history of non-polyposis colorectal cancer syndrome, or inflammatory bowel disease of the colon such as ulcerative colitis and Crohn's disease are all non-modifiable risk factors for colorectal cancer. (Johnson et al., 2013).

1.3 Pathogenesis of colorectal cancer

Colorectal cancer is a hereditary disease that can be inherited or acquired. Only around 5% of all occurrences of colorectal cancer are caused by hereditary disorders. Colorectal cancer develops in phases, with each step resulting in the transformation of a normal epithelial cell into an adenocarcinoma. Colonocytes with particular genetic mutations were able to multiply at an abnormally high pace. As the process progresses, the cells develop malignant traits such as invasiveness and the ability to spread. Environmental variables, in addition to genetic predisposition, are thought to be linked to an increased risk of colorectal cancer. (Jass, 2002).

Colorectal cancer is a slow-growing illness that can go years without causing symptoms. Polyps, which are tiny, non-cancerous growths that

originate in the colon and rectum, are the most common cause of colon and rectum cancer. These polyps, also known as precancerous lesions, are a precursor to colorectal cancer. The "dwell time" is the average period between the development of a polyp and the commencement of cancer. However, dwell time appears to vary with the location of cancer. It is longer in the distal colon than in the proximal colon, and it is the shortest in the rectosigmoid segment (Grady & Markowitz, 2015).

1.4 Clinical Manifestation

Changes in bowel habits and recurrent rectal bleeding are two major clinical characteristics of big bowel malignancies. The tumor's location has an impact on the presenting signs and symptoms. It frequently presents late with a palpable lump, right iliac fossa pain, or hypochromic microcytic anemia due to prolonged occult blood loss if it arises in the caecum and ascending colon. Because the left colon is smaller and stores more solid stuff than the right colon, blockage, bowel irregularities and rectal bleeding are all typical symptoms. When a tumor is found in the rectum, bleeding is a common sign, leading the patient to assume he has piles. A feeling of incomplete evacuation of the rectum is common after defecation and the patient may experience urgency and the frequent passage of slime and blood. As the rectum is capacious, obstruction is unusual (Bohorquez et al., 2016).

1.5 Prognosis

The outcome of colorectal cancer depends on how advanced the disease when it was first diagnosed. Therefore, the diagnosis of early-stage cancer results in better survival. Curtbert Dukes described a pathologic staging system for colorectal cancer based on invasion through the bowel wall and lymph node involvement (Dukes, 1949). It has major prognostic implications. In the early stages (Dukes A-invasion of muscularis propria), survival is excellent through surgical intervention with 62% to 98% of 5 years survival (Haq, Schneeweiss, Kalsi, & Arya, 2009).

1.6 TNM classification

The TNM classification, which is based on the degree of cancer invasion into the intestinal wall, lymph node involvement, and distant metastases (T: tumor size, N: lymph node involvement, M: distant metastases). There are different stages for each one:

- Tis =carcinoma in situ; T1 = submucosa; T2 = muscularis propria; T3 = penetrates all layers (for rectal cancer, includes perirectal tissue); T4 = adjacent organs or peritoneum.
- N0 = none; N1 = 1–3 regional nodes; N2 \geq 4 regional nodes; N3 = apical or vascular trunk nodes.
- M0 = none; M1 = present.

TNM classification is used by the American Joint Committee on Cancer and the Union for International Cancer Control, and mostly all over the world.

Studies have demonstrated that there is a link between stage at diagnosis and survival, the survival rate for stages 0 and 1 was up to 100%, but just 3% for stage 4. (Puppa, Sonzogni, Colombari, & Pelosi, 2010).

However, because the majority of patients were asymptomatic at the start, earlier symptomatic diagnosis was unlikely to obtain; even if it was, the total increase in survival was expected to be minor. As a result, screening offers an alternative for detecting CRC before cancer becomes symptomatic, which improves the survival rate. (Compton, Fenoglio-Preiser, Pettigrew, & Fielding, 2000).

1.7 Treatment

The therapy for colorectal cancer is determined by the disease's stage. It was practically treatable in its early stages. It was less likely to be cured if it was discovered at a late stage with distant metastases.

Surgery is the most common therapy for colorectal cancer since it has a greater cure rate. More than 85 percent of patients with colon cancer have surgical resection with anastomosis, while rectal cancer patients have a locoregional resection. A large number of resections are conducted with the goal of curing the affected segment-bearing tumor, which is removed with acceptable margins of normal-appearing tissue, as well as its vascular

pedicle and lymphatic drainage, followed by an anastomosis or colostomy. Palliative (noncurative) excision of the main tumor is still an option in the case of many metastases to reduce future morbidity caused by tumor bleeding, invasion, or obstruction (Wolpin & Mayer, 2008).

Chemotherapy is used to decrease the chances of metastasis, lower tumor size, and limit tumor growth. Chemotherapy is frequently used as adjuvant therapy after surgery, as a precursor to surgery (neoadjuvant treatment), or as the primary therapy (palliative). Chemotherapy is normally administered after surgery for colon cancer only if the disease has progressed to the lymph nodes (Stage III) (Moertel, 1994). Depending on the stage, patient with CRC will get chemo and/or targeted therapies to control the cancer. Some of the most commonly used regimens include:

- FOLFOX: leucovorin, 5-FU, and oxaliplatin (Eloxatin)
- FOLFIRI: leucovorin, 5-FU, and irinotecan (Camptosar)
- CAPEOX or CAPOX: capecitabine (Xeloda) and oxaliplatin
- FOLFOXIRI: leucovorin, 5-FU, oxaliplatin, and irinotecan
- One of the above combinations plus either a drug that targets VEGF, (bevacizumab [Avastin], ziv-aflibercept [Zaltrap], or ramucirumab [Cyramza]), or a drug that targets EGFR (cetuximab [Erbix] or panitumumab [Vectibix])
- 5-FU and leucovorin, with or without a targeted drug

- Capecitabine, with or without a targeted drug
- Irinotecan, with or without a targeted drug
- Cetuximab alone
- Panitumumab alone
- Regorafenib (Stivarga) alone
- Trifluridine and tipiracil (Lonsurf)

Radiotherapy is not commonly utilized in the treatment of colon cancer because it might cause radiation enteritis and is difficult to target particular areas of the colon. Because the rectum does not move as much as the colon and is thus simpler to target, it is more commonly utilized in rectal cancer (Häfner & Debus, 2016).

