COLORECTAL CANCER AT KENYATTA NATIONAL HOSPITAL FROM 2014 TO 2018: CLINICOPATHOLOGICAL CHARACTERISTICS, OUTCOMES & CORRELATES

A RETROSPECTIVE CHART REVIEW

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I. DECLARATION

This dissertation is my original work as a requirement for the degree of Masters of Medicine in Internal medicine and has not been presented for a degree to any other university.

Signature ……. Date…….

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II. APPROVAL BY SUPERVISORS

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III. DEDICATION

I dedicate this work to all cancer patients seen at Kenyatta National Hospital

IV. ACKNOWLEDGEMENT

I am grateful to the following for their contribution to this project:

Almighty God,

My supervisors

My family

My colleagues and friends

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LIST OF ABBREVIATIONS

APR……..Abdominoperineal resection

CEA…….carcinoembryonic antigen

CRC ……...colorectal cancer

CTC…….Cancer treatment centre

FOLFOX……...folinic acid, fluorouracil, and oxaliplatin

FOLFIRI…….....folinic acid, fluorouracil, and irinotecan hydrochloride

GLOBOCAN……...Global Cancer Incidence, Mortality and Prevalence

KNH…….….Kenyatta National Hospital

LAR……Lower anterior resection

PNI…….….Perineural invasion

R classification……...…tumour residual classification

SES……Socio-economic status

SEER ……....Surveillance, Epidemiology and End results reporting program

SPSS……...Statistical Packages for Social Sciences

US……United States

XELOX…….…Xeloda and oxaliplatin

ABSTRACT

Background: Colorectal cancer is one of the most common cancers diagnosed amongst males and females worldwide. The incidence has stabilised in the developed world but seems to be rising in developing countries. It is likely that after various government programmes and guidelines targeting cancer being established since 2011, there is improved awareness of colorectal cancer, better access to healthcare, earlier diagnosis of the disease and more widespread availability of better treatment over time. It is thus expected that the presentation and outcome of the disease at Kenyatta National Hospital has changed since 2011. The study was done to determine the clinicopathological characteristics and outcomes of colorectal cancer at Kenyatta National Hospital over a five-year period from 2014 to 2018 and the data generated can be used to delineate the trends.

Objective: To describe the clinicopathological characteristics and outcomes of colorectal cancer at Kenyatta National Hospital and correlate mortality with the clinicopathological characteristics.

Design: Retrospective chart review.

Setting & Duration: Kenyatta National Hospital cancer treatment centre and Kenyatta National Hospital records department. The study covered a 5-year period from 1st January 2014 to 31st December 2018.

Population: All patients with biopsy proven colorectal cancer diagnosed between January 2014 and December 2018 and having records at the aforementioned centres.

Methods: Chart reviews of patients with histologically proven colorectal cancer between January 2014 and December 2018 were done. Clinico-pathologic and socio-demographic data were retrieved from the patient's files and entered into a study proforma.1 year outcomes of treatment of colorectal cancer were also determined from the files.

Results: A total of 478 patient charts were reviewed, 248 were males and 230 were females. The mean age of patients with colorectal cancer was 53. The most common clinical manifestations were abdominal pain, hematochezia, altered bowel habits and anemia. Most cancers occurred on the left side. Metastatic disease was present in 37.5% of patients at presentation. The most common treatment modality was chemotherapy. The one year mortality rate was 18%.

Conclusion: Colorectal cancer occurs in a relatively young population in our country and most patients present with advanced disease. Young patients have a more aggressive histology. Folinic acid, fluorouracil, plus oxaliplatin is now the most common chemotherapy prescribed. The one year mortality of colorectal cancer still remains high compared to developed countries.

1.0. INTRODUCTION AND LITERATURE REVIEW

1.1 EPIDEMIOLOGY

Worldwide, Colorectal cancer (CRC) is the third most commonly diagnosed cancer in men and the second most common in women. 1,800,000 new cases and 881000 deaths are estimated to have occurred in 2018 (1).

The regional incidence of CRC varies more than 10 fold. The incidence rates are highest in North America, Europe, Australia and New Zealand and the lowest rates occur in South-Central Asia and Africa (2).

Amongst western populations, the risk of development of CRC is higher in lower socio-economic status (SES) populations; one study estimated that the risk is higher in the lower SES quintile as compared to the highest quintile by 30 percent (3). Physical inactivity, unhealthy diet, smoking, and obesity are the potentially modifiable risk factors thought to account for about 33 to 50 percent of the difference in the incidence of new onset CRC between the higher and lower SES populations (3). Lower rates of CRC screening in the lower SES population also contributes significantly to the increased risk in this population (4).

The incidence of CRC has declined in the United states (US) by about 2 percent per year (5). The incidence rates, during this period, in most other western nations have stabilised or have gone up slightly. In contrast, the incidence in historically low risk nations such as Spain and those in Eastern Asia and Eastern Europe has increased (6).

The occurrence of non-hereditary CRC has a strong association with increasing age. The incidence of CRC is low in under 40 year olds. The frequency of occurence of Coolorectal malignat tumours increases during the 5 the decade of life and every decade following (7). According to more current data, the incidence of CRC is increasing in the population aged under 50 while it is decreasing in the older population. (8)(9). These increases are more of left-sided cancers and especially of rectal cancer (10). In the under 50 age group, more than 86 percent are symptomatic at diagnosis which points to a more advanced presentation and therefore higher mortality (11). In the US, the incidence of CRC over the lifetime of individuals at average risk is around 5 percent with 90 percent of cases occurring in older individuals above 50 years of age. In African Americans, the incidence is higher by 20 percent compared to white and higher by 25 percent in males compared to females. Patients with Hereditary conditions that predispose to CRC also have a high incidence (8).

Studies have shown that the incidence of CRC in the right side of the bowel has been gradually increasing both in the United States (12) and in Europe (13) with a relatively greater increase in primary caecal cancer (14). This change may partly reflect increased rates of screening via colonoscopy with excision of precancerous polyps in the distal sites of the large bowel. Colonoscopy better prevents left-sided as compared to right-sided CRC (15).

1.1.2 MORTALITY

CRC related mortality has progressively declined since the mid-1980s in many western countries (16). This decline in mortality may partly be related to increased screening for and removal of colonic polyps, earlier diagnosis of CRC in terms of stage, and availability of better treatment. However, the decline in death rates from CRC started much earlier before screening was widely adopted and prior to widespread availability of effective adjuvant therapy (17). We could not find any explanation for these findings from our literature review.

According to the Surveillance, Epidemiology, and End results (SEER) programme, the 5 year survival for CRC, all stages and sites combined, is 61 percent in the US which thus has one of the highest 5 year survival rates for the disease (18).

On the other hand, in countries with less resources and more limited health infrastructure particularly in Central and South America and Eastern Europe, the mortality rates continue to rise (19).

1.1.3 AFRICAN PERSPECTIVES

In Africa, CRC has historically been considered an insignificant problem, although the mortality is high (20). Ugandan and Zimbabwean studies showed a 5 year survival rate of 8.3% and 17.4% respectively for patients diagnosed between 1993 and 1997 (21,22). The outcomes of gastrointestinal cancers in Africa are poorer at least in part due late presentation and diagnosis (21).

That Colorectal cancer is rare in Africa is supported by evidence available from cancer registries (20). The age standardised incidence rate ranges from 1.5/100000 in males and 2.5/100000 in females in the Gambia to 8.5/100000 in males and 7.1/100000 in females in Zimbabwe (20). Current Global Cancer Incidence, Mortality and Prevalence (GLOBOCAN) estimates the age standardized incidence rate of CRC in zimbabwe to be 10/100000 while that in Gambia to be 1.1/100000 in both sexes and all ages (1). In comparison, the age-standardised incidence rate per 100000 among Caucasians in Zimbabwe is similar to that in the western world at 49.8 and 35.5 in males and females respectively (20). As a comparison ,the average age-standardised incidence rate in the developed world is 37.6 (6).

This may be due to differences in health seeking behaviour and access to comprehensive health services. The apparent low incidence may then actually reflect an underdiagnosis of CRC among black Africans which may be more common amongst black Africans than is thought to be (23). However, the current belief is that it is a rare condition (24).

