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Treatment outcomes and Prognostic Factors for Survival in Patients with Gastric Cancer at Adult Oncology Unit of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia

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A Thesis Submitted to the Department of Pharmacology and Clinical Pharmacy, School of Pharmacy, College of Health Sciences, Addis Ababa University in Partial Fulfillment for the Requirements of the Degree of Master of Sciences in Pharmacy Practice.

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This is to certify that the thesis prepared by Hilina Tsegaw, entitled: "***Treatment outcomes and Prognostic Factors for Survival in Patients with Gastric Cancer at Adult Oncology Unit of TikurAnbessa Specialized Hospital, Addis Ababa, Ethiopia***" and submitted in partial fulfillment of the requirements for the degree of Master of Sciences in Pharmacy Practice complies with the regulations of the University and meets the accepted standards concerning originality and quality.

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Abstract

Treatment outcomes and Prognostic Factors for Survivalin patients with Gastric Cancer at Adult Oncology Unit of TikurAnbessa Specialized Hospital, Addis Ababa, Ethiopia

Hilina Tsegaw,Addis Ababa University, 2022

Gastric cancer is the fifth most often diagnosed cancer and the third most frequent reason for cancer death worldwide. In Ethiopia, the survival status of patients diagnosed with gastric cancer was not well understood. This study, therefore,aimed to determine treatment outcomes and prognostic factors for survival status of patients diagnosed with gastric cancer at TikurAnbessa Specialized Hospital, oncology unit; Addis Ababa, Ethiopia.This hospital-based retrospective cohort study was conductedon164 study participantsselected from patient's registry between January 01, 2016 to December 31, 2020. Data were collected using a structured tool from medical records and telephone interviews. A Kaplan–Meier survival analysis with a log-rank test and bivariate and multivariable analysis using the Cox proportional hazard model wereused. The median (±SD) age of the study participant at diagnosis was 48.50 ±14.48 years (range:18–87),with amale to female ratio of 1.8:1. Adenocarcinoma accounted for 73.8% of the cases. Regarding clinical-stage,92(56.1%) of the patients were diagnosed with stage IV. About 39.6% (65) of the cases were treated with partial gastrostomy followed by bypass surgery. The commonest chemotherapy regimen was cisplatin with paclitaxel (85, 51.8%) followed by cisplatin with 5- Fluorouracil (5-FU), and 84 (51.2%) of the cases had metastasized cancer, of which47 (28.7%) of them had liver metastasis.110 (67.1%) of the patients were dead at the end of the treatment follow-up. A 5-year overall survival rate was 11% with a median survival time of 18.6 months.In multivariate logistic regression, ECOG ≥ 2, Adenocarcinomahistologic type, ovary metastasis, liver+lung metastasis, and paclitaxel + carboplatin chemotherapy were found to significantly affect survival of thepatients.The survival outcome of gastric cancer is low and requires early detection.

Keywords: Gastric cancer, chemotherapy, treatment outcome, survival, prognostic factor

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Abbreviations and acronyms

5-FU: 5-fluorouracil

AAU: Addis Ababa University

AC: Adenocarcinoma

AOR: Adjusted odds ratio

CI:Confidence interval

COR: Crude odds ratio

DCF: Docetaxel,cisplatin, and fluorouracil

ECF: Epirubicin, cisplatin, and fluorouracil

ECOG PS: Eastern Cooperative Oncology Group performance status

ECX:Epirubicin, cisplatin, and oxaliplatin

EOF: Epirubicin, oxaliplatin, and fluorouracil

FLOT:Fluorouracil, leucovorin, oxaliplatin and docetaxel

GC: Gastric Cancer

HER-2: Human epidermal growth factor receptor 2

MAGIC: Medical Research Council Adjuvant Gastric Infusional Chemotherapy trial

OS: Overall survival

PFS:Progress free survival

RO: Resection with negative microscopic disease

SCC: Squamous cell carcinoma

SPSS: Statistical Package for the Social Sciences

TASH: TikurAnbessa Specialized Hospital

WHO: World Health Organization

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1. Introduction

1.1. Background

Cancer is the world's leading cause of death and the second leading cause of death in the United States (Siegel RL, 2019). It is also the single most important barrier to increasing lifespan in every country of the world(Bray F, 2018).

Gastric cancer (GC) could be a leading cause for cancer-related death worldwide throughout the twenty-first century, andit's also related to an absence of standard treatment strategies, significantly following first-line therapy (Ferlay J, 2010).Risk factors for GC include male gender (incidence is double), *Helicobacter pylori* infection, tobacco use, atrophic gastritis, partial gastrectomy, and Ménétrier's disease (Smyth EC, 2016).

Improved imaging techniques allowpatients to be staged more adequately than antecedently. Minimally invasive techniques like endoscopic resections, sentinel nodes, and laparoscopy have been developed and may be used for early stages of the disease. For advanced GC, achievement of loco-regional control remains a considerable problem. To boost outcomes, the extension of surgery has been studied widely(Wang Y, 2017).

Surgical resection is the cornerstone for the treatment of patients with localized GC. On condition, resection was curative and, surgery thrives good survival outcomes, with a 5-year survival rates of up to 98% with early-stage GC(Park HJ, 2014).

The FLOT4-AIO phase III clinical trial showed theregimen of FLOT (fluorouracil, leucovorin, oxaliplatin, and docetaxel) was superior to ECF/ECX (epirubicin, cisplatin, and fluorouracil/Epirubicin, cisplatin, and oxaliplatin),once it's given before and after radical surgery:Patients-derived benefits regarding of median overall survival (OS) and progression-free survival werehigher; thus, it's considered the standard of care(Al-Batran SE, 2019).

Triplets containing taxanes are also an evidence-based treatment alternative for first-line chemotherapy. The addition of docetaxel to 5-FU/cisplatin in an exceedingly 3-weekly regimen (DCF) was related to improvedOS. However, conjointly significant toxic effects, as well as increased rates of febrile neutropenia, were observed.As an alternative to platinum-based therapy, irinotecan plus leucovorin and

infusional 5-FU (FOLFIRI) has been studied in each phase II trial and one phase III randomized trial within the first-line setting and can be considered for selected patients(Smyth EC, 2016).

In the majority of cases, palliative treatment is given for recurrence and metastatic disease. It helps to manage symptoms, improve quality of life, and lengthening life (Zhou K, 2021). Therefore, there has been abundant interest in using adjuvant therapies to boost the outcomes of GC patients after surgical resection of the primary tumor. Sadly, though numerous ways are tried, few have been shown to be clinically useful (Paoletti X, 2010).

In metastatic GC, chemotherapy is the mainstay treatment, with capecitabine and oxaliplatin being as effective as fluorouracil and cisplatin,and adding chemotherapy to HER-2 positive metastatic GC, trastuzumabconsiderably prolonged survival (Bang YJ, 2010).

According to the American Cancer Society, several patients with GC present with distant metastasis.Theprognosis for advanced GC is poor, and the 5-year relative survival rate for these patients with distant metastasis is only 6%(Amin, 2017).

1.2. Statement of the problem

GC is the fifth most often diagnosed cancer and also the third most frequent causefor cancer death worldwide. In 2016, it was estimated that about 26,370 individuals would bediagnosed and 10,730 individuals eventually die of the illness within the United States (Ajani JA, 2016). In 2018, GC accounted for 1,033,000 cases and 783,000 deaths worldwide. In the United States, approximately 27,600 cases have been diagnosed each year, with a 5-year survival rate of 32%(Teh SH, 2021).

There is a large variation in the incidence of GC in several geographical regions. Whereasthe incidence of GC is high in China, Japan, and Korea;- the incidence is relativelylow in most of Europe, North America, and Africa (Mabula JB, 2012). Large variationswithin the 5-year relative survival rates– starting from 10 to 54% – have also been observed among countries on the four continents (Al-Moundhri MS, 2006).In Spain, the estimated incidence of GC in 2019 was 7865 cases,with a higher incidence in menthanwithin the remainder of the Western countries (Martín-Richard M, 2020). The region of Romagna in Italy had one of thehighest incidence rates of GC, estimated at 13,000 new cases in 2018, with overall deaths of about 10,000(Monti M, 2020). In Sweden, the prognosis ofesophageal and GC is poor, with an overall 5-year survival rate of15–29%(Dalhammar K, 2020).

The survival ratesafter curative operation for GCare higher in East Asian countries than in Western countries (Yang K, 2016).The survival of gastric adenocarcinoma in Taiwan was poor, with a 5-year survival rate of 29%(Hu HM, 2021). Nearly amillion new cases of GC were diagnosed each year, and 50% of them occurred in Eastern Asia.Although an improvement of 5-yearsurvival for GC was determined within the past ten years,the prognosis of Chinese GC patients was still poor (Zhao L, 2019).

World Health Organization (WHO) estimated a 15% increase in non-communicable illness worldwide, with more than a 20% increase occurring in Africa between 2010 and 2020. Mali, West Africa, is ranked 15th(Asombang AW, 2014). The highest prevalence of GC was found in a region involvingRwanda, Burundi, South Western Uganda, and Eastern Kivu province of the Democratic Republic of Congo (Ahmed A, 2011). There is a great deal of variation in reported incidence and mortality among the individual African countries. For example,in Ethiopia, and East Africa, GC is the most common cancer in men with a mortalityrate of3.4/100000 (Asombang AW, 2014). In Ethiopia,available works in the literature place GC 9thamong all cancers in incidence (Woldeamanuel YW, 2013).

