

# **Saint Paul's Hospital Millennium Medical College**

## **Department of Public Health**



Survival and its Predictors among Colorectal Cancer Patient at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, 2012-2016: A Retrospective Cohort Study.

Investigator – Mohammed Ahmed Teka (B.Sc.)

A Thesis Report Submitted to Department of Public Health St. Paul's Hospital Millennium Medical College in Partial Fulfillment of the Requirement for Degree of Master of Public Health in Field Epidemiology

July, 2018

Addis Ababa, Ethiopia



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Investigator: Mohammed Ahmed Teka <sup>1</sup>

Advisors:

Dr. Mamo Wubshet (MPH, PhD) <sup>2</sup>

Mr. Aman Yesuf (BSc. MPH) <sup>2</sup>

## Affiliations

1. St. Paul's Hospital Millennium Medical College FETP Resident
2. St. Paul's Hospital Millennium Medical College, Department of Public Health

July, 2018

Addis Ababa, Ethiopia

**SAINT PAUL'S HOSPITAL MILLENNIUM MEDICAL COLLEGE  
DEPARTMENT OF PUBLIC HEALTH**

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I, the under signed, declared that this is my bona fide original work, has never been presented in this or any other University, and that all the resources and materials used for the body of work with thesis, have been fully acknowledged.

Student Name: MOHAMMED AHMED TEKA

Signature: \_\_\_\_\_

Date: \_\_\_\_\_

Place: ADDIS ABABA, ETHIOPIA

Date of submission: \_\_\_\_\_

This body of work with thesis has been submitted for examination with our approval as Candidate's adviser.

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|-----------------------------------|--------------------|---------------|
| _____<br>Name of Primary adviser  | _____<br>Signature | _____<br>Date |
| _____<br>Name of Co-adviser       | _____<br>Signature | _____<br>Date |
| _____<br>Name of FETP Coordinator | _____<br>Signature | _____<br>Date |

## DEPARTMENT OF PUBLIC HEALTH GRADUATE STUDIES

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As members of the Board of Examiners of the final body of work with thesis open defense, we certify that we have read and evaluated the body of work with thesis prepared by Mohammed Ahmed Teka under the title “**Survival and its Predictors among Colorectal Cancer Patients at TASH 2012-2016, Addis Ababa, Ethiopia: A Retrospective Cohort Study**” and recommencement for the degree of Master of Public Health in Field Epidemiology.

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| Name of Co-adviser | Signature | Date  |

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| Name of Internal Examiner | Signature | Date  |

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***Final approval and acceptance of the body work with thesis is contingent upon the submission of the final both hard and soft copies of the body work with thesis to the department of public health.***

## **Acknowledgement**

First and foremost, I would like to say Alhamdulillah, for His (Allah's) unlimited favor in my life, for giving me patience during my study period and for accomplishing this particular work.

Secondly I would like to extend my heartfelt gratitude for my advisers Dr. Mamo Wubshet and Mr. Aman Yesuf for their unreserved comments and suggestion during the undertakings of this thesis and also St. Paul's Hospital Millennium Medical College, Department of Public Health for funding this study.

Thirdly, I wish to pass my heartfelt thanks to Dr. Jilcha Dirbi for his excellent and unforgettable contribution during tool development and data collection; Mr. Neme Wolkite and Mrs. Muluemebet H /Mariam for their cooperation during data collection and study participants and their families for their kind cooperation throughout the study period.

Last, but not least I would like to give all the credit to my lovely family for supporting me entirely during my study period, and especially for my two little angels Mariah and Afnan Mohammed who encourage me by sitting beside me while I undertake this work and inspiring my future success!!

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## List of abbreviation and acronyms

|                |                                 |
|----------------|---------------------------------|
| A.A-----       | Addis Ababa                     |
| AHR-----       | Adjusted Hazard Ratios          |
| ASIR -----     | Age Standardized Incidence Rate |
| ASMR-----      | Age Standardized Mortality Rate |
| B.Sc. -----    | Bachelor of Science             |
| CEA-----       | Carcino Embryonic Antigen       |
| CI-----        | Confidence Interval             |
| CI5-----       | Cancer in Five Countries        |
| CRC -----      | Colorectal Cancer               |
| CT-----        | Computed Tomography             |
| DM-----        | Diabetes Mellitus               |
| EHR-----       | Excess Hazard Ratio             |
| EpiData -----  | Epidemiologic Data              |
| FMOH-----      | Federal Ministry of Health      |
| GLOBOCAN ----- | Global Burden of cancer         |
| HR-----        | Hazard Ratio                    |
| IQR-----       | Interquartile Range             |
| MRI-----       | Magnetic Resonance Imaging      |
| MPH-----       | Master of Public Health         |
| M.Sc. -----    | Master of Sciences              |
| NCDs-----      | Non communicable Diseases       |
| OR -----       | Odds Ratio                      |
| RVI-----       | Retroviral Infection            |

|      |       |                                           |
|------|-------|-------------------------------------------|
| SD   | ----- | Standard Deviation                        |
| SEER | ----- | Surveillance Epidemiology and End Results |
| SPSS | ----- | Statistical Package for Social Sciences   |
| SSA  | ----- | Sub Saharan Africa                        |
| TNM  | ----- | Tumor Node Metastasis                     |
| TASH | ----- | Tikur Anbessa Specialized Hospital        |

## Abstract

**Background:** Colorectal cancer (CRC) is the third most commonly diagnosed malignancy and the fourth leading cause of cancer death globally, and it is also the first and fourth diagnosed cause of cancer in males and females respectively, accounting for about 1.4 million new cases and almost 700,000 deaths in 2012 according to the latest global burden of cancer report. In Ethiopia, it represents the fourth cause of morbidity and mortality.

**Objective:** To estimate survival time and identify its predictors among colorectal cancer patients treated at Tikur Anbessa Specialized Hospital in Addis Ababa, Ethiopia, from 2012-2016.

**Methodology:** A retrospective cohort study was conducted at Tikur Anbessa Specialized Hospital. Data was extracted from 161 colorectal cancer patient's charts and telephone interviews were conducted to ascertain vital status of the patients. Finally, data was checked for completeness and consistency each day after data extraction, and entered into EpiData v.3.1, before being exported to SPSS v.23 for final analysis. Descriptive analyses such as median, range, interquartile range, life table and Kaplan Meier analysis were computed. The overall survival was estimated using the Kaplan-Meier product limit technique. Bivariate and multi variate Cox-regression analyses were used to determine predictors of survival time for colorectal cancer patients. Adjusted Hazard Ratios with 95%CI and p values < 0.05 were considered statistically significant.

**Result:** The median age was 45 years with an interquartile range of 22 years, while the median duration of follow-up was 14 months with an interquartile range of 16 months. The median survival time was 21 months, and the overall survival rates were 71.9% and 34.7% at one year and five years, respectively. The predictors of overall survival of colorectal cancer were found to be: surgery (AHR 3.37, 95%CI:1.32-8.57), baseline carcino embryonic antigen levels >5ng/ml (AHR 2.01, 95%CI:1.14-3.57), mucinous/singent cell type (AHR 3.52, 95%CI:2.08-14.67), chemotherapy (AHR 0.52, 95%CI:0.27-0.98) and distant metastasis (AHR 2.8, 95%CI:1.32-3.94).

**Conclusion:** We found that the overall 1 year & 5 years' survival rate were 71.9% and 34.7%, respectively, with a median survival time of 21 months, and that mucinous /singent cell types, surgery, chemotherapy, distant metastasis and baseline CEA levels >5ng/ml were all strong predictors of colorectal cancer survival, indicating that these specific predictors are deserving of further attention.

**Key words:** colorectal cancer, survival time, predictors, Tikur Anbessa Specialized Hospital, Ethiopia.

# 1. Introduction

## 1.1. Background

Non communicable diseases are increasing worldwide, with cancer leading, the non-communicable diseases as a primary cause of morbidity and mortality worldwide, second only to the cardiovascular diseases ([1](#)). In numbers, this means that there are an estimated 14.1 million cancer cases and 8.2 million cancer deaths worldwide, according to the Global Burden of Cancer 2012 report ([2](#)).

The crude incidence and mortality rates of colorectal cancer in sub Saharan African countries are estimated to be approximately 28,214 (4.5%) and 21,076 (4.7%), with a five-year prevalence of 57,297(4.4%) and proportion of 1.5%. In sub Saharan Africa, the ASIR and ASMR reveal that 5.8% and 4.5% per 100,000 persons respectively, are affected by CRC. Being a sub Saharan country, Ethiopia finds itself a member of this cohort, with estimated total incidence and mortality rates of 3,805 (6.2%) and 7,361 (4.5%) respectively and a five-years prevalence of 7,361 (5.7%). The ASIR and ASMR for Ethiopia reveal that 5.3% and 7.8 % per 100,000 persons respectively, are affected by CRC. This data reveals that Ethiopia alone accounts for 14.2% of all CRC cases in sub Saharan Africa ([3](#)).

Colorectal cancer (CRC) is the third most commonly diagnosed malignancy and the fourth leading cause of cancer death in the world, accounting for approximately 1.4 million new cases and nearly 700,000 deaths in 2012 (3,4). The distribution of CRC burden varies widely, with more than two-thirds of all cases and about 60% of all deaths occurring in developed countries ([3](#)). Given the temporal profiles and demographic projections, the global burden of CRC is expected to increase by 60% to more than 2.2 million new cases and 1.1 million cancer deaths by the year 2030([3](#)). CRC, together with other cancers predominantly linked to western lifestyles are widely considered to be the clearest markers of the cancer transition; only replacing infection-related cancers in countries undergoing the rapid societal and economic changes that bring them in line with the lifestyles found in high-income countries ([4](#), [5](#)).