1.8 Colorectal cancer screening

The American Cancer Society recommends that persons over the age of 50 get a CRC screening since most sporadic CRCs in industrialized nations occur in adults over the age of 50. The CRC screening test allows for cost-effective early diagnosis and treatment of early-stage cancer. Individuals who have frequent fecal occult blood testing have been demonstrated to have a lower risk of CRC death. (Kronborg et al., 1996; Mandel et al., 2000). Further reduction can be achieved by performing sigmoidoscopy and colonoscopy followed by colonoscopic polypectomy. However, many studies showed the obstacle to implementing a CRC screening program

were limited by knowledge on CRC, the inconvenient and embarrassing nature of the test, and lack of physician recommendation.

1.9 Colorectal cancer in Palestine

Globally, cancer is considered the primary cause of death, cancer caused by various factors, such as sedentary lifestyle, unhealthy nutrition, and other environmental causes (Singh, Singh, Murad, Singh, & Samadder, 2014). In Palestine, the first leading cause of death is cardiovascular diseases, and cancer is ranked as the second leading cause of death. Colon cancer is ranked number one among cancers affecting men in Palestine. However, colon cancer is ranked as the second cancer type with a rate of 9.4% and lung cancer considered as third (8.7%). A few years ago, males who died out of colon cancer were 11.2%. Per year, 12.3 new cases per 100,000 males in Palestine develop colon cancer (Palestinian Ministry of Health, 2019).

Breasts, lung, colon, leukemia, and brain cancers account for 58.6% of cancer cases resulting in death among Palestinians, accounting for more than half of all cancer fatalities in Palestine, according to statistics from the National Cancer Registry in Palestine, a division of the Health Information Center (Halahleh & Gale, 2018).

Palestinian Ministry of Health official statistics revealed that the total number of cancer cases reported in the governorates of the West Bank was 3,174 cases in 2019, an increase of 2.2% over the number of cases reported in 2018, which reached 3,102 cases. In 2019, the incidence of cancer in the

West Bank was 117.8 per 100,000 inhabitants. The number of new cases registered among females reached 1,664 cases, accounting for 52.4% of new cancer cases, and 1,510 cases were registered among males, accounting for 47.6% of the total cases registered in 2019. 1,095 cancer cases were registered in the age group over 64 years, or 34.5% of the total cases recorded in the year 2019, noting that this age group represented only 3.3% of the total population, and 1,936 cases were recorded, 61.0% of the cases in the 15-64 age group. Per year there were 143 cases in the age group under 15 years old, and the percentage of this group was 38.4% of the total population (Palestinian Ministry of Health, 2019).

1.10 Statement of problem

Epidemiologic studies are still lacking in Palestine, it is mandatory to follow up on the treatment protocols that are being implemented, the risk factors behind disease development among the Palestinian population, and survival rates. There have been no studies investigating the survival of colorectal cancer patients in Palestine, and there is a shortage of studies exploring adherence to international therapeutic guidelines. Thus, the current study aimed at investigating colorectal cancer among the Palestinian population in the West Bank in terms of disease prevalence, survival rates, treatment protocols, and risk factors. Such studies would enlighten the health care providers toward the Palestinian population in order to deliver optimal health care.

1.11 Objectives

1.11.1 General Objective

The study aims to assess the colorectal cancer treatment protocols and the survival of patients in Palestine.

1.11.2 Specific objectives

1. To determine the distribution of the cases according to gender, age, and stages of colorectal cancer among Palestinian patients.
2. To present the common modes of treatment protocols used by physicians to treat patients with colorectal cancer in Palestine.
3. To explore the relevant factors affecting the prognosis of colorectal cancer patients.

1.12 Significance of the study

This study undertaken to document colorectal cancer survival and associated prognostic factors in Palestine. It helps to give data about the used treatment protocols and the stages of disease among our patients, in addition to the outcomes of treatment which will help in evaluating the situation and developing policies in this field.

Chapter Two

Literature Review

2.1 Overview

The current study's research aim, design, and methodological approach have been developed from a close understanding and analysis of the existing literature. This part reviews previous research and published data that is directly relevant to the research objectives. It involves cancer in Palestine, the methods to treat colorectal cancer, and the gaps in the knowledge related to the study objectives.

2.2 Cancer in Palestine

Palestinian health care became increasingly important since the 1994 Oslo agreement when the Palestinian Authority ruled the West Bank and Gaza strip, this included the health care organization. The WHO and foreign donors supported this administration, especially the US Government. Nevertheless, there were major economic and social challenges, health care in Palestine is one of the best among Arab countries in terms of life expectancy and maternal, infant, and child mortality rates (Bailony et al., 2011).

As cancer is a global major concern, cancer diagnosis is increasing among Palestinians as it became the second most common cause of death. However, the diagnosis happens at late stages due to certain causes.

Particularly, the social perspectives, uneasy access to health care systems, and lack of insurance.

There are limited hospitals in Palestine that provide care for cancer patients. In terms of cancer diagnosis and treatment, four hospitals in the West Bank and three in Gaza are available. Radiation therapy and personalized oncology are only available at Augusta Victoria Hospital, while bone marrow transplantation is only available at An-Najah University Hospital. Palestinian hospitals refer patients to Israeli, Jordanian, and Egyptian hospitals. Some diagnostic tests are not available in Palestinian hospitals such as PET-CT, hence, all cases are referred to Israeli hospitals (Kharroubi & Seir, 2016).

Cancer care is improving in Palestinian hospitals with time; however, services like palliative care, targeted therapy, bone-marrow transplantation, and individualized therapy are still limited. This is due to many causes, the lack of specialized physicians, shortage of drugs, and other causes.

The cancer burden in Palestine is likely to rise, putting extra strain on the present healthcare system's financial and technical resources, with financial instability exacerbating the situation (Qumseya et al., 2014).

A study was conducted to evaluate the quality of mortality data to explore the cancer mortality patterns in Palestine. The study used Death certificates of Palestinians in the West Bank. The most common cause of death out of all cancer types was lung cancer among males (22.8 %) and breast cancer among females (21.5 %) succeeded by prostate cancer for males (9.5 %) and

by colon cancer for females (11.4 %). The study concluded that the Palestinian mortality registry has improved over time. There were different mortality patterns among cancers, which might be devoted to many factors including environmental and individual factors (Abu-Rmeileh et al., 2016).

2.3 Colorectal cancer treatment

In the United States, colorectal cancer is the fourth most prevalent noncutaneous malignancy and the second leading cause of cancer-related mortality. Significant progress has been achieved in the systemic treatment of this malignant illness in recent years. Six new chemotherapeutic drugs have been approved, bringing the median overall survival for patients with metastatic colorectal cancer from less than 9 months to around 24 months with no therapy (Wolpin & Mayer, 2008).