1.1.4 KENYAN PERSPECTIVES

According to GLOBOCAN 2018, CRC accounts for 4.8 % of all cancers diagnosed in both sexes making it the 5th most commonly diagnosed malignancy overall; in male, it accounts for 5.9% of all cases while in females it accounts for 4.1% of all cases, making it the 3rd and 4th most common diagnosed malignancy in males and females respectively (1).

Between 2004 and 2008, the Nairobi cancer registry recorded a total of 538 cases of colorectal and anal cancer in Nairobi county. Of these, 296 were in males and 242 were in females. CRC and anal cancer together accounted for 7.6% of all cancers in males and 4.8% of all cancers in females making it the 3rd and 4th most common malignancy respectively (25).

According to previous Kenyan research by Saidi et al (2005), emergency surgery, poorly differentiated cancer, age over 50 years, and advanced disease were associated with poor prognosis. The incidence was recorded to have increased 2.7 fold between 1993 and 2005 (26).

According to another Kenyan study by Saidi et al (2010), overall recurrence rate was 37.5% and mortality rate was 29.4%. Lesions located in the rectum accounted for just over half (50.5%) of the cases (rectosigmoid lesions comprised 63.3% of all cases). The highest incidence was in individuals aged between 41 and 50 yrs. Age, gender, sub-site, chemotherapy receipt or presence of comorbidity were not associated with recurrence. Male gender, presence of co-morbidity, recurrence, curative intent, disease stage and receipt of chemotherapy were associated with mortality (27).

Since 2011, the government of Kenya has implemented various policies and guidelines targeting cancer in general. These include the Cancer Prevention and Control Act (2012), cancer prevention and control bill (2015), National guidelines for management of cancer in Kenya (2013), National Cancer Control Strategy (2011-2016 and 2017-2022), and National Health Insurance fund coverage of cancer treatment in local hospitals since 2016. These policies and guidelines aim to allow better access to healthcare for cancer patients, earlier diagnosis of the disease and more widespread availability of better treatment over time. With these steps it would be expected that the presentation and outcomes of cancer in Kenya, including colorectal cancer, has changed, possibly significantly, since 2011 (28).

1.1.5 YOUNG ONSET COLORECTAL CANCER

It has been reported that the frequency with which CRC occurs in patients aged under 40 years is increasing; this has been theorised to be due to low index of suspicion of CRC in young symptomatic individuals as well as different molecular features. Compared to older patients, young onset CRC seems to differ in many aspects with respect to issues such as stage at diagnosis, outcomes and biological aggressiveness (29). A Kenyan study by Saidi et al (2005) showed that patients younger than 40 years of age bear a significant burden of the disease at 27.3% of CRC. However, in contrast to international data, the clinicopathological characteristics and outcomes did not differ significantly from older patients (30).

1.2 CLINICOPATHOLOGICAL CHARCTERISTICS OF PROGNOSTIC SIGNIFICANCE

1.2.1 DISEASE PATHOLOGY

Local tumour extent: Local tumour extent has strong prognostic significance with the prognosis being significantly worse for tumours that reach the serosa/peritoneum or invade extramurally. Local peritoneal involvement consistently predicts recurrent disease in the peritoneum. Tumours within 1 mm of a fibroinflammatory reaction on the serosa likely reflect involvement of the peritoneum by the tumour. Extent of local invasion correlates well with nodal metastases and the histological grade (31,32,33,34).

Tumour size: appears to be an independent factor predictive of outcome for colorectal cancer; with a stronger prognostic significance in the colon but of minor value for rectal tumours. Tumour sizes associated with worse prognosis vary with the site of the bowel involved; 5 cm, 5.3 cm, 3.9 cm, and 3.4 cm are values with the strongest distinguishing capacity on average in the colon, the right colon, the left side and the rectum respectively (35).

Residual tumor: A consensus statement by the American college of pathologists considered residual tumor after definitive therapy as one of the most important markers of poor prognosis after a critical review of medical literature (36). The residual tumour (R) classification describes the tumour status following curative treatment. According to R classification, R0 means no residual tumour, R1 means microscopic residual tumour while R2 means macroscopic residual tumour. The residual tumour can be in the area of the primary tumour, the regional lymph nodes, at a distant site or a combination thereof. Studies have found the R classification to have strong prognostic significance. Of the 3 classes, only R0 has a good long term prognosis and although R classification correlates with the stage ,the difference in prognosis between R0 and other R classes cannot accounted for by the difference in stage alone (37).

Regional lymph node involvement: The number of lymph nodes infiltrated with malignant cells has a strong prognostic significance (38). Detection of isolated tumour cells in regional lymph nodes using molecular methods such as reverse transcriptase PCR has been found to have a poor prognosis in terms of increased recurrence and mortality according to some studies (39).

Tumor regression after neoadjuvant therapy: Among patients who receive neo adjuvant chemotherapy, studies have shown that the best prognosis is for patients whose tumour been eradicated histologically followed by minimal residual disease due to a small but not trivial risk of distant recurrence. The worst prognosis is for gross residual disease (40).

Lymphovascular invasion: On univariate and multivariate analysis, venous and lymphatic invasion by the tumour has been proven to be of prognostic significance (41). Lymphovascular invasion –positive can therefore be used to identify aggressive tumours and stage 2 tumours that may benefit from adjuvant chemotherapy (42).

Perineural invasion: A meta-analysis of 58 studies showed that PNI is independently associated with increased rate of local recurrence, decreased disease free survival at 5 years, decreased overall and cancer specific survival at 5 years (43).

Histologic type: Histologically, most cases of CRC are adenocarcinomas; mucinous and signet ring adenocarcinomas are variants which constitute 10% and 1-2.4% of adenocarcinomas. Both are associated with a poor prognosis. Mucinous cancers have large quantities of extracellular mucin. Mucinous metastatic CRC also have reduced response to chemotherapy and targeted treatment agents (44).

Histological grade and mucin production: Histologic grade refers to the degree of tumor differentiation and is a factor that has been proven to be an independent prognostic factor regardless of stage (45). Some (46), but not all (47), data suggest that the presence of mucin is on its own associated with adverse outcomes in rectal cancers.

Tumor border: An infiltrative growth pattern at the tumour margin refers to pathological evidence of extensive dissemination into normal tissue of cancerous cells such that the boundary between normal host tissue and the tumour becomes indistinct. This sort of pattern is associated with a worse prognosis (48).

Tumor location: A meta-analysis of 66 studies showed that a left sided tumour location is associated with a significantly improved survival compared to tumour location on the right side of the colon independent of other factors such as stage, and adjuvant chemotherapy (49).

Focal neuroendocrine differentiation: The data on the prognostic significance of focal neuroendocrine differentiation is conflicting; some studies show it to have an independent adverse prognostic impact (50) but others do not (51).

Host immune response: Many studies have shown that the presence of tumour-infiltrating lymphocytes is associated with a favourable prognosis. A high density of CD 8+ T cells and memory T cells amongst these infiltrating cells is linked to the absence of pathologic evidence of early metastasis, to earlier stage, and improved patient survival (52).

1.2.2 CLINICAL FACTORS

Clinical presentation: Patients may be asymptomatic and CRC may be detected via screening colonoscopy; in these patients, the disease is usually of an earlier stage than in those with symptomatic cancer thus they have a better prognosis. In addition, these patients may have a better prognosis independent of the stage at diagnosis (53).

Typical symptoms of CRC include change in hematochezia, iron deficiency anemia, bowel movements, and abdominal pain (54). CRC presenting with hematochezia has a good prognosis due to earlier presentation but hematochezia on its own is not an independent prognostic factor. On the other hand, presentation with anemia portends a poor prognosis due to the advanced stage

of presentation. In malignant tumours located in the colon, but not in the rectum presence of a greater number of symptoms may be associated with a poor prognosis (55). A review of 40 studies showed no association between diagnostic delay from onset of symptoms and outcome (56).

Several studies have shown that clinical presentation with bowel perforation or obstruction due to the tumour are independent predictors of worse outcomes on multivariate analysis (57). However, it may also be that CRCs needing emergency surgery due to perforation or intestinal obstruction are generally reflective of a more aggressive histopathological profile as compared to cases which undergo elective surgery (58).

1.2.3 TREATMENT RELATED FACTORS

Surgical resection in stage 4 colorectal cancer : A meta-analysis of 66 studies of patients with stage 4 CRC showed that patients patients who received primary tumour resection plus chemoradiotherapy/chemotherapy had longer overall survival as compared to patients who received medical management alone (59).