GC is an aggressive malignancy whose management and early detection are challenging. The survival rate of patients diagnosed with gastric cancer in Ethiopia was unknown. Furthermore, there are no national or institutional guidelines on GC. Besides that, no previous research had been conducted on the treatment pattern, histologic types, survival status, and associated factors in GC patients at TikurAnbessa Specialized Hospital (TASH). This study was also used as a good input for further research in related topics within the institution.

1.3. Significance of the study

Generating a shred of evidence on histologic types, treatment patterns, treatment outcomes of various cancers, survival status, and associated prognostic factors has important practical value for patients, healthcare providers, and researchers. Aproper understanding of prognosis/treatment outcomemay also facilitate clinicians to decide on treatment options, prioritize interventions, estimate the survival rate of patients, support the planning systems of cancer management and prevention program,and balance personal values for quality versus quantity of life. Health care providers can build use of survival information to more objectively verify the suitable timing of follow-up visits and aggressiveness of surveillance testing based on patient's current risk profile. It also offers a piece of knowledge for health policymakers, researchers, and all concerned stakeholders by creating a benchmark for planning and a foundation for further studies in GC.

2. Literature review

2.1. Treatment outcome and associated factors of gastric cancer

Caldero-Guardia *et al.*(Cordero-García E, 2018)conducted a retrospective analysis among 236 GC patients in four major public hospitals in Central America. The finding indicated that 57 cases(24.2%) were less than 50 years old and 77 patients (32.6%) were older than 70 years.Male cases were predominant (1.4:1). Overall, a total of 131 patients died throughout the follow-up. Median OS was 47.6 months, and therefore the OS rate at 5 years was 45.1%.

A retrospective analysis by Hoffman*et al*. (Hoffman KE, 2013)in Canada also found that the median follow-up was 25.5 months and 62% died. Patients with lymph node involvement, T3 or T4 disease, worse grade disease, and more comorbidities were more likely to die (p=0.0411).

Monti*et al.*(Monti M, 2020)conducted a retrospective analysis of GC management in Italy, identifying all 573 consecutive patients with GC histologic diagnosis.Only 5 (1.5%) of the patients received neoadjuvant chemotherapy, while 67 (19.5%) received adjuvant chemotherapy.The 5-year survival for patients was 54.5%. The odds ratio (OR) for patients with comorbidities was 0.31 and 0.87 for every unit increase in patient age, according to a crude analysis.

Similarly, the median age in an Italian retrospective study by Catalano *et al.*(Catalano V, 2008),was sixty-four years with a range of 38–83 years. Sixty-six percent of the patients were male, and 23.4% hadanECOG PS >2. A prior gastrectomy was performed in nearly 80% of the patients and 5-FU, 5-FU, and cisplatin (n=141) or 5-FU and oxaliplatin were used as first-line chemotherapy.The overall response rate was 16.0%.The presence of more than or equal to three metastatic sites of disease (HR, 1.72), performance status >2 (HR, 1.79),and time-to-progression under first-line chemotherapy ≤6 months were all found to be independently associated with poor OS.

A cohort study by Kim *et al.*(Kim JG, 2008)in Seoul, Republic of Korea included 304 patients, with 197 malesand 107 females. The median age was 54 years (range 19–75 years), and 218 patients (72%) had metastaticdiseasewith newly diagnosed metastatic or recurrent GC treated with one or more cycles of cisplatin-based chemotherapy. The median survival time for all patients was 7.3 months (95% CI, 6.3–8.2). Poor performance status ECOG 2-3 (HR: 1.46), excessivetotal bilirubin, presence of peritoneal

metastasis, presence of bone metastasis, and presence of more than one metastatic site significantly increased the risk of death.

In another study conducted in Korea between September 1994 and February 2005, the median age of 725 advanced GC patients treated with first-line chemotherapy in Korea was 56 years (range, 22 to 86);139 (19 %) had an ECOG ≥ 2, and 96% of them died. The median progress-free survival was 2.9 months, while the median OS was 6.7 months.Low baseline hemoglobin levels and poor performance status were found to be independent significant predictive variables for OS in multivariate analysis (Ji SH, 2009).

In Japan, a retrospective study on chemotherapy for patients with advanced gastric cancer with performance status ≥ 2 was conducted by Shitara*et al.*(Shitara K, 2009). In this study, 657 patients with advanced GC,who had first-line chemotherapy,and a few patients with PS≥2 were included. PS≥ 2 patients had a shorter median survival time (5.8 vs. 13.9 months; P.001). Oral agents were associated with a better outcome in patients with PS 0–1 (HR: 0.76), whereas they were associated with a poorer prognosis in those with PS≥ 2 patients(HR 1.52).

Ali*et al*(Ali ZA, 2014)carried out ahistorical study. The mean age at diagnosis was 65.7 ±11.22 years for men and 65.41±10.56 forwomen. Majority of the patients (239, 72.4%) died before the study ended, and the rest were censored. Patients with adenocarcinoma pathology had a poorer survival rate than those with other pathologies (18.7 months vs. 23.14 months). Age, marital status, number of renewed treatments, recurrence, type of gastrectomy(Subtotal, Distal, Partial), proximal liver metastases (HR=1.79), distant metastases (HR=1.84), and disease stage factors all had a significant effect on patients' survival, according to the multivariate analysis.

In a retrospective study in Tehran, Iran by Alimoghaddam*et al.*(Alimoghaddam K, 2014)368 patients were included. With a median age of 57.0 and a male-to-female ratio of 71.8%.Adenocarcinoma was found in majority of the GC patients (208, or 88.9%).In adenocarcinoma, the one-year survival rate was 63.5%.The median follow-up was 10 months. With GC, 65.4% of people had stage III or IV. At the time of presentation, nearly half of them (50.8%) had unrespectable illness or metastases. The 1-year OS rate was 68.2% ($p<0.001$).

Aretrospective survival analysis conducted by Lin *et al*. (Lin WL, 2014)in Taiwan reviewed the records of patients with adenocarcinoma of the stomach. The study included 64 patients, including 39

male(60.9%) and 25 women (39.1%) (male/female = 1.56). The patients were 64.4±12.4 years old on average (62.8±13 for men and 66.9±11 for women) (p=0.315).

Yaprak*et al.*(Yaprak G, 2019) conducted a retrospective study of prognostic factors for survival in patients with GC in Istanbul, Turkey and found that the median follow-up time was 34 months. The median survival time was 51 months. The OS rate for the 1st, 3rd, and 5thyears was 72%, 49%, and 38%, respectively.

Basaran*et al* (Basaran H, 2015)conducted a similar study on survival at Erzurum Regional Training and Research Hospital's Medical Oncology and Radiation Oncology Clinics. The study included 228 patients, with a male/female ratio of 1.47. The median OS time was 18.0(± 1.190) months. The median follow-up period was 22.3 months (range: 3 to 96). One hundred and twenty-six patients (55.3%) had surgery, while 51.3 % had adjuvant chemotherapy. The median OS rates was68%, 36%, 24%, and 15%for the 1st, 2nd, 3rd, and 5thyear, respectively. OS rates did not differ for histopathological diagnoses (p=0.520).Median OS times for these CT protocols were calculated as 24, 21, 16, and 14 months, respectively, and there were no statistically significant differences between them.

A retrospective study conducted by Uyeturk*et al.*(Uyeturk U, 2013)on patients diagnosed with GC between January 2005 and January 2012 at Ankara Oncology Education and Research Hospital in Ankara, Turkey showed that eight patients (0.45%) were adenocarcinoma,histopathologicallyidentified. The median age was 42.2 years (range, 32–69 years). At the time of diagnosis, two (25%) of the patients were in stage 3A, two (25%) were in stage 3C, and four (50%) were in stage 4. After the initial diagnosis, the median OS was 16.7 months (1–41 months), and after ovarian metastasis, the median OS was 3.6 months (1–10 months).

Ahmed*et al.* (Ahmed A, 2011) conducted a prospective study with 179 patients in Zaria, Nigeria. There were 105 males and 74 females, with a male-to-female ratio of 1.4:1. Their age ranged from 21 to 89 years old, with a mean (SD) of 51±6.3. Fifty-four (30.2 %) patients were < 40 years, while 52.0 were 40-60 years.The overall median survival was 13.6 months. Overall, 70.1% of patients survived for one year, while 49.4% and 21.8% survived 2 and 5years, respectively. The factors that significantly affected survival were patient age (0.03), tumor location (0.01), presence of peritoneal metastasis (0.001), and histological type (0.01). Medical conditions (0.001), presence of pre-operative comorbidity (OR; 1.55), resection of adjacent organs, and D2 lymphadenectomy were independent predictors of postoperative morbidity.

According to a retrospective study by Gebresillasse *et al* (Gebresillasse HW, 2019)on patients with GC in the GI surgery unit of TASH,(54, 56.8 %) were male and the rest were female, with a male to female ratio of 1.3:1. The patient's age ranged from 23 to 76 years, with a mean age of 52 years. According to histopathology reports, 69.5 % of the patients had adenocarcinoma;20% had a malignant gastrointestinal stromal tumor, and 8/95 (8.4%) had gastric lymphoma.