In 2012, the estimated incidence rates in males varied from <5 (per 100,000) in several African countries to over 40 in certain countries in Europe, North America, and Oceania. The highest rates in males were observed in Slovakia (61.6), Hungary (58.9), and the Republic of Korea (58.7), while the lowest were seen in The Gambia and Mozambique (both 1.5 per 100 000) ([6](#)).

While the annual incidence rate of CRC is 30–50/100,000 individuals in North America and Europe, it is still hovers around 37/100,000 in most Middle-Eastern countries. Cultural changes in the third-world countries have led to a rapid increase in the incidence of CRC in these countries (7, 8).

## **1.2. Statement of the Problem**

Ethiopia's large population size means that more than 86,538 Ethiopians are at risk of developing colorectal cancer (3). Each year, this terrible disease afflicts an estimated 3,805 men and women in Ethiopia, with a mortality rate of 2,947 deaths per year.(3). Crude incidence rates of colorectal cancer in the Ethiopian population aged 15 years or more are estimated to be 6.2 per 100,000 persons per year, with an ASIR of 5.3 per 100,000 persons per year: note that this incidence rate is still considerably lower than the global ASMR (in 2012), of 7.8 per 100,000 persons per year.(3).

As far as statistical measures go, the survival rate remains the best index available for evaluating the effectiveness of healthcare, diagnostic, and curative interventions in colorectal cancer patients. The difference in survival time in various geographical areas is hypothesized to be due to a number of factors, including: demographics, economic status, genetics, the environment, availability of healthcare services, histology type, tumor grade, tumor size, tumor stage, and number of co-morbid conditions such as cardiovascular disease and diabetes(3, 9). Within Ethiopia, the exact survival time and prognosis predictors for colorectal cancer remain an untouched area of study, despite their status as major and growing public health concerns. Hence, this study aims to assess the survival time and prognosis predictors for Ethiopian colorectal cancer patients, up to and including: age at time of diagnosis, gender, occupation, level of education, marital status, place of residence, smoking history, family history, co-morbidity, tumor site, tumor stage, histology type, and tumor grade. The source of the data used in this population based study stems from the Tikur Anbessa Hospital, in Addis Ababa, Ethiopia.

## **1.3. Significance of the Study**

Studying the predictors of survival for different cancers has important practical value for patients, care providers, and researchers(10). Cancer patients may wish to know how their prognosis will be changing over time, and what their life expectancy is based on the disease status, in order to make important decisions about their, or their families', future. A proper understanding of the most likely prognosis for the patient may also help both care givers and the patients themselves decide

on the best possible treatment options, carefully balancing the competing demands for the quality and quantity of the patient's life ([11](#)).

Furthermore, care providers can make use of improved survival information to more objectively determine the appropriate frequency of follow-up visits and aggressiveness of surveillance testing based on patient's current risk profile. The findings of this study might also be used as a base line for further research, in addition to its benefit for care providers and the actual victims of colorectal cancer, with regards to selecting a treatment modality in line with the survival time of the patients.

To summarize, the author hopes that the outcome of this research will further the cause of identifying CRC survival time and its predictors, and subsequently aid in planning different treatment options for patients with CRC, with the ultimate goal of decreasing morbidity and mortality from CRC. Secondly, this research may give the evidence necessary for increased efforts to develop the proper guidelines for early diagnosis and the planning of effective treatments for CRC. Finally, this paper will also contribute to filling the research gap on survival time and its predictors for CRC in Ethiopia.

## **2. Literature review**

### **2.1. Burden of cancer**

According to the latest GLOBOCAN report, published in 2012, 14.1 million new cancer cases and 8.2 million cancer-related deaths occurred in 2012, compared with 12.7 million and 7.6 million, respectively, in 2008. Prevalence estimates for 2012 show that there were 32.6 million people (over the age of 15 years) alive who had had a cancer diagnosis in the previous five years([7](#)).

The most commonly diagnosed cancers worldwide were those of the lung (1.8 million, 13.0% of the total), breast (1.7 million, 11.9%), and colorectum (1.4 million, 9.7%). The most common causes of cancer death were cancers of the lung (1.6 million, 19.4% of the total), liver (0.8 million, 9.1%), and stomach (0.7 million, 8.8% of the total cancer ) ([7](#)).

As indicated previously, global statistics indicates that colorectal cancer is the second most common cancer in women (570,000 cases, 9.4 percent of the total) and the third most common cancer in men (663,000 cases, 10.0 percent of the total) with almost 60 percent of the cases occurring in developed regions. The ASR for males was 20.4 percent versus 24.6 percent for females. Estimated deaths from colorectal cancer account for 8 percent of all cancer deaths, making colorectal cancer the fourth most common cause of death from cancer([12](#)).

The incidence of colorectal cancer, drawn from cancer registries for 1983 through 1987 and 1998 through 2002, shows that colorectal cancer increased significantly for both 27 of 51 males and females. This rise in incidence mainly involves economically transitioning countries in Eastern Europe, significant parts of Asia, and certain countries in South America. Increases in incidence were more frequent among men than among women. Considerable variations in colorectal cancer incidence trends were detected both within the aforementioned countries, as well as among various ethnicities ([12](#), [13](#)).

Drawing from information abstracted from various cancer registries (1998-2002), the highest worldwide colorectal ASR for males was found in the Czech Republic at 59.1%, followed by males in New Zealand at 49.0%. For females the highest ASR was found in New Zealand at 39.5%, followed by Australia (South) at 34.1%. The lowest ASR for males was reported in Mumbai, India at 5.9%, followed by Quito, Ecuador at 8.4%. For females, the lowest ASR was also reported in Mumbai, India at 4.4%, followed by Quito, Ecuador at 8.9%([14](#)).

## 2.2. Survival time and its predictors

The correlation between colorectal cancer survival and age is still uncertain. Although worse prognoses of the disease in young patients were reported by many researchers ([15](#)), upon analyzing the data obtained from the Ontario (Canada) cancer registry, the relative odds of early death at 1 year in fact increased by 85 percent in the age range of 65-69 years, as compared with the age range of 40-49 years ([16](#)). Hazard ratios of death at 1 year for white and black patients registered in the national cancer data base increased by 37 and 38 percent, respectively, within the age range of 61-64 years, as compared with the age range of 18-49 years([17](#)). Contrary to these findings, a study conducted on 230 colorectal cancer patients with stage I-III cancer at a Beijing cancer hospital found no significant differences in survival rates among younger ( $\leq 40$  years) patients and older ( $\geq 40$  years) patients ([18](#)).

Furthermore, another study demonstrated that survival for patients younger than 65 years of age improved over time when compared to older patients. The study attributed this improvement to an increase in the use of adjuvant treatment in younger patients, as well as greater resilience to the negative effects of surgery([19](#)).The effect of adjuvant therapy on improving cancer-related survival rate was also reported for patients younger than 50 years of age with rectum cancer([19](#)).

The relationship between sex and colorectal cancer survival varies from one population to another, and is generally an area needing further investigation, as the causal relationships between this factor and survival outcomes are not well established. Results of one study showed that within most of the included regions, the survival rate of CRC patients was not significantly affected by the patient's sex. However, some studies have demonstrated better survival among females, but this advantage did not exceed five percent in most of the registries([20](#)). The same study found these differences between the two sexes in a few specific regions. In Malta, the 5year relative survival rates for female patients were better than those of male patients by a difference of 20 percent for colon cancer, 17.8 percent for rectum cancer, and 19.8 percent for colorectal cancer. In the Navarre region, among the Spanish registries, the survival rate for females was higher by 15.4 percent for rectum cancer. Conversely, better survival rates for male patients with rectum cancer were observed in the Ragusa, Italy registry and the Netherlands (South) registries where the differences were 12.5 percent and 12.9 percent, respectively([20](#)).

In another study, the effect of sex on survival rate was investigated for 52,822 patients with metastatic colorectal cancer from 1988-2004. Patients were registered in the Surveillance, Epidemiology and End Results (SEER) programme. As per the study, it was found that young women less than 45 years of age had better overall survival rates than men of the same age by 20 percent at the seventeenth month, whereas the rates became worse for women more than 55 years of age as compared with men of the same age ([21](#)).

Rectum surgery is technically more difficult in men, so local spread and nodal clearance may be inadequate. Reasons for better survival rates in younger females when compared to men of the same age need further investigation. Many researchers have suggested that oestrogen inhibits CRC progression, thus explaining why better survival is often observed in premenopausal women([22](#)).

All other factors aside, stage of tumour at time of diagnosis is indisputably the most important predictor of survival. Patients' survival from CRC was estimated for the different stages (i.e. Stage I through IV) of tumour at diagnosis([23](#)). The findings indicated that survival rates became shorter as the cancer spread beyond the origin site. Thus, the highest survival rate was found for patients with localized tumour stage (Stage I) and the lowest for the distant tumour stage (Stage III). This result was found regardless of patient's race ([24](#)), quality of health care services ([25](#)), treatment type ([26](#)), and/or the site of the tumour ([27](#)). In a cohort study undertaken to examine the prognosis factors in CRC patients, the 5-year survival rates of CRC were 68 percent for Stage II, 44 percent for Stage III and 2 percent for Stage IV([28](#)).