Adjuvant chemotherapy: In stage 3 colon adenocarcinomas, adjuvant chemotherapy post curative resection decreases recurrence and improves survival (60). The current standard adjuvant chemotherapy therapy regimens include 5Fluorouracil with leucovorin (61), 5fluorouracil and leucovorin with oxaliplatin (62), and cepecitabine monotherapy (63). In contrast, adjuvant chemotherapy in stage 2 colon cancer remains controversial athough there might be role for adjuvant chemotherapy in selected patients with high risk features such as tumours involving the serosa, poor differentiation, perforation, and inadequately number of evaluated lymph nodes (64).

Timing of adjuvant chemotherapy in stage 3 CRC: Surgery can lead to growth of tumours by stimulating angiogenesis (65). It is thought that adjuvant chemotherapy eradicates micrometastasis after surgical resection and thus increases cancer cure rates. Initiation of adjuvant chemotherapy early within 8 weeks of curative resection increases overall survival but relapse free survival is not impacted upon significantly (66).

1.2.4 PATIENT RELATED FACTORS

Age: Young patients under the age of 40 years present with a more aggressive disease biology and a more advanced stage of presentation when compared to older patients. The advanced stage at presentation may at least partly be due to clinicians having a lower index of suspicion in these patients leading to delays in diagnosis. In addition, screening programmes are less likely to include younger patients. However, despite the aggressive biology and late presentation, younger patients have a superior 5 year survival when controlling for other prognostic factors (67).

Comorbidities: CRC most commonly occurs in older individuals who are likely to be burdened by coexisting diseases. In these comorbidities such as dementia, renal disease, liver disease and hemiplegia have been shown to interact with CRC and increase the 30 day post-operative mortality and 1 year mortality after diagnosis (68).

Gender of the patient: A meta-analysis of 13 retrospective cohort studies and 1 randomised controlled trial from 1960 to 2017 showed that among patients with CRC, women have significantly better overall and cancer specific survival when compared to men. This was true even after adjusting for all baseline characteristics. Thus sex may be an independent prognostic factor in CRC (69).

1.2.5 TUMOUR MARKERS

Preoperative carcinoembryonic antigen (CEA) levels: Many studies have elucidated that pre-operative CEA levels above 5ng/ml correlate with worse survival rates independent of other prognostic variables (70). The prognostic significance of preoperative CEA levels is independent of the number of infiltrated nodes on histology, and correlates with the degree of lumen encirclement, lumen obstruction, and treatment failure regardless of the dukes stage (70).

2.0 JUSTIFICATION

CRC has not been described at KNH since 2010; the last description was between 2005 and 2010 (26), its occurrence is on the rise and previous studies have found poor outcomes with 5 year survival rates of 10-30%. It is likely that after various government programmes targeting cancer being established since 2011, there is improved awareness of CRC, better access to healthcare, earlier diagnosis and more widespread availability of better treatment with time. It is therefore likely that the presentation and outcomes of cancer (including CRC) have changed, possibly significantly, at KNH since 2011. This study seeks to update the knowledge on the clinicopathological characteristics and outcomes of CRC at KNH; the data generated can be used to delineate trends.

3.0 STUDY QUESTION

What are the clinico-pathologic characteristics and outcomes of CRC at KNH and how do the clinicopathological characteristics correlate with mortality?

4.0 STUDY OBJECTIVES

4.1 BROAD OBJECTIVE

We conducted this study to determine the clinicopathologic characteristics and outcomes of CRC at KNH from 2014 to 2018, and to correlate patient mortality from the disease with the clinicopathological characteristics.

4.2 SPECIFIC OBJECTIVES

4.2.1 PRIMARY OBJECTIVES

1. To describe the clinical and sociodemographic characteristics of patients with CRC at KNH from 2014-2018.

2. To describe the pathological characteristics of CRC at KNH from 2014 to 2018.

3. To determine the outcomes at one year among patients with CRC at KNH from 2014 to 2018.

4.2.2 SECONDARY OBJECTIVES

1. To correlate 1-year mortality with the clinicopathological characteristics that we described.

5.0 METHODOLOGY

5.1 SITE
We obtained our data from the records at the Cancer treatment centre and at the KNH records department. From the cancer treatment centre we obtained data of all patients who received chemotherapy and radiotherapy for CRC as outpatients while records from the KNH records department provided us with information on patients seen at the haemato-oncology clinic, the surgical outpatient clinic and admitted to ward 8C, surgical wards and ground floor ward D.

5.2 DESIGN
This was a comprehensive chart review of patients with biopsy proven CRC diagnosed between 2014 and 2018.

5.3 STUDY POPULATION
Our study population was patients with biopsy proven CRC diagnosed between 2014 and 2018 and having records at KNH records department and KNH cancer treatment centre.

5.4 INCLUSION AND EXCLUSION CRITERIA

5.4.1 INCLUSION CRITERIA
We included anybody diagnosed with biopsy proven CRC between January 2014 and December 2018 with records at the KNH cancer treatment centre and the KNH medical records department.

5.4.2 EXCLUSION CRITERIA
We excluded from our study all patients with other colorectal malignancies such as lymphomas, patients whose diagnosis was not clear and patients who did not have records at KNH.

5.5 CASE DEFINITION
CRC was defined as histologically proven carcinoma of the colon and of the rectum.

5.6 SAMPLE SIZE

Sample size was calculated using the formula (71):

$$n = \frac{Z^2 x\ P(1-P)}{d^2}$$

Where,

n = Desired sample size

Z = value from standard normal distribution corresponding to desired confidence level (Z=1.96 for 95% CI)

P = expected true proportion (estimated at 63.3%, from a study done by Saidi et al in Kenya (26) looking at subsite of the CRC found that rectosigmoid lesions comprised 63.3% of them).

d = desired precision ($p < 0.05$)

$$n_0 = \frac{1.96^2 x\ 0.633(1-0.633)}{0.05^2} = 357$$

A minimum sample size of 357 patient charts was required for the study.

5.7 SAMPLING METHOD

We sampled all files under colorectal cancer from January 2014 to December 2018 at the KNH records department and at the cancer treatment centre.

5.9 STUDY PROCEDURE & METHODS

5.9.1 RECRUITMENT

The principle investigator with the aid of the records officer retrieved all files from 1st January 2014 to 31st December 2018 using ICD codes c19, c20 and c21 from the KNH records department and using the diagnosis indicated in the register at the cancer treatment centre.

The files which met the inclusion criteria were selected and checked for histologic confirmation of diagnosis and completeness of information. From these files study variables of interest were captured in a study proforma (Appendix I). These included sociodemographic characteristics of the patients such as age, gender, county of residence, education level, occupation and marital status as well as clinical characteristics such as the clinical presentation, comorbidities, location of the tumour, presence and site of distant metastasis and the treatment modality, and also the pathological characteristics of the tumour including the histological grade, the histological type, the extent, and lymph node involvement. We also obtained the outcome data from the files.

We described the location of the tumour as right sided if the tumour was located anywhere from the caecum to the splenic flexure and left sided if it was located distal to the splenic flexure.

The treatment modality was categorized under surgery, chemotherapy and radiotherapy. The type of surgery, the chemotherapy regimen and the dose of radiotherapy given was also documented.

The outcomes recorded were alive, dead, lost to follow up and undetermined.

The date on the biopsy report was used as the date of diagnosis. Any patient seen at the end of 12 months or beyond after the date of diagnosis was recorded as ‘alive’. Death within 1 year of diagnosis was recorded as such. Any patient diagnosed at less than 1 year before date of data collection had their outcome recorded as ‘undetermined outcome’. Any patient whose last visit in the file was less than 1 year from the date of diagnosis was recorded as ‘lost to follow up’.

5.9.2 STUDY ADMINISTRATION AND QUALITY ASSURANCE

The principal investigator collected all the data himself to ensure high quality data and timely collection. Files were retrieved daily in the morning with the help of records officers and data was collected on most afternoons on weekdays from 1st March 2019 to 14th June 2019. Files for continuing patients during clinic attendance days were noted and retrieved at a later date once available. Throughout the process, frequent contact was made with supervisors for guidance. The statistician offered guidance during proposal development, data entry, analysis and presentation of the final statistical analysis.