For nearly all patients with resectable lesions who can tolerate general anesthesia, resection of the main colonic or rectal cancer is the therapy of choice. Multiple studies show that a minimally invasive laparoscopically assisted colectomy has similar outcomes and rates of recurrence to an open colectomy for colon cancer (Al-Hajeili, Marshall, & Smaglo, 2016).

Chemotherapy and radiation have been shown to enhance overall and tumor-free survival in colorectal cancer patients depending on stage:

1. Stage I- No adjuvant therapy is advised due to the outstanding 5-year survival rate (90-100%).

2. Stage II (node-negative illness) has a 5-year survival rate of around 80%. In most randomized clinical studies for stage II colon cancer, no substantial survival advantage from adjuvant chemotherapy has been observed. Patients who are otherwise healthy but have stage II illness are at a greater risk of recurrence (perforation, obstruction, T4 tumors, or fewer than 12 lymph nodes sampled) may benefit from adjuvant chemotherapy.
3. Stage III (node-positive disease): The predicted 5-year survival rate with surgical resection alone is 30-50 percent. Adjuvant chemotherapy given after surgery improves disease-free survival and overall survival by up to 30% and is indicated for all healthy patients.
4. Stage IV (metastatic illness)-Approximately 20% of patients had a metastatic illness at the time of their first diagnosis, with another 30% developing metastasis later. A small percentage of these individuals have a condition that can be treated by surgical resection. In 35-55 percent of instances, resection of isolated liver or lung metastases can result in long-term (over 5 years) survival. (Hatcher & Kumar, 2014).

2.4 Colorectal cancer prognosis

Rectal cancer has lower long-term survival rates and a significantly higher rate of local tumor recurrence with surgery alone (approximately 25%) than colon cancer, which can be attributed to the difficulty of achieving adequate surgical resection margins and the lack of serosal encasement of the rectum. Surgery may be performed initially if early imaging scans

indicate stage I illness. Preoperative chemoradiation with 5-fluorouracil or capecitabine as radiation therapy for stage II and III cancers by clinical staging (with endorectal ultrasound or pelvic MRI). The use of a -sensitizing drug increases disease-free survival and lowers the likelihood of pelvic recurrence (Walther et al., 2009).

The stage of disease at presentation is the most important determinant of long-term survival in colon cancer: stage I has a survival rate of more than 90%, stage II has a survival rate of 70-85%, stage III has a survival rate of 67 percent, stage III with more than 4 positive lymph nodes has a survival rate of 33 percent, and stage IV has a survival rate of 5-7 percent. Rectal malignancies have a poorer prognosis at each stage. Palliative care efforts must be thorough for people whose disease advances despite treatment. (Shaukat et al., 2013).

An overall survival advantage for fluorouracil-based chemotherapy in patients with stage III (lymph node-positive) colon cancer has been well documented, and new studies have indicated even more effectiveness with the inclusion of oxaliplatin in such adjuvant treatment regimens. Adjuvant chemotherapy for patients with stage II colon cancer is contentious, but it may be suitable in a group of patients who are at a higher risk of disease recurrence (Morris, Maughan, Forman, & Quirke, 2007).

Chapter Three

Methodology

This part describes the method that was implemented to achieve the research objectives.

3.1 Study Design

This was a retrospective study through data collection from medical records in a hospital specialized in cancer patients' care.

3.2 Study Setting

The medical records of colorectal cancer patients from An-Najah National University Hospital were reviewed during January and February 2021. This hospital is a tertiary hospital for cancer treatment in the Northern region of the West Bank.

3.3 Population

Patients with confirmed colorectal cancer (stages I, II, III, IV) undergoing surgical or medical treatment.

3.3.1 Inclusion criteria and exclusion criteria

The study included the following:

1. Patients above 18 years.
2. Males and females

3. Confirmed diagnosis of colorectal cancer
4. Patients with CRC who received surgical treatment (resection, laparotomy, colectomy) and/or radiotherapy and/or chemotherapy.

Exclusion criteria were as follow:

1. Pregnant patients.
2. Patients who did not receive any type of treatment.

3.4 Sample Size

This study included the files of all patients who were treated at An-Najah National University Hospital and met the inclusion criteria.

3.5 Data collection

Considering the importance of data standardization for the internal validity of a study; data collection was standardized by using Data Collection Form to gather information from included medical records (Appendix A).

All clinical cases and their follow-up data were recorded. The data includes sex, age at diagnosis, clinical symptoms, severe complications, location of the primary tumor, histological type, tumor differentiation, lymphovascular invasion, depth of invasion, numbers of retrieved lymph nodes and metastatic lymph nodes, date of surgery, date of recurrence (if applicable), cause of recurrence (if applicable), date of death (if applicable), cause of death (if applicable), postoperative treatment, and date of follow-up.

3.6 Ethical Considerations

The study protocol was authorized by An-Najah National University Institutional Review Boards (IRB) (Appendix B) and An-Najah National University Hospital before the initiation of this study.

All information obtained from medical records were kept confidential and only summarized data was presented in reports or publications

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

3.7 Statistical analysis

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS version 21). Mean \pm standard deviation was computed for continuous data. Frequencies and percentages were calculated for categorical variables. Categorical variables were compared using the Chi-square test or regression analysis as appropriate. A p-value of less than 0.05 was considered to be statistically significant for all analyses.

Chapter Four

Results

4.1 Overview

This section presents the results obtained from a sample of 252 patients with colorectal cancer from An-Najah National University Hospital (NNUH). The medical records were obtained with approval from the Archive Department-NNUH using the Medical Record System at NNUH.

4.2 Socio-demographics of patients

The socio-demographic of patients are shown in table 4-1. Male patients were more than females with a ratio of 1.31:1, they ranged in age between 27 – 86 years with a mean of 60.64 (± 11.4), most of them were married, non-drinker and non-smoker. Information about socio-demographics including age, gender, marital status, smoking, weight, height, blood group, education, nutrition, work was meant to be evaluated. Noticeably, there was a lack of information in the medical records about weight, height, blood group, education, nutrition, and work, hence, no meaningful results can be obtained from them.

Almost half of the patients did not have any disease history other than colorectal cancer. The comorbid diseases that the patients had been shown in Table 4-2.

Table 4.1: Sociodemographic information of patients.