The different histological types of colorectal cancer tumors have also been investigated. In one study, it was reported that patients with rectum cancers that rose from a polyp, adenoma, and/or carcinoid had 5-year survival rates ranging from 85 percent to 90 percent the highest rate among various histological types. In the same study, the poorest 5-year survival rates (i.e. less than 30 percent) were estimated for small cell and adenosquamous colon cancer, whereas for rectum cancer, the poorest 5-year survival rates were for undifferentiated, small cell and melanoma histological types ([29](#)). Another study demonstrated that patients with different papillary adenocarcinoma had the best survival; moderately differentiated and mucinous adenocarcinoma had moderate survival; and poorly differentiated adenocarcinoma had the poorest prognosis ([30](#)). Furthermore, researchers found that five-year survival rates between sub-sites or between colon cancer and rectum cancer were not significantly different (64.0 percent for colon cancer and 62.7

percent for rectum cancer), but the other two sub-sites (overlapping and non-overlapping sites) had much poorer survival outcomes. Distinct differences, however, were shown for patients with stage II colorectal cancer, where the 5-year survival rate was 82.7 percent and 69.7 percent for colon and rectum cancers, respectively(30). In addition, mucinous tumors were found to have worse survival when compared with non-mucinous tumors; their 5-year survival rates were 51 percent and 69 percent, respectively, while signet ring tumors were worse (for both mucinous and non-mucinous tumors) with a 5-year survival rate of 27 percent(31).

Another study found somewhat different results, asserting that the survival rate for colon cancer was significantly higher than that of rectum cancer(32). In a recent study in which the survival rates of colon and rectum cancers were investigated at different survival times, patients with colon cancer had a worse 1 year survival rate, whilst they had better 2, 3, 4, and 5 year survival rates compared to patients with rectum cancer(33). Definitive surgery and adjuvant chemotherapy were found to contribute to the variations in colon cancer survival in New Zealanders. The hazard ratio was reduced significantly to 0.24 for patients who underwent definitive surgery and to 0.55 for patients who received adjuvant chemotherapy(34).

In a study done to evaluate laparoscopic surgery versus open colectomy in colorectal cancer patients, no significant differences were observed in the 5-year survival rates between the two methods. Depending on cancer stage, 5-year survival rates ranged from 0 to 100 percent for the laparoscopic method and 0 to 89.7 percent for the open surgical method(35).

In a retrospective cohort study done to identify the prognostic factors of survival of colorectal cancer in Kurdistan province, Iran, with a total number of 335 patients affected by CRC, the results showed that 1 and 5 year survival rates were 87% and 33%, respectively(36).

In a similar retrospective cohort study conducted at the University Malaya Medical Centre (UMMC) in Kuala Lumpur, Malaysia to determine the survival rate and its predictors among 1,212 patients, the median survival for colorectal, colon, and rectal cancers were 42.0, 42.0, and 41.0 months respectively; while the 1, 3, and 5 year relative survival rates ranged from 73.8 to 76.0%, 52.1 to 53.7%, and 40.4 to 45.4% respectively(37).

In a retrospective overall survival (OS) analysis of CRC data for the period 1994–2004 done in Saudi Arabia, the five-year OS was 63.3% for patients with localized disease, 50.2% for those with

regional disease, and 14.7% for patients with metastases. According to the Cox regression analysis, age and extent were significant prognostic factors of survival in patients with colon cancer the risk was higher in patients with distant metastasis (HR 2.53; 95%CI: 1.17-5.45;  $p=0.01$ )([38](#)). In a study conducted in Jordan, a total of 3,005 patients with CRC were registered during 2005–2010. The overall 5 years and 10years survival rates for patients with CRC were 58.2% and 51.8%, respectively. The 5-year survival rate decreased significantly from 60.4% for the age <50 years to 49.3%for the age  $\geq 70$  years ( $P < 0.005$ ). The 5-year survival rate was 72.1% for the localized stage, 53.8% for the regional stage, and 22.6% for the distant metastasis. In the multivariate analysis, the only factors that were significantly associated with survival were age, grade, stage, and location of tumor([39](#)).

In a retrospective single institution review done in department of surgery, the Royal Brisbane and Women's Hospital in Australia investigated outcomes for 379 patients undergoing surgical resection of their primary colon or rectal cancer. Of these patients, thirty-five (9.2%) died in the post-operative period, with an overall morbidity of 48.3%. Furthermore, it was demonstrated that the thirty days post-operative mortality was independently associated with medical complication ( $p=0.001$ ) and age ( $\geq 70$ ;  $p=0.007$ ) using regression analysis([40](#)).

A case control study done to identify risk factors and survival from colorectal cancer in black patients in Soweto,South Africa demonstrated a relatively short median survival time of only 7.5months([41](#)).

In Ethiopia studies assessing knowledge and attitude towards colorectal cancer and colorectal cancer screening are limited, and there is no data on the survival time of colorectal cancer patients and the predictors of this survival time. Studying survival time and its predictors in our country will help health professionals in cancer treatment centers accurately assess the quality of care they provide. Prediction of prognosis would as such be based on evidence and local circumstances. This research will also provide the concrete evidence necessary to make effective recommendations for improving the survival time of colorectal cancer patients. Thus, this study will assess and contribute to the current knowledge about survival time and predictors of survival for colorectal cancer patients in TASH Addis Ababa, Ethiopia, 2017.

### **3. Objectives**

#### **3.1. General Objective**

- To estimate survival time and identify its predictors among colorectal cancer patients treated at Tikur Anbessa Specialized Hospital in Addis Ababa, Ethiopia, from 2012-2016.

#### **3.2. Specific Objectives**

- To estimate survival time of colorectal cancer patients treated at Tikur Anbessa Specialized Hospital
- To identify predictors of survival time of CRC patients treated at Tikur Anbessa Specialized Hospital.

## **4. Methods and Materials**

### **4.1. Study Design**

A Hospital based Retrospective Cohort Study Design was conducted.

### **4.2. Study Area and Period**

This study was conducted in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia. The study period was from January 1<sup>st</sup>, 2012 to December 31<sup>st</sup>, 2016, selected purposively with the intent of acquiring relatively complete data by consulting the senior oncologist working in the hospital while the data collection period was from October 1<sup>st</sup> to 30<sup>th</sup>, 2017. TASH is a teaching and central tertiary generalized referral hospital with approximately 800 in-patient beds, and was constructed in the early 1960's([42](#)).

The hospital serves as the only oncologic center which provides outpatient day care and inpatient chemotherapy and radiotherapy service. There are currently four oncologists, one hematologist, three radiotherapists, and 15 nurses working at the cancer center ([42](#)).

TASH aspires to become a center of excellence in the diagnosis, treatment, and care of patients with cancer. With the support of Ethiopia's governmental institutions, non-governmental organizations, and international partners, the hospital hopes to develop a comprehensive cancer care program; including a cancer registry, early detection measures, prevention techniques, standard treatment practices and palliative care([42](#)).

### **4.3. Source & study populations**

#### **4.3.1. Source Populations**

All newly diagnosed colorectal cancer patients in TASH who were diagnosed from January, 2012 to December, 2016.

#### **4.3.2. Study Populations**

All colorectal cancer patients in TASH who were diagnosed from January, 2012 to December, 2016 and who fulfill the eligibility criteria.

### **4.4. Inclusion and Exclusion Criteria**

All histopathologically confirmed colorectal cancer patients who also started the treatment during the required period (2012-2016) were included in the study.

Patients whose follow up periods were less than a month, and patients with diagnoses of precancerous lesions were excluded from the study.

## **4.5. Study Variables**

### **4.5 .1. Dependent (outcome) Variable:**

- Survival time of patients from confirmed CRC

### **4.5.2. Independent Variables /Covariates:**

- Age of patients at time of diagnosis
- Marital status
- Sex
- Presence of co-morbid illness
- Place of residence
- Stage of cancer at time of diagnosis
- Location of cancerous lesion
- Vascular invasion
- Regional LN involvement
- Residual tumor
- Histological types
- Treatment modality

## **4.6. Operational Definitions**

- Follow up time: In this study follow up time was from first date of confirmed diagnosis with CRC to death from CRC, lost follow up /withdrawal, or end of the study (December 31<sup>st</sup>, 2016).
- Follow up: In this study follow up was defined as the time from December 31<sup>st</sup>, 2016 to January 1<sup>st</sup>, 2012 retrospectively.
- Event: For this study the event of interest is defined as death of CRC patient before the end of study period (December 30<sup>th</sup>, 2016).
- Censored: For this study censored cases are those patients who are alive at the end of the study period (December 31<sup>st</sup> 2017), who were lost to follow up, or whose status was unknown during the study period.
- Survival time: In this study survival time is defined as the time from date of confirmed diagnosis to death from colorectal cancer.

## **4.7. Data Collection Tools and procedure**

### **4.7.1. Data Collection Tools/Checklists**

Data extraction checklist which consists of socio-demographic characteristics, natural history of the disease, and prognostic predictors/clinical characteristics variables about the study subjects were prepared; no personal identifiers were included. Instead, individuals were given unique identifiers/code numbers to be attached to the data extraction checklists (Annex II).

### **4.7.2. Data Collection Procedure and Data collector**

Data was collected by two clinical oncology residents who were working at the cancer treatment center from October 1<sup>st</sup> to 30<sup>th</sup>, 2017.

Before the actual data extraction task was started, all medical registration numbers of colorectal cancer patients in the years 2012 to 2016 were obtained from the data base of the cancer registry, from outpatient's register, and from the inpatients register. In addition, all identified colorectal cancer patient's charts were retrieved from the cancer treatment center chart archives/card room by two card handlers who were working in the archive.

All the retrieved patient's charts were checked for eligibility by the principal investigator daily and data extraction was made by the above mentioned data collector.