3. Objective

3.1. General objective

- ✓ To assesstreatment outcomes and prognostic factors for survival status ofGC patients at TASH adult oncology unit; Addis Ababa, Ethiopia.

3.2. Specific objectives

- ✓ To determine treatment outcomes of patients treated for GC in the adult oncology unit of TASH.
- ✓ To describe the histologic type and treatment pattern of patients treated for GC in the adult oncology unit of TASH.
- ✓ To determine 5 year survival rate of patients treated for GC in the adult oncology unit of TASH.
- ✓ To determine prognostic factors associated with poor survival of patients treated for GC in the adult oncology unit of TASH. Cancer

4. Methods

4.1. Study design and period

A retrospective hospital-based cohort study design was used and data were collected from March 10 to July 12, 2021.

4.2. Study Setting

The study was conducted at the adult oncology unit of TASH, Addis Ababa, Ethiopia. The hospital was founded in 1972 and serves as the country's primary referral center. The TASHradiotherapy center is the first facility in the country that has one functional radio-therapeutic machine. It serves over 6,000 new cancer patients annually.Most patients with cancer also present in the surgical, gastrointestinal, and gynecology units. Six full-time consultant oncologists, three medical physicists, and five radiotherapists are currently working in the center. The center started training in clinical oncology in 2013 and currently,36 residents are enrolled. Activities of the center includeoutpatient clinics for newpatient evaluation and follow-up. It has also two wards for inpatient chemotherapy with a total of 33 beds, where two of the beds are dedicated for emergency patient admission. The center also has a daycare center for outpatient chemotherapy administration.Currently, the oncology unit provides management services for more than 10,000 cancer patients including chemotherapy and radiotherapy.

4.3. Source and studypopulation

All GC patients who were diagnosed and treated in the adult oncology unit of TASH formed the source population.

All GCpatients who had been histologically confirmed andtreated in the adult oncology unit ofTASH fromJanuary1, 2016 to December31, 2020fulfillingthe eligibility criteria constituted the study population.

4.4. Eligibility criteria

Adult patients aged ≥ 18 years old with histologically confirmed GC and, on chemotherapy were included.

Patients who had incomplete information on registration and medical charts (noreport about of histopathology, treatment, phone number, and cancer stage)were excluded.

4.5. Sample size determination and sampling procedure

As the number of patients were small to calculate sample size, all GC patients receiving treatment during the study period and fulfilling the inclusion criteria were included in the study.The totalnumber of GC patients registered during the study periodwere 263. Data (no report of histopathology, treatment, phone number, and cancer stage) were incomplete for99 patients. Finally, the records of 164 patients were used for analysis.

4.6. Data collection and management

4.6.1 Data collection instrument

A data abstraction form (Annex I) was used, which was prepared based on the availability of information on patient charts and reviewing the literature onSocio-demographic features, clinical and pathological characteristics, and treatment approaches used. Data were collected retrospectively from patients' medical records and phone interviews.Patients' or their families' phone interviews were also used to collect current event status, date of death if they died, and the presence of co-morbidities, which were not explicitly recorded in the patient charts.

4.6.2 Data collectors' recruitment and training

Data were collected by one pharmacist and one nurse.A one-day training was organizedon the use of data collection instruments, uniform interpretation of questions, implementation of sampling techniques, and confidentiality of collected data.Pre-test was conducted on 5% of the patient charts, which were not included in the study. It was performed to ensure that the instruments would allow to capture all the required data from charts as well as patients. An appropriate modification was then made based on the pre-test result.

4.6.3 Data collection procedure

The medical charts of all GC patients were identified and retrieved using the medical registration number from the Health Management Information System record. Then, data collectors reviewed baseline and follow-up characteristics of the patient from the medical charts. To determinethe main outcome, as there were no mortality data within the patient charts, a telephone call was made to all patients and/or their

caregivers. During the phone interview, we collected current event status, date of death if died, presence of co-morbidities.

4.6.4 Data quality control

The quality of the data was maintained through appropriate training of the data collectors and pretesting of the instrument. Additionally, daily follow-up was made by the supervisor to confirmaccuracy and consistency of the collected data.

4.7. Study variables

4.7.1. Dependent variables

- ✓ Treatment outcome (Death/ survival)

4.7.2. Independent variables

- ✓ **Patient-related variables:** Age of the patient at diagnosis, Sex.
- ✓ **Disease-related variables**: Stage of cancer at diagnosis, histologic type /grade, duration of symptoms, Initial cancer site, ECOG.
- ✓ **Medication-related variables**: Durationofchemotherapy(numberofcycles),typeofchemotherapyregimen.

4.8. Data processing and analysis

Data cleaning wasdoneon a daily basis. The collected data wereentered in Epi Info and transported to SPSS software version 21. Basic descriptive statistics like frequency, proportion, mean and median wereused and presented using tables and graphs. Kaplan Meier analyses with a life table were used to identify the overall survival rates and median survival time. Variations in survival among different variables were compared using the log-rank test. Before running the Cox regression model, the assumption of proportional hazard was performed and variables having a P-value > 0.05 were considered. Variables with $p<0.2$ in the bi-variable Cox regression model were included in a multivariable Cox regression model analysis. Variables in the multivariable Cox model with a p-value < 0.05 were considered to havea significant association with the survival of patients ata 95%confidence interval.

4.9. Ethical considerations

Ethical approval (Annex III) was obtained from theEthics Committee of the School of Pharmacy, College of Health Sciences, Addis AbabaUniversity (Ref No: ERB/SOP/173/08/2020).Permission to conduct the study was also sought from the Oncology Unit of the Department of Internal Medicine, School of Medicine, College of Health Sciences, Addis Ababa University. In addition, informed verbal consent (Annex II) was obtained from patients/caregivers before starting the phone interview after getting phone numbers from the cancer registry.Confidentialityand privacy of information were kept through anonymity and restricting data access.

4.10. Operational definitions and definitions of standard terms

Stage of GC:this implies a diagnosis stage of a tumor with pathological confirmation (from stage I to stage IV).

Treatment pattern: in this study treatment pattern is defined as the frequency of GC patients treated with chemotherapy, radiotherapy, or surgical treatment in TASH

Treatment outcome:in this study treatment outcome refers to the status of patients after starting treatment (survived, death).

ECOG Performance Status: Eastern Cooperative Oncology Group is a scale developed by the Eastern Cooperative Oncology Group that is used to assess how a patient's disease is progressing, how the disease affects the patient's daily living abilities, and to determine appropriate treatment and prognosis.

Survival status: was defined as the outcome of patients which was classified into survived, or death from patient’s clinical data file from scheduled or unscheduled visits or interview.

Time to death: was the time between the date of diagnosis of GC and the date of death (in a month).

Median survival: the time at which the survival curve crosses 50% survival.

Prognostic factors:in this study refers to any barrier, positive or negative that has an effect on treatment outcome (treatment-related, tumor-related, socio-demographic).

4.11. Plan for dissemination of the results

The thesis work will be prepared both in hard and soft copy tobe submitted to the Department of Pharmacology and Clinical Pharmacy, School of Pharmacy, College of Health Sciences, Addis Ababa

University. In addition, the findings of the study will be disseminated to TASH and other key stakeholders involved in cancer management. Publication of the result in scientific journals will be considered through peer review and presentation at different meetings/conferences.

5. Results

5.1 Socio-demographic characteristics

Out ofthe 164 GC patients included in the study,males comprised 64%of the sex category, with a male to female ratio of 1.8:1. The median (SD ±) age of the study participant at diagnosis was 48.50±14.48 years(range: 18– 87), Of these, 83(50.6 %) were between 40-60 years of age, and(74,45.1%) came from the Oromia Region. A sizable proportion of the study participants were married (143, 87.2%) (Table 1).

Table 1: Socio-demographic characteristics of gastric cancer patients treated at the Oncology Unit of Tikur Anbessa Specialized Hospital between 1January 2016 to 31December 2020 Addis Ababa, Ethiopia (n= 164).

Variables	**N (%)**
Gender	
Male	105(64.0)
Female	59(36.0)
Age	
<40 years	50(30.5)
40-60years	83(50.6)
>60 years	31(18.9)
Region	
Oromia	74(45.2)
Addis Ababa	52(31.7)
SNNPR	24(14.6)
Amhara	12(7.3)
Dire Dawa	2(1.2)
Religion	
Orthodox	93(56.7)
Muslim	56(34.2)
Protestant	15(9.1)
Marital status	
Married	143(87.3)
Single	14(8.5)
Widowed	3(1.8)
Divorced	4(2.4)

5.2 Clinical and Pathological Characteristics

All the 164GC patients hada documented initial functional status at the time of diagnosis. For instance, nearly two-thirds of the patients (113, 68.9%) had ECOG Performance Status (ECOG PS)score of 0-1, andalmost half of the cases (87, 53%) had more than or equal to six monthssince the first symptom started.The most common site of the tumors and cancer cell type was the antrum(101, 61.6%), and adenocarcinoma (AC)(121,73.8%).Eighty two (50.0%) of participants have Poorly-Differentiatedof Pathological grading.Regarding clinical-stage,92(56.1%) of the patients were diagnosed with stageIV, and84(51.2%) of the cases had metastasized cancer, of which47 (28.7%) of them had liver metastasis (Table 2).