6.0 DATA MANAGEMENT AND ANALYSIS

Data gathered by the principal investigator was entered continuously in a coded proforma, cleaned and verified. Data was then entered into a password protected Microsoft Access database handled by the statistician**.** Data analysis was performed using Statistical Package for Social Science (SPSS) version 21.0 for windows.

Continuous data was presented as means and median while categorical data was presented as frequencies, ratios and percentages**.** Univariate and multivariate analysis was be used to determine the association between the clinicopathological and socio demographic characteristics with mortality.

95% confidence interval was calculated. A p value of < 0.05 was be considered significant.

Among the sociodemographic characteristics, gender was presented as ratio and age was presented as percentages, mean plus standard deviation and median. Residence, education level, occupation, and marital status were presented as percentages.

The clinical characteristics and pathological characteristics were all presented as percentages.

Outcomes were presented as percentages.

Association between 1-year mortality and clinicopathological characteristics was determined and p-values provided.

7.0. ETHICAL CONSIDERATIONS

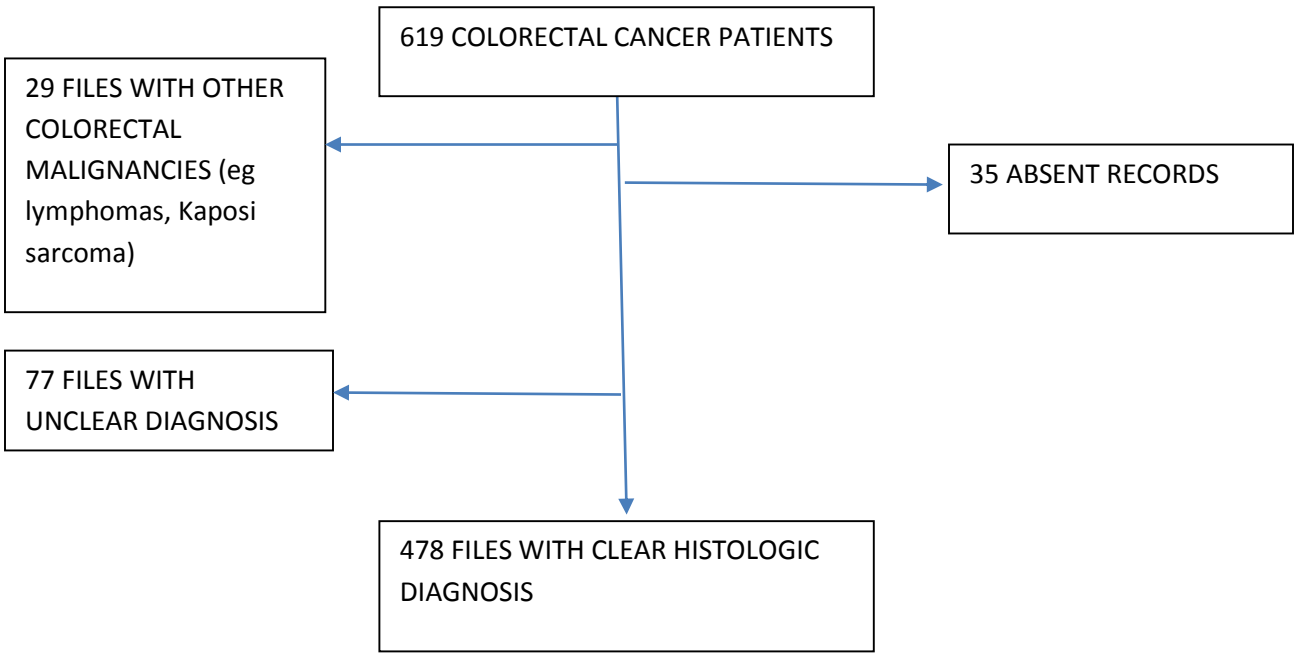
The project commenced after approval by the Kenyatta National Hospital/University of Nairobi Ethics and Research Committee (Reference: KNH-ERC/A/62). This was a low risk study. Absolute confidentiality was observed throughout the process.

All data collected was de-identified; randomly coded unique identifier numbers were used in the data collection forms. The links between the randomly coded unique identifier numbers and the file numbers were documented and stored under lock and key as was the data collected.

8.0 RESULTS

Data was collected between 1st March 2019 and 14th June 2019.

Total of 619 patients with CRC diagnosed between January 2014 and December 2018 were seen at KNH. Of these 30 had missing files, 25 had other malignancies of the colon/rectum and 77 had an unclear diagnosis.



8.1 SOCIODEMOGRAPHIC CHARACTERISTICS OF PATIENTS WITH CRC

A total of 478 CRC cases were included.

Males were 248 (51.9%) while females were 230 (48.1%) with a ratio of 1:1.08.

The ages ranged from 14 years to 96 years. The mean age at diagnosis was 53.26 with a standard deviation of 15.33 years. The median age at diagnosis was 54 years. The mean age of male patients at diagnosis was 54.5 while that of females was 52 years.

Patients at and below 40 years of age accounted for 21.1% of patients while 78.9% were above 40 years. The peak incidence occurred in the age group 51-60 years with 112 (23.4%) of the cases.

The most common county of residence was Kiambu county (14.6%) followed by Murang'a (10.7%) and Nairobi county (7.9%).

Secondary education level (19%) was most common amongst the patient followed by primary level (14.2%).

The most common occupation was farming (26.1%) followed by business (9.2%).

More than 70% of the patients were married while just over 14% were recorded as single.

Table 1: Socio-demographics Characteristics of Patients with CRC

	Frequency	**Percent**
Sex	**(n=478)**	
Male	248	51.9
Female	230	48.1
Age (mean = 53.26 years)	**(n= 478)**	
<=40	101	21.1
41 – 50	96	20.1
51 – 60	112	23.4
61 – 70	110	23.0
>70	59	12.3
Residence (county)	**(n=478)**	
Kiambu	70	14.6
Kirinyaga	28	5.9
Murang'a	51	10.7
Nairobi	38	7.9
Others	291	60.9
Education	**(n=186)**	
Missing	292	61.1
Tertiary	27	5.6
Primary	68	14.2
Secondary	91	19.0

Occupation	**(n=321)**	
Missing	157	32.2
Farmer	127	26.1
Business	45	9.2
Housewife	35	7.2
Others	123	25.3
Marital status	**(n=433)**	
Missing	45	9.4
Divorced	8	1.7
Married	336	70.3
Single	68	14.2
Widowed	14	2.9
Widower	7	1.5