Sociodemographic information		Frequency	Percent %	Total
Gender	Male	143	56.7	252
	Female	109	43.3	
Age (years)	Mean	60.64 ±11.4		252
	Minimum	27		
	Maximum	86		
Marital Status	Single	67	26.6	252
	Married	173	68.7	
	Widowed	10	4.0	
	Divorced	2	0.8	
Smoking	Non-smoker	187	74.2	252
	Ex-smoker	28	11.1	
	Smoker	37	14.7	
Alcohol	Non-drinker	251	99.6	252
	Drinker	1	0.4	
Nutrition	Well	183	72.6	252
	Malnutrition	69	27.4	
Height (cm)	Mean	167.4819±12.4		83
	Minimum	150		
	Maximum	185		
Weight (Kg)	Mean	74.3 ± 3.1		95
	Minimum	33		
	Maximum	120		

Table 4.2: Past medical history of patients.

Disease	Frequency	Percent %
Diabetes Mellitus	64	25.4
Hypertension	73	29.0
Ischemic Heart Disease	13	5.2
Heart Failure	3	1.2
Hypothyroidism	15	2.0
Chronic Kidney Disease	4	1.6
End Stage Renal Disease	3	1.2
Asthma	5	2.0
None	128	50.8

4.3 Colorectal cancer characteristics

Out of the 252 patients, most of the patients had colon cancer only (183 patient, 72.6%) and (29 patient, 11.5%) had rectal cancer only, while the rest had both rectal and colon cancer (40 patients, 15.9%) as shown in

Figure 4-1. The stages of colorectal cancer using (I, II, III, IV) and (TNM) systems are shown in Table 4-3, Table 4-4. A high percentage of patients (63.1%) were unfortunately in stage IV.

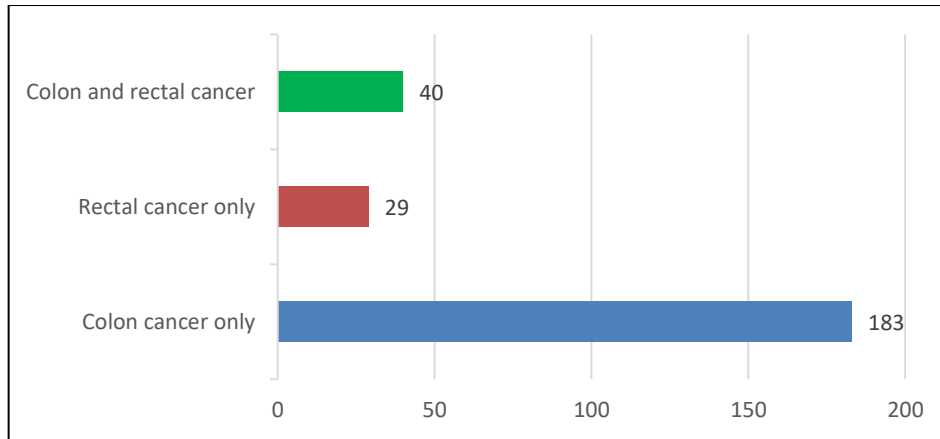


Figure 4.1: Colorectal cancer distribution among patients.

Table 4.3: Stages of colorectal cancer at diagnosis.

CRC Stage	Frequency	Percent (%)
Stage I	3	1.2
Stage II	33	13.1
Stage III	57	22.6
Stage IV	159	63.1

Table 4.4: TNM stages of colorectal cancer among patients.

TNM Stage*	Frequency
T1	1
T2	40
T3	133
T4	43
M0	87
M1	161
N0	61
N1	125
N2	36
N3	2

*(T: tumor size, N: lymph node involvement, M: distant metastases)

In a Chi-square analysis, there has been no significant difference between gender and stage ($p = 0.553$). In terms of rectal or colon cancer, there was also no significant difference between gender and type of cancer; colon or rectal as p values were $p = 0.539$, and $p=0.965$ respectively, as shown in Table 4-5.

Table 4.5: Association between gender and colorectal cancer and stages.

Gender	Colon cancer		Rectal cancer		Stage (I, II, III, IV)			
	No	Yes	No	Yes	I	II	III	IV
Female	11	98	79	30	1	13	21	74
Male	18	125	104	39	2	20	36	84
P value*	0.539		0.965		0.553			

* Chi square test .

4.4 Treatment strategies

The data collection form had specific questions regarding the treatment of CRC, for instance, about the strategy in general (surgery, radiotherapy, or chemotherapy) as shown in Table 4-6. Followed by questions regarding the chemotherapy protocol used to treat the patients in terms of the protocol used and the number of cycles of each protocol.

Table 4.6: Treatment strategies among colorectal cancer patients.

Treatment Strategy	Frequency	Percentage (%)
Surgical	230	91.3
Radiotherapy	38	15.1
Chemotherapy	227	90.1

Regarding chemotherapy, FOLFOX is a combination of chemotherapy drugs used to treat CRC, it consists of: folinic acid, fluorouracil, and oxaliplatin.

FOLFIRI is the name of a chemotherapy combination that includes: folinic acid, fluorouracil, and irinotecan.

Some patients received other chemotherapy protocols, by using monoclonal antibodies such as (cetuximab or bevacizumab) or capecitabine. Or patients who used FOLFOX or FOLFIRI in addition to any of these agents. Table 4-7 shows the distribution of chemotherapeutic protocols used among patients. FOLFOX was more prevalent among patients and the physicians tend to choose it compared to FOLFIRI.

Table 4.7: Treatment protocols among colorectal cancer patients.

Treatment	Frequency	Percent (%)
FOLFOX alone	35	13.89
FOLFOX + MAB	4	1.59
FOLFOX + ZA	1	0.40
FOLFIRI alone	17	6.75
FOLFIRI+MAB	8	3.17
Capecitabine	28	11.11
Capecitabine + oxaliplatin	68	26.98
Bevacizumab	18	7.14
Cetuximab	6	2.38
Regorafenib	1	0.40
Cisplatin + Etoposide	1	0.40
Gemcitabine + Oxaliplatin	1	0.40
Others	43	17.06
Unknown	21	8.33

FOLFOX: Folinic acid "FOL", Fluorouracil "F", and Oxaliplatin "OX"

FOLFIRI: Folinic acid "FOL", Fluorouracil "F", and Irinotecan "IRI"

MAB: monoclonal antibody drug, ZA: Zolendronic acid

4.5 Outcomes of treatment

The disease outcomes after treatment were categorized into six categories, namely, Death, Cure, Disease Progression, Disease Recurrence, Undertreatment, or Unknown outcomes. The results are presented in Table 4-8. The mortality of the disease is high as most of the patients (41.3%) have died.

Table 4.8: Colorectal cancer disease outcomes.