Since most of the patient's charts had no documented vital status of the patients, phone calls were made by the principal investigator to ascertain the vital status of the patients and some other variables which were missed in the chart each day during data collection.

All colorectal cancer patients with unknown vital status, who were lost to follow up, and/or who did not develop the event of interest at the end of the study period were considered as censored in this study.

#### **4.7.3. Data Quality Assurance**

The data extraction check list was prepared in English language and pretesting of the checklist was done on ten randomly selected colorectal cancer patient's charts, of which five of the charts were preceding 2012 and the remaining five charts were from 2017. Patient charts were examined for clarity, comprehensibility, flow of the questions, and the time needed to fill the checklists: based on these findings, some of the questions were restructured.

During data collection the principal investigator daily checked the filled checklists for completeness and consistency. Incomplete and misfiled checklists were sent back to the data collector for correction.

#### **4.7.4. Data Processing and Analysis**

Data entry and analysis were performed by the principal investigator (PI) using EpiData v.3.1 and Statistical Software for Social Sciences (SPSS) v.23 statistical software package.

The principal investigator before and during the actual data entry performed coding and data cleaning; any error identified during data entry was corrected after tracing and revising the originally completed data extraction checklists.

Once the cleaned and edited data was ready for statistical analysis, data analysis was performed by the principal investigator using SPSS v.23 statistical software.

Descriptive analysis such as median, standard deviation, range, interquartile range, life table and Kaplan Meier analysis was also performed.

For the bivariate analysis, Cox regression was fitted at less than 20% level of significance, and all independent variables with p-values less than 0.2, as well as some clinically important variables which were included in the multivariable analysis.

For the multivariable analysis, Cox regression was fitted at 5% level of significance to identify the independent predictors of survival time from colorectal cancer patients.

The proportional hazard assumption for the model was checked by Schoenfeld residual test and the result of the model was expressed as adjusted hazard ratios with 95% confidence interval, and all results with p-values less than 0.05 were considered significant.

#### **4.8. Ethical Considerations**

An ethical clearance was obtained from the research and ethical committee of St. Paulos Hospital Millennium Medical College, Department of Public Health and a letter of cooperation was obtained from Tikur Anbessa Specialized Hospital research directorate to Oncology department and Surgery department.

Informed verbal consent was also obtained from the respondents before starting phone call interviews by the principal investigator. Privacy of participants was highly maintained throughout the study by anonymously excluding their names as identification from data extraction checklists and confidentiality was highly maintained by using the data for the purpose of the proposed study only.

## 5. Result

### 5.1. Socio-demographic characteristics of Colorectal Cancer patients in TASH

A total of 161 colorectal cancer patient charts were accessed and reviewed in this study. Accordingly, the median age (range) at diagnosis was 45 (16-85) years with interquartile range (IQR) of 23 years. Ninety-nine (61.5%) of colorectal cancer patients were below 50 years and male patients account for 102 (63.4%) of colorectal cancer patients and 127 (78.9%) of colorectal cancer patients were married and almost half (50.9%) of colorectal cancer patients were residents of Addis Ababa (Table 1).

**Table 1. Distribution of socio-demographic characteristics of colorectal cancer patients treated at TASH, Addis Ababa, Ethiopia 2012-2016 (N=161)**

| Variables          | Outcome          |              |               |
|--------------------|------------------|--------------|---------------|
|                    | Censored<br>N(%) | Dead<br>N(%) | Total<br>N(%) |
| Gender             |                  |              |               |
| Male               | 53(52)           | 49(48)       | 102(63.4)     |
| Female             | 33(55.9)         | 26(44.1)     | 59(36.6)      |
| Marital Status     |                  |              |               |
| Single             | 12(38.7)         | 19(61.3)     | 31(19.3)      |
| Ever Married       | 74(56.9)         | 56(43.1)     | 130(80.7)     |
| Age category       |                  |              |               |
| <50                | 53(53.5)         | 46(46.5)     | 99(61.5)      |
| 50-59.9            | 14(51.9)         | 13(48.1)     | 27(16.8)      |
| 60-69.9            | 15(57.7)         | 11(42.3)     | 26(16.1)      |
| 70+                | 4(44.4)          | 5(55.6)      | 9(5.6)        |
| Educational Status |                  |              |               |
| Illiterate         | 22(50)           | 22(50)       | 44(27.3)      |
| Primary Level      | 25(62.5)         | 15(37.5)     | 40(24.8)      |
| Secondary Level    | 27(47.4)         | 30(52.6)     | 57(35.5)      |
| Tertiary Level     | 12(60)           | 8(40)        | 20(12.4)      |
| Residence (Region) |                  |              |               |
| Addis Ababa        | 52(63.4)         | 30(36.6)     | 82(50.9)      |
| Oromia             | 11(35.5)         | 20(64.5)     | 31(19.3)      |
| Amhara             | 8(33.3)          | 16(66.7)     | 24(14.9)      |
| Others             | 9(37.5)          | 15(62.5)     | 25(14.9)      |

Others\_SNNPR, Somali, Diredawa, Tigray & Harari Regional States of Ethiopia.

## 5.2. Clinical and pathological characteristics of colorectal cancer patients in TASH

Out of 161 colorectal cancer patients who sought care at Tikur Anbessa specialized hospital 109(67.7%) patients had colonic cancer followed by 32(19.9%) of patients with rectal cancer with the dominant histologic type of adenocarcinoma 156(96.9%) of all colorectal cancer patients. Ninety (55.5%) of colorectal cancer patients had well differentiated carcinoma, followed by moderately differentiated and poorly differentiated carcinoma while 77(48.8%) of patients were diagnosed as stage IV disease followed by 57(35.4%) of them as stage II disease whereas 82(50.9%) of colorectal cancer patients had elevated baseline carcino embryonic antigen level before surgery with 81(50.3%) of colorectal cancer had distant metastasis to one or more adjacent organs (Table 2).

**Table 2. Clinical & pathological characteristics of colorectal cancer patients treated at TASH Addis Ababa, Ethiopia 2012-2016 (N=161).**

| Variables                 | Outcome          |              |               |
|---------------------------|------------------|--------------|---------------|
|                           | Censored<br>N(%) | Dead<br>N(%) | Total<br>N(%) |
| Tumor location            |                  |              |               |
| Colon                     | 63(57.8)         | 46(42.2)     | 109(67.7)     |
| Recto sigmoid             | 9(52.9)          | 8(47.1)      | 17(10.6)      |
| Rectum                    | 12(37.5)         | 20(62.5)     | 32(19.9)      |
| Anorectal                 | 2(66.7)          | 1(33.3)      | 3(1.9)        |
| Histologic Type           |                  |              |               |
| Adenocarcinoma            | 86(55.1)         | 70(44.9)     | 156(96.9)     |
| Mucinous/singent          | 0(0)             | 5(100)       | 5(3.1)        |
| Histologic Grades         |                  |              |               |
| Well differentiated       | 56(62.2)         | 34(37.8)     | 90(55.9)      |
| Moderately differentiated | 17(47.2)         | 19(52.8)     | 36(22.4)      |
| Poorly differentiated     | 12(35.5)         | 22(64.7)     | 34(21.1)      |
| Anaplastic                | 1(100)           | 0(0)         | 1(0.6)        |
| TNM staging               |                  |              |               |
| Stage I                   | 4(80)            | 1(20)        | 5(3.1)        |
| Stage II                  | 41(71.9)         | 16(28.1)     | 57(35.4)      |
| Stage III                 | 13(59)           | 9(40.9)      | 22(13.7)      |
| Stage IV                  | 28(36.4)         | 49(63.6)     | 77(47.8)      |
| Surgery                   |                  |              |               |
| No                        | 20(80)           | 5(20)        | 25(15.5)      |
| Yes                       | 66(48.5)         | 70(51.5)     | 136(84.5)     |
| Chemotherapy              |                  |              |               |
| No                        | 13(50)           | 13(50)       | 26(16.1)      |
| Yes                       | 73(54.1)         | 62(45.9)     | 135(83.9)     |
| Distant Metastasis        |                  |              |               |
| No                        | 55(68.8)         | 25(31.2)     | 80(49.7)      |
| Yes                       | 31(38.3)         | 50(61.7)     | 81(50.3)      |
| Vascular Invasion         |                  |              |               |
| No                        | 85(54.5)         | 71(45.5)     | 156(96.9)     |
| Yes                       | 1(20)            | 4(80)        | 5(3.1)        |
| Baseline CEA              |                  |              |               |
| Not elevated (>5ng/ml)    | 56(70.9)         | 23(29.1)     | 79(49.1)      |
| Elevated (<5ng/ml)        | 30(36.6)         | 52(63.4)     | 82(50.9)      |

### 5.3. Survival time of colorectal cancer patients from initial diagnosis

From a total of 161 colorectal cancers whose charts were reviewed, 75(46.6%) of them died during the entire 60 months of follow-up period. The median(range) duration of follow up was 14 months (1-60 months) with interquartile range of 16 months while median survival time was 21 months. The overall 1-year and 5-year survival rates were 71.9 % and 34.7% respectively (Annex I). As we can see from survival curve below the overall survival was less than 40% at the end of the follow up period for those who survive till the end of the follow-up period that is 60 months (Figure 1).

As depicted by the life table below the proportion of surviving beyond the time interval 0-5 was 94% with cumulative survival of 94% while the survival proportion beyond 12-17 months was 72% with cumulative survival of 55% and the survival proportion beyond 24-29 months was 92% with cumulative proportion of 42% (Table 3).