Figure 1: Pie chart of the sex distribution of colorectal cancer

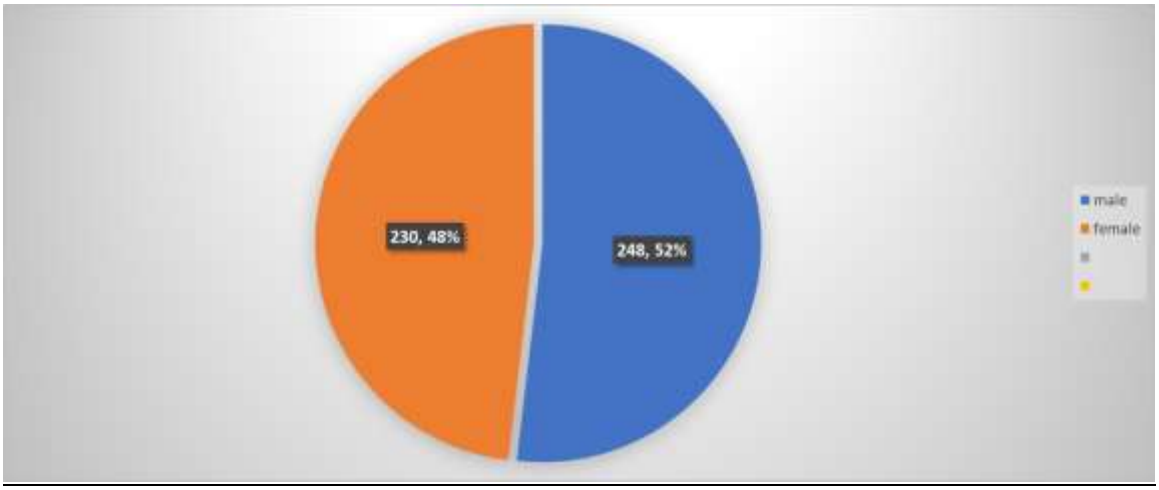
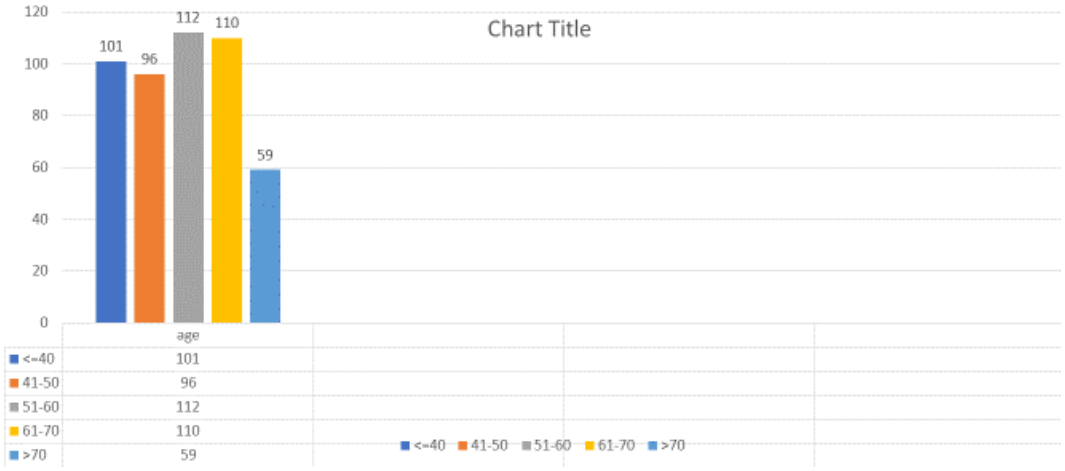


Figure 2: Bar graphs showing age distribution of colorectal cancer



8.2 CLINICAL CHARACTERISTICS OF PATIENTS WITH CRC

Hematochezia was the most common presenting complaint at 51 % followed by change in bowel habits and pain in the abdomen at 42.4% and 37.7 % respectively. Intestinal obstruction was a presenting feature in 12.3% of patients.

Just over 80% of the patients received chemotherapy, 59.1% were operated for their tumours while just over a third of the patients received radiotherapy. The most common chemotherapy regimen prescribed was FOLFOX 4 followed by FOLFOX 6. Almost 21% of those who received surgical management were operated with palliative intention. The most commonly prescribed radiotherapy dose treatment of rectal cancer was the adjuvant/neoadjuvant long course dose of 50.4 grays (72.7%) followed by the palliative dose of 30 grays (16.2%).

The most common comorbidity was hypertension (17.2%) followed by diabetes (5%).

Almost 77% of the patients had left sided tumours with almost all of the rest having right sided neoplasms. A minority (1%) had metachronous tumours.

More than half (54%) of the patients did not have a metastatic cancer. Of those who did have metastasis, the liver (27.8%) followed by the lung (13.8%) were the most common sites.

Table 2: Clinical Characteristics of Patients with CRC

Clinical characteristics	Frequency	Percent
Clinical presentation	**(n=478)**	
Abdominal pain	176	37.7%
Hematochezia	238	51.0%
Altered bowel habits	198	42.4%
Anemia (hemoglobin < 11g/dl)	32	6.9%
Intestinal obstruction	59	12.3%
Weight loss	43	9.2%
Others	86	18.4%
Treatment Modality	**(n=478)**	
Surgery	278	58.2%
APR	60	21.6%
LAR	24	8.6%
Colostomy/debulking/bypass	84	20.7%
Left hemicolectomy	34	12.2%
RT hemicolectomy	52	18.7%
Sigmoidectomy	24	8.6%
Chemotherapy	389	81.4%
FOLFOX4	179	46.0%
FOLFOX6	104	26.7%
Folfiri	21	4.5%
Xeloda	75	19.3%
Xelox	66	17.0%
Others	22	5.8%
Radiotherapy	154	32.2%
30.00 grays	25	16.2%
50.40 grays	112	72.7%
Other doses	17	11.0%
No treatment	10	2.1%
No record	33	6.9%
Comorbidities	**(n=478)**	
None	361	75.5%
Diabetes	24	5.0%
HIV Positive	8	1.7%
Hypertension	82	17.2%
Others	32	6.7%
Location	**(n=476)**	
Left side	367	76.8
Right side	104	21.8
Both sides	5	1.0

Missing information	2	0.4
Sites of metastasis	**(n=433)**	
Absent	254	53.1%
Bone	12	2.5%
Liver	133	27.8%
Lung	66	13.8%
No record	45	9.4%
Others	13	2.7%
Peritoneum	27	5.6%

8.3 PATHOLOGICAL CHARACTERISTICS OF CRC

Adenocarcinoma was the most common histologic type of CRC diagnosed with 405 (84.7%) patients having it. Mucinous adenocarcinoma was diagnosed in 39 (8.2%) and signet ring cell in 17(3.6%) patients.

Moderately differentiated tumours were present in 59.6% of patients with the rest having well and poorly differentiated tumours in almost equal proportions.

Lymph node involvement was present in almost 60% of the tumours.

Table 3: Pathological characteristic of CRC

Pathologic characteristics	**Frequency**	**Percent**
Histologic type	**(n= 477)**	
Adenocarcinoma	405	84.7
Adenocarcinoma, Papillary	3	.6
Adenosquamous ca	1	.2
Mucinous	39	8.2
Papillary adenocarcinoma	11	2.3
Signet Ring Cell	17	3.6
Squamous	1	.2
No record	1	.2
Histologic grade	**(n=462)**	
Moderately Differentiated	285	59.6
Poorly differentiated	86	18.0
Well differentiated	90	18.8
No record	17	3.6
Tumour Extent	**(n=405)**	
Involvement of Mucosa	2	.4

Involvement of Submucosa	13	2.7
Involvement of muscularis propria	128	26.8
Involvement of serosa	136	28.5
Involvement of surrounding organs	126	26.4
No record	73	15.3
Lymph node involvement	**(n=437)**	
Absent	153	32.0
Present	284	59.4
No record	41	8.6

8.4 ANALYSIS OF CLINICAL CHARACTERISTICS ACCORDING TO THE AGE OF THE PATIENT AND THE SITE OF THE TUMOUR

When an analysis by age groups >40 years versus ≤40 years was done, the presence of metastasis (p = 0.812) did not differ significantly between the two groups and neither did the frequency of left sided (p = 0.404), right sided tumours (p = 0.575) or metachronous tumours (p = 0.243).

Table 4: Clinical characteristics according to age of the patients

Distance Metastases	**≤40**	**>40**	**Total**	**P value**
Absent	55 (54.5)	203 (53.8)	258 (54)	0.913
Present	38 (37.6)	137 (36.3)	175 (36.6)	0.812
No record	8 (7.9)	37 (9.8)	45 (9.4)	0.563
Location				
Left	81 (80.2)	286 (76.3)	367 (77.1)	0.404
Right	20 (19.8)	84 (22.4)	104 (21.8)	0.575
Both	0 (0.0)	5 (1.3)	5 (1.1)	0.243

***P<0.05 was considered significant.**

Hematochezia (p = < 0.001), altered bowel habits (p= < 0.001), weight loss (p= <0.001), intestinal obstruction (p= < 0.001) and abdominal pain (p= 0.002) were significantly more common in left sided tumours. The location of the tumour did not predict the presence of metastasis (p = 0.145).

Table 5:Clinical characteristic according to site of tumour

Distance Metastases	**Right**	**Left**	**Both**	**Total**	**P value**
Absent	201 (54.8)	57 (54.8)	0 (0)	258 (54.2)	0.057
Present	133 (36.2)	37 (35.6)	4 (80)	174 (36.6)	0.145
Clinical presentation					
Abdominal pain	69 (39.7)	105(60.3)		171(100)	0.002
Hematochezia	8 (3.4)	226 (96.6)		234(100)	<0.001
Altered bowel habits	25 (12.6)	173(87.4)		198(100)	<0.001
Clinical anemia	21 (65.6)	11(34.4)		33(100)	0.077
Intestinal obstruction	16 (27.1)	43 (72.9))		59(100)	<0.001
Weight loss	9 (20.9)	34 (79.1)		43(100)	<0.001

***P<0.05 was considered significant.**

8.5 ANALYSIS OF THE PATHOLOGICAL CHARACTERISTICS ACCORDING TO THE PATIENT GENDER AND AGE, AND THE SITE OF THE TUMOUR

Adenocarcinomas (85.1% vs 84.3%), papillary adenocarcinomas (1.2% vs 0.0%) and mucinous adenocarcinomas (8.5% vs 7.8%) were more common in males while signet ring cell tumours (4.3% vs 2.8%) were more common in females.

