PREVALENCE, CLINICOPATHOLOGIC FINDINGS AND ASSOCIATED FACTORS OF ADVANCED COLORECTAL NEOPLASIA AMONG PATIENTS UNDERGOING COLONOSCOPY AT MUHIMBILI NATIONAL HOSPITAL

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By

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A Dissertation Submitted in (Partial) Fulfillment of the Requirements for the Degree of Master of Medicine (Internal Medicine) of Muhimbili University of Health and Allied Sciences

October, 2024

CERTIFICATION

The undersigned certify that they have read and hereby recommend for acceptance by the Muhimbili University of Health and Allied Sciences a dissertation entitled: "**Prevalence, Clinicopathologic Findings and Associated Factors of Advanced Colorectal Neoplasia Among Patients Undergoing Colonoscopy at Muhimbili National Hospital**" in partial fulfillment of the of the requirements for the degree of Master of Medicine (Internal Medicine) of the Muhimbili University of Health and Allied Sciences.

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DECLARATION & COPYRIGHT

I, Jacqueline Mtage Kihwele declare that to the best of my knowledge this dissertation is my own original work; it has not been presented and will not be presented to any other university for a similar or any other degree award.

Signature: _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ Date: _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _

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DEDICATION

To my loving parents, Dr. David Kihwele and Ms Mboni Mgaza for the immense sacrifices they went through to ensure I get educated. They are persons behind all my success.

ABSTRACT

Colorectal Cancer (CRC) is the 3rd most common cancer worldwide. It is the second most common cancer in women and the third most common cancer in men. In 2020 there were more than 1.9 million new cases of CRC worldwide. As the third most common malignancy and the second leading cause of cancer death.

It is Africa's fourth most common cause of death secondary to a malignancy, although slight regional variations exist. CRC ranks third amongst all types of cancers in North Africa, while in East, Central, South, and West Africa it is ranked fourth. Factors such as alcohol intake, high red meat diet and a strong family history have been linked to increase occurrence of advanced colorectal neoplasia.

The Aim: To determine the prevalence, clinical, colonoscopic, histopathological findings, and associated factors among patients with advanced colorectal neoplasia at Muhimbili National Hospital (MNH) identified between November, 2023 – March 2024.

Methodology: This was a hospital-based cross-sectional study. A sample of 200 participants fulfilling the eligibility criteria were included in the study. Colonoscopy and pathological confirmation of advanced colorectal neoplasia were the measures of interest. A structured questionnaire was used to obtain patients' socio-demographic, clinical, and laboratory data. All study patients had a colonoscopy done at MNH – Upanga or Mloganzila site.

Data processing was through SPSS v 23. Variables were summarized as means and proportions. Multivariate analyses of variance were used to evaluate the relationships between ACRN and associated factors.. Ethical approval was sought from the Muhimbili University of Health and Allied Sciences (MUHAS) Research and Ethics Committee. Permission to conduct the study was obtained from the MNH administration.

Results: A total of 200 participants were studied with an age of 56 years, with an IQR 42-66. Over half of the participants were male (59%) and the majority were married/cohabiting (74%).

A slight higher proportion had completed primary education (51%), followed by completed secondary education (25.5%). A higher proportion of participants were unemployed (34.2%). Most participants did not have any comorbidities (60%). Of the 40% with comorbidities, the most common were hypertension (30%), heart disease (19%) and Diabetes Mellitus (10%). Most participants presented with abdominal pain (60.2%), blood in stool (57.1%) and constipation (51.1%).

Majority of participants presented a lesion (81%), with most presenting with one lesion (64.%), while some had up to 10 or more lesions (2%). Most participants presented a lesion in the rectum (32.47%), followed by the sigmoid and ascending colon (8.23%). Most participants presented a fungating mass (14.7%), followed by polypoid/polyp (10.17%) and internal hemorrhoids (6.9%). Among all participants, 25.5% were found to have advanced colorectal neoplasia compared to the remaining 74.5%. Assessment of factors associated with the presence of an ACRN, grouping of the sample by age showed that participants 45 years and older had 1.2 more odds of having an ACRN but it was not significant. Gender did not have an effect on odds of having an ACRN. A positive family history increased the odds of having an ACRN. Having a first degree relative with CRC increased the odds of having an ACRN by 4.6 (4.56,4.8), p-value = 0.031.

Conclusion: The prevalence of ACRN among patients undergoing colonoscopy at MNH was 25.5%. About 81% of patients undergoing colonoscopy have a visible lesion. There are various relationships between age, sex, social/behavioral history and diet with the presence of an ACRN at colonoscopy but the only statistically significant relationship was the increased odds of an ACRN at colonoscopy if a participant has a first-degree relative with a history of CRC.

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LIST OF ABBREVIATIONS

AIDS	Acquired immunodeficiency syndrome
APC	Adenomatous polyposis Coli gene
BMI	Body mass index
CRC	Colorectal Cancer
FAP	Familial adenomatous polyposis
WHO	World Health Organization
HB	Hemoglobin
HIV	Human Immunodeficiency Virus
PLWHIV	People Living with HIV
MNH	Muhimbili National Hospital
MUHAS	Muhimbili University of Health and Allied Sciences
SSA	Sub-Saharan Africa

DEFINITION OF KEY TERMS

Advanced Colorectal Neoplasia: An advanced colorectal neoplasm was defined as a tubular adenoma ≥ 10 mm in size, an adenoma of any size with villous features or high-grade dysplasia, a dysplastic serrated lesion of any size, or invasive cancer.

Colorectal Cancer: Colorectal cancer (CRC), also known as bowel cancer, colon cancer, or rectal cancer, is the development of cancer from the colon or rectum.

Microsatellite Instability: Microsatellites are regions of repeated Deoxyribo Nucleic Acid (DNA) that change in length (show instability) when mismatch repair is not working properly. MSI testing looks at the length of certain DNA microsatellites from the tumor sample to see if they have gotten longer or shorter as a measure of instability.

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background

1.1.1 Burden of Advanced Colorectal Neoplasia

Colorectal cancer (CRC) is the 3rd most common cancer worldwide (1). It is the second most common cancer in women and third most cancer in men. In 2020 there were more than 1.9 million new cases of colorectal cancer worldwide. As the third most common malignancy and the second most deadly cancer, CRC is estimated to have caused about 0.9 million deaths worldwide in 2020 (2).

The incidence of colorectal cancer was estimated to be 1·8 million (95% confidence interval of 1·8–1·9) in 2017, this is a rise of 9·5% (4·5–13·5). Since 1990, there has been an estimated 896, 000 (876 300–915 700) deaths from colorectal cancer. Predictions of cancer incidences in older adults show a doubling of new cases by 2035 worldwide. and this includes less developed regions, with colorectal cancer being one of the major contributors (4).

Some high-income countries have seen an increase in colorectal cancer at young ages (younger than 50 years) (5). Young adults with cancer tend to experience large burdens including psychosocial and fertility issues and premature morbidity and death. Currently, Australia/New Zealand and Western Europe see the highest burden of CRC, while in Africa it is the fourth most fatal malignancy, although there are slight regional referral variations.

IN TANZANIA In the last decade, Tanzania has seen six times increase CRC incidence (7). The rapid increase of CRC in Tanzania like many African countries has been attributed to a change in lifestyle choices and other risk factors like infections, familial and genetic factors (8). Incidences are higher in; Dar es Salaam with an incidence of 20.2 per 100,000, in Pwani 7.2 per

100,000, Kilimanjaro 4.4 per 100,000, Arusha 4.2 per 100,000, and 3.6 per 100,000 in Morogoro (7).

In addition, specific groups such as People Living with HIV (PLWHIV) are at average risk of CRC, although there are inconsistent reports on the epidemiology of CRC in this population. The Standardized Incidence Ratio (SIR) for CRC in PLWHIV to the general population has ranged from 0.45 to 2.3 (42). The prevalence of adenomatous polyps and mucosal abnormalities known precursors of malignancy, among people with HIV, surpasses the prevalence of the general population (range 1.0%–34.3%) in most, but not all, studies (43).

1.1.2 Investigations for Advanced Colorectal Neoplasia

Colonoscopy

The mainstay of identifying advanced colorectal neoplasia remains to be colonoscopy. Studies have reported that 7.4%-14% of colorectal polyps larger than 20 mm were submucosal carcinoma. A previous report showed that only 0.07%-5.80% of polyps less than 20 mm in size were more likely to be sub-mucosal carcinoma (33).