Table 2: Clinical and pathological characteristics of gastric cancer patients treated at the Oncology Unit of TikurAnbessa Specialized Hospital between 1January 2016 to 31December 2020 Addis Ababa, Ethiopia (n= 164).

Variables	N (%)
ECOG performance at diagnosis	
ECOG 0-1	113(68.9)
ECOG ≥2	51(31.1)
Duration since the first symptom start	
<6month	77(47.0)
≥6month	87(53.0)
Site of tumor	
Antrum	101(61.6)
Body	21(12.8)
Cardia	17(10.4)
Gastro-oesophageal junction	15(9.1)
Fundus	10(6.1)
Histopathology	
Adenocarcinoma	121(73.8)
Squamous cell carcinoma	30(18.3)
Lymphoma	13(7.9)
Pathological grading	
Poorly-Differentiated	82(50.0)
Moderately-Differentiated	45(27.4)
Well-Differentiated	37(22.6)

Stage	
4	92(56.1)
3	32(16.5)
2	27(17.7)
1	13(7.9)
Recurrences	
Yes	26(15.9)
No	138(84.1)
Metastasis of disease	
Yes	84(51.2)
No	80(48.8)
Site of Metastasis (n=84)	
Liver	47(28.7)
Lung	17(10.4)
Ovary	10(6.1)
Lung and liver	10(6.1)

*ECOG PS; Eastern Cooperative Oncology Group Performance Status

5.3 Treatment approaches used

The approaches used for treating GC patients are depicted in Table 3. Out of the 164 patients with a confirmed diagnosis of GC, 80(48.7%) were given palliative care. Whilst (68, 41.5%) patients did not undergo surgery, about 40%(65) of the cases were treated with a partial gastrectomy surgical procedure followed by bypass surgery. The duration between surgery and chemotherapy for almost half (83, 50.6%),of the patients was ≥3months.The commonest chemotherapy regimen was Cisplatin with paclitaxel (85, 51.8%) followed by Cisplatin with 5- Fluorouracil (5-FU) (49, 29.9%) (Table 3). One hundred forty-nine (90.9%)of the casestook < 7 cycles of chemotherapy.Of the study participants,36(22.0%) hadcomorbidityand 110 (67.1%) patients died after 15.5 months of median follow-up.

Table 3: Description of a pattern of treatment used to treat gastric cancer patients at the Oncology Unit of TikurAnbessa Specialized Hospital between 1January 2016 to 31December 2020Addis Ababa, Ethiopia (n= 164).

Variables	**N (%)**
Sequence of Treatment	
Palliative	80(48.7)
Adjuvant	78(47.6)
Neo-adjuvant	6(3.7)

Surgery	
No surgery	68(41.5)
Partial Gastrostomy	65(39.6)
Bypass surgery	28(17.1)
Total Gastrostomy	3(1.8)
Duration between surgery and chemotherapy	
<3 months	46(28.1)
≥ 3 months	83(50.6)
Unknown	35(21.3)
Chemotherapy	
Cisplatin + Paclitaxel	85(51.8)
Cisplatin + 5 FU	49(29.9)
carboplatin + Paclitaxel	17(10.4)
CHOP	13(7.9)
Regimen change	
No	130(79.3)
Yes	34(20.7)
Co-morbidity	
No	128(78.0)
Yes	36(22.0)
Chemotherapy cycles	
< 7 cycles	149(90.9)
≥ 7 cycles	15(9.1)
Follow up	
Yes	41(25.0)
No	123(75.0)
Treatment outcomes	
Dead	110(67.1)
Survived	54(32.9)

*5-FU: 5-fluorouracil*CHOP: Cyclophosphamide, doxorubicin, vincristine, prednisone

5.4 Overall Survival rate of gastric cancer patients

A 5-year overall survival rate was 11% with a median survival time of 18.6 months(1-54 months) (95% CI:16.4-19.6).The estimated cumulative survival rates of GC patients atthe 1st,2nd, 3rd, and 4thyears were 66%, 32%,18%, and 13% respectively. The probability of survival was highest on the first year of diagnosis of GC, but it was relatively shorten as follow-up time increased (Figure 1).

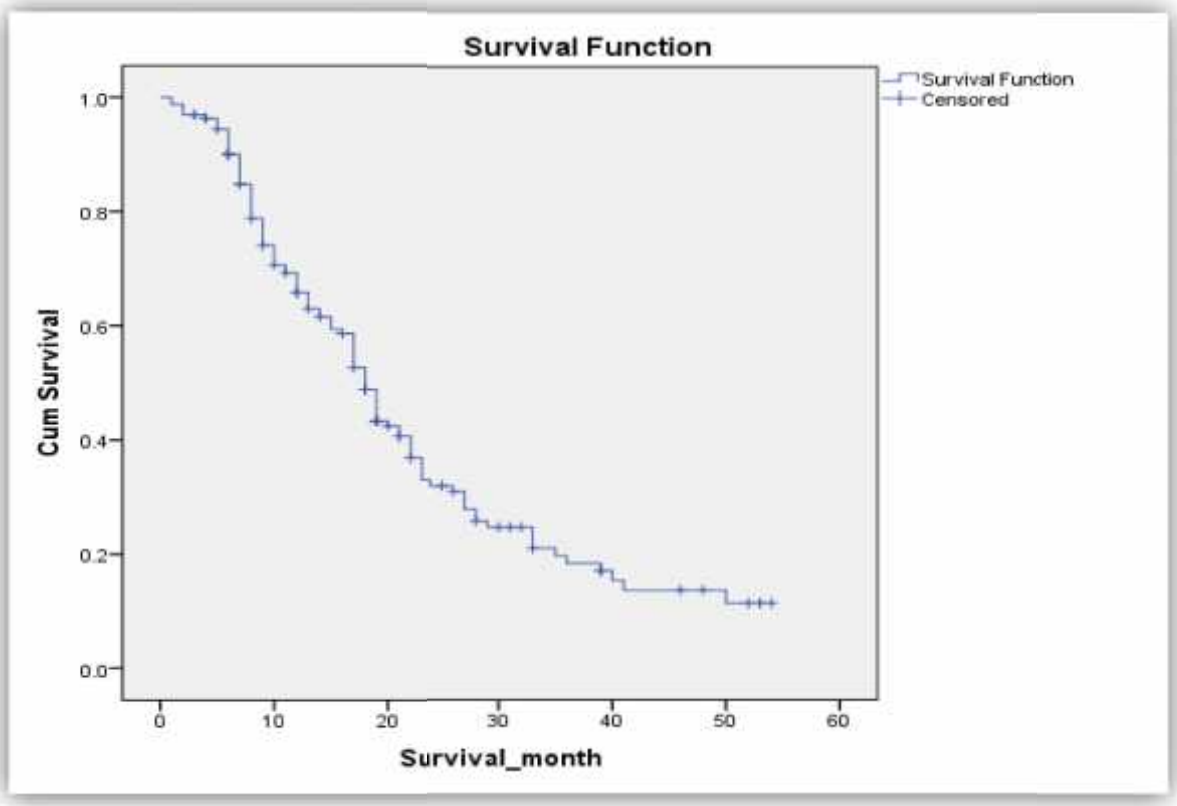


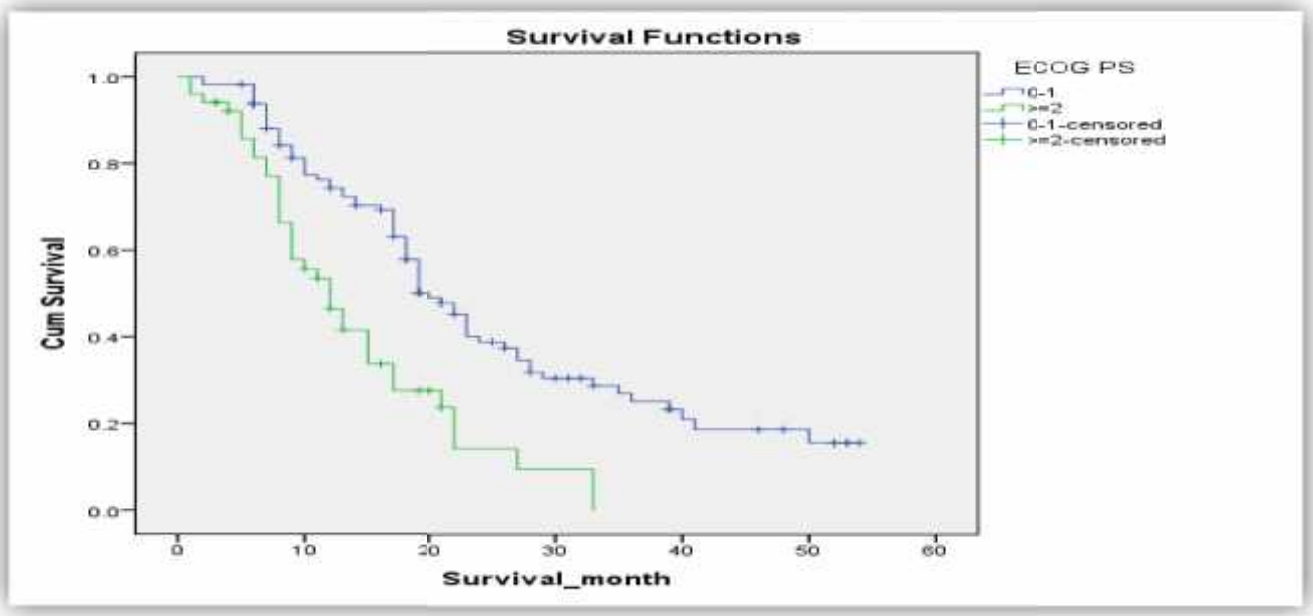
Figure 1: Kaplan Meier Plot for overall survival function in months ofpatients treated for gastric cancerat the Oncology Unit of TikurAnbessa Specialized Hospital between 1January 2016 to 31December 2020Addis Ababa, Ethiopia (n= 164).