Moderately differentiated tumours were present in 61.7% of males versus 57.4% of females (p=0.338), poorly differentiated tumours were present in 16.5% of females versus 19.6% of females (p = 0.388) while well differentiated tumours were present in 19.1% of females versus 18.5% of males (p = 0.871).

As far as tumour depth of invasion was concerned, Tumour involvement of the serosa and beyond was slightly more common in females compared to males (56.5% vs 53.2%).

This is shown in the table below (table 6) which also shows that the differences did not achieve statistical significance.

Table 6: Pathological characteristic according to patient gender

Pathologic characteristic	Male	Female	Total	p-value
Histological type				
Adenocarcinoma	211 (85.1)	194 (84.3)	405 (84.7)	0.824
Adenocarcinoma, Papillary	3 (1.2)	0 (0.0)	3 (0.6)	0.094
Adenosquamous ca	0 (0.0)	1 (0.4)	1 (0.2)	0.299
Mucinous	21 (8.5)	18 (7.8)	39 (8.2)	0.798
Papillary adenocarcinoma	6 (2.4)	5 (2.2)	11 (2.3)	0.858
Signet Ring Cell	7 (2.8)	10 (4.3)	17 (3.6)	0.363
Squamous	0 (0.0)	1 (0.4)	1 (0.2)	0.299
No record	0 (0.0)	1 (0.4)	1 (0.2)	0.299
Histological grade				
Moderately Differentiated	153 (61.7)	132 (57.4)	285 (59.6)	0.338
Poorly differentiated	41 (16.5)	45 (19.6)	86 (18.0)	0.388
Well differentiated	46 (18.5)	44 (19.1)	90 (18.8)	0.871
No record	8 (3.2)	9 (3.9)	17 (3.6)	0.685
Tumor extent				
Involvement of muscularis propria	67 (27)	61 (26.5)	128 (26.8)	0.903
Involvement of Mucosa and Submucosa	9 (3.6)	4 (1.7)	13 (2.7)	0.204
Involvement of Mucosa only	0 (0.0)	2 (0.9)	2 (0.4)	0.141
Involvement of serosa	69 (27.8)	67 (29.1)	136 (28.5)	0.752
Involvement of surrounding organs	63 (25.4)	63 (27.4)	126 (26.4)	0.565
No record	40 (16.1)	33 (14.3)	73 (15.3)	0.557
Lymph node involvement				
Absent	80 (32.3)	73 (31.7)	153 (32)	0.903
Present	148 (59.7)	136 (59.1)	284 (59.4)	0.903
No record	20 (8.1)	21 (9.1)	41 (8.6)	0.678

***P<0.05 was considered significant.**

Adenocarcinomas (85.3% vs 82.7%) and papillary adenocarcinomas (4.3% vs 1.0%) were more common in left sided tumours while signet ring cell tumours (3.8% vs 3.5%) and mucinous tumours (11.5% vs 7.4%) were more common in right sided tumours.

Moderately differentiated tumours were present in 60.6% of right sided tumours versus 59.1% of females (p = 0.756), poorly differentiated tumours were present in 22.1% of right sided tumours versus 17.2% of right sided tumours (p = 0.396) while well differentiated tumours were present in 21.0% of left sided tumour versus 12.0% of right sided tumours (p = 0.068).

As for tumour depth of invasion, Tumour involvement of the serosa and beyond more common in left side tumours compared to right sided tumours (55.6% vs 51.9%).

This is tabulated below (table 7). None of the differences reached statistical significance.

Table 7: Pathological characteristics according to site of tumour

Pathologic	Left	Right	Both	Total	p-value
Histological type					
Adenocarcinoma	313 (85.3)	86 (82.7)	5 (100)	404 (84.9)	0.516
Adenocarcinoma, Papillary	3 (0.8)	0 (0.0)	0 (0.0)	3 (0.6)	0.639
Adenosquamous ca	0 (0.0)	1 (1.0)	0 (0.0)	1 (0.2)	0.167
Mucinous	27 (7.4)	12 (11.5)	0 (0.0)	39 (8.2)	0.311
Papillary adenocarcinoma	10 (2.7)	1 (1.0)	0 (0.0)	11 (2.3)	0.528
Signet Ring Cell	13 (3.5)	4 (3.8)	0 (0.0)	17 (3.6)	0.812
Squamous	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	1.000
Histological grade					
Moderately Differentiated	217 (59.1)	63 (60.6)	4 (80.0)	284 (59.7)	0.756
Poorly differentiated	63 (17.2)	23 (22.1)	0 (0.0)	86 (18.1)	0.396
Well differentiated	77 (21.0)	12 (11.5)	1 (20.0)	90 (18.9)	0.068
No record	10 (2.7)	6 (5.8)	0 (0.0)	16 (3.4)	0.271
Tumor extent					
Involvement of muscularis propria	93 (25.3)	34 (32.7)	1 (20.0)	128 (26.9)	0.314
Involvement of Mucosa and Submucosa	10 (2.7)	3 (2.9)	0 (0.0)	13 (2.7)	1.000
Involvement of Mucosa only	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.4)	1.000
Involvement of serosa	109 (29.7)	24 (23.1)	2 (40.0)	135 (28.4)	0.331
Involvement of surrounding organs	95 (25.9)	30 (28.8)	1 (20.0)	126 (26.5)	0.818
No record	58 (15.8)	13 (12.5)	1 (20.0)	72 (15.1)	0.497
Lymph node involvement					
Absent	119 (32.4)	32 (30.8)	1 (20.0)	152 (31.9)	0.936
Present	218 (59.4)	62 (59.6)	4 (80.0)	284 (59.7)	0.801
No record	30 (8.2)	10 (9.6)	0 (0.0)	40 (8.4)	0.711

***P<0.05 was considered significant.**

When the pathological characteristics were compared between patients > 40 years and patients ≤40 years it was found that adenocarcinomas (p = 0.018) and moderately differentiated tumours (p = 0.003) were more common in patients over 40 years old while signet ring cell tumours (p = 0.008) and poorly differentiated tumours (p = <0.001) were more frequent amongst younger patients.

Table 8: Pathological characteristics according to patients age

Pathologic Characteristic	≤40	>40	Total	p-value
Histological type				
Adenocarcinoma	78 (77.2)	327 (86.7)	405 (84.7)	0.018
Adenocarcinoma, Papillary	0 (0.0)	3 (0.8)	3 (0.6)	0.368
Adenosquamous ca	0 (0.0)	1 (0.3)	1 (0.2)	0.604
Mucinous	13 (12.9)	26 (6.9)	39 (8.2)	0.051
Papillary adenocarcinoma	2 (2.0)	9 (2.4)	11 (2.3)	0.809
Signet Ring Cell	8 (7.9)	9 (2.4)	17 (3.6)	0.008
Squamous	0 (0.0)	1 (0.3)	1 (0.2)	0.604
No record	0 (0.0)	1 (0.3)	1 (0.2)	0.604
Histological grade				
Moderately Differentiated	47 (46.5)	238 (63.1)	285 (59.6)	0.003
Poorly differentiated	31 (30.7)	55 (14.6)	86 (18.0)	<0.001
Well differentiated	19 (18.8)	71 (18.8)	90 (18.8)	0.996
No record	4 (4.0)	13 (3.4)	17 (3.6)	0.805
Tumor extent				
Involvement of muscularis propria	25 (24.8)	103 (27.3)	128 (26.8)	0.605
Involvement of Mucosa and Submucosa	2 (2.0)	11 (2.9)	13 (2.7)	0.607
Involvement of Mucosa only	0 (0.0)	2 (0.5)	2 (0.4)	0.463
Involvement of serosa	28 (27.7)	108 (28.6)	136 (28.5)	0.855
Involvement of surrounding organs	31 (30.7)	95 (25.2)	126 (26.4)	0.185
No record	15 (14.9)	58 (15.4)	73 (15.3)	0.886
Lymph node involvement				
Absent	31 (30.7)	122 (32.4)	153 (32)	0.750
Present	64 (63.4)	220 (58.4)	284 (59.4)	0.362
No record	6 (5.9)	35 (9.3)	41 (8.6)	0.287

***P<0.05 was considered significant.**

8.6 OUTCOMES

Among patients with CRC at KNH from January 2014 to December 2018, 86 (18%) were recorded as having died in less than a year after diagnosis, 176 (36.8%) were alive at 1 year after diagnosis, 152 (31.8.%) were lost to follow up and the outcome of 58 (12.1%) was undetermined.