Histology

Advanced colorectal neoplasia are a heterogeneous disease, and the subtypes that affect prognosis and therapeutic response (2). An accurate CRC type and subtype classification system is important in determining clinical outcomes (2).

About 90% of colorectal carcinomas are adenocarcinomas from epithelial cells of the colorectal mucosa (35). Other rare types of colorectal carcinomas include neuro-endocrine, squamous cell, adenosquamous, spindle cell (36) and undifferentiated carcinomas. Conventional adenocarcinoma is characterized by glandular formation, which is the basis for histologic tumor grading. In well differentiated adenocarcinoma >95% of the tumor is gland forming. Moderately differentiated adenocarcinoma shows 50-95% gland formation. Poorly differentiated adenocarcinoma is mostly solid with <50% gland formation (37).

An important part of microscopic examination is to look for evidence of invasion. To be termed as invasive carcinoma, the carcinoma has to at least invaded into the submucosa of the colorectum. Invading the muscularis mucosae into the submucosa, and close to submucosal blood vessels is termed as invasive carcinoma (37).

Tumors can also be classified by the level of tumor invasion where T1 the tumor invades submucosa, T2 invades muscularis propria and T3 invades through the muscularis propria into pericolorectal tissues, T4a penetrates to the surface of the visceral peritoneum and T4b directly invades or is adherent to other organs or structures per the American Joint Committee of Cancer TNM staging system (38).

Early detection and treatment of CRC is associated with improved prognosis and facilitated by period screening using endoscopic visualization or fecal occult blood testing (39). It is known that removal of precursor adenomas reduce the incidence of colorectal cancer (40). Identification of important risk factors for advanced colorectal neoplasia could inform both risk stratification and development of risk reduction strategies.

1.2 Problem Statement

High-quality population-based cancer registry data are not available in all countries (44). This brings challenges to properly account for the prevalence and incidence of colorectal cancer worldwide, and underscores the challenges that observational studies have had in studying CRC risk factors and conditions that affect disease type and progression.

A study by Selik et al in 1998 suggested an increased risk of rectal cancer in patients with comorbidities such as HIV, but data on risk factors such as Human Papilloma Virus (HPV) infection were lacking, and the specific type of cancer within the umbrella of colorectal cancer was not reported (45). Hermal et al Northern Tanzania reviewed entries between 1998 – 2008 and found that earlier onset of CRC, patients younger than 50 years was 41.5%, and that most patients presented more than 3 months after symptom debut; 62.6% first sought care at lower-level health facilities. Most (64.9%) presented as emergencies, necessitating emergency surgery (7).

Literature is limited on the burden of CRC in sub-Saharan with a few studies reporting prevalence with inconsistent findings, and less on risk factors including HIV infection. A retrospective CRC database of about 715 patients by Pillay SK et al in South Africa on CRC patients showed that 20% of participants were HIV positive and the median age was 45 vs 53 (HIV +ve vs HIV –ve).

There is lack of data on the burden of CRC at MNH, and due to the lack of high-quality registry data and most studies completed being low power retrospective observational studies. There has also been inconsistent evidence on the prevalence of CRC and association between clinical, colonoscopic and histopathological findings among patients with advanced colorectal neoplasia.

1.3 Conceptual Framework

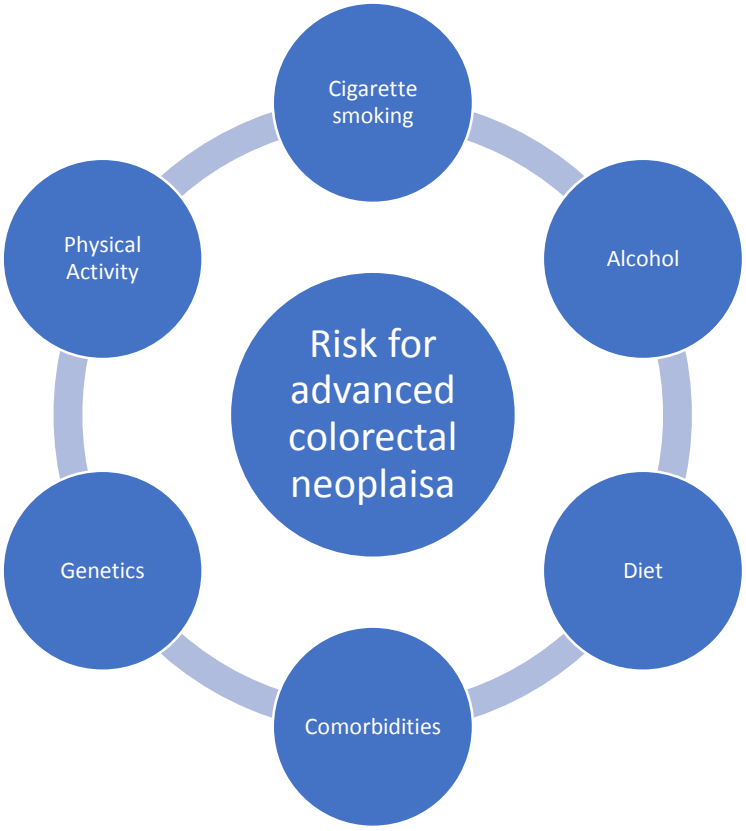


Figure 1 Conceptual Framework

Studies on risk factors associated with CRC have shown a strong correlation with alcohol, level of physical activity, genetics, diet, and comorbidities with diseases such as IBD. The strength of association varies between studies stipulated to be due to study design, geographical locations, and population.

1.4 Rationale

Due to the increased prevalence of advanced colorectal neoplasia in Tanzania reported, and highest incidences reported in coastal regions such as Dar es salaam and Pwani (7), it is important to identify risk factors associated with advanced colorectal neoplasia in the region together with clinical and pathology findings.

In this study, risk factors such as diet, smoking, alcohol intake, level of physical activities and family history of advanced colorectal neoplasia were captured to help in risk stratification of patients at MNH. Data was collected during colonoscopy to record colonoscopy findings. Data was collected on the histological type and pathological staging at diagnosis, this will enable the possible identification of patients at increased risk of advanced colorectal neoplasia at MNH.

1.5 Research Question

1.5.1 Overall research question

What is the prevalence, clinicopathologic findings and associated factors of advanced colorectal neoplasia among patients undergoing colonoscopy at Muhimbili National Hospital?

1.5.2 Specific research questions

a. What is the prevalence of advanced colorectal neoplasia among patients undergoing colonoscopy at Muhimbili National Hospital?
b. What are the clinical characteristics in patients with advanced colorectal neoplasia undergoing colonoscopy Muhimbili National Hospital?
c. What are the histopathological findings in patients with advanced colorectal neoplasia undergoing colonoscopy Muhimbili National Hospital?
d. What are the factors associated with advanced colorectal neoplasia among patients undergoing colonoscopy at Muhimbili National Hospital?

1.6 Research Hypothesis

Patients at increased risk for advanced colorectal neoplasia pertaining to diet, level of physical activity, strong family histories, and comorbidities present with advanced clinicapathologic findings of colorectal neoplasia.

1.7 General Objective

To determine the prevalence, clinicopathologic findings and associated factors of advanced colorectal neoplasia among patients undergoing colonoscopy at Muhimbili National Hospital identified between September 2023 – January, 2024.

1.7.1 Specific Objectives

i. To determine the prevalence of advanced colorectal neoplasia among patients undergoing colonoscopy at Muhimbili National Hospital identified between September 2023 – January, 2024.
ii. To describe the clinical characteristics in patients with advanced colorectal neoplasia undergoing colonoscopy Muhimbili National Hospital identified between September 2023 – January, 2024.
iii. To describe the histopathological findings in patients with advanced colorectal neoplasia undergoing colonoscopy Muhimbili National Hospital identified between September 2023 – January, 2024.
iv. To determine factors associated with advanced colorectal neoplasia among patients undergoing colonoscopy at Muhimbili National Hospital identified between September 2023 – January, 2024.

CHAPTER FOUR

2.0 LITERETURE REVIEW

2.1 Advanced Colorectal Neoplasia

Advanced colorectal neoplasias are recognized as precursors in most new cases of CRC, and are categorized as conventional adenomas or sessile serrated polyps (52).

Serrated polyps heterogeneous and are characterized by saw-tooth luminal serrations with dilatation, branching, and distortion in the bases of the colonic crypts, found mostly in the proximal colon (53).