5.5 Survival estimates among associated variables

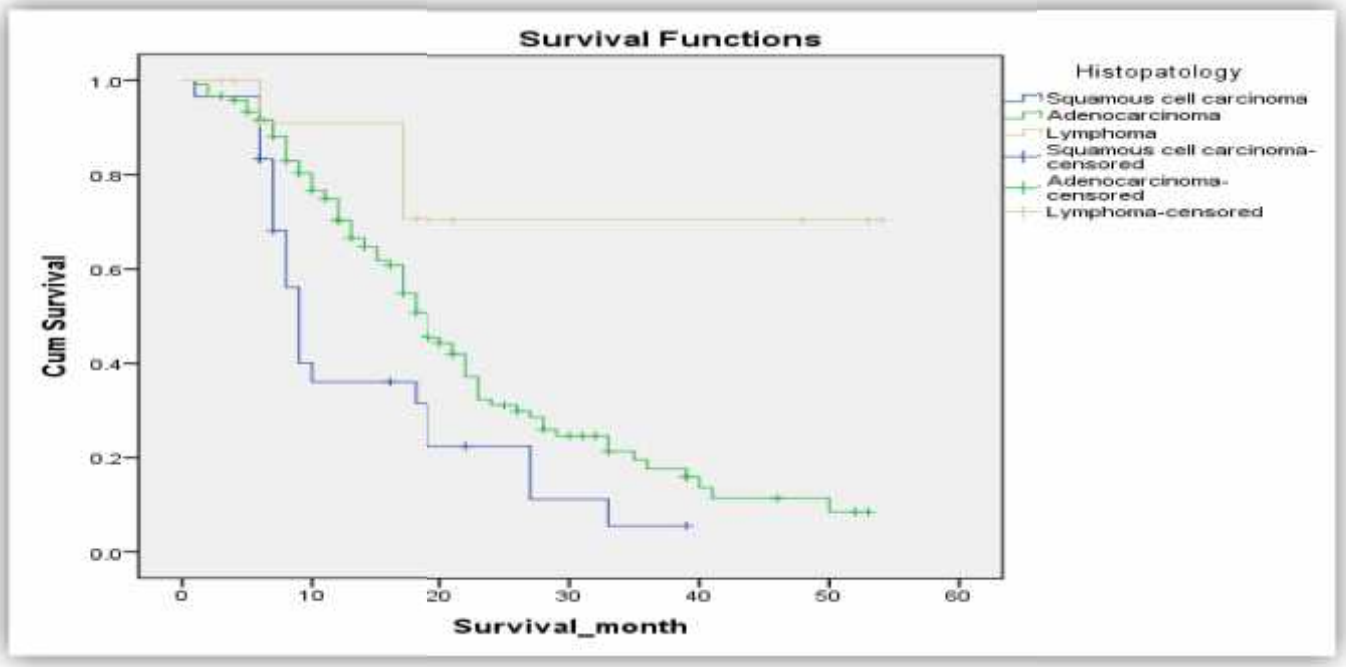
The study found that the median survival time of GC having ECOG PS≥2 was significantly (p<0.001) shorter than those with ECOG PS0-1 (12.0 months) (Figure 2A). Patients with Adenocarcinoma (AC)had alonger median survival time (22.0 months) (p< 0.004) than those with squamous cell carcinoma (SCC) (Figure 2B).Patients withcomorbidity had less survival time as compared to those without comorbidity(17.0 months) (P < 0.037) (Figure 2C). Survival time forthose withovarian (9.0 months)and

liver+lung (11.0 months)metastaseswas significantly lowercompared tothose with other sites of metastasis(Figure 2D).Patients oncarboplatin + paclitaxelhadmore survival time (23.0 months) ($p<0.006$)compared to those who received cisplatin + paclitaxel(Figure 2E).

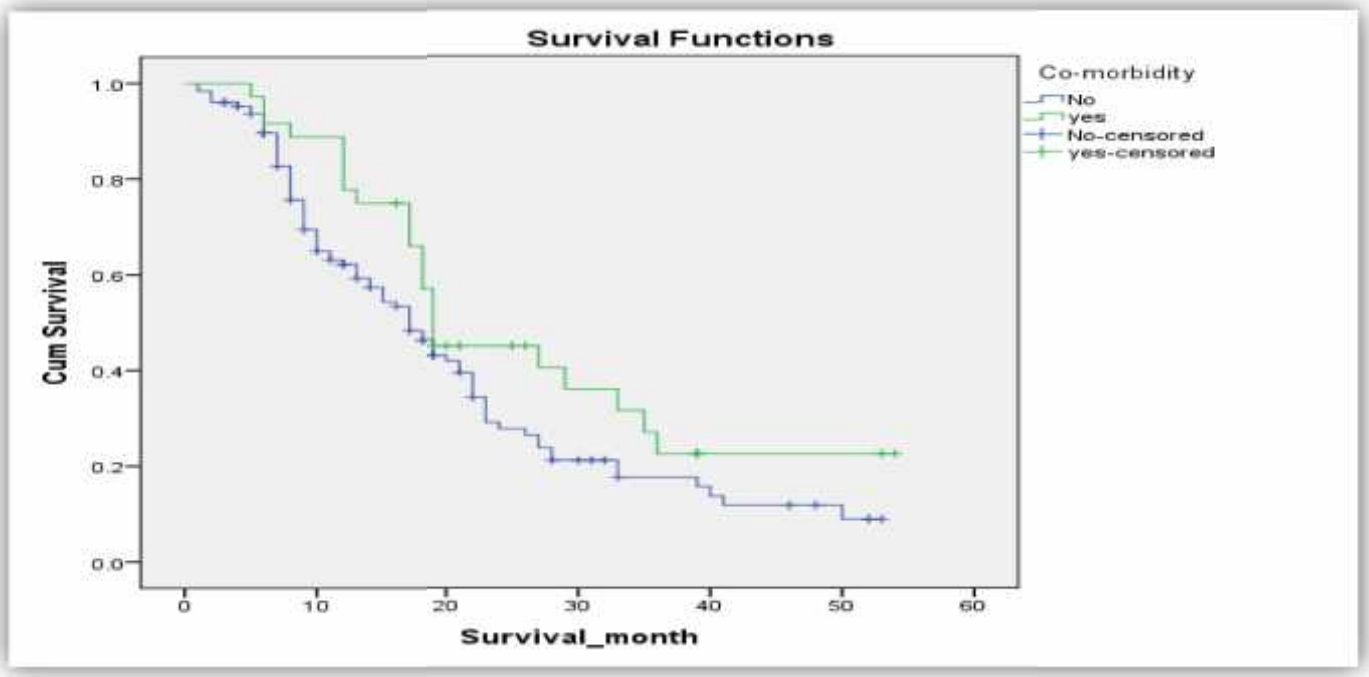
(A)



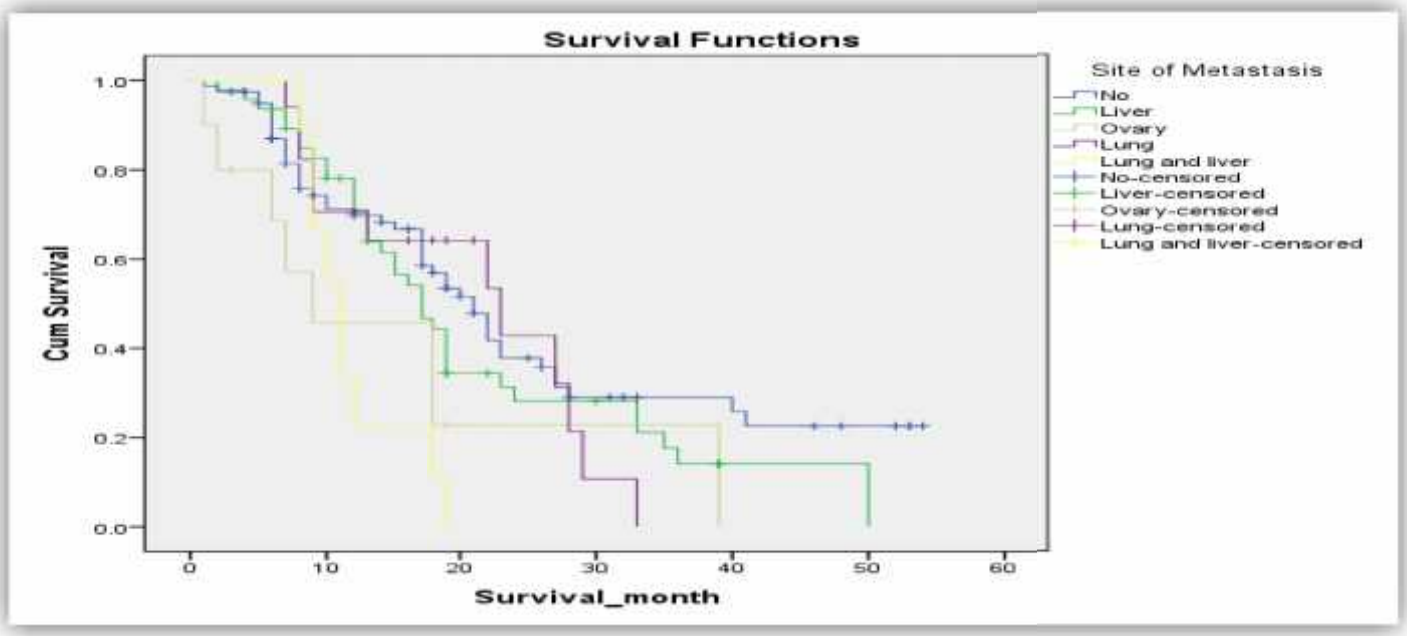
(B)