Disease outcome	Frequency	Percent (%)
Death	104	41.3
Cure	30	11.9
Disease Progression	96	38.1
Disease Recurrence	7	2.8
Undertreatment	6	2.4
Unknown	9	3.6

Regression analysis of disease outcome (death, cure, progression, recurrence, under-treatment) to the type of therapy that the patient received ($R^2 = 0.066$) was significant ($p = 0.001$). Patients who received surgical treatment tend to have cure outcomes much higher than patients who received radiotherapy or chemotherapy.

Besides, by analyzing the disease outcomes and their relation to the protocol that the patients received, as shown in table 4-9. The results were not of significant difference ($p = 0.7$).

Table 4.9: FOLFOX protocol compared to disease outcomes.

Disease Outcome	Medical treatment protocol FOLFOX			
	Yes	Percentage	No	Percentage
Death	58	23.0%	46	18.3%
Cure	8	3.2%	22	8.7%
Progression	44	17.5%	52	20.6%
Unknown	4	1.6%	5	2.0%
Recurrence	3	1.2%	5	2.0%
Undertreatment	4	1.6%	1	.4%

FOLFIRI protocol was also linked to disease outcomes, and it had no significant difference as well ($p = 0.13$). Table 4-10 presents the FOLFIRI protocol and disease outcomes.

Table 4.10: FOLFIRI protocol and CRC disease outcomes.

Disease Outcome	Medical treatment protocol FOLFIRI			
	Yes	Percentage	No	Percentage
Death	60	20.4%	44	17.5%
Cure	2	.8%	28	11.3%
Progression	41	18.3%	54	21.4%
Non known	5	2.3%	4	1.6%
Recurrence	2	1.8%	6	2.4%
Undertreatment	0	0.0%	5	2.0%

4.6 Years of survival

The years of survival were collected in two ways, either if it was clearly mentioned in the medical record, or from the date of diagnosis and date of the last visit. However, the years of survival were not clear in the medical records, the current study calculated the survival based on the difference between the date of diagnosis and the date of the last visit, the mean of days was 1062.2 ± 974.15 .

Regression analysis of days between last visit and diagnosis date and the type of treatment received (Chemotherapy, Surgical Treatment, Radiotherapy) ($R^2 = 0.035$) was significant ($p = 0.033$).

Surgical treatment had a positive impact on increasing the days of survival and it was significant ($p = 0.021$), radiotherapy has a positive impact on increasing the days of survival as well, but it was lower than surgical treatment positive, however, the difference was not significant ($p = 0.407$). Besides, chemotherapy had a positive impact, but it was the lowest amongst all therapeutic options, though it was not significant ($p = 0.096$). The table below (Table 4-11) shows the regression analysis for the type of treatment and days of survival.

Table 4.11: Regression analysis of colorectal treatment and years of survival.

ANOVA	Sum of Squares	df	Mean Square	F	Sig.
Regression	8212897.0	3	2737632.33	2.954	0.033 ^b
Coefficients	Unstandardized Coefficients		Standardized Coefficients	t	Sig.
	B	Std. Error	Beta		
Surgical Treatment	500.671	215.509	0.147	2.323	0.021
Radiotherapy	141.995	170.848	0.053	0.831	0.407
Chemotherapy	347.936	208.352	0.106	1.670	0.096

^a Dependent Variable: Days between last visit and diagnosis date

^b Predictors: (Constant), Chemotherapy, Surgical Treatment, Radiotherapy

A Chi-square analysis of the stage at diagnosis and the prognosis of CRC patients using existing data revealed that there is a significant difference ($p < 0.05$) between the stage at diagnosis and the disease outcome (Table 4-12).

Table 4.12: Disease outcome after treatment.

Disease outcome after treatment	Stage I		Stage II		Stage III		Stage IV	
Death	0	0.0%	5	4.8%	6	5.8%	93	89.4%
Cure	3	10.0%	19	63.3%	7	23.3%	1	3.3%
Disease Progression	0	0.0%	4	4.2%	35	36.8%	56	58.9%
Disease Recurrence	0	0.0%	2	28.6%	4	57.1%	1	14.3%
Under-treatment	0	0.0%	3	50.0%	3	50.0%	0	0.0%
Unknown	0	0.0%	0	0.0%	2	22.2%	7	77.8%

On the other hand, Chi-square analysis for the chemotherapy protocol used among patients in comparison with disease outcomes, cure rates were highest with the use of FOLFOX (26.7%), death rates were similar between FOLFIRI and FOLFOX patients. These results were significantly different ($p < 0.05$) (Table 4-13).

Table 4.13: Chemotherapy protocol and disease outcomes.

Disease outcome after treatment	FOLFOX		FOLFOX + mab		FOLFIRI		FOLFIRI + mab	
	Freq.	%	Freq.	%	Freq.	%	Freq.	%
Death	49	47.1%	9	8.7%	49	47.1%	11	10.6%
Cure	8	26.7%	0	0.0%	2	6.9%	0	0.0%
Disease Progression	35	36.5%	9	9.4%	31	32.3%	10	10.4%
Disease Recurrence	3	42.9%	0	0.0%	2	28.6%	0	0.0%
Under-treatment	4	66.7%	0	0.0%	0	0.0%	0	0.0%
Unknown	4	44.4%	0	0.0%	4	44.4%	1	11.1%

The number of cycles of any chemotherapy regimen in the current sample ranged between one cycle and 28 cycles. However, analysis of the number of cycles with the survival of patients or better or worse outcomes was not statistically significant.

Chapter Five

Discussion

The current study aimed to capture the scope of colorectal cancer in Palestine by studying the distribution of the cases in terms of colorectal cancer stages among Palestinian patients. Moreover, the study evaluated the prevailing treatment methods and management strategies of CRC employed by physicians. Besides, investigating the disease progression and its relation to the treatment strategy, protocol of chemotherapy, number of cycles. In addition, disease outcomes have been explored from the sample post-treatment in order to related disease outcomes with decisions made by physicians. A random sample of 252 patients was included in the study from An-Najah University Hospital, Nablus, Palestine, retrospective review of medical records was done to collect the required data to achieve the objectives of the study.

5.1 Colorectal cancer in Palestine

The current study gave an insight on the epidemiology of colorectal cancer in Palestine, it showed that male patients are more prone to develop CRC with a mean age of 60.64 ± 11.4 years. Although these results are from one hospital in one city in Palestine, the results coincide with the global epidemiology of CRC and especially in CRC in the Arab World as shown in the review by Arafa and Farhat (Arafa & Farhat, 2015). As the CRC patients mostly of older age, they tend to have more comorbidities, the current sample had many comorbid conditions such as hypertension and

diabetes mellitus, this can be related to the high prevalence of chronic disease in Palestine (Husseini et al., 2009).