A systematic review and meta analysis on 4308 studies, published from 1999 to 2018 with the sample size per study ranging from 584 to 1,426,000 found overall, the prevalence of adenoma (AD) was 23.9% (95% CI, 22.2–25.8), advanced adenomas (AAD) was 4.6% (95% CI, 3.8–5.5) and CRC was CRC was 0.4% (95% CI, 0.3–0.5) (54).

Patients with advanced adenomas, the 10-year cumulative risk of developing CRC has been projected to range from 25.4% to 42.9% in women, and from 25.2% to 39.7% in men (55).

Recent decades have shown a rapid predilection of an unhealthy diet and physical inactivity, alcohol consumption, and smoking, which could predispose to the higher risk of colorectal neoplasia in the general population.

2.2 Risk Factors

2.2.1 Genetic Factors

Colorectal cancer is a diverse group of diseases often associated with genetic changes which are associated with transformation of benign adenomas to invasive disease [9]. Mutations in the Adenomatous Polyposis Coli gene (APC) were first to be linked to familial adenomatous polyposis (FAP) which is important in the activation of oncogenes c-myc and cyclin D1. Some other important genes also involved in colon cancer carcinogenesis include, mutations in deletion of the short arm of chromosome 17 and mutations of p53 cause reduced apoptosis and linked to development of invasive disease [9].

A case control study by JL Duncan and Jkyle was one of the initial studies in 1982 conducted in Scotland on 50 participants with adenocarcinoma of the colon showed that 16% of participants with adenocarcinoma of the colon had a close relative with intestinal cancer, with on 2% of control with a history of a close relative with intestinal cancer [10].

The results were similar to a prospective study for family history and risk for CRC conducted on 32, 085 men and 87,031 women who provided data on first degree relatives colorectal cancer. The study found that the age adjusted relative risk factor of 1.72 (95 percent confidence interval, 1.34 to 2.19) and 2.75 (95 percent confidence interval, 1.34 to 5.63) for participants with two or more affected first-degree relatives [10].

2.2.2 Lifestyle & Physical Activity

CRC incidence has increased in the last decade, specifically in developing countries (9). Associated factors are often related to the adoption of westernized diets, obesity, and reduced physical activity [11]. There is a strong relationship between the increase in CRC incidence and lifestyle changes can be seen in second and at times, third generations of migrants have a higher risk of colorectal cancer compared to generations before. This attribution to the environment is

also observed when comparing rural and urban areas together with people of different races in the same country (12).
In addition, a prospective cohort by Brook A Carlton et al on 31,783 participants showed that although there was no statistically significant association between overall physical activity and colorectal cancer, participants in the lowest range of physical activity had a 30% increased of colorectal cancer compared to participants in the highest physical activity quartile. The analysis did not include BMI in the multivariate model.

Studies have shown that physically active individuals are at lower risk for CRC, this was independent of other risk factors (26). Different types of physical activity, including relatively moderate activity level, reduce the risk of colon cancer. The level of physical inactivity is different between genders and between rural and urban residents in Tanzania (27).

A study by Fraisa et al did find a statistically significant difference in BMI between participants with colorectal cancer and control group. The mean BMI for participants with colorectal cancer was 28.3 ± 5.5 kg/m2 compared to a BMI of 25.9 ± 6.9 kg/m2 in the control group (10).

2.2.3 Diet

Dietary associated factors account for about 30% to 50% of all CRC incidences (13). Developing countries are going through a drastic change in behavioral patterns, where there is a shift in dietary patterns influenced by socioeconomic changes, changes in food markets, urbanization, an increase in technology, and economic growth (15).

A study by Firas et al in Saudi Arabia showed that consumption of dairy products (servings/day) and legumes (servings/week) were different ($P < 0.05$) between participants in the control and the CRC groups. Although this study did not find differences ($P > 0.05$) were detected in consumption of red and processed meat (servings/day), poultry (servings/day) as well as fruits and vegetables (servings/ day) between the two groups.

The study also found that a weekly intake of 3–5 servings of legumes was protective of colorectal cancer with an odds ratio of 0.28, 95% CI = 0.09–0.85, P = 0.025. The study also found that the protection increased with number of servings; 1–2 servings had a 28% decrease in odds, 95% CI = 0.08–0.96, P = 0.04) and 3–5 servings of leafy vegetables had an 18% decrease in odds, 95% CI = 0.05–0.67, P = 0.01). This was also noted in servings of olive oil, 1–2 servings had a 24% decrease in risk, 95% CI = 0.11–0.52, P < 0.001(10).

Results also showed that healthy participants in the control group tended to consume more black tea (cup/day) than people suffering from CRC.

A relationship between red meat consumption and CRC has brought about recommendations that meat should rarely be eaten or should be completely avoided. One mechanism suggests that red meat carcinogenesis stipulates that carcinogens are released during the cooking process (17) and therefore meat prepared at high temperatures increases the production of heterocyclic amines compared to that prepared at lower temperatures (18).

In Tanzania, changes in nutrition tendency within the last decade have moved to a low fiber, high sugar, and saturated fatty diets due to increased access to processed foods (16). The availability of higher-sugar foods such as cakes, soda, and sweets, has led to difference in calorie content between rural and urban populations (7).

2.2.4 Alcohol

The relationship between alcohol consumption and CRC has been shown in a number of studies and they indicate no difference in the risk for colon and rectal cancers. Cho et al studied 489,979 women and men with no history of cancer other than nonmelanoma skin cancer at baseline in North America and Europe and found 4687 cases of colorectal cancer in a follow up of 6 to 16 years and found that participants with an alcohol intake of 45g/day or more, the equivalent of almost four units per day had a 41 % increased risk for colorectal cancer compared to participants who did not consume alcohol (22).

A pooled analysis of two cohort studies and twenty-two case control studies by Yue Wang et al in 2015 found that a pooled relative risk (RR) for any alcohol intake compared with non/occasional drinking was 1.13 [95% confidence interval (CI), 1.09-1.17] (23)

A subgroup analysis for light (≤12.5 g/day), moderate (12.6 to 49.9 g/day) and heavy drinking (≥50 g/day) showed risk ratios of RRs were 1.07 (95% CI, 1.02-1.13), 1.23 (95% CI, 1.15-1.32) and 1.37 (95% CI, 1.26-1.49) respectively. The results were consistent for both men and women although there was a stronger association between men compared to women (22). In these results, the association was stronger in European studies compared to studies conducted in Asia and Europe with paucity of data from South America and African countries (23).

2.2.5 Cigarette Smoking

Smoke from cigarettes contains over 60 known carcinogens and free radicals, which irritate the colonic mucosa and thus increase the likelihood of malignant transformation (25). The number of cigarettes smoked, length of exposure, and age of initiation, individually affect the association between smoking and CRC (25). There have been differing results from different studies on the risk of colorectal cancer and smoking. A meta-analysis that included 36 studies in 2009 examined the association between smoking and CRC, colon cancer and rectal cancer in terms of incidence and mortality, they included 34 cohort studies and 2 nested cohort studies (24).

Compared to never smokers, current smokers had a 17% (95% CI: 0.97–1.40) higher risk of developing CRC and a 40% (95% CI: 1.06–1.84) higher risk of CRC mortality. The analysis also found a significant increased risk of CRC incidence and mortality ($p < 0.0001$) with increased daily cigarette consumption [24]. An increase of 20 cigarettes/day (1 pack/day) had a 17.5% increase in RR for CRC incidence and a 40.7% increase in RR for CRC mortality. An increase of 40 cigarettes/day (2 packs/day) led to a 38.0% increase in RR for CRC incidence and a 98.0% increase in RR for CRC mortality (24).

There is a limited information regarding tobacco smoking in Tanzania, K Jagoe et al determined population based smoking prevalence using expired alveolar carbon monoxide as a validation tool and found that an estimate of 18% of males and 1.3% of females are daily smokers in the age range of 25–64 (25). The prevalence did not capture unconventional smoking such as the use of electronic cigarettes and its link to malignancy (25).

The Tanzania Global Adult Survey in 2018 found that the overall tobacco use in Tanzania is 8.7%, with tobacco smoking at 6.8% and smokeless tobacco use at 2.2%

CHAPTER THREE

3.0 METHODOLOGY

3.1 Study Design

A hospital based cross sectional study was conducted at a tertiary hospital, Muhimbili National Hospital, Upanga and Mloganzila sites.

3.2 Study Duration

This study data collection was over a period of five months from November 2023 to March 2024.