Table 9: Outcomes of Patients with CRC

	Frequency (n=478)	Percent
Alive	182	38.1
Dead	86	18.0
Lost to follow up	152	31.8
Undetermined outcome	58	12.1

8.7 ASSOCIATION BETWEEN SOCIODEMOGRAPHIC AND CLINICOPATHOLOGICAL CHARACTERISTICS OF CRC AND MORTALITY AT 1 YEAR

The association between clinicopathological and sociodemographic characteristics was assessed by univariate analysis (table 10). Age of the patient. Location of the tumour, presence of comorbidities, histologic subtype, and lymph node involvement were not significant factors but presence of distant metastasis ($p<0.001$), poorly differentiated histology ($p = 0.008$) and involvement of surrounding organs ($p<0.001$) were associated with mortality within 1 year.

The factors found to be significant on univariate analysis were assessed using multivariate analysis (table 11). On multivariate analysis, the degree of differentiation was not significantly associated with mortality but involvement of surrounding organs ($p = 0.02$) had significant effect. The presence of distance metastases was also significant ($p < 0.001$).

Table 10: Univariate analysis of patient and tumour characteristics associated with mortality

Demographic characteristics	Alive	Dead	Total	p-value
Age				
<=40	36 (19.8)	21 (24.4)	57 (21.2)	0.386
41 – 50	34 (18.7)	22 (25.6)	56 (20.9)	0.195
51 – 60	47 (25.8)	14 (16.3)	61 (22.8)	0.082
61 – 70	49 (26.9)	18 (20.9)	67 (25.0)	0.290
>70	16 (8.8)	11 (12.8)	27 (10.1)	0.280
Age				
<=40	36 (19.8)	21 (24.4)	57 (21.3)	0.386
>40	146 (80.2)	65 (75.6)	211 (78.7)	
Distance Metastases				
Absent	133 (76.0)	22 (27.8)	155 (61.0)	<0.001
Present	42 (24.0)	57 (72.2)	99 (39.0)	
Location				
Left	143 (78.6)	63 (74.1)	206 (77.1)	0.419
Right	38 (20.9)	20 (23.5)	58 (21.7)	0.625
Both	1 (0.5)	2 (2.4)	3 (1.1)	0.193
Comorbidities				
Yes	50 (27.5)	25 (29.1)	75 (28.0)	0.786
No	132 (72.5)	61 (70.9)	193 (72.0)	
Histological type				
Adenocarcinoma	159 (87.8)	71 (82.5)	230 (86.1)	0.243
Mucinous	13 (7.1)	7 (8.1)	20 (7.5)	0.781
Papillary adenocarcinoma	4 (2.2)	2 (2.3)	6 (2.2)	0.952
Signet Ring Cell	5 (2.8)	5 (5.8)	10 (3.7)	0.220
Squamous	0 (0.0)	1 (1.2)	1 (0.4)	0.144
Histological grade				

Moderately Differentiated	112 (64.0)	50 (59.5)	162 (60.4)	0.486
Poorly differentiated	21 (12.0)	21 (25.0)	51 (19.0)	0.008
Well differentiated	42 (24.0)	13 (15.5)	55 (20.5)	0.116
Tumor extent				
Involvement of subserosal tissues	74 (44.0)	11 (16.9)	85 (36.0)	<0.001
Involvement of Serosa	59 (35.1)	24 (35.3)	83 (35.1)	0.980
Involvement of surrounding organs	35 (20.8)	33 (48.5)	68 (28.8)	<0.001
Lymph node involvement				
Absent	65 (36.9)	20 (26.3)	85 (33.7)	0.102
Present	111 (63.0)	56 (73.7)	167 (66.3)	

***P<0.05 was considered significant.**

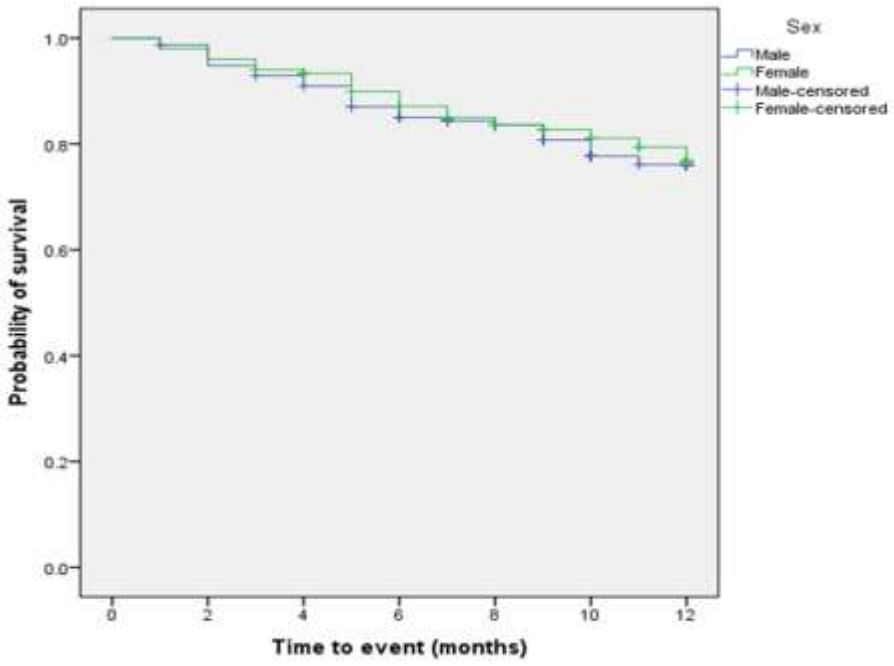
Table 11: **Multivariate analysis of patients and tumour characteristics associated with Mortality**

	p-value	**OR**	**95% C.I. for OR**	
			Lower	**Upper**
Histological grade	0.194			
Moderately diff.	0.301	1.618	0.650	4.023
Poorly diff.	0.070	2.853	0.916	8.887
Well diff. (Ref)				
Tumor extent	0.054			
Involvement of Mucosa (Ref)				
Involvement of Serosa	0.361	1.508	0.624	3.644
Involvement of surrounding organs	0.020	2.994	1.187	7.552
Distance Metastases (Present)	0.001	7.202	3.583	14.476

***P<0.05 was considered significant.**

The Kaplan-Meier survival curves for overall survival, and according to gender (figure 3) are shown in the figures below. There was trend towards a worse outcome but did not reach statistical significance (p=0.804)

Figure 3: Kaplan-Meier survival curves for overall survival, and according to gender



Mean Survival Time				
Sex	Mean			
	Estimate	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
Male	10.520	.247	10.035	11.005
Female	10.700	.243	10.225	11.176
Overall	10.608	.173	10.268	10.948

Overall Comparisons			
	Chi-Square	Df	Sig.
Log Rank (Mantel-Cox)	.062	1	.804
Test of equality of survival distributions for the different levels of Sex.			

9.0 DISCUSSION

In our study, which covered a duration of 5 years between January 2014 and December 2018, 51.9% of cases occurred in males while 48.1 % occurred in females showing only a slight male preponderance. In comparison, a previous Kenyan study showed males accounting for 58.8 % of CRC cases pointing to a higher incidence in females now compared to before (26). Our data also aligns itself with international data which records males having a slightly higher incidence than females in most regions with a ratio of 1:1.1 (1).

Our findings suggest that CRC still remains a disease of younger patients in our country and even more patients below 40yrs in age are being diagnosed with the disease; the proportion of patients aged under 40 years was slightly higher than in a previous local study (26). Our mean age was 53.33 years which is well below the mean in developed countries such as the US (7). Why CRC occurs more commonly in younger patients in Kenya as compared to patients in developed countries is a question that remains to be fully answered. However, recent data also suggest an increasing incidence amongst younger patients in the developed nations (8).