5.1.1 Colorectal cancer stages among Palestinian patients

The survival rate for patients with colorectal cancer is strictly correlated with the stage of the disease at diagnosis, the earlier the stage at diagnosis, the higher the chance of survival. Most patients in the current sample were of stage IV (63.%) and thus considered as a triggering mark to raise the awareness of CRC disease screening, as the patients stay not diagnosed for a very long period until they reach the worst stage, which will highly increase the mortality rate of the disease. Many studies have also revealed that most patients were presenting themselves late (Korsgaard, Pedersen, & Laurberg, 2008; Pita-Fernández et al., 2016). However, it should be noticed that An-Najah University Hospital is a tertiary hospital where some advanced cancer cases from Gaza Strip or other hospitals in the West Bank are referred to for medical treatment, this could explain in part the very high percentage of advanced stage IV patients.

The Palestinian ministry of health publishes an annual health report stating the distribution of cancer diseases among Palestinians and they provide large data sets, however, they do not provide the staging of cancer, the treatment, and survival of patients.

The current study sample found that 41.3% of the patients died even after treatment, followed by 38.1% developed disease progression, with a low cure rate of only 11.9%. The high mortality rate due to colorectal cancer in

Palestine could be correlated to the findings on the stages of colorectal cancer at presentation, which emphasizes the need for developing a colorectal cancer screening program at a national level. Colorectal cancer screening programs can detect and diagnose cases much earlier and provide health promotion, one can anticipate a reduction in the incidence of colorectal cancers diagnosed at late stages in Palestine, thus improving survival.

5.2 Management of colorectal cancer

Management of colorectal cancer depends on whether it is rectal cancer or colon cancer in the first place. In the current study sample, 27.3% had rectal cancer and its treatment differs in early stages, as anatomic conditions are distinctive from the rest of the colon, and local recurrence is a major problem for morbidity and quality of life. Surgical therapy counted as the highest mode of treatment for all patients, also, chemotherapy had almost the same percentage, which means that most patients who receive chemotherapy either end up getting surgery or start with surgery and end with chemotherapy. There was no clear trend in the treatment strategy among patients with CRC in Palestine. We found that patients receive FOLFOX or FOLFIRI or either any of them in addition to a monoclonal antibody (e.g., cetuximab or bevacizumab) or simply using other protocols either capecitabine alone, irinotecan, bevacizumab alone, or else. The treatment outcomes were not as bright as the physicians expected we presume, because the mortality rate is high. It is difficult to prospect that

the physicians do not truly follow the international guidelines. However, there should be distinctive centers for oncology and treatment of cancer patients, where the patients get healthcare from highly specialized physicians and consultants, in addition, to deal with healthcare staff that is well-trained to follow up these guidelines, especially, clinical pharmacists.

There have been numerous studies confirming the role of the clinical pharmacist in hematology/oncology and their contribution to better therapy outcomes and improving morbidity and mortality rates (Delpeuch, Leveque, Gourieux, & Herbrecht, 2015; Duarte et al., 2019; Moukafih et al., 2021). In Palestine, the role of the clinical pharmacist is almost negligible (Naseef, Amria, & Dreidi, 2020), it is highly recommended to include them in the healthcare team of colorectal cancer in Palestine.

Lab results were obtained from the medical records of the patients with CRC for 3 intervals. The lab results were complete blood count, blood sugar, renal function test. The chemotherapy protocols were analyzed to link them with white blood cells and platelet count. FOLFOX was found to reduce platelet counts and FOLFIRI was found to reduce leukocytes. However, it was found that the effect of both treatment regimens is not significant on platelets and leukocytes.

5.3 Disease outcomes

After treatment, the disease outcomes were categorized into six categories, namely, Death, Cure, Disease Progression, Disease Recurrence, Under-treatment, or Unknown outcomes. Despite that the retrospective chart

reviews were only for one year, unfortunately, the mortality rate was high (41.3%). It is known that the second cause of death in Palestine is cancer which comes after cardiovascular diseases. There are 15.5% of the Palestinian population dies because of cancer (Palestinian Ministry of Health, 2019).

In the current sample, regression analysis of disease outcome (death, cure, progression, recurrence, under-treatment) to the type of therapy that the patient received ($R^2 = 0.066$) was significant ($p = 0.001$). patients who received surgical treatment tend to have cure outcomes much higher than patients who received radiotherapy or chemotherapy. In addition, by comparing FOLFOX and FOLFIRI chemotherapy in terms of treatment outcomes, FOLFIRI protocol had higher death rates compared to FOLFOX which had higher cure rates, however, the difference was not significant.

5.4 Colorectal cancer survival in Palestine

Information on cancer survival is an important indicator of the cancer system's effectiveness in detecting and treating cancer. Colorectal cancer survival is highly dependent on the stage of disease at diagnosis. Theoretically, the diagnosis of the disease is the most crucial point that determines whether the patient would survive or not, i.e. the later the diagnosis the worst the outcomes. This issue was investigated by Fernandez et. al., as the study came to conclude that the delay in diagnosis of rectal cancer was linked to poor survival, while delay in colon cancer was not associated with poor survival, hence, the researchers believe that delay in

diagnosis is not the sole factor that affects poor survival. (Pita-Fernández et al., 2016) In the current study, Regression analysis of days between last visit and diagnosis date and the type of treatment received (Chemotherapy, Surgical Treatment, Radiotherapy) ($R^2 = 0.035$) was significant ($p = 0.033$). A chi-square correlation analysis of the stage at diagnosis and the prognosis of CRC patients using existing data revealed that there is a significant difference ($p < 0.05$) between the stage at diagnosis and the disease outcome.

Surgical treatment had a positive impact on increasing the days of survival and it was significant ($p = 0.021$), radiotherapy has a positive impact on increasing the days of survival as well, but it was lower than surgical treatment positive, however, the difference was not significant ($p = 0.407$). Besides, chemotherapy had a positive impact, but it was the lowest amongst all therapeutic options, though it was not significant ($p = 0.096$). This could be explained by the fact that many patients with advanced metastatic stage IV disease are not eligible for surgery. Having surgery means that the tumor is operable which may reflect a less advanced stage and better survival.

On the other hand, chi-square analysis for the chemotherapy protocol used among patients in comparison with disease outcomes, cure rates were highest with the use of FOLFOX (26.7%), death rates were similar between FOLFIRI and FOLFOX patients. These results were significantly different ($p < 0.05$).