3.3 Study Area

This study was conducted at Muhimbili National hospital, a tertiary hospital, located at Upanga, in the city of Dar es Salaam. Muhimbili hospital is the country's national referral hospital receiving patients from District and Regional hospitals across Tanzania. Muhimbili National Hospital, has a bed capacity of 1500 and attends about 1000 to 1200 outpatients a week, with admissions of 1000 to 1200 patients a week. MNH has 12 specialized units offering medical and surgical services having about 460 doctors and 1125 nurses within the same compound.

3.4 Study Population

The study population was patients undergoing colonoscopy at Muhimbili National Hospital between November 2023 – March 2024.

3.4.1 Inclusion criteria

a. Patient aged 18 years and above and able to consent
b. Patients less than 18 years but older or equal to 15 years able to assent, and whose parents were willing to consent

3.4.2 Exclusion criteria

a. Patients with a history of advanced colorectal neoplasia
b. Patients colonoscopies could not be completed

3.5 Sample Size Calculation

A pre-study survey at the East Africa Gastroenterology center at MNH, located at Muhimbili Upanga Campus found that 900 colonoscopies are performed per year, while the MNH Mloganzila campus about 200 colonoscopies per year, and about 10% of participants from each hospital have a final diagnosis of coloreactal cancer. A study in Oman, by Alsumait AF, et al "found a prevalence of 12% of colorectal cancer among scoped patients.

$n = Z2\ P\ (100 - P)/\varepsilon\ 2$

n = minimum sample size required

Z = SD set at 1.96 (CI of 95%)

P = Prevalence of colorectal cancer among patients scoped. A study in Oman, by Alsumait AF, et al found a prevalence of 12%

ε = marginal error to be used of 5.0%

n = 1.962 *X* 12 (100-12)/5*5 equals 139.9 patients.

n = 140

But since our population is a finite population is a finite population and data will be collected for a period of five months, the formula for sample size calculation was:

N = n/(1+((n-1)/population)))

N = Adjusted sample size for a finite population

n = Calculated sample size from above

Population: Population from which the study participants was obtained

N= 140/(1+((140-1)/400)))

N= 104

The final sample size required was 104 study participants.

3.6 Sampling Technique and Enrolment of Study Participants.

All patients undergoing colonoscopy were included. Patients were enrolled consecutively, where all patients undergoing colonoscopies between November 2023 and March of 2024 at MNH were recruited. A structured questionnaire was administered before the colonoscopy session. The questionnaire was structured to measure the demographic characteristics, symptomatic presentation, and co-morbid conditions.

3.7 Study Variables

3.7.1 Dependent Variables

- Pathologically confirmed advanced colorectal neoplasia

3.7.2 Independent Variables

Socio demographic factors

- sex
- Age
- Occupation
- Residency
- Body mass index
- Level of income
- Level of education

Clinical factors

- Physical activity
- Alcohol intake
- Cigarette smoking
- Symptoms
- Comorbid conditions

3.8 Data Collection Methods

A Structured questionnaire for socio-demographic, clinical and colonoscopic data collection was used. Data was also be collected from the pathology reports. Patients once consented were be tested for HIV if they have not tested in the last three months.

3.9 Data Management and Statistical Analysis

The data obtained from the questionnaires was entered into computerized software program of SPSS v 23. The social demographic characteristics, presentation and clinical information were summarized by measures of central tendency and dispersion; as mean and standard deviation for symmetrically distributed data and as median with interquartile range for asymmetrical distributed data. Categorical variables were summarized as frequencies and proportions. Association between numerical variables were be tested using student t-test for normally distributed data and Chi-square test will be used to determine association between categorical variables. Logistic regression was used to evaluate associated factors. Independent variables was analyzed by bivariate model. All variables that are statistically significant with a p-value of <0.2 were entered in a multivariate model where p-value of <0.05 was considered statistically significant.

3.10 Ethical Issues

Ethical clearance was sought form the MUHAS Research and Ethics Committee and permission was sought from Muhimbili National Hospital. Written informed consent were obtained from all participants prior to enrollment into the study. Adults 18 years and above signed informed consent forms, informed consent forms clearly stated that subjects had the rights to decline answering any question and to withdraw from the study at any point in time. A signed copy of the informed form was to the participant. All information obtained is maintained with maximum confidentiality. Study participants that will be found to have ACRN will be directed to appropriate clinics for follow up.

CHAPTER FOUR

4.0 RESULTS

A total of 203 participants were approached for eligibility screening during the study period, of which 200 fulfilled the inclusion criteria and were enrolled.

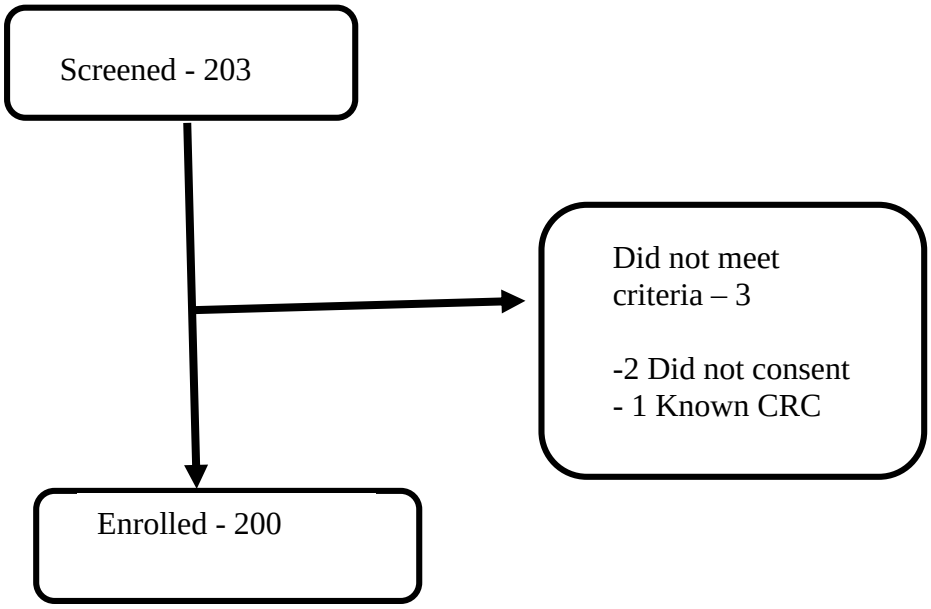


Figure 2: Consort Diagram

Table 1: Socio-demographic characteristics of study participants N=200

Variable		Frequency (n)	Percent (%)
Age (In Years)	18-24	10	5
	25-34	18	9
	35-44	28	14
	45-59	51	25.5
	60+	93	46.5
Sex	Male	118	59
	Female	82	41
Marital Status	Single	34	17
	Married/cohabiting	147	74
	Divorced/separated/widow/widower	19	9.5
Education	No formal education	9	4.5
	Completed primary level	102	51
	Completed Secondary	51	25.5
	College/ University	38	19
Employment Status	Formally Employed	54	23.4
	Informally Employed	42	18.2
	other	25	10.8
	Unemployed	79	34.2

Table 1: About half of our participants (46.5%) were aged 60 years and above, with a median age (IQR) 56 (42.66). Over half of the participants were male (59%) and the majority were married/cohabiting (74%). A slight higher proportion had completed primary education (51%), followed by completed secondary education (25.5%). A higher proportion of participants were unemployed (34.2%).

Table 2: Participant comorbidities at study entry N=200

	Frequency (n)	Percent (%)
Comorbidities	Yes 80	40
	No 120	60
Heart Disease	38	19
Diabetes Mellitus	20	10
Hypertension	60	30
Liver Disease	3	1.5
Malignancies (Prostate, Cacx)	3	1.5
Easy Fatigability	6	3
Previous Stroke	3	1.5

Table 2: Most participants did not have any comorbidities (60%). Of the 40% with comorbidities, the most common were hypertension (30%), heart disease (19%) and Diabetes Mellitus (10%).

Table 3: Participant clinical presentation at study entry N=200

	Frequency	Percent
Abdominal Pain	139	69.5
Abdominal Fullness	73	36.5
Abdominal Distention	27	13.5
Diarrhea	56	28
Constipation	118	59
Blood in Stool	132	66
Easy Fatigability	120	60
Dizziness	77	33.5
Awareness of Heart Beat	60	30
Lower Limb Swelling	31	15.5

Table 3: Most participants presented with abdominal pain (69.5%), blood in stool (66%) and constipation (59%).