Most of our patients were from Kiambu, Muran'ga and Nairobi. This likely reflects more on the geographic proximity of these counties to KNH rather than a disproportionately higher incidence of CRC in these areas. However, given that Kiambu and Muran'ga are farming communities and the most common profession of our patients was farming, the role of exposure to agrochemicals as risk factors for CRC needs to be studied.

Majority of CRC occurred in the bowel's left side with most of the rest occurring on the right side. This was also reflected in the patients symptomatology since the most common symptoms were hematochezia and altered bowel habits. Our observation corroborates with other African studies (72) and other Kenyan studies (26). The proportion of left and right sided CRC seems stable in Kenya (26) unlike in western countries where the proportion of right sided tumours is gradually increasing (12,13). Colonoscopy has been found to be highly effective at preventing left sided tumours (15) and it has been reported that screening rates in asymptomatic patients in Kenya is very low (73).This could at least partly explain our findings.

We observed that 37.5% of our patients had metastasis at diagnosis. This percentage was higher than in the previous local study (26) and much higher than in a study done in china (74) in which distant metastasis was present in 18% of patients. This implies that our patients present late which we postulate may be due to health seeking behaviours in our patients and/or lack of awareness of symptoms of CRC.

The rate of metastasis did not defer between younger versus older patients or left versus right sided CRC; the late presentation of most of our patients means that other factors such as age and site of tumour were not significant in determining the presence or absence of metastasis.

Chemotherapy was prescribed to a greater percentage of patients than in an older study by Saidi et al (26) which could be because of increased availability likely due to NHIF funding. In

addition, since chemotherapy is indicated for adjuvant treatment of stage 3 colon cancer (59) and palliative treatment of stage 4 colon cancer (60), its status as the most common treatment modality in our study further supports the theory that many of our patients indeed present late. The current standard of care chemotherapeutic regimens for adjuvant treatment of CRC include FOLFOX and XELOX (61,62). A striking finding in this study was that these regimens were much more frequently prescribed for this indication between 2014 and 2018 as compared to a decade earlier (26) when a regimen consisting of 5 Flourouracil plus Leucovorin was far more common. This could be due, at least in part, to greater availability of oxaliplatin to our patients as a result of government funding of chemotherapy treatment and more evidence in favour of oxaliplatin based regimens (75).

Abdominoperineal resection was previously the surgical treatment of choice for low rectal cancers but due to advances in surgical techniques, the use neoadjuvant chemoradiotherapy to downstage the tumour, and also due the morbidity associated with the procedure, it is now becoming less common. In contrast, sphincter saving procedures are becoming more common. (76). However, it was the most common surgical procedure for treatment of rectal cancer in our study as was the case in the previous decade (26). This may imply that the most common location of the tumour largely remains unchanged. However, our data may also point to lack of advancement in our surgical techniques, lack of availability of staplers, inadequate utilization of neo-adjuvant chemoradiotherapy to downstage low rectal cancers or a combination thereof. Further studies need to be done to explore these theories.

More than half of the tumours at presentation involved the serosa or extended beyond pointing to a high frequency of locally advanced disease. Lymph node involvement was present in just less then 60% of patients in our study. In contrast, lymph node positive CRC occurred in almost 90% of patients in an Iranian study (77). Lower lymph node positivity in our study compared to Iranian study could at least partly be attributed to sampling of fewer nodes in our setting.

The pathological characteristics of CRC were similar in males and females, and in right sided and left side tumours but were different in younger patients from patients over 40 years in age. Younger patients tended to have a more aggressive histology compared to older patients. This is congruent with an international publication by Campos FG et al (28) but contradicts the findings in a previous Kenyan study (29). However, despite this, age was not a significant predictor of mortality probably because of the overriding effect of advanced disease presentation across the age groups.

The 1-year mortality rate in this study was 18% which is lower than in the 29.4% in an older Kenyan study (26) but still higher than in the US (7). The lower mortality in our research could be explained by the large number of patients who are lost to follow up, some of them could be deceased while others could have gone elsewhere for treatment. More research is needed to determine the real mortality of CRC in KNH and to elucidate the large lost to follow ups.

10.0 LIMITATIONS

The main limitation of this study was missing information. To mitigate this, the principal investigator collected data himself ensuring that every piece of information from clerking notes, histology reports, surgical notes, chemotherapy notes and treatment sheets was captured.

In addition, during analysis of the data to determine associations between the clinicopathological characteristics, the missing data was not analysed as it would introduce significant inaccuracy.

11.0 CONCLUSION

Kenyan CRC is a disease of a relatively younger population with more than 40% of the patients below the age of 50. The disease occurs in almost equal numbers in males and females.

Younger patients have a more aggressive pathology but outcomes do not differ between older and younger patients.

The bulk of the colorectal cancers in this country still occur on the left side of the bowel.

FOLFOX chemotherapy is much more commonly used than before.

A large number of patients with CRC in KNH present late, as an example 37.5% had metastatic disease at presentation.

1-year mortality from CRC still remains high at 18% as compared to developed countries.

12.0 RECOMMENDATIONS

A prospective study with long follow ups would greatly aid in revealing the changing face of colorectal cancer in this country.

Better documentation and record keeping, for example with check lists and electronic medical records respectively, would greatly enhance the accuracy and availability of information.

More research are needed to try and elucidate the large number of lost to follow ups; did they seek treatment elsewhere? Is this the result of NHIF cancer cover allowing patients who would normally seek care at KNH to seek care in private facilities and even abroad ?

Given the advanced presentation of CRC in a significant number of patients, studies that look into the availability and awareness of screening colonoscopy in this country need to be done.

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APPENDIX I: STUDY PROFORMA

STUDY TITLE: CLINICOPATHOLOGICAL CHARACTERISTICS OF COLORECTAL CANCER AT KNH

STUDY ID NUMBER: _____

Section 1 :SOCIODEMOGRAPHIC INFORMATION (TICK WHERE APPROPRIATE):

AGE:

SEX: MALE

FEMALE

OCCUPATION:

MARITAL STATUS:

RESIDENCE:

EDUCATION LEVEL:

Section 2 :PATIENT RELATED INFORMATION(TICK WHERE APPROPRIATE**):**

COMORBIDITY(S)

HYPERTENSION

DIABETES

OTHERS

NONE

Section 3 :DISEASE INFORMATION (TICK WHERE APPROPRIATE):

DATE OF DIAGNOSIS

CLINICAL FEATURES AT PRESENTATION: _____

LOCATION OF TUMOUR: RIGHT SIDE LEFT SIDE

HISTOLOGIC TYPE:

ADENOCARCINOMA

SIGNET RING CELL

MUCINOUS

OTHER

NO RECORD

HISTOLOGIC GRADE OF TUMOUR:

WELL DIFFERENTIATED

MODERATELY DIFFERENTIATED

POORLY DIFFERENTIATED

NO RECORD

TUMOUR EXTENT :

INVOLVEMENT OF MUCOSA ONLY

INVOLVEMENT OF MUCOSA AND SUBMUCOSA

INVOLVEMENT OF MUSCULARIS PROPRIS

INVOLVEMENT OF SEROSA

INVOLVEMENT OF SURROUNDING ORGANS

NO RECORD

LYMPH NODE INVOLVEMENT:

PRESENT

ABSENT

NO RECORD

DISTANT METASTASIS :

LIVER

LUNG

BONE

BRAIN

PERITONEUM

OTHERS

ABSENT

NO RECORD

Section 4 :TREATMENT INFORMATION(TICK WHERE APPROPRIATE):

TREATMENT MODALITY :

SURGERY ONLY

SURGERY AND ADJUVANT CHEMOTHERAPY

SURGERY AND ADJUVANT RADIOTHERAPY

SURGERY PLUS ADJUVANT CHEMOTHERAPY AND RADIOTHERAPY

NEO-ADJUVANT CHEMOTHERAPY AND SURGERY

RADIOTHERAPY ONLY

CHEMOTHERAPY ONLY

NO RECORD

Section 5 :OUTCOME AT DATE OF DATA COLLECTION(TICK WHERE APPROPRIATE):

DEAD

ALIVE

UNDETERMINED

LOST TO FOLLOW UP