Gaps in the survival rates probably reflect the difference in the management practices among countries. A lack of cohesive practice guidelines for colorectal management and inadequate development to deal with the increasing demand for diagnostic, therapeutic, and follow-up care interventions could be reasons for the lower survival rate in Palestine.

5.5 Strength and limitations

To the best of our knowledge, it is the first time in Palestine to evaluate the stages and outcomes of colorectal cancer along with treatment protocols.

This study is a retrospective study and as a limitation of all retrospective studies, the data can be considered inadequate since upon documentation it was not meant for research purposes. Clinical data such as weight, height, lab tests, were not truly available.

In addition, since the data collection was from one hospital in Nablus only, the study's generalizability is weak and further national studies need to be undertaken in order to generalize the results.

Chapter Six

Conclusions and Recommendations

6.1 Conclusion

A high percentage of patients were diagnosed in advanced stages. The modes of treatment generally were adopted from international guidelines, however, the cure rates and good disease prognosis were not high, the disease mortality rate was high.

6.2 Recommendations

More studies need to be undertaken to investigate the actual application of chemotherapy protocols and involve clinical pharmacists in the chemotherapy protocol choice, dosing, frequency, follow-up.

Besides, the palliative care of patients and their emotional state and wellbeing during the suffering of disease was not studied, and many studies have shown the importance of this care of patients with colorectal cancer. Hence, this is an area of research in Palestine to investigate the application of such optimum care in Palestinian hospitals.

On the other hand, the economic components of economic burden include direct medical care and nonmedical costs, and productivity losses among patients and caregivers were not included in this research. These are substantial parts of studying colorectal cancer in the future.

Hence, According to the present analysis of the existing colorectal cancer pattern in Palestine, a wide range of actions are needed to lower the disease's burden. These include investments in public awareness campaigns aimed at the general public and primary care clinicians, with the goal of increasing understanding of colorectal cancer symptoms and risk factors, awareness of benefits of screening, and promotion of healthy lifestyles to prevent this important disease. In order to diagnose the disease much earlier which makes health care providers intervene earlier to promote a better prognosis.

Furthermore, in a country like Palestine where patients seek primary care first, it is grossly important to empower primary care providers by providing them with resources to undertake preliminary screening, or developing a referral strategy for early clinical diagnosis of symptomatic patients, which is an important approach that requires to be promoted.

National campaigns need to be implemented to organize screening programs for the early detection of cancer, which can ultimately reduce the burden of colorectal cancer.

Further research on the epidemiology and characteristics of colorectal cancer in the Palestinian population, and public perception and professional attitude on screening and screening behavior of the population is required.

The treatment of colorectal cancer requires significant system resources and has many possibilities and guidelines, involving surgery, chemotherapy, radiotherapy, palliative care, and rehabilitation. The

development and implementation of evidence-based management guidelines and follow-up care for colorectal cancer should be reinforced for effective and optimum care.

In rural regions, awareness of colorectal cancer among the general public and preventative actions among primary care physicians are noticeably lacking. More public health emphasis should be directed to raising colorectal cancer screening knowledge and awareness among the general public in Palestine. The role of primary care providers in colorectal cancer prevention should be well defined, and policymakers need to take initiatives to improve colorectal cancer screening services in primary clinics.

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Appendix

Appendix (A) Data Collection Form

MEDICAL RECORD # _____		GENDER <input type="radio"/> Male <input type="radio"/> Female		DATE OF BIRTH _____ Age _____	
BLOOD GRP _____		HEIGHT _____	WEIGHT _____	BMI _____	
MARITAL STATUS	<input type="radio"/> Single	<input type="radio"/> Married		<input type="radio"/> Divorced	<input type="radio"/> Widowed
EDUCATION	<input type="radio"/> No formal Edu.	<input type="radio"/> Primary		<input type="radio"/> Secondary	<input type="radio"/> Tertiary
SMOKING	<input type="radio"/> Smoker		<input type="radio"/> Non-Smoker		<input type="radio"/> Ex-smoker
ALCOHOL	<input type="radio"/> Drinker		<input type="radio"/> Ex-drinker		<input type="radio"/> Non-drinker
NUTRITION	<input type="radio"/> Well Nourished		<input type="radio"/> Malnourished		<input type="radio"/> Vegetarian
Allergy	<input type="radio"/> None		<input type="radio"/> Allergic to _____		
DISEASE HISTORY	<input type="radio"/> Diabetes	<input type="radio"/> Dyslipidemia		<input type="radio"/> Hypertension	<input type="radio"/> IHD _____
	<input type="radio"/> Stroke	<input type="radio"/> Heart Failure		<input type="radio"/> Arrhythmia	<input type="radio"/> IBD _____
	<input type="radio"/> Asthma	<input type="radio"/> IBS		<input type="radio"/> L. Cirrhosis	<input type="radio"/> R. Arthritis _____
	<input type="radio"/> COPD	<input type="radio"/> CKD		<input type="radio"/> Gout	<input type="radio"/> Osteoporosis _____
FAMILY HISTORY	<input type="radio"/> Cancer (Type _____)			<input type="radio"/> NONE	

B: COLORECTAL CANCER CHARACTERISTICS

Colon cancer	<input type="radio"/> Yes <input type="radio"/> No
Rectum cancer	<input type="radio"/> Yes <input type="radio"/> No
Stage (TNM)	
Diagnosis date	
Last visit date	
Treatment method	<input type="radio"/> Surgi <input type="radio"/> Radiotherapy <input type="radio"/> Chemotherapy

	cal
Medical treatment protocol	<input type="radio"/> FOL <input type="radio"/> Other _____ <input type="radio"/> FOLFIRI <input type="radio"/> FOX _____
Number of cycles completed	

C: LAB RESULTS (last readings)

Na				135-145 mmol/L	RBC				4-11 x103/m m3	R.B Glu		
K				3 -5 mmol/L	WBC				4-6.2 x103/m m3	HbA1c		
Urea				1.7 – 8.3 mmol/L	HGB				11-18 g/dL	INR		
Cr				53-97 μmol/L 44- 80μmol/ L	HCT				35-55%	CRP		
Cr Cl					MCV				80-100			
Uric acid				210-420 μmol/L	PLT				150- 400 x103/m m3			
Mg				0.7-1.05								
Ca				2.3- 2.5mmo l/L								
Phosp				0.9-1.3 mmol/L								

Outcomes of treatment: cure death recurrence not known

Years of survival after diagnosis: _____

Appendix (B): Ethical Approval

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



جامعة النجاح
الوطنية
كلية الطب وعلوم الصحة
لجنة أخلاقيات البحث
العلمي

Ref: Mas Sep. /2020/3

IRB Approval Letter

Study Title:

“Evaluation of Stages, Treatment Protocols and Outcomes of Colorectal Cancer among Palestinian.”