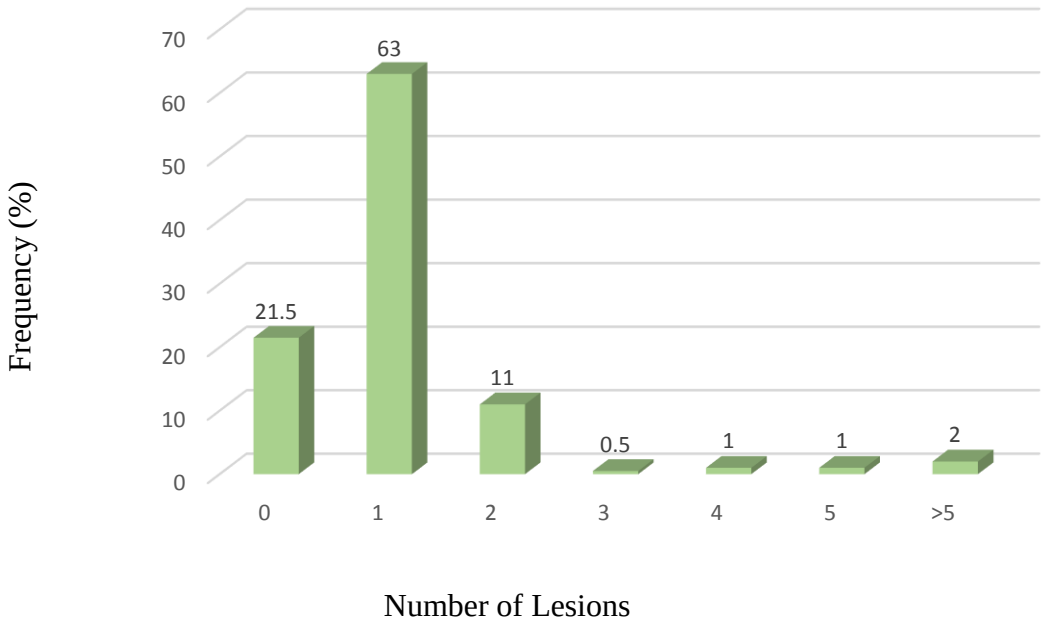


Figure 3 showing the number of lesions per patient during colonoscopy

Figure showing the number of lesions per patient during colonoscopy N=200**.** The majority of participants presented with a lesion (78.5%), with most presenting with one lesion (63.%), while some had more lesions than 5 lesions (2%).

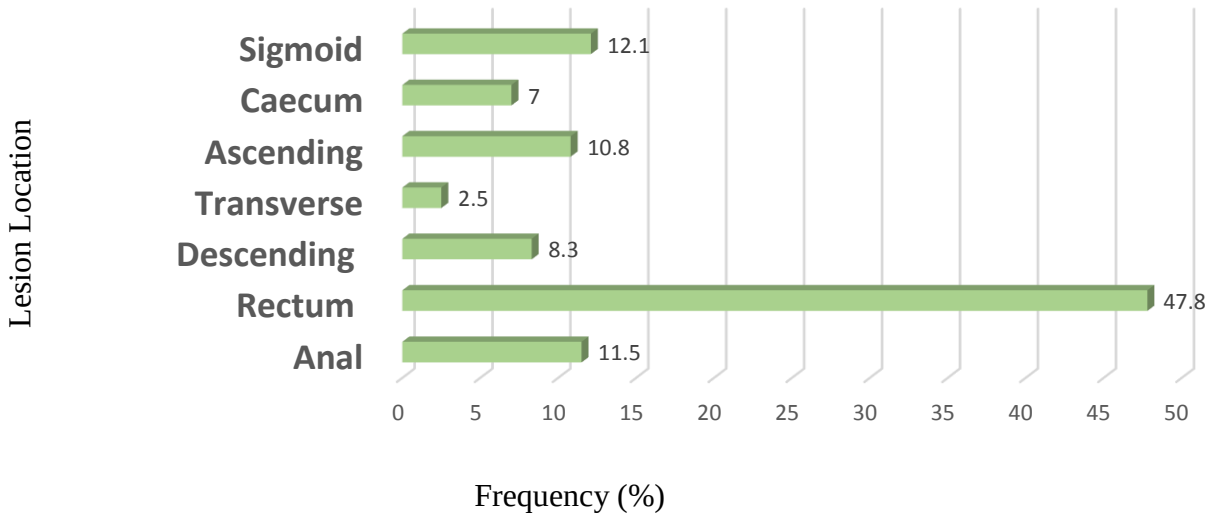


Figure 4: Showing frequency of location of lesions

Figure showing frequency of location of lesions (N = 157). Most participants presented a lesion in the rectum (47.8%), followed by the sigmoid (12.1%).

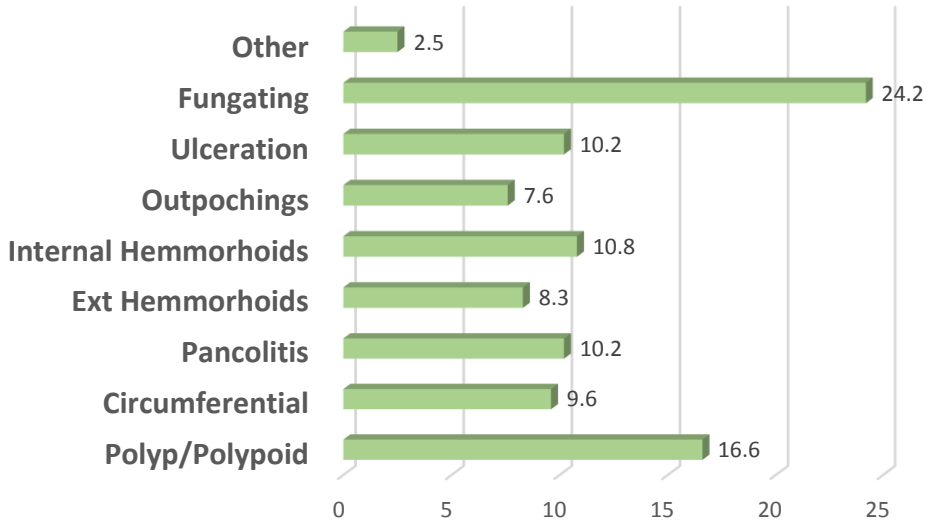


Figure 5: Showing the Frequency of Lesion Description Among Participants

Showing the frequency of lesion description among participants (N = 157). Most participants presented a fungating mass (24.2%), followed by polypoid/polyp (16.6%) and internal hemorrhoids (10.8%).

Figure showing the prevalence of advanced colorectal neoplasia among participants (N=200)



Figure 6: Among all participants, 25.5% were found to have advanced colorectal neoplasia compared to the remaining 74.5%.

Figure showing the frequency of histological type of biopsied lesions among participants (N=98)

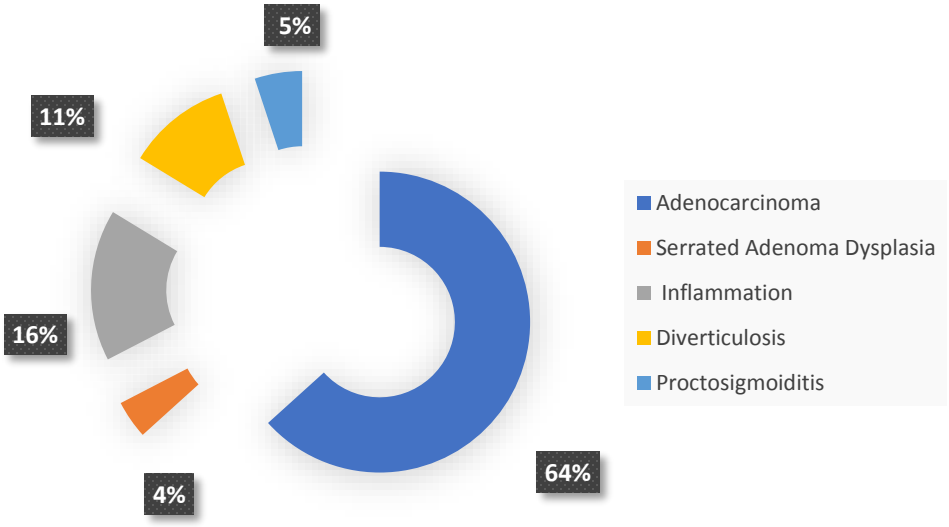


Figure 7: Frequency of histological type of biopsied lesions among participants (N=98)

Table 4: Demographic factors associated with Advanced Colorectal Neoplasia

VARIABLE	***TOTAL N=200 (%)***	**Univariate**	**P-value**	**Multivariate (CI)**	**P-value**
Age, Median = 56, IQR (42-66)					
<45	11 (20)	Ref			
>/=45	40 (27.6)	1.208	0.272		
Sex					
Female	30 (25.4)	Ref			
Male	21 (25.6)	0.001	0.976		
1st degree relative with CRC					
No	40 (22.9)	Ref		Ref	
Yes	11 (44)	3.3	0.000	4.6(4.56,4.8)	0.031
2nd degree relative with CRC					
No	47 (24.2)	Ref		Ref	
Yes	4 (66.7)	2.5	0.019	0.56 (0.16,0.96)	0.42

Table 4: The median age of the sample was 56 years, with an IQR 42-66. Grouping of the sample by age showed that participants 45 years and older had 1.2 more odds of having an ACRN but it was not significant. Gender did not have an effect on odds of having an ACRN. A positive family history increased the odds of having an ACRN. Having a first degree relative with CRC increased the odds of having an ACRN by 4.6 (4.56,4.8), p-value = 0.031.