(C)


Survival Functions
Co-morbidity
No
yes
No-censored
yes-censored
Cum Survival
1.0
0.8
0.6
0.4
0.2
0.0
0
10
20
30
40
50
60
Survival_month

(D)


Survival Functions
Site of Metastasis
No
Liver
Ovary
Lung
Lung and liver
No-censored
Liver-censored
Ovary-censored
Lung-censored
Lung and liver-censored
Cum Survival
1.0
0.8
0.6
0.4
0.2
0.0
0
10
20
30
40
50
60
Survival_month

(E)

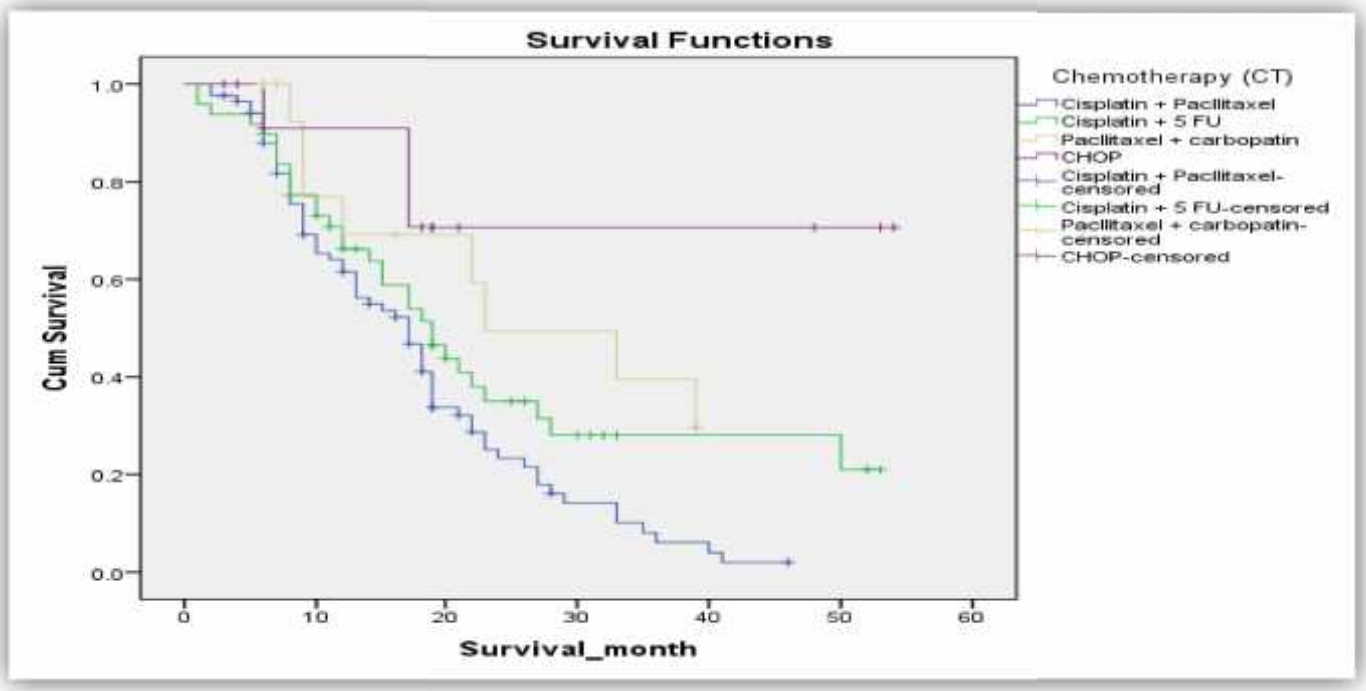


Figure 2: Kaplan-Meier survival function among different groups of gastric cancer patients: (A); ECOG PS (B); Histopathology (C); comorbidity (D); metastasis (E); Chemotherapy at TikurAnbessa Specialized Hospital between 1 January 2016 to 31 December 2020, Addis Ababa, Ethiopia (n= 164).

5.6 Predictors of gastric cancer mortality

In bivariate Cox regression analysis, factors such as age, sex, ECOG, histopathology, pathologic grading, stage, comorbidity, and metastasis site, surgical treatment modality, chemotherapy, and regimen change had a p value less than 0.2 and hence included in the multivariate analysis. In multivariate Cox regression gastric patients those with ECOG, histopathology, comorbidity, and metastasis site, chemotherapy were found to have a significant impact on survival ($p < 0.05$)(Table 4). Patients who had ECOG PS ≥ 2 were 2.5 times at higher risk for death (adjusted hazard ratio (AHR) =2.5, 95% CI: 1.4-4.5) as compared to those ECOG PS 0-1patients. Patients with AChad a 40% less chance to die (AHR = 0.4,95% CI: 0.2-0.7) as compared to SCC. GC patients who had comorbid conditionswere 1.8 fold (AHR = 1.8, 95% CI:1.2-3.3) more likely to quickly die as compared to non-co-morbidconditions. Patients who had ovarian metastasis as well as liver and lung metastaseswere 2.9 and 2.4 times at a higher risk of death, respectively, than those without metastasis (AHR = 2.9, 95% CI:1.1-7.9), (AHR = 2.5, 95% CI:1.9-6.5).

Patients who were on carboplatin + paclitaxel had a 30% less risk of death as compared to those who received cisplatin + paclitaxel (AHR = 0.3, 95% CI: 0.1-0.9) (Table 4).

Table 4: Univariate and multivariate analysis of factors contributing to survival in gastric cancer patients treatedat the Oncology Unit of Tikur Anbessa Specialized Hospital between 1 January 2016 to 31 December 2020 Addis Ababa, Ethiopia (n= 164).

Variable	**Patients**		**Events**		**Median Survival Time**	**CrudeHR (95% CI)**	**Adjusted HR (95% CI)**	**P-value**
	N	**%**	**N**	**%**				
Age								
<40	50	30.5	30	18.3%	18.9	1	1	
40-60	83	50.6	56	34.1%	19.2	1.3(0.7-2.1)	0.7(0.4-1.4)	0.342
>60	31	18.9	24	14.6%	17.5	1.5(0.8-2.7)	0.8(0.4-1.8)	0.654
Sex								
Male	105	64.0	74	45.1	18.0	1	1	
Female	59	36.0	36	22.0	19.0	0.6(0.4-1.0)	0.6(0.4-1.2)	0.158
ECOG								
ECOG 0-1	113	68.9	72	43.9	20.0	1	1	
ECOG ≥2	51	31.1	38	23.2	12.0	2.4(1.5-3.5)	2.5(1.4-4.5)	0.001*
Histopathology								
Squamouscellcarcinoma	30	18.3	23	14.0	14.0	1	1	
Adenocarcinoma	121	73.8	84	51.2	22.0	0.5(0.3-0.7)	0.4(0.2-0.7)	0.004*
Lymphoma	13	7.9	3	1.8	42.0	0.1(0.0-0.5)	0.4(0.1-2.1)	0.292
Pathological grading								
Well-Differentiated	37	22.6	22	13.4	21.0	1	1	
Moderately-	45	27.4	26	15.9	19.0	0.9(0.5-	0.8(0.4-1.7)	0.522

Differentiated						1.7)		
Poorly-Differentiated	82	50.0	62	37.8	17.0	1.6(1.0-2.6)	0.9(0.5-1.9)	0.915
Stage								
Stage 1	13	7.9	8	4.9	20.0	1	1	
Stage 2	27	16.5	12	7.3	23.0	0.6(0.2-1.5)	0.2(0.0-1.6)	0.07
Stage 3	32	19.5	21	12.8	18.0	1.4(0.6-2.9)	0.4(0.1-1.3)	0.136
Stage 4	92	56.1	69	42.1	17.0	1.8(0.9-3.6)	0.5(0.2-1.4)	0.198
Co-morbidity								
No	128	78.0	86	52.4	19.0	1	1	
Yes	36	22.0	24	14.6	17.0	1.4(0.9-2.3)	1.8(1.2-3.3)	0.037*
Metastasis								
No	80	48.8	46	28.0	21.0	1	1	
Liver	47	28.7	35	21.3	17.0	1.3(1.8-2.0)	0.9(0.5-1.8)	0.965
Ovary	10	6.1	8	4.9	9.0	2.1(1.0-4.6)	2.9(1.1-7.9)	0.035*
Lung	17	10.3	12	7.3	23.0	1.1(0.6-2.2)	0.4(0.2-1.1)	0.100
Lung and liver	10	6.1	9	5.5	11.0	2.9(1.4-6.1)	2.4(1.9-6.5)	0.048*
Surgical								
No surgery	68	41.5	49	29.9	16.0	1	1	
Total Gastrostomy	3	1.8	1	0.6	26.0	0.3(1.0-2.3)	0.3(0.0-4.5)	0.391
Partial Gastrostomy	65	39.6	40	24.4	23.0	0.5(0.3-0.8)	0.3(0.1-1.1)	0.067
Bypass surgery	28	17.1	20	12.2	11.0	1.0(0.6-	0.4(0.1--1.3)	0.150