**Table 3. Life table of colorectal cancer cases treated in the period of 2012–2016 at Tikur Anbessa Specialized Hospital Addis Ababa Ethiopia.**

| Interval Start Time(in months) | Number at the beginning of interval | Number of Withdrawal cases | Number of patients exposed to risk | Number of deaths | Survival proportion | Cumulative survival proportion |
|--------------------------------|-------------------------------------|----------------------------|------------------------------------|------------------|---------------------|--------------------------------|
| 0-5                            | 161                                 | 12                         | 155.000                            | 10               | 0.94                | 0.94                           |
| 6-11                           | 139                                 | 15                         | 131.500                            | 23               | 0.83                | 0.77                           |
| 12-17                          | 101                                 | 17                         | 92.500                             | 26               | 0.72                | 0.55                           |
| 18-23                          | 58                                  | 9                          | 53.500                             | 9                | 0.83                | 0.46                           |
| 24-29                          | 40                                  | 8                          | 36.000                             | 3                | 0.92                | 0.42                           |
| 30-35                          | 29                                  | 3                          | 27.500                             | 2                | 0.93                | 0.39                           |
| 36-41                          | 24                                  | 6                          | 21.000                             | 1                | 0.95                | 0.37                           |
| 42-47                          | 17                                  | 5                          | 14.500                             | 1                | 0.93                | 0.35                           |
| 48-53                          | 11                                  | 4                          | 9.000                              | 0                | 1.00                | 0.35                           |
| 54-60                          | 7                                   | 7                          | 3.500                              | 0                | 1.00                | 0.35                           |

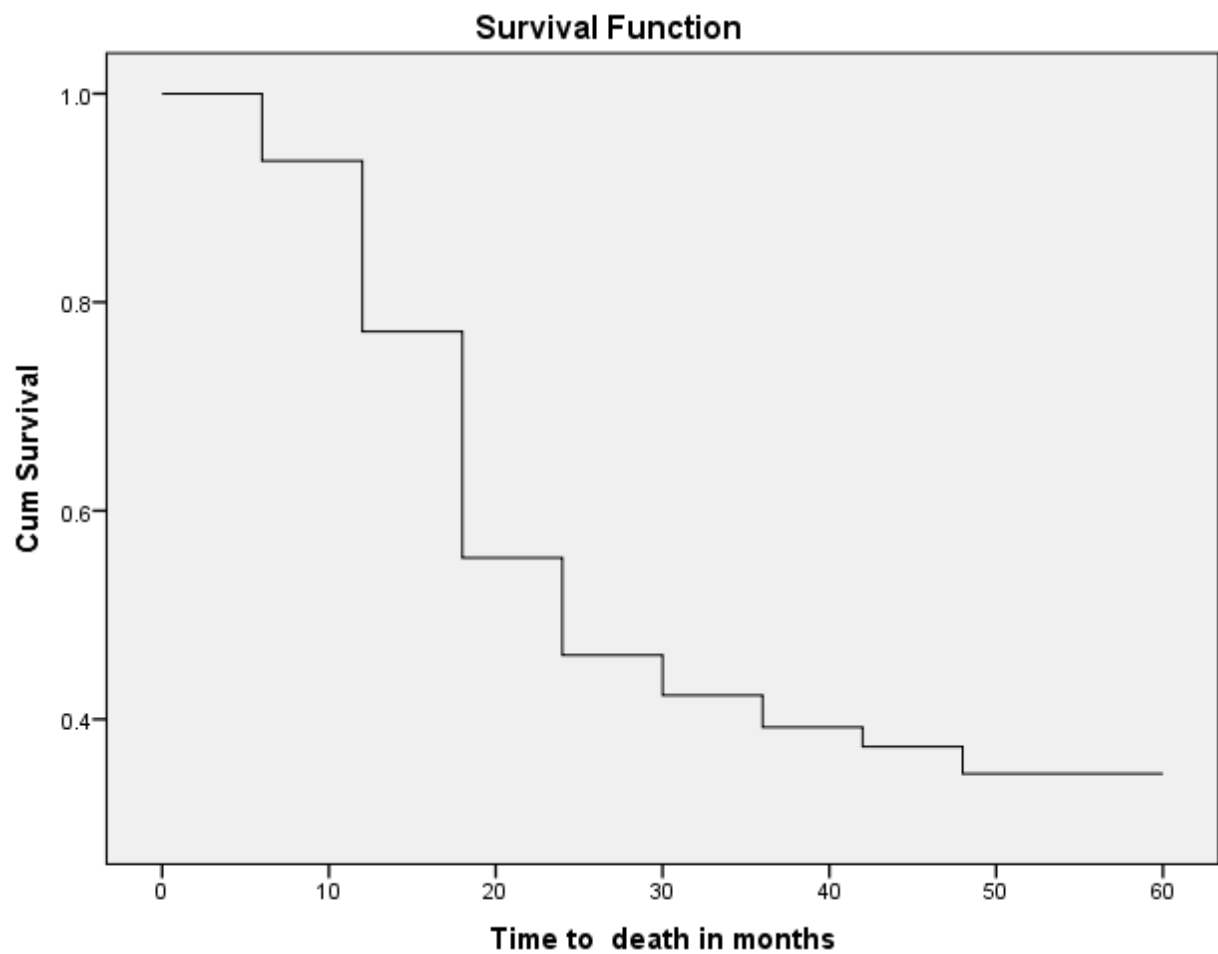


**Figure 1.** Kaplan Meier survival curve for time to death among colorectal cancer patients treated at TASH, Addis Ababa, Ethiopia 2012-2016.

### 5.3. Bivariate Cox's Regression Analysis result of colorectal cancer patients in TASH

The bivariate Cox's regression analysis showed that, marital status( $P=0.046$ ), histologic type of cancer ( $P=0.001$ ), vascular invasion ( $p=0.032$ ), undergoing surgery ( $P=0.034$ ), and baseline CEA level ( $P=0.0001$ ) were significantly associated whereas the rest variables were not significant during bivariate cox's regression analysis (Table 4).

**Table 4. Bivariate Cox's regression analysis result of predictors of colorectal cancer survival in TASH**

| Variables              | N(%)      | Crude HR | P-Value |
|------------------------|-----------|----------|---------|
| Sex                    |           |          |         |
| Male                   | 102(63.3) | 1.0      | -       |
| Female                 | 59(36.7)  | 0.75     | 0.244   |
| Marital Status         |           |          |         |
| Single                 | 31(19.3)  | 1.0      | 0.046*  |
| Ever married           | 130(80.7) | 1.70     |         |
| Educational Status     |           |          |         |
| Illiterate             | 44(27.3)  | 1.0      | -       |
| Primary education      | 40(24.8)  | 1.06     | 0.830   |
| Secondary & Above      | 77(47.8)  | 0.75     | 0.348   |
| Tumor location         |           |          |         |
| Colon                  | 109(67.7) | 1.0      | -       |
| Recto –Sigmoid J.      | 17(10.6)  | 1.09     | 0.927   |
| Rectum                 | 32(19.9)  | 1.07     | 0.946   |
| Anorectal              | 3(1.8)    | 1.20     | 0.859   |
| Histologic Type        |           |          |         |
| Adenocarcinoma         | 156(96.9) | 1.0      |         |
| Mucinous /singent      | 5(3.1)    | 4.87     | 0.001*  |
| Histologic Grades      |           |          |         |
| Well Diff.             | 90 (55.9) | 1.0      | -       |
| Moderately Diff.       | 36(22.4)  | 1.13     | 0.666   |
| Poorly Diff.           | 34(21.1)  | 2.31     | 0.002*  |
| Anaplastic             | 1(0.6)    | 0.000    | 0.970   |
| TNM staging            |           |          |         |
| Stage I                | 5(3.1)    | 1.0      | -       |
| Stage II               | 57(35.4)  | 1.14     | 0.897   |
| Stage III              | 22(13.7)  | 1.91     | 0.539   |
| Stage IV               | 77(47.8)  | 3.69     | 0.197   |
| Vascular Invasion      |           |          |         |
| No                     | 156(96.9) | 1.0      | -       |
| Yes                    | 5(3.1)    | 3.02     | 0.032*  |
| Surgery                |           |          |         |
| No                     | 25(15.5)  | 1.0      | -       |
| Yes                    | 136(84.5) | 2.68     | 0.034*  |
| Chemotherapy           |           |          |         |
| No                     | 26(16.1)  | 1.0      | -       |
| Yes                    | 135(83.9) | 0.72     | 0.274   |
| Baseline CEA           |           |          |         |
| Not elevated (<5ng/ml) | 79(49.1)  | 1.0      | -       |
| Elevated (>=5ng/ml)    | 82(50.9)  | 2.723    | 0.0001* |
| Distant Metastasis     |           |          |         |
| No                     | 80(49.7)  | 1.0      | -       |
| Yes                    | 81(50.3)  | 2.584    | 0.001*  |

\*all variables less than P- value 0.2 were included in the bivariate Cox's regression model

#### 5.4. Predictors of survival time of colorectal cancer patients treated in TASH

The multivariable Cox's regression showed that histologic type (HR, 5.52,95%CI:2.08-14.67), baseline CEA level (AHR,2.01,95%CI:1.14-3.57), surgery (AHR3.37,95%CI:1.32-8.57), chemotherapy (AHR,0.52,95%CI:0.27-0.98), and distant metastasis (AHR,2.82,95%CI:1.32-3.94) were significant predictors of survival time of colorectal cancer patients (Table 5) for all significance levels between 0.80 and 0.95.