Table 5: Behavioral factors Associated with Advanced Colorectal Neoplasia

VARIABLE	TOTAL N=200 (%)	Univariate	P-value	Multivariate	P-value
Smoking Hx					
No	43 (24.7)	Ref			
Yes	8 (32)	0.96	0.62		
Alcohol Hx					
No	45 (25.7)	Ref			
Yes	6 (26.1)	0.63	0.87		

Table 5: A history of ever smoking reduced the odds of an ACRN by 0.96 but this was not statistically significant. A history of alcohol intake reduced the odds of an ACRN by 0.63 but this was not statistically significant.

Table 6: Factors Associated with Advanced Colorectal Neoplasia

VARIABLE	TOTAL N=200 (%)				
		Bivariate	P-value	Multivariate (CI)	P-value
Diet					
Dairy Products (> 5* week)	3 (75)	8.0	0.03	0.5 (-1.7,0.7)	0.477
Dairy Products (3-5 * week)	28 (30.8)			Ref	
Dairy Products (1-2 * week)	20 (19.2)			0.26(-0.42,0.1)	0.612
Dairy Products (0* week)	0				
Red Meat (> 5* week)	10 (76.9)	45.4	<0.001	1.17(-0.08,0.23)	0.28
Red Meat(3-5 * week)	36 (37.9)			Ref	
Red Meat(1-2 * week)	5 (6)			2.32(2.2.2.4	0.128
Red Meat (0* week)	0				
Poultry (> 5* week)	0	12	0.007	Ref	
Poultry (3-5 * week)	8 (12.3)			0.011(-0.86;0.78)	0.916
Poultry (1-2 * week)	43 (33.3)			0.164(-0.98;0.64)	0.685
Poultry (0* week)	0				
Green Leafy Vegetables (> 5* week)	1 (50)	3.7	0.156	0.10(-1.32,2.3)	0.75
Green Leafy Vegetables (3-5 * week)	35 (22.4)			Ref	
Green Leafy Vegetables (1-2 * week)	15 (35.7)			0.37(-0.37,0.65)	0.54
Green Leafy Vegetables (0* week)	0				
Legumes (> 5* week)	9 (56.3)	9.1	0.028	0.88(0.45,1.31)	0.349
Legumes (3-5 * week)	30 (21.9)			Ref	
Legumes (1-2 * week)	10 (24.4)			0.002(-0.27,0.257)	0.962
Legumes (0* week)	2 (33.3)			0.034(-0.593,0.661)	0.855
Fruit (> 5* week)	0	24.7	<0.001		
Fruit (3-5 * week)	21 (15.2)			Ref	
Fruit (1-2 * week)	30 (48.4)			2.56(-2.4,7.6)	0.107
Fruit (0* week)	0				

Table 6: A diet of dairy products more than 5 times a week had 8 higher odds of having an ACRN compared to 3-5 * week, while diet of red-meat products more than 5 times a week had 45.4 higher odds of having an ACRN compared to 3-5 * week. A diet of poultry products more than 5 times a week had 12 higher odds of having an ACRN, A diet of legumes more than 5 times a week had 9.1 higher odds of having an ACRN, while diet of fruit less than 5 times a week had 24.7 higher odds of having an ACRN compared to 3-5 * week. Although none of the associations were statistically significant in the multivariate model.

A diet frequency per week of green-leafy vegetables had no association to ACRN in both univariate and multivariate model.

CHAPTER FIVE

5.0 DISCUSSION

This study discovered three significant findings worthy of noting. First, the prevalence of ACRN is high at MNH. Second, there are various demographic variations in clinical presentations of symptoms, colonoscopic and pathologic findings of ACRN. Third is that there are various factors identified to have a strong statistical association with advanced colorectal neoplasms.

CRC arises from neoplastic epithelial polyps including adenomatous and sessile serrated polyps. The most common precancerous colon polyp is the adenoma, which is believed to be the precursor for about 80% of CRC.

Evidence has demonstrated that the polyp features most strongly associated with the future risk of an advanced adenoma or CRC include large size (≥10 mm), number of polyps (>2), high-grade dysplasia and presence of villous features in the polyp, these are termed as advanced colorectal neoplasms. In this study, it was found that the prevalence of ACRN is 25.5% among patients undergoing colonoscopies at MNH. This finding is higher than previous retrospective observational studies and is possible due to the different population studied. Our study by design, was not designed as a screening study, but rather studies symptomatic participants.
Other findings include a study by Eduardo et al in 2018 in Mexico that screened 4694 participants and found an overall prevalence of ACRN from retrospective screening colonoscopy data to be 2.9% but 19.8% in the higher risk tier defined by the Asia Pacific Screening score.

A meta analysis conducted in 2020 included 70 observational studies involving 637,414 individuals found that the overall prevalence rates of adenoma (23.9%; 95% CI, 22.2%–25.8%), AAD (4.6%; 95% CI, 3.8%–5.5%), and CRC (0.4%, 95% CI, 0.3%–0.5%), The studies did not perform a subgroup analysis for ACRNs due to the nature of original data (50).

The 2019 WHO classification of digestive system tumors significantly reformed the classificatory definition of serrated lesions of colorectal mucosa and added new essential diagnostic criteria for both conventional adenomas and hereditary gastrointestinal polyposis syndromes. This would explain the higher prevalence of ACRN in our study using the new classification.

This study found that individuals under the age of 45 (23.8%) of the sample, had a slightly higher odds of having an ACN although this finding was not statistically significant. The lack of a statistically significant difference between the two age groups (<45 and >45) could be attributed to the broadening of definition of ACN to include polyps up to 10 mm in size and serrated lesion, or the capturing of symptomatic adenomas prior to recommended screening age as per American Gastro Enterology Society in 2019. This could have also affected the strength of the relationship between other associated factors and the presence of ACRN.

In 2003, a study by Kathryn L. Lynch et al on self-reported family history of CRC showed that Subjects with adenomas were more likely to have a family history of colorectal cancer than were subjects without polyps (odds ratio [OR], 1.36; 95% confidence interval [CI], 1.09-1.70) 52. Similarly, Siew C. Ng et al in 2013 found that advanced neoplasms was 7.5% among siblings of patients and 2.9% among controls (matched odds ratio [mOR], 3.07; 95% confidence interval [CI], 1.5–6.3; P = .002). The prevalence of adenomas larger than 10 mm was higher among siblings of patients than in controls (5.9% vs 2.1%; mOR, 3.34; 95% CI, 1.45–7.66; P = .004), as was the presence of colorectal adenomas (31.0% vs 18.2%; mOR, 2.19; 95% CI, 1.52–3.17; P < .001) (53).

A positive family history, specifically a first degree relative with CRC showed an increased odds of having an ACRN by 4.6 (4.56,4.8), p-value = 0.031. These findings are consistent with other studies such as a study by Enrique Quintero in 2016, on 8,498 found that advanced neoplasia was significantly more prevalent in individuals having two FDR with colorectal cancer (odds ratio [OR] 1.90; 95% confidence interval [CI] 1.36-2.66, p < 0.001).

They are also consistent with a case control study by JL Duncan and Jkyle was one of the initial studies in 1982 conducted in Scotland on 50 participants with adenocarcinoma of the colon showed that 16% of participants with adenocarcinoma of the colon had a close relative with ACRN, with on 2% of control with a history of a close relative with intestinal cancer (10).
The results were similar to a prospective study for family history and risk for CRC conducted on 32, 085 men and 87,031 women who provided data on first degree relatives colorectal cancer. The study found that the age adjusted relative risk factor of 1.72 (95 percent confidence interval, 1.34 to 2.19) and 2.75 (95 percent confidence interval, 1.34 to 5.63) for participants with two or more affected first-degree relatives (10).