						1.7)		
Chemotherapy								
Cisplatin+ Paclitaxel	85	51.8	68	41.5	17.0	1	1	
Cisplatin + 5 FU	49	29.9	31	18.9	19.0	0.6(0.4-1.0)	0.6(0.3-1.1)	0.081
carboplatin + Paclitaxel	17	10.4	8	4.9	23.0	0.4(0.2-0.9)	0.3(0.1-0.9)	0.044*
CHOP	13	7.9	3	1.8	35.0	0.2(0.0-0.6)	0.6(0.3-1.2)	0.162
Regimen change								
No	130	79.3	82	50.0	19.0	1	1	
Yes	34	20.7	28	17.1	17.0	0.7(0.5-1.1)	1.6(0.7-3.4)	0.184

**Variables that showed significant association with mortality*

6. Discussion

This is the first study that assessed outcome of GC patients in a tertiary care hospital in Ethiopia. There was a preponderance of male patients (1.8:1) in this study, which is in line with studies conducted elsewhere, including US-Mexico(1.4:1)(Cordero-García E, 2018), Turkey (1.5:1)(Lin WL, 2014), Taiwan (1.6:1)(Basaran H, 2015), Nigeria (1.4:1)(Ahmed A, 2011), and Ethiopia (1.3:1)(Gebresillasse HW, 2019). This gender difference is not fully related to the prevalence of risk factors that are known to exist in both genders, apart from the GC hypothesis, the risk may rise after a brief lifetime of estrogen action, as shown in early menopause and a brief reproductive period. As a result, the mechanism by which estrogen-mediated GC protection works is a reduction in gastric secretion (Park HJ, 2014).

The present study showed that the median age at diagnosis was 48.5 and 50.6 % of those diagnosed were between 40-60 years old, which shows that the majority of GC patients are middle-aged adults. This is consistent with studies done in Nigeria (Ahmed A, 2011), and Ethiopia (Gebresillasse HW, 2019), although the finding of this study is lower than those in Taiwan (Lin WL, 2014).This discrepancy could be due to different life expectancies, and socio-demographic and socio-economic status of the patients. Moreover, Ethiopians have a trend of eating red meat and high-fat content, and also lack of birth registration, as most patients in rural areas may not know their exact years of age.

The distribution of GC patients based on their region showed that (74, 45.1%) were from Oromia followed by Addis Ababa. This finding was consistent with the previous study done in TASH(Gebresillasse HW, 2019). The proximity of the region to TASH and the absence of adequate tertiary hospitals that provide cancer treatment services may explain the high number of GC patients from Oromia.

The predominant tumor location in this study was the antrum (101, 61.6%) followed by the body (21, 12.8%). This finding was consistent with studies conducted in Nigeria (64.8%) (Ahmed A, 2011) and Ethiopia (40.7%) (Gebresillasse HW, 2019), as most lesions were located in the Antrum portion of the stomach. However, the location was predominantly in the proximal area of the

stomach in other studies conducted in the US-Mexico (51.1%) (Cordero-García E, 2018), Turkey (39.5%) (Basaran H, 2015), and Taiwan (76.5%) (Lin WL, 2014). This might be because of the geographical difference, genetic polymorphisms, time trends, migratory effect of gastric cancer, and lifestyle of the patients.

In the present study, the most common histopathological type was adenocarcinoma (AC) (73.8%)followed by squamous cell carcinoma (SCC) (18.3%). The finding is consistent with other studies conducted by Basaran*et al*. (77.6%) (Basaran H, 2015) in Turkey, Ali et al. (85.2%) (Ali ZA, 2014) in Iran, and Zhang *et al.* (78.9%) in China (Zhang YF, 2012). According to the pathologic grading of GC patients, half had a poorly differentiated carcinoma. Another study in China (54.9%) (Zhu HP, 2011) and Korea (65.4%) (Kwon JY, 2011) also reported poor differentiation.

The stage of GC was not significantly associated with survival contrary to two different studies conducted showing stage was a major predictor of mortality among GC patients and had the most significant influence on patient outcome. The Italian study showed that the 5-year OS decreased from 75.0% for stage 0–I disease to 1.7% for stage IV disease(Monti M, 2020). The other study done by Basaran*et al.*(Basaran H, 2015)showed that the 1-, 2-. and 5-year survival rates were 79.5%, 50.6%, and 42% in stage II, 73.3%, 37.4%, and 14% in stage III, and 43.2%, 13.6%, and 0% in stage IV.Stage was a strong predictor of death in GC patients and had a significant impact on patient outcomes, according to the findings. This discrepancy may be due to sample size, study design, study setup, and follow-up period.

Around 51.2% of the patients had metastatic cancer at presentation. This is similar to a report from Turkey (69%)(Zhao L, 2019), Iran (30.3%) (Alimoghaddam K, 2014), and Ethiopia(54.4%)(Gebresillasse HW, 2019). The late presentation could be attributable to asymptomatic nature of the disease, a lack of screening programs, a higher proportion of advanced-stage cancer at the time of diagnosis, patients' lack of awareness of stomach cancer signs and symptoms, Ethiopia's prolonged waiting and referral system,patients' low socioeconomic level especially for patients living far from TASH, and the scarcity of cancer treatment centers. This could explain why TASH patients had metastatic disease at presentation.

In this study, from a total of 164 patients, 39.6% of cases were treated with partial gastrectomy followed by bypass surgery. This is in line with reports from China (78.9 %)(partial gastrectomy)(Zhang YF, 2012) and US-Mexico (Cordero-García E, 2018) 59.8% (subtotal gastrectomy).However, in a study conducted in Japan and Iran, more than half of the patients received complete resection (Park HJ, 2014, Ali ZA, 2014).

The study revealed that the treatment outcome of gastric cancer patients was survived for 32.9%patients and death occurred among 67.1% of gastric cancer patients. . This finding was in line with the finding in the study conducted inLatin america(Cordero-García E, 2018)(55%),Italy(Catalano V, 2008)93.1%,China(Zhang YF, 2012)(48%), Turkey (Yaprak G, 2019)59%,Turkey(Basaran H, 2015)73.2%. The similarity of the result might be due todelayed diagnosis and detection the more advanced lymph node metastasis, the more frequent peritoneal dissemination at first operation and also low resection rate (Park JM, 2006). Absence of screening program in this region may contribute to advance at the time of diagnosis, lack clinical symptom in early stage of gastric cancer,lack of awareness of the disease, and also poor accessibility to health care facilities.

The present study demonstrated that the overall 1-, 3-,and 5-year survival rates of GC patients were found to be 66%, 18%, and 11%,respectively. In the focus of 5- year survival, this finding isconsistent with the study done in Italy (Catalano V, 2008). Overall, the present finding is lowerthan other studies conducted in US-Mexico(Cordero-García E, 2018), Turkey(Ali ZA, 2014), and Iran(Yaprak G, 2019). This discrepancy may be due to limited access to healthcare services in low-income countries, a lack of early-stage cancer screening programs, a longer follow-up period, variations in waiting time for treatment after confirmed GC diagnosis, early initiation of different treatment modalities, and insufficient health information about the disease nature. Also, a higher number of patients are diagnosed at an advanced stage, resulting in a low survival rate. Furthermore, inconsistencies in survival may be related to varied approaches used in each study, including study design, sample size, sampling techniques, population factors as well as differences in local cancer care and Ethiopia's poorly developed cancer health care system.

In the multivariable Cox regression model, ECOG ≥ 2, AChistologic type, ovary metastasis, liver+ lung metastasis, paclitaxel + carboplatin were significant prognostic factors for GC patient's poor survival.

Patients who had ECOG performance status ≥ 2 were 2.5 times at higher risk for death than those with ECOG performance 0-1patients. This finding is supported by studies conducted in Italy (1.79)(Catalano V, 2008), Korea (1.46)(Kim JG, 2008), and Japan (1.52)(Shitara K, 2009)timeshigher rate of mortality. This similarity is due to the fact the patient's deterioration with GC results in an increase in the ECOG performance of the patient. HighECOG performance was a contributing factor to the low survival of GC patients.

In the current study, patients with AC were 40% less likely to die thanthose with SCC.This is similar to a study done inUSA(Akce M, 2019)and China (Feng F, 2017)which revealed that SCC had a worse chance of survival as compared to AC histology. This similarity is due to the fact that gastric SCC is quite uncommon. It's frequently identified at a later stage when it's poorlydifferentiated and it has a lower overall survival rate (Dong C, 2016).