**Table 5. Predictors of time to death of colorectal cancer patients treated at TASH, Addis Ababa, Ethiopia 2012-2016**

| Variables                        | N(%)      | CHR       | AHR(95%CI)       | P-value |
|----------------------------------|-----------|-----------|------------------|---------|
| Histologic types                 |           |           |                  |         |
| Adenocarcinoma                   | 156(96.6) | 1.0       | 1.0              | 0.001*  |
| Mucinous /singent cell carcinoma | 5(3.1)    | 4.8<br>67 | 5.52(2.08-14.67) |         |
| Baseline CEA level               |           |           |                  |         |
| Not elevated (<5ng/ml)           | 79(40.1)  | 1.0       | 1.0              | 0.017*  |
| Elevated (≥5ng/ml)               | 82(50.9)  | 2.7<br>23 | 2.01(1.14-3.57)  |         |
| Surgery                          |           |           |                  |         |
| No                               | 25(15.5)  | 1.0       | 1.0              | 0.011*  |
| Yes                              | 136(84.5) | 2.6<br>8  | 3.37(1.323-8.57) |         |
| Chemotherapy                     |           |           |                  |         |
| No                               | 26(16.1)  | 1.0       | 1.0              | 0.042*  |
| Yes                              | 135(83.9) | 0.7<br>16 | 0.52(0.27-0.98)  |         |
| Distant Metastasis               |           |           |                  |         |
| No                               | 80(49.7)  | 1.0       | 1.0              | 0.003*  |
| Yes                              | 81(50.3)  | 2.5<br>84 | 2.82(1.32-3.94)  |         |

\*Statistically significant at P-value 0.05, CHR (Crude Hazard Ratio), AHR (Adjusted Hazard Ration)

## 6. Discussion

The aim of this retrospective cohort study was to estimate survival time (rate) and associated predictors of CRC patients in Tikur Anbessa Specialized Hospital. Our study shows 1-to -5 years' survival rates of 71.9 % and 34.7 % respectively. The median survival time was 21 months. The results of multivariate Cox's regression showed that histologic type, baseline CEA level, surgery, chemotherapy and distant metastasis to one or more organs to be significant predictors of colorectal cancer survival.

In our study the median survival found was 21 months in which more than fifty percent of colorectal cancer patients in our setup survive nearly for two years and this finding is better than the study finding of Soweto, South Africa where the median survival found was 7.5 months([41](#)).

Overall survival of 1 year and 5 years among colorectal cancer patients in the study was 71.9% 34.7% respectively. There were no similar study in our set up for comparison with our finding but this study similar with the findings in Asian countries like Kurdistan province of Iran([36](#)) , but this finding was lower than developed countries, which can be explained by the great disparities in socio economic, quality of health care services and life style of colorectal cancer patients.

Both bivariate and multivariable Cox's regressions showed that there was significant association between histologic type and survival time of colorectal cancer patients (AHR,5.52,95%CI,2.08-14.67) which showed that colorectal cancer patients with mucinous / singent cell carcinoma type had 5.5 times greater risk of dying compared to colorectal cancer patients with adenocarcinoma histologic type, this finding is consistent with the study finding done ([30](#)).

Both bivariate and multivariate Cox's regressions showed that surgery had significant association with survival from colorectal cancer (AHR, 3.37, 95%CI: 1.32-8.07),that colorectal cancer who underwent surgery had 3.37 times more risk of dying as compared to colorectal cancer patients who had no surgery, this finding was similar to the study finding in Australia([40](#)) but against with the study findings among New Zealanders ([34](#))which can be explained that since our patients come from different region of the country and most of them were at advanced stage of cancer they might be unable to cope up the post-surgery complication but this finding needs further investigation.

Both bivariate and multivariate analyses showed that there was significant association between chemotherapy and survival time of colorectal cancer patients (AHR,0.52,95%CI,0.27-0.98), which shows that colorectal cancer patients who took chemotherapy had 52% less risk of dying compared

to colorectal cancer patients who did not take chemotherapy, this finding was consistent with the study finding done in New Zealand ([34](#)).

Both the bivariate and multivariate Cox's regressions showed that elevated carcino embryonic antigen level was significant predictor of time to death from colorectal cancer with (AHR 2.31, 95%CI: 1.30-4.11) in which colorectal cancer patients with elevated baseline CEA level had 2.31 times more likely to die from colorectal cancer compared to patients with low baseline CEA level, this finding was similar with the findings done in Malaysian tertiary hospital, Malaysia([37](#)).

Both bivariate and multivariate Cox's regression showed that there was significant association between distant metastasis and survival from colorectal cancer (AHR 2.82, 95%CI: 1.32-3.94) which indicates that colorectal cancer with distant metastasis had 2.8 times risk of dying compared to colorectal cancer patients who had no distant metastasis, this finding was similar with the findings of study conducted in Saudi Arabia([38](#)).

There is no significant difference in time to death between males and female both in bivariate and multivariate Cox's regression analysis, this finding was similar with the Jordanian study ([39](#)) and can be explained that there is no difference in the incidence of colorectal cancer in both sexes.

## **7. Strength and Limitation of the study**

### **Strength of the study**

- Despite the burden of colorectal cancer in our country, there was no published work regarding to the survival of colorectal cancer, our study was first of its kind in survival study.
- Despite the presence of some limitation related to being secondary data, we believe that the finding of our study brought strong evidence regarding predictors of survival of colorectal cancer patients in our country.
- Phone interview was done to ascertain the vital status of the patients.

### **Limitation of the study**

- Inadequate record keeping and documentation was the main limitation faced to this study which affect in recruiting more patients.
- There were incomplete patients charts during data collection, though the incomplete charts were less than 10% of the total charts it doesn't affect the overall result of the study and we tried to fill the incomplete data as much as we can with telephone interview.

## **8. Conclusion**

The overall 1 year & 5 years' survival rate were 71.9% and 34.7%, respectively, with a median survival time of 21 months which is comparable with Asian countries but lower than population from developed nations. We found that mucinous /singent cell types, surgery, chemotherapy, distant metastasis and baseline CEA levels >5ng/ml were all strong predictors of colorectal cancer survival, indicating that these specific predictors are deserving of further attention.

## **9. Recommendation**

### **The following recommendations were drawn from our study**

#### **Patients**

- We strongly recommend colorectal cancer patients to improve their health seeking behavior since most patients were in advanced stage that contribute for poor overall survival

#### **TASH/Care providers**

- We strongly recommend the hospital to utilized the findings of our study to work on the modifiable predictors of survival time such as CEA level and Surgery so as to prolong the survival time of colorectal cancer patients.
- We believe that chemotherapy prolong patient's survival, it is better to focus on chemotherapy for all candidate patients as per the standard.

#### **FMOH /Policy Makers**

- We found that the overall survival is poor, FMOH shall work on comprehensive colorectal cancer care including early detection, treatment and palliative care is mandatory

#### **Researchers**

- We strongly recommend that further research has to be conducted that will overcome the limitation of our study particularly a variety of prospective study.

## 10. Reference

- 1.Global burden of cancer. Yale journal of Biology and MEDICINE2010;.79(3-4):85-94.
- 2.Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics. 2005;55:74-108.
- 3.Ferlay J, Soerjomataram I, Ervik M, et al. Cancer Incidence and Mortality Worldwide,GLOBOCAN 2012 v1.0. 2013.
- 4.Bray F. Transitions in human development and the global cancer burden. 2012 54-68.
- 5.Center MM, Jemal A, Smith RA, et al. Worldwide variations in colorectal cancer. CA Cancer J Clin. 2009; 59:366–78.
- 6.Arnold M, Sierra MS, Laversanne M, et al. Global pattern and trends in colorectal cancer incidence and mortality. Gut Published Online First:27 jan 2016. 2015:310-91.
- 7.Saberi Firoozi M, Kamali D, Yousefi M, Mehrabani D, Khademolhosseini F, Heydari S, et al. Clinical characteristics of colorectal cancer in Southern Iran,2005. iran RedCrescentMedJ. 2007;9(4):209-11.
- 8.Abdifard E, Ghaderi S, Hosseini S, Heidari M. Incidence trends of colorectal cancer in the West of Iran during 2000–2005. Asian Pac J Cancer Prev. 2013;14(3):1807-11.
- 9.Morris EJA, Sandin F, Lambert PC, et al. A population-based comparison of the survival of patients with colorectal cancer in England, Norway and Sweden between 1996 and 2004. Gut 2011;60:1087-93.
- 10.Blanke CD, Shwartz RE, Bonin SR. Cancer management: a multidisciplinary approach. 2005;9.
- 11.Kato I SR, Shwartz A. Conditional median survival of patients with advanced carcinoma. 2001;92:2211-9.
- 12.Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008.GLOBOCAN 2008. International journal of cancer. 2010 Dec 15;127(12):2893-91
- 13.Parkin DM, Ferlay J, Curado MP, Bray F, Edwards B, Shin HR, et al. Fifty years of cancer incidence: CI5 I-IX. International journal of cancer. 2010 Dec 15;127(12):2918-27.
- 14.Curado MP, Edwards B, Shin HR, Storm H, Ferlay J, Heanue M, et al. Cancer incidence in five continents. 2008.
- 15.Schellerer VS, Merkel S, Schumann SC, Schlabrakowski A, Fritsch T, Schildberg C, et al. Despite aggressive histopathology survival is not impaired in young patients with colorectal cancer. International journal of colorectal disease 2012;27(1):71-9.