In this study, age, sex, diet, alcohol and cigarette smoking did to have a statistically significant association with the presence of an ACRN although literature has shown CRC has increased in the last decade due to lifestyle changes, specifically, adoption of westernized diets, obesity, and reduced physical activity (11). There is a strong relationship between the increase in CRC incidence and lifestyle changes can be seen in second and at times, third generations of migrants have a higher risk of colorectal cancer compared to generations before. This attribution to the environment is also observed when comparing rural and urban areas together with people of different races in the same country (12).
Study results have varied by region, a prospective cohort by Brook A Carlton et al on 31,783 participants showed that there was no statistically significant association between overall physical activity and colorectal cancer.

A study by Firas et al in Saudi Arabia showed that consumption of dairy products (servings/day) and legumes (servings/week) were different ($P < 0.05$) between participants in the control and the CRC groups. Although this study did not find differences ($P > 0.05$) were detected in consumption of red and processed meat (servings/day), poultry (servings/day) as well as fruits and vegetables (servings/ day) between the two groups. This similar to this study that found a diet of dairy products more than 5 times a week had 8 higher odds of having an ACRN compared to 3-5 times a week, while diet of red-meat products more than 5 times a week had 45.4 higher

odds of having an ACRN compared to 3-5 times week although the findings are not statistically significant.

A relationship between red meat consumption and CRC has brought about recommendations that meat should rarely be eaten or should be completely avoided. One mechanism suggests that red meat carcinogenesis stipulates that carcinogens are released during the cooking process [17] and therefore meat prepared at high temperatures increases the production of heterocyclic amines compared to that prepared at lower temperatures (18)..

The relationship between alcohol consumption and CRC has been shown in a number of studies and they indicate no difference in the risk for colon and rectal cancers. Similar to this study that found alcohol to be protective although not statistically significant. Although the association was stronger, despite not being statistically significant in European studies compared to studies conducted in Asia and Europe with paucity of data from South America and African countries (23).

CHAPTER SIX

6.0 STRENGTHS OF THE STUDY CONCLUSION AND RECOMMENDATIONS

6.1 An overview

The strengths of this study are that it is a hospital based cross-sectional study capturing patients at colonoscopy compared to a significant number of literature in ACRN that is based on observational studies and registries. Another strength is that the study was conducted at two different sites, ensuring that a more diverse type of patient samples is collected

6.1.1 Study Limitations and Mitigations

The limitations for the study include: Biases, recall bias due to slow progression of symptoms in advanced colorectal neoplasia. This was mitigated by ensuring that the questions in the tool were structured in a manner that allowed from broad approximations instead of exact specific details.

A second limitation was that pathological diagnosis was concluded by one pathologist as per hospital protocol.

The study is cross-sectional study, whereby we cannot infer causality, which would require longitudinal studies.

6.2 Data dissemination

The study results will be presented to the department of internal medicine and the final report will be available at the MUHAS library.

6.2.1 Conclusion and Recommendations

Overview

In this study, we concluded that the prevalence of ACRN among patients undergoing colonoscopy at MNH was 25.5%. About 81% of patients undergoing have a lesion at colonoscopy.

There are various relationships between age, sex, social/behavioural history and diet with the presence of an ACRN at colonoscopy but the only statistically significant relationship was the increased odds of an ACRN at colonoscopy if a participant has a first-degree relative with a history of CRC.

This conclusion supports the current screening guidelines that recommend colonoscopy every 5 or 10 y, starting at the age of 40 for first degree relatives of patients diagnosed with CRC, depending on whether colorectal cancer in the index-case is diagnosed at <60 or ≥60 y, respectively 51.

In addition, individuals with advanced colorectal adenomas should be counseled about the increased risk of colorectal cancer among their relatives 52.

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7.0 APPENDICES

Appendix I: Questionnaire on the prevalence, clinicopathologic findings and associated factors of advanced colorectal neoplasia among patients undergoing colonoscopy Muhimbili National Hospital

Instructions:

1. This questionnaire consists of six sections. Sections A, B, C, D, and E shall be filled by participant and research assistant

SECTION A: SOCIO DEMOGRAPHIC FACTORS

Questionnaire number		MRN	
Age in years			
Sex		1.Male	
		2.Female	
		3.Other	
Marital status		Single	
		Married/cohabiting	
		Divorced/separated/widow/widower	
Occupation		1.Formally Employed	
		2. Informally Employed	
		3. Unemployed	
		4.Other	
Area of residence			
Participants phone number			
Next of kin phone number			
Level of education		1.Never studied	
		2.Completed primary level	
		3. Completed secondary	

	4. College/ University	
Do you have a history of treatment for any of the following? (tick as appropriate)	Cardiac diseases	
	Diabetes Mellitus	
	Hypertension	
	Liver diseases	
	Malignancies	
	Peripheral vascular diseases	
	Stroke	
	Others	

SECTION B: MEDICAL PRESENTATION AND HISTORY

Put a mark (tick) where appropriate

		Yes	No
1	**Presenting symptoms**		
	Abdominal pain?		
	Abdominal fullness?		
	Abdominal distension?		
	Diarrhea?		
	Constipation?		
	Blood in stool?		
	Easy fatigability?		
	Dizziness?		
	Awareness of heartbeats?		
	Lower limb swelling?		
	Yellowish discoloration of the eyes?		
	Facial puffiness?		

	LOC?				
	Convulsions?				
2	**Past Medical History**				
	History of previous admission(s)?				
	If yes, please elaborate				
	History of blood transfusion(s)?				
	If yes, please elaborate				
	History of smoking?				
	If yes, number of pack years?				
	History of alcohol consumption?				
	If yes, how many units per year?				
3	**Dietary History (Circle the appropriate response)**	**Servings per week**			
	Dairy Products	**0**	**1-2**	**3-5**	**>5**
	Red meat	**0**	**1-2**	**3-5**	**>5**
	Poultry	**0**	**1-2**	**3-5**	**>5**
	Legumes (Lentils, Peas, Broad beans, Chickpeas, Soybeans, Peanuts)	**0**	**1-2**	**3-5**	**>5**
	Green leafy vegetables	**0**	**1-2**	**3-5**	**>5**
	Fruit	**0**	**1-2**	**3-5**	**>5**
4	**Family and Social History**				
	Number of siblings				
	History of advanced colorectal neoplasia in 1st degree relative?				
	History of advanced colorectal neoplasia in 2nd degree relative?				
	History of neoplasia in family?				
	Positive family history of diabetes?				

	Positive family history of hypertension?	

SECTION C: LABORATORY PARAMETERS

No	Item	Value	Unit
1	Hemoglobin levels		g/dl
2	Albumin levels		g/dl
3	Creatinine		Mmol/l
	Urea		mmol/l
4	ALT		mmol/l
5	AST		mmol/l
6	ALP		mmol/l
7	HIV Status		

SECTION D: COLONOSCOPIC FINDINGS

No	Item	
1	Lesion location	
2	Number of lesions	
3	Lesion(s) size	
4	Lesion description	
	Loss of lobulation: loss of normal lobulation	
	Excavation: a crumbled, damaged area of the tumor that prevents observation of the surface structure	
	Demarcated depressed areas: depressed demarcations on the surface of the tumor;	
	Stalk swelling: a thickened and expanded stalk	
	Fullness: a bursting appearance due to expansive growth of the tumor;	
	Fold convergence: fold convergence towards the tumor	

	Bleeding ulcer	
5	Pit pattern	
	Normal mucosa, star-shaped crypts	
	Regular crypts with or without demarcated areas or irregular pits without demarcated areas	
	Invasive pattern: irregular and distorted crypts in demarcated areas	

SECTION E: PATHOLOGICAL FINDINGS

No	**Item**	**Yes**	**No**
1	**Histological type**		
	Mucinous adenocarcinoma		
	Signet ring cell adenocarcinoma		
	Medullary carcinoma Mixed type		
2	**Histopathological Tumor Stage**		
	pT1		
	pT2		
	pT3		
	pT4a		
	pT4b		
3	**Grade**		
	Low Grade		
	High Grade		

7.1 Appendix II: Informed Consent-English Version **Consent to participate in the study titled, 'Prevalence, clinicopathologic findings and associated factors of advanced colorectal neoplasia among patients undergoing colonoscopy Muhimbili National Hospital'**

"Greetings:

I am Dr. Jacqueline Kihwele, a postgraduate student doing research titled, 'Clinicipathologic findings and associated factors in patients suspected to have advanced colonirectalneoplasia at Muhimbili National Hospital'

Purpose of the study: To determine the prevalence, clinicopathologic findings and associated factors of advanced colorectal neoplasia among patients undergoing colonoscopy Muhimbili National Hospital, this study will help in map out patterns of patients diagnosed with advanced colonrectal neoplasia at Muhimbili National Hospital at both Upanga and Mloganzila sites.