Submitted by:

Ibrahim Sawaied

Supervisor:

Rawa Alramahi . Husam Salameh

Date Approved:

3rd Sep 2020

Your Study Title **“Evaluation of Stages, Treatment Protocols and Outcomes of Colorectal Cancer among Palestinian Patients.”**, was reviewed by An-Najah National University IRB committee and was approved on 3rd Sept.2020

Hasan Fitian, MD

IRB Committee Chairman

An-Najah National University



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جامعة النجاح الوطنية

كلية الدراسات العليا

تقييم مراحل، بروتوكولات ونتائج علاج سرطان القولون والمستقيم لدى المرضى الفلسطينيين

إعداد

ابراهيم سواعد

إشراف

د. رواء الرمحي

قدمت هذه الأطروحة إستكمالاً لمتطلبات الحصول على درجة الماجستير في برنامج الصيدلة السريرية، من كلية الدراسات العليا، في جامعة النجاح الوطنية، نابلس - فلسطين.

2021

ب

تقييم مراحل، بروتوكولات ونتائج علاج سرطان القولون والمستقيم لدى المرضى الفلسطينيين

إعداد

ابراهيم سواعد

إشراف

د. رواء الرمحي

الملخص

مقدمة: في فلسطين، السبب الرئيسي الأول للوفاة هو أمراض القلب والأوعية الدموية، ويحتل السرطان المرتبة الثانية من حيث أسباب الوفاة. يصنف سرطان القولون والمستقيم على أنه النوع الثاني من السرطانات بين المرضى الفلسطينيين. تتحسن رعاية مرضى السرطان في المستشفيات الفلسطينية بمرور الوقت؛ ومع ذلك، لا تزال الخدمات مثل الرعاية التلطيفية والعلاج الموجه وزرع نخاع العظام والعلاج الفردي محدودة. تهدف الدراسة إلى تقييم مراحل سرطان القولون والمستقيم وبروتوكولات العلاج ومدى بقاء المرضى على قيد الحياة في فلسطين.

المنهجية: هذه دراسة مقطعية من خلال جمع البيانات من السجلات الطبية في مستشفى متخصص في رعاية مرضى السرطان. تم تضمين المرضى الذين يعانون من سرطان القولون والمستقيم (المراحل الأولى والثانية والثالثة والرابعة) الذين يخضعون للعلاج الجراحي أو الطبي في الدراسة. تم توحيد جمع البيانات باستخدام نموذج جمع البيانات لجمع المعلومات من السجلات الطبية. تم تصنيف نتائج المرض بعد العلاج إلى ست فئات، وهي الموت، الشفاء، تفاقم المرض، تكرار المرض، العلاج غير كاف، أو النتائج غير المعروفة. تم إجراء التحليل الإحصائي باستخدام SPSS الإصدار 21.

النتائج: عينة من 252 مريض بسرطان القولون والمستقيم من مستشفى النجاح الجامعي، منهم 143 (56.7%) كانوا ذكوراً وتراوحت أعمار المرضى بين 27 - 86 سنة بمتوسط 60.64 (± 11.4) سنة. كان معظم المرضى مصابون بسرطان القولون فقط (183 مريضاً، 72.6%) و(29 مريضاً، 11.5%) مصابون بسرطان المستقيم فقط، بينما الباقي لديهم سرطان القولون

والمستقيم معاً (40 مريضاً، 15.9%) معظمهم في المرحلة الرابعة (159 مريضاً، 63.1%). كانت الجراحة هي الطريقة الأكثر شيوعاً في العلاج لمرضى سرطان القولون والمستقيم (230: 91.3%)، من ناحية أخرى، المرضى الذين تلقوا العلاج الكيميائي، كان FOLFOX أكثر انتشاراً بين المرضى ويميل الأطباء إلى اختياره مقارنة بـFOLFIRI. معدل الوفيات بسبب المرض مرتفع حيث مات معظم المرضى (41.3%) خلال فترة زمنية قصيرة بين التشخيص والوفاة. وتجدر الإشارة إلى أن هناك تأخيراً واضحاً في تشخيص المرض حيث تم تشخيص معظم المرضى في مرحلة متأخرة من المرض. كان للعلاج الجراحي أثر إيجابي في زيادة أيام البقاء على قيد الحياة وكان معنوياً ($p = 0.021$). كشف تحليل chi square لمرحلة التشخيص وتفاقم الحالة لمرضى سرطان القولون باستخدام البيانات الموجودة أن هناك فرقاً جوهرياً ($p < 0.05$) بين درجة الحالة عند التشخيص ونتائج المرض. من ناحية أخرى، فإن تحليل Chi-square لبروتوكول العلاج الكيميائي المستخدم بين المرضى مقارنة بنتائج المرض، كانت معدلات الشفاء الأعلى باستخدام FOLFOX (26.7%)، وكانت معدلات الوفيات متشابهة بين مرضى FOLFIRI وFOLFOX، كانت هذه النتائج ذات اختلاف جوهري ($P < 0.05$).

الاستنتاجات: تم تشخيص نسبة كبيرة من المرضى في مراحل متقدمة من المرض. تم اعتماد طرق العلاج بشكل عام من الدلائل الإرشادية الدولية، ومع ذلك، لم تكن معدلات الشفاء والتشخيص الجيد للمرض عالية، وكان معدل الوفيات بسبب المرض مرتفعاً. يجب إجراء المزيد من الدراسات للتحقيق في التطبيق الفعلي لبروتوكولات العلاج الكيميائي وإشراك الصيادلة السريريين في اختيار بروتوكول العلاج الكيميائي، والجرعات، والتكرار، والمتابعة. وبالتالي، فإن الدراسة الحالية لنمط سرطان القولون والمستقيم الموجود في فلسطين تدعو إلى مجموعة متنوعة من التدخلات للحد من عبء المرض. ويشمل ذلك الاستثمار في برامج التوعية التي تستهدف عامة السكان ومقدمي الرعاية الأولية، والتي تركز على زيادة المعرفة بأعراض وعوامل الخطر لسرطان القولون والمستقيم، والوعي بفوائد الفحص، وتعزيز أنماط الحياة الصحية للوقاية من هذا المرض المهم. من أجل تشخيص المرض في وقت مبكر مما يجعل مقدمي الرعاية الصحية يتدخلون في وقت مبكر لتعزيز التشخيص الأفضل.