- 16.Booth CM, Li G, Zhang-Salomons J, Mackillop WJ. The impact of socioeconomic status on stage of cancer at diagnosis and survival: a population-based study in Ontario, Canada. *Cancer*. 2010 Sep 1;116(17):4160-7.
- 17.Groome PA, Schulze KM, Keller S, Mackillop WJ. Demographic differences between cancer survivors and those who die quickly of their disease. *Clin Oncol (RColl Radiol)* 2008 Oct;20(08):647-56.
- 18.Li M, Li JY, Zhao AL, Gu J. Do young patients with colorectal cancer have a poorer prognosis than old patients? *J Surg Res* 2011 May 15;167(2):231-6.
- 19.Van den Broek CB, Dekker JW, Bastiaannet E, Krijnen P, De Craen AJ, Tollenaar RA, et al. The survival gap between middle-aged and elderly colon cancer patients. Time trends in treatment and survival. *Eur J Surg Oncol* 2011 Oct;37(10):904-12.
- 20.Coleman MP, Quaresma M, Berrino F, Lutz JM, De AR, Capocaccia R, et al. Cancer survival in five continents: a worldwide population-based study (CONCORD). *Lancet Oncol*. 2008 Aug;9(8):730-56.
- 21.Hendifar A, Yang D, Lenz F, Lurje G, Pohl A, Lenz C, et al. Gender disparities in metastatic colorectal cancer survival. *Clin Cancer Res*. 2009 Oct 15;15(20):6391-7.
- 22.Bardin A, Boulle N, Lazennec G, Vignon F, Pujol P. Loss of ER beta expression as a common step in estrogen-dependent tumor progression. *Endocr Relat Cancer*. 2004 Sep;11(3):537-51.
- 23.Ciccolallo L, Capocaccia R, Coleman MP, Berrino F, Coe Bergh JW, Damhuis RA, et al. Survival differences between European and US patients with colorectal cancer: role of stage at diagnosis and surgery. *Gut*. 2005 Feb;54(2):268-73.
- 24.The American Cancer Society .Cancer Facts & Figures for African Americans 2011-2012. The American Cancer Society. 2013.
- 25.Sankaranarayanan R. Cancer survival in Africa, Asia, the Caribbean and Central America. Introduction. *IARC Sci Publ*. 2011;162:1-5.
- 26.Folkesson J, Birgisson H, Pahlman L, Cedermark B, Glimelius B, Gunnarsson U. Swedish Rectal Cancer Trial: long lasting benefits from radiotherapy on survival and local recurrence rate. *J Clin Oncol* 2005 Aug 20;23(24):5644-50.
- 27.Christodoulidis G, Spyridakis M, Symeonidis D, Kapatou K, Manolakis A, Tepetes K. Clinicopathological differences between right-and left-sided colonic tumors and impact upon survival. *Techniques in coloproctology* 2010;14:45-7.

- 28.Laohavinij S, Maneechavakajorn J, Techatanol P. Prognosis factors for survival in colorectal cancer patients. *J Med Assoc Thai*. 2010 Oct;93(10):1156-66.
- 29.Kevin C, Ward JLY, Jra LAGR. Cancers of the Colon and Rectum. SEER Survival Monograph.National Cancer Institute. 2010.
- 30.Grande M, Milito G, Attina GM, Cadeddu F, Muzi MG, Nigro C, et al. Evaluation of clinical, laboratory and morphologic prognosis factors in colon cancer. *World Journal of Surgical Oncology*. 2008;6:98.
- 31.King-Yin LA, Ong K, Ho YH. Colorectal mucinous adenocarcinoma: the clinicopathological features and significance of p16 and p53 expression. *Dis Colon Rectum* 2006 Sep;49(9):1275-83.
- 32.Li F, Lai M. Colorectal cancer, one entity or three *Journal of Zhejiang University- Science B*. 2009;10(3):219-29.
- 33.Akhoond MR, Kazemnejad A, Hajizadeh E, Ghanbari Motlagh A. Comparison of colon and rectum cancer: survival and prognosis factors. *Gastroenterology and Hepatology from bed to bench*. 2010;3(4).
- 34.Hill S, Sarfati D, Blakely T, Robson B, Purdie G, Chen J, et al. Survival disparities in Indigenous and non-Indigenous New Zealanders with colon cancer: the role of patient comorbidity, treatment and health service factors. *J Epidemiol Community Health*. 2010 Feb;64(2):117-23.
- 35.Braga M, Frasson M, Vignali A, Zuliani W, Civelli V, DiC V. Laparoscopic vs. open colectomy in cancer patients: long-term complications, quality of life, and survival. *Dis Colon Rectum* 2005 Dec;48(12):2217-23.
- 36.Mohammad Aziz Rasouli, Ghobad Moradi, Daem Roshani, Bahram Nikkhoo, Ebrahim Ghaderi, Bahman Ghaytasi. Prognostic factors and survival of colorectal cancer in Kurdistan province, Iran. *Medicine* 2017;96:6.
- 37.Magaji, et al. Survival rates and predictors of survival among colorectal cancer patients in a Malaysian tertiary hospital. *BMC Cancer* 2017;17:339.
- 38.Al-Ahwal , et al. First national survival data for colorectal cancer among Saudis between 1994 and 2004: what's next? *BMC Public Health*.13:73.
- 39.Ghazi Faisal Sharkas, Kamal H. Arqoub, Yousef S. Khader, et al. "Colorectal Cancer in Jordan: Survival Rate and Its Related Factors," *Journal of Oncology*. 2017;vol. 2017: 6 pages.

40. Stillwell AP, Buettner PG, Siu SK, Stitz RW, Stevenson AR, Ho YH. Predictors of postoperative mortality, morbidity, and long-term survival after palliative resection in patients with colorectal cancer. *Diseases of the colon and rectum*. 2011;54(5):535-44.
41. Walker AR, Walker BF, Funani LS, Segal I. Risk factors and survival from colorectal cancer in black patients in Soweto, South Africa. *Tropical gastroenterology : official journal of the Digestive Diseases Foundation*. 1989;10(4):220-4.
42. Amha Gebremedhin, Tesgayeaster, Aziza Shad , Marcia Landskroene Partner profile. International Network for Cancer Treatment and Research. 2012.

## 11. Annexes

### Annex I. Kaplan Meier cumulative survival of colorectal cancer patients in Tikur Anbessa specialized hospital Addis Ababa Ethiopia 2012-2016.

Survival Table

| #cases | Time   | Status | Cumulative Proportion Surviving at the Time |            | N of Cumulative Events | N of Remaining Cases |
|--------|--------|--------|---------------------------------------------|------------|------------------------|----------------------|
|        |        |        | Estimate                                    | Std. Error |                        |                      |
| 1      | 0.000  | Dead   | .994                                        | .006       | 1                      | 160                  |
| 67     | 12.000 | Dead   | .719                                        | .038       | 40                     | 94                   |
| 121    | 23.000 | Dead   | .468                                        | .046       | 68                     | 40                   |
| 136    | 35.000 | Dead   | .395                                        | .049       | 73                     | 25                   |
| 148    | 46.000 | Dead   | .347                                        | .054       | 75                     | 13                   |

## Annex II. Data abstraction tools

Cell Phone \_\_\_\_\_

| Part I: Socio _ Demographic Characteristics Of CRC Patients               |                             |                                                                                                     |        |
|---------------------------------------------------------------------------|-----------------------------|-----------------------------------------------------------------------------------------------------|--------|
| S.No                                                                      | Variables                   | Codes                                                                                               | Remark |
| 100                                                                       | Age at Diagnosis(in Years ) | _____ years                                                                                         |        |
| 101                                                                       | Sex of Patients             | 1. Female      2. Male                                                                              |        |
| 102                                                                       | Marital Status              | 1. Single<br>2. Married<br>3. Separated /Divorced<br>4. Widowed                                     |        |
| 103                                                                       | Educational Status          | 1. Read & Write<br>2. Primary Level<br>3. Secondary Level<br>4. Tertiary Level                      |        |
| 104                                                                       | Family History Of Cancer    | 1. Yes              2. No                                                                           |        |
| 105                                                                       | Alcohol History             | 1. Yes              2. No                                                                           |        |
| 106                                                                       | Smoking History             | 1. Yes              2. No                                                                           |        |
| 107                                                                       | Region                      | _____                                                                                               |        |
| Part II: Natural History Of The Disease And Associated Prognostic Factors |                             |                                                                                                     |        |
| 200                                                                       | Date Diagnosis              | -----/-----/-----                                                                                   |        |
| 201                                                                       | Location Of Cancer          | Colon<br>Rectum<br>Rectosigmoid                                                                     |        |
| 202                                                                       | Method Of Diagnosis         | 1. Histopathology<br>2. Colonoscopy<br>3. Imaging (CT/MRI)<br>4. Other Specify                      |        |
| 203                                                                       | Histologic Type             | 1. Adenocarcinoma<br>2. Mucinous\signet ring-cell carcinoma                                         |        |
| 204                                                                       | Histologic Grades           | 1. Well Differentiated<br>2. Moderately Differentiated<br>3. Poorly Differentiated<br>4. Anaplastic |        |

|     |                                    |                                                                                    |                            |
|-----|------------------------------------|------------------------------------------------------------------------------------|----------------------------|
|     |                                    | 5. Unknown                                                                         |                            |
| 205 | TNM Staging                        | 1. T -----<br>2. N-----<br>3. M-----                                               | Grouped<br>Staging---<br>- |
| 206 | Stage Of Cancer                    | 1. Localized<br>2. Locally Advanced<br>3. Metastasis<br>4. Unknown                 |                            |
| 207 | Treatment Modality                 | 1. Surgical<br>2. Chemotherapy<br>3. Radiotherapy<br>4. Combination Of All         |                            |
| 208 | Date Treatment Started             | -----//-----//-----                                                                |                            |
| 210 | Involved regional LNs              | 1. Yes            2.No                                                             |                            |
| 211 | Vascular Invasion                  | 1. Yes            2. No                                                            |                            |
| 212 | Residual Tumor                     | 1. Yes            2. No                                                            |                            |
| 213 | Base Line CEA (Preoperative)       | 1.Elevated (>5ng/MI)<br>2. Not Elevated (<5ng/MI)<br>3. Write Specific Figure----- |                            |
| 214 | Distant Metastatic Organs Involved | 1. Liver<br>2. Lung<br>3. Peritoneum<br>4. Other                                   |                            |
| 215 | Comorbid Illness                   | 1. RVI<br>2. HTN<br>3. DM<br>4. UC<br>5. Other specify                             |                            |
| 216 | Date Of Last Follow Up             | -----/------/------                                                                |                            |
| 217 | Patient Status At Last Follow Up   | 1. Alive            2. Died                                                        |                            |
| 218 | Date Of Death(Dd/Mm/Yy)            | -----/------/------                                                                |                            |