What participation involves: If you agree to participate in this study, your medical information will be used for research purpose-but will not be linked to you directly. This means your information will not bear identity, and this information will help us map out patterns of patients diagnosed with advanced colorectal neoplasia at Muhimbili National Hospital but there is no financial implication to you but through the research you will be able to get medical interventions when needed.

Confidentiality: All information collected will be entered into a computer with identification numbers only, no names included.

Risk: We expect no physical harm to happen to you during the course of this study.

Right to withdrawal: Taking part in this study is completely voluntary and refusal to participate or withdrawal will not involve penalty or loss of any benefits to which you are entitled.

Benefits: The results from this study will be used as evidence-based information for proposing better understanding factors associated with advanced colonrectal neoplasia at Muhimbili National Hospital. This study has sought approval from proper and informed authorities.

Who to contact? If you have any questions regarding this study, feel free to contact me, the investigator, Dr. Jacqueline Kihwele, MUHAS, PO BOX 65001, Dar-es-salaam, Tanzania. Mobile phone +255 687 082334. Email: jacquelinekihwele@gmail.com

If you have any questions concerning your right as a participant, you may contact Dr. Ewaldo Komba, supervisor of the study, MUHAS, PO Box 65000, Dar es salaam, Tanzania. Phone number: +255 713 200171 **,** Email: kombaewaldo@gmail.com

Dr. Nahya Masoud, Acting Director of Research, Publications and Innovation (DRPI) of MUHAS, contacts P. O. Box 65001, Dar es Salaam, Tanzania. Tel: +255-022-2152489, Fax: +255-022-2152489, Email: drp.muhas.ac.tz.

Do you agree; Patient/Relative…….

I' …… have read the consent form and my questions have been answered and I agree to participate in this study.

Signature:

Participant/Relatives…….....

Signature of investigator…….....

Date of signed consent……

7.1.1 Appendix IV: Fomu Ya Kuomba Idhini

Ruhusa ya kushiriki kwenye utafiti kuhusu kuangalia kiwango na tabia zinazohusiana na saratani ya utumbo mkubwa katika hospitali ya taifa Muhimbil Upanga na Mloganzila. Mimi naitwa Dr Jacqueline Kihwele, ni mwanafunzi wa uzamili Chuo Kikuu cha Tiba Muhimbili. Ninafanya utafiti kuangalia uangalia tabia zinazohusiana na saratani ya utumbo mkubwa katika hospitali ya taifa Muhimbil.

Dhumuni la utafiti huu: Kuchunguza kiwango na tabia zinazohusiana na saratani y autumbo mkubwa katika hospitali ya taif aMuhimbili.

Usiri: Taarifa zote za uchunguzi zitaingizwa kwenyekompyuta na nambari ya utambulisho; jina halitanukuliwa.

Madhara: Tunategemea kwamba hakuna madhara yoyote kimwili yatokanayo na utafiti huu.

Haki ya kujitoa kwenye utafiti: Kushiriki katika utafiti huu ni hiari na kutokubali kushiriki au kujitoa hautaadhibiwa au kupoteza haki yako ya matibabu.

Kutokea kwa madhara: Tunategemea kwamba hakuna madhara yoyote ya kimwili yatokanayo na utafiti huu. Hata hivyo kama madhara ya mwili yakitokea kutokana na utafiti huu utatibiwa kilingana na kanuni na taratibu za matibabu ya Tanzania.

Faida za kushiriki kwenye utafiti: Kama kuchunguzwa hali yako ya maambukizi ya VVU ikiwa utaridhia.

Kwa mawasiliano zaidi: Kama una maswali kuhusu utafiti huu uwe huru kuwasiliana na mtafiti, Dr. Jacqueline Kihwele, Namba ya simu: +255 687 082334, Barua pepe:jacquelinekihwele@gmail.com. Chuo kikuu cha afya na tiba Muhimbili, P.O Box 65001,

Kama una swali kuhusu haki yako kama mshiriki wasiliana na Dr. Ewaldo Komba, msimamizi wa utafiti, MUHAS, PO Box 65000, Dar es salaam, Tanzania. simu: +255 713 200171, Email: kombaewaldo@gmail.com

Dr. Nahya Masoud, Mkurugenzi wa Utafiti na Uchapishaji MUHAS,
contacts P. O. Box 65001, Dar es Salaam, Tanzania. Tel: +255-022-2152489, Fax: +255-022-2152489, Email: drp.muhas.ac.tz.

Saini:

Je, umekubali kushiriki? …….

Mimi …… Nimesoma maelezo na kuyaelewa vizuri, na nimekubali kushiriki kwenye utafiti huu.

Sahihi ya mshiriki/ndugu…….

Sahihi ya mtafiti ……..

Tarehe ……..

7.1.2 Appendix IV: Fomu Ya Kuomba Idhini

UNITED REPUBLIC OF TANZANIA

MINISTRY OF EDUCATION, SCIENCE AND TECHNOLOGY

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES

OFFICE OF THE DIRECTOR – RESEARCH, PUBLICATIONS AND INNOVATION

Ref. No.DA.282/298/01.C/1921

Date: 03/10/2023

MUHAS-REC-10-2023-1921
JACQUELINE KIHWELE
SCHOOL OF MEDICINE
MUHAS

RE: APPROVAL FOR ETHICAL CLEARANCE FOR A STUDY TITLED: PREVALENCE,CLINICOPATHOLOGIC FINDINGS AND ASSOCIATED FACTORS OF ADVANCED COLONIC NEOPLASIA AMONG PATENTS UNDERGOING COLONOSCOPY AT MUHIMBILI NATIONAL HOSPITAL

Reference is made to the above heading,

I am pleased to inform you that the Chairperson has on behalf of the University Senate, approved ethical clearance of the above-mentioned study, on recommendations of the Senate Research and Publications Committee meeting accordance with MUHAS research policy and Tanzania regulations governing human and animal subjects research.

APPROVAL DATE: 03/10/2023
EXPIRATION DATE OF APPROVAL: 03/10/2024

STUDY DESCRIPTION:
Purpose:

The purpose of this study is to determine the prevalence, clinical, colonoscopic, histopathological findings, and associated factors among patients with advanced colonic neoplasia at Muhimbili National Hospital.

The approved protocol and procedures for this study is attached and stamped with this letter, and can be found in the link provided:
https://irb.muhas.ac.tz/storage/Certificates/Certificate%20-%2014801.pdf and in the MUHAS archives

The PI is required to:

1. Submit bi-annual progress reports and final report upon completion of the study.
2. Report to the IRB any unanticipated problem involving risks to subjects or others including adverse events where applicable.
3. Apply for renewal of approval of ethical clearance one (1) month prior its expiration if the study is not completed at the end of this ethical approval. You may not continue with any research activity beyond the expiration date without the approval of the IRB. Failure to receive approval for continuation before the expiration date will result in automatic termination of the approval for this study on the expiration date.
4. Obtain IRB amendment (s) approval for any changes to any aspect of this study before they can be implemented.
5. Data security is ultimately the responsibility of the investigator.
6. Apply for and obtain data transfer agreement (DTA) from NIMR if data will be transferred to a foreign country.
7. Apply for and obtain material transfer agreement (MTA) from NIMR, if research materials (samples) will be shipped to a foreign country,
8. Any researcher, who contravenes or fail to comply with these conditions, shall be guilty of an offence and shall be liable on conviction to a fine as per NIMR Act No. 23 of 1979, PART III section 10 (2)
9. The PI is required to ensure that the findings of the study are disseminated to relevant stake holders.
10. PI is required to be versed with necessary laws and regulatory policies that govern research in Tanzania. Some guidance is available on our website https://drp.muhas.ac.tz/.

Dr. Nahya Salim Masoud,
Chairperson, MUHAS Research and Ethics Committee

Muhimbili University of Health and Allied Sciences
DIRECTOR
Research, Publications & Innovations
Box 65001