GC patients with a comorbid condition had a1.8 times higher risk of death than non-co-morbid conditions.This is in agreement with the studies conducted in Canada (1.15) (Hoffman KE, 2013) and Nigeria(1.55)(Ahmed A, 2011). The similarity might be due to the fact that patients with comorbid conditions are less capable to receive standard treatments due to treatment-related increased side effects and toxicity; increased disabilities, patient's pill burden as well as Carlson comorbidity index, which states that the presence of comorbidity, shortens life-based on the severity of each comorbidityand have an important impact on survival(Brusselaers N, 2017).

In the present study, patients who had an ovary, as well as liver + lung metastasis,were 2.9 and 12.5 timesmore likely to die. This is supported by studies done in Japan,patients with GC metastasis to the female genital tract have an exceedingly bad prognosis, which is even worse when compared to other primary sites like the breast and colorectal (Matsushita H, 2016). In addition, Kim *et al.*(Kim JG, 2008)and Catalano *et al.*(Catalano V, 2008)confirmed that more than 1 metastatic siteincreased the risk of death. Andalso,patients with regional and distance metastases have a reduced patients' survival (Ali ZA, 2014).

The finding of this study demonstrates that patients who received Paclitaxel + Carboplatinhad a 30%lesserrisk of deaththan those who received cisplatin + paclitaxel. The median survival time for GCpatients who received carboplatin + paclitaxelwas 23 months more as compared to patientswho received cisplatin + paclitaxel.This finding was not consistent with other studies likeItaly(Monti M, 2020), and Turkey (Basaran H, 2015)Such differences are expecteddue to a different standard of treatment protocolused for the management of GC among different countries, short supply of anticancer agents in oncology centers, most anticancer drugs are expensive, and due to toxicity profile of cisplatin.

7. Strengths and limitations of the study

Because the data was gathered retrospectively, it is possible that not all of the relevant information from the patients' charts was extracted. It was also difficult to generalize the findings of a small sample size study conducted at a single facility.Patients with incomplete records were excluded, which may have induced selection bias during secondary data collection. As data on the particular causes of death were not available, cause-specific survival could not be ascertained. The underestimation of several critical variables could potentially be attributed to poor patient data documentation and record-keeping. Some predictive factors, such as nutrition and physical activity, alcohol consumption, smoking history, *H-pylori* status, and treatment problems, were not included in our study.Despite the limitations listed above, the study's main strength was that it examined the entire treatment pattern for GC in Ethiopia as well as the median survival rate to determine the patients' status using chart review and a phone interview.This study was carried out at the TASH Radiotherapy Center, the country's first and largest radiotherapy facility, which may represent the majority of the country's population. Additionally, it generated baseline data for future researchers.

8. Conclusions

The study found that patients with GC had a low five-year overall survival rate. In patients with gastric cancer, ECOG PS ≥2, adenocarcinoma histology, comorbidities, ovary, and liver + lung metastases, as well as carboplatin+ paclitaxel, were revealed to be significant predictors of mortality.

9. Recommendation

As a result of this research, the following recommendations have been made.

Tikur Anbessa Specialized Hospital

- ✓ The need to enhance early detection and prompt treatment using feasible and effective regimens, particularly to immediately begin radiation for individuals who completed chemotherapy according to protocol.
- ✓ To improve utility of the data for further research and policy formulation, health professionals working in oncology units should record detailed patient characteristics on patient charts as well as the cancer registry form.

Federal Ministry of Health

- ✓ The Federal Ministry of Health (FMOH) should develop a comprehensive GC treatment program that includes possible prevention, early identification, diagnosis, treatment, and palliative care services.
- ✓ In partnership with the public media, raise awareness of prevention techniques for GC risk factors.

Researchers

- ✓ It is recommended that more research be conducted using large sample sizes and research designs.
- ✓ A larger multi-center prospective study on a cohort of GC patients is recommended, as it will allow researchers to collect as much data as feasible.

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11. Annexes

11.1 Annex I: Data abstraction format

Study checklist

Please circle the answer that applies

Part 1: basic Socio-demographic

No	Question	Answer
1.	Medical registration number	
2.	Study number	
3.	Date of diagnosis	Day month year
4.	Mobile number	

5.	Age at diagnosis	Years
6.	Sex	1. Male 2. Female
7.	Family history of Gastric cancer	1. yes 2. No 3. Unknown
8.	Region	…… …….

Part 2: Co-morbidities

9.	Any co-morbidity	1. yes 2. no If yes, specify……

Part 3: Physical examination

10.	ECOG performance at diagnosis	1. 0 2. 1 3. 2 4. 3 5. 4 6. 5
11.	Duration since the first symptom started	……..

Part 4: Assessment

12.	Location of tumor evaluated	1. Abdominal U/S 2. CT-Scan 3. Endoscopy 4. Biopsy 5. Chest-Xray 6. other……
13.	Tumor location of the patient	1.Gastroesophageal junction 2. Cardia 3. Fundus 4. Body 5. Antrum 6. Unknown/ not mentioned
14.	Histopathology	1. Squamous cell carcinoma 2. Adenocarcinoma 3. Adenosquamous 4. Other …….
15.	Pathological grading	1. well differentiated 2. Moderately differentiated 3. poorly differentiated 4. Unknown
16.	TNM staging	T……. N…….. M……..
17.	Group stage	1.One 2. Two 3. Three 4. Four 5.Local recurrence
18.	Final assessment	……
19.	Recurrence of symptoms	1. Yes 2. No 3. Unknown
20.	Metastasize of the disease	1. No 2. Yes, 3. Unknown If yes, specifythe site of metastasis detected ……..

Part 5: treatment-related characteristics

21.	Treatment started date	……../……./…….(DD/MM/YY)
22.	chemotherapy as	1. Adjuvant 2. Neo-adjuvant 3. Palliative 4. Other……
23.	Treatment taken can be more than one answer	1. Radiotherapy (EBRT) only 2. Chemotherapy only 3. EBRT& Chemotherapy 4. surgery &EBRT 5. Surgery, EBRT & Chemotherapy 6. Surgery only 7. Palliative care 8. Surgery and Chemotherapy 9. other ……..
24.	Type of surgery performed	1. Total gastrectomy 2.Eshophagogastrectomy 3. Subtotal gastrectomy 4. Wedge resection 5. Metastenectomy 6. Bypass surgery
25.	The time duration between	1. 0-3 Months 2. 3-6 Months

	surgery and chemotherapy	3. 6-9 Months 4. 9-12 Months 5.> 1 Year
26.	Type of combination chemotherapy regimen taken	1. …….. 2. ……..
27.	Any change in the treatmentsand reason's for treatment change.	……..
28.	Type of radiotherapy treatment taken as a primary treatment.	1. Radical radiotherapy 2. Adjuvant to surgery 3. Palliative radiotherapy 4. Single shoot 5. Unknown
29.	The radiotherapy dose the patient has taken	1. Adjuvant …..Gy#..... 2. Radical …….Gy#..... 3. Palliative …..Gy#.....

Part 6: Response assessment

30.	Start day of follow up	……./……/……..(DD/MM/YY)……..
31	If chemotherapy was given, the number of cycles taken	……...
32.	Treatment-related complications	Surgical ……. Radiotherapy…….. Chemotherapy……
33	Response of the patient	1. Alive. If alive, functional status A) ECOG 0 B) ECOG 1 C) ECOG 2 D)ECOG 3 E) ECOG 4 2. Disease recurrence: A. within 1 month B. within 2 months CWithin 3 monthsD. within 6 and above months 2.1. If the disease recurred what type of treatment was given? a. …….. b…… 3. Lost to follow up, if lost to follow up, date(DD/YY/MM)……../……/…… 4. Died, if died, date of death (DD/MM/YY)……/…..…/……. What was the cause of death…….. 5. Unknown

11.2 Annex II:Consent Form

Hello, my name is ……., and I am a ……..at TikurAnbessa Specialized Hospital. I am calling because I am conducting a study about Treatment outcomes and Prognostic Factors for Survival in Patients with Gastric Cancer at Adult Oncology Unit of TikurAnbessa Specialized Hospital by Hilina Tsegaw, who is the clinical pharmacist. and would like to ask you a few minutes and the information you provide will only be used in the study.

Information which is necessary for the study will be taken from your medical. As the study will be conducted through review your medical records alone, it will not cause any harm as far as the confidentiality is kept. The information will be taken when you give permission, participation is totally voluntary. Your name and other personal identifiers will not be recorded on data collection form and the information that you give us will be kept confidential and will also be used for this study purpose only. You have full right not to let your information on medical record to be used for this study. But the information that would be taken will be quite useful for the study. You will not face any problem if you do not allow the information to be taken from your records and you will not also be denied of getting any medical services from the hospital. If you have any questions about this study you may ask me or the principal investigator Hilina Tsegaw: Tel: 0921303173

E-mail: Hilinats30@gmal.com

Are you willing to let your information to be used for this study? 1. Yes 2. No

Signature of the interviewer which shows that the respondent has consented (verbally) to take part in the study _____

11.3 **Annex-III**: Consent Form (Amharic Version)/ለጥናቱተሳታፊዎችየፈቃደኝነትመጠየቂየቅጽ

ጤናይስጥልኝ,

ስሜ.....ስራ.....የምደውልለውከጥቁርአንበሳስፔሻላይዝድሆስፒታልነው።;