### Annex III. Conceptual Frame work

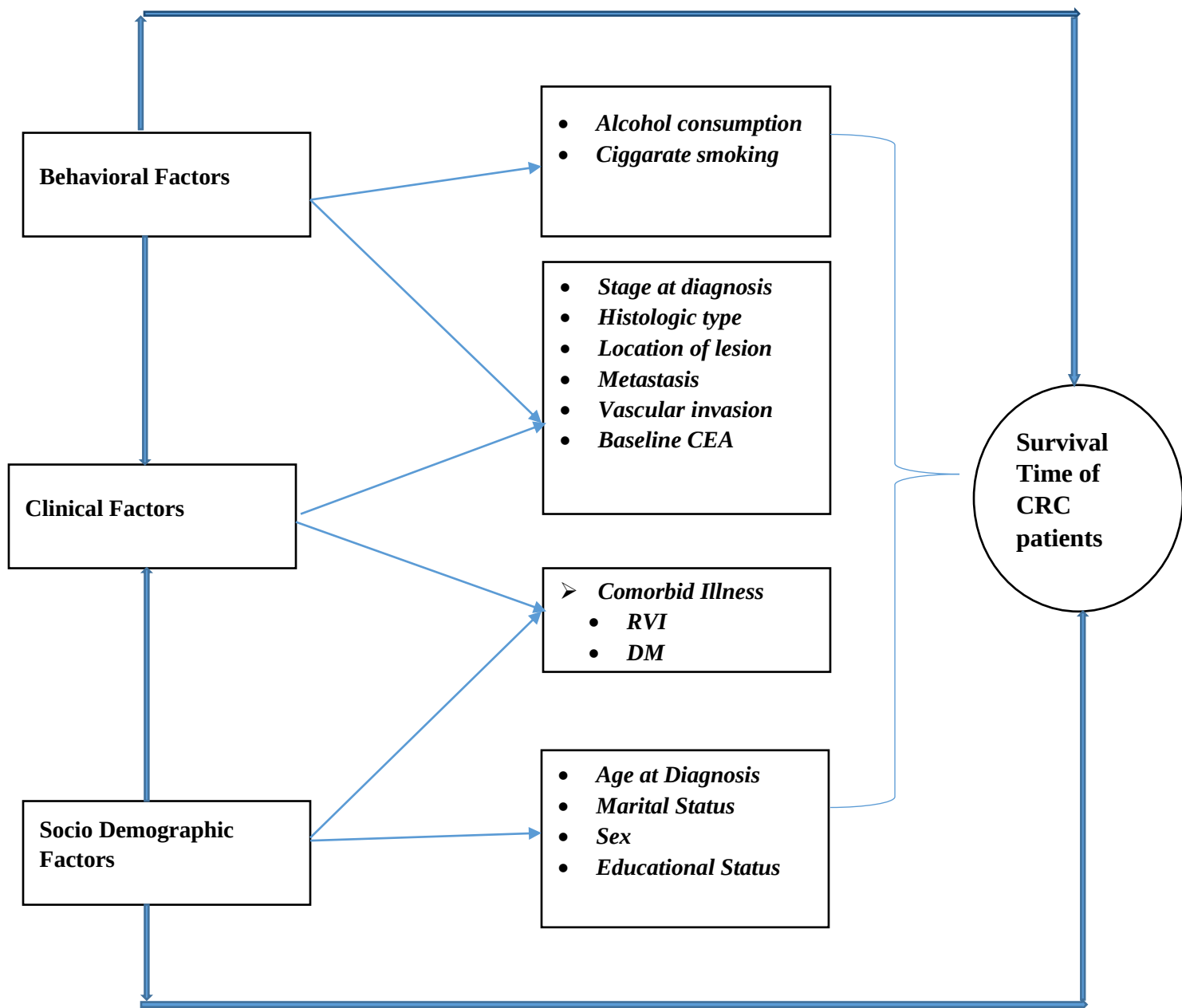


**Figure 2.** Conceptual Frame Work for the study of Survival Time and Prognosis predictors of Colorectal Cancer Patients at Tikur Anbessa Specialized Hospital Addis Ababa Ethiopia 2012 -2016

#### **Annex IV. Information & Consent form (English version)**

Hello. My name is \_\_\_\_\_. I am collecting data for Mr. Mohammed Ahmed who is currently a student in St. Paul's Hospital Millennium medical college and conducting research on colorectal cancer. It is one of the commonest cancer disease which claiming the life of many. The result that will come out of this study will be used by the government and nongovernmental organizations to base rational decision to develop appropriate strategies to combat this problem. The research is intended to benefit the community specifically those suffering from the disease to the extent of death including the people that will be participating in this research. It will introduce no risk to the participant. The interview requires the maximum of 20 minutes to complete. You are selected on the basis of having the disease. Your participation is entirely voluntarily, and you can quit from the study any time you want. You will have no penalty if you fail to show desire to participate. I, however, do hope that you will participate in the study since the data that will come from you will be important for us. Your name and other personal identity will not be used, and hence the information I will collect from you will completely be kept confidential and will not be disclosed to any third person other than the people participating in this study. For any question you want to ask me, you can use the contact address here under.

Mohammed Ahmed: mobile 0912618775, [jemsmoh@gmail.com](mailto:jemsmoh@gmail.com)

May I now begin the interview? If yes, continue interviewing If No, thank and stop interviewing

Name of the interviewer \_\_\_\_\_ Sign. \_\_\_\_\_ Date \_\_\_\_\_

Name of the supervisor \_\_\_\_\_ Sign. \_\_\_\_\_ Date \_\_\_\_\_

## Annex V. የተጠያቂ መረጃና ፈቃድ መጠየቂያ ቅጽ

ጤና ይስጥልኝ \_\_\_\_\_ እባላለሁ። በቅዱስ ጳውሎስ ሆስፒታል ሚሊኒየም ህክምና ኮሌጅ ፊልድ ኢፒዴሚዮሎጂ ተማሪ ከሆኑት አቶ መሀመድ አህመድ ጋር መንስኤው ባልታወቀውና የብዙ ሰዎችን ህይወት በመቅጠፍ ላይ ባለው ኮሎሬክታል ካንሰር በተባለው በሽታ ላይ ጥናትና ምርምር በማድረግ ላይ እንገኛለን። የጥናትና ምርምር ውጤቱ በዞን፣ በክልልና በሀገር አቀፍ ደረጃ ያሉ የጤና ቢሮዎችና ሌሎች አጋር ድርጅቶች በጉዳዩ ላይ አስፈላጊውን ትኩረት እንዲሰጡና ተገቢውን የህክምና መስጠት እንዲቻል ያደርጋል። በዚህም ሁሉንም ማህበረሰብ ተጠቃሚ የሚያደርግ ችግር ፈቺ ምርምር ነው። በዚህ ላይ ለሚሰጡት ምላሽ ምንም አይነት ጉዳት አይደርስበትም። መጠየቁን ከ20ደቂቃ ባነሰ ጊዜ ውስጥ የሚፈጸም ነው። ለዚህ የተመረጡት በዚህ በሽታ የተያዙ በመሆንዎት/ለታማሚው ወይም ህይወታቸው ላለፈባቸው ሰዎች ቤተሰብ፣ አሊያም ቅርብ ዘመድ በመሆንዎት ነው። የሚያደርጉት ተሳትፎ ሙሉ በሙሉ በእርስዎ ፈቃድ ላይ የተመሰረተና በፈለጉበትም ሰዓት የማቋረጥ መብትዎ የተጠበቀ ነው። ማንነትዎና የሚሰጡት መረጃ ለሶስተኛ ወገን ተላልፎ አይሰጥም። እገዛዎ ለሚደረገው ጥናትና ምርምር ትልቅ አስተዋጽዖ ያለው መሆኑን እንደሚገነዘቡ ተስፋ አደርጋለሁ። ማንኛውንም ጥያቄ ካልዎት ከዚህ በታች ባለው አድራሻዉ ሊጠይቁት ይችላሉ።

መሀመድ አህመድ፡- ሞባይል : 0912618775፣ኢሜይል፡ [jemsmoh@gmail.com](mailto:jemsmoh@gmail.com)

መጠየቁን መጀመር እችላለሁ? ምላሹ እሺ ከሆነ መጠየቁን ይቀጥሉ፣ ምላሹ አይሆንም ከሆነ አመሰግነው ይሰናበቱ።

የጠያቂ ስም \_\_\_\_\_ ፊረማ \_\_\_\_\_ ቀን \_\_\_\_\_

የተቆጣጣሪ ስም \_\_\_\_\_ ፊረማ \_\_\_\_\_ ቀን \_\_\_\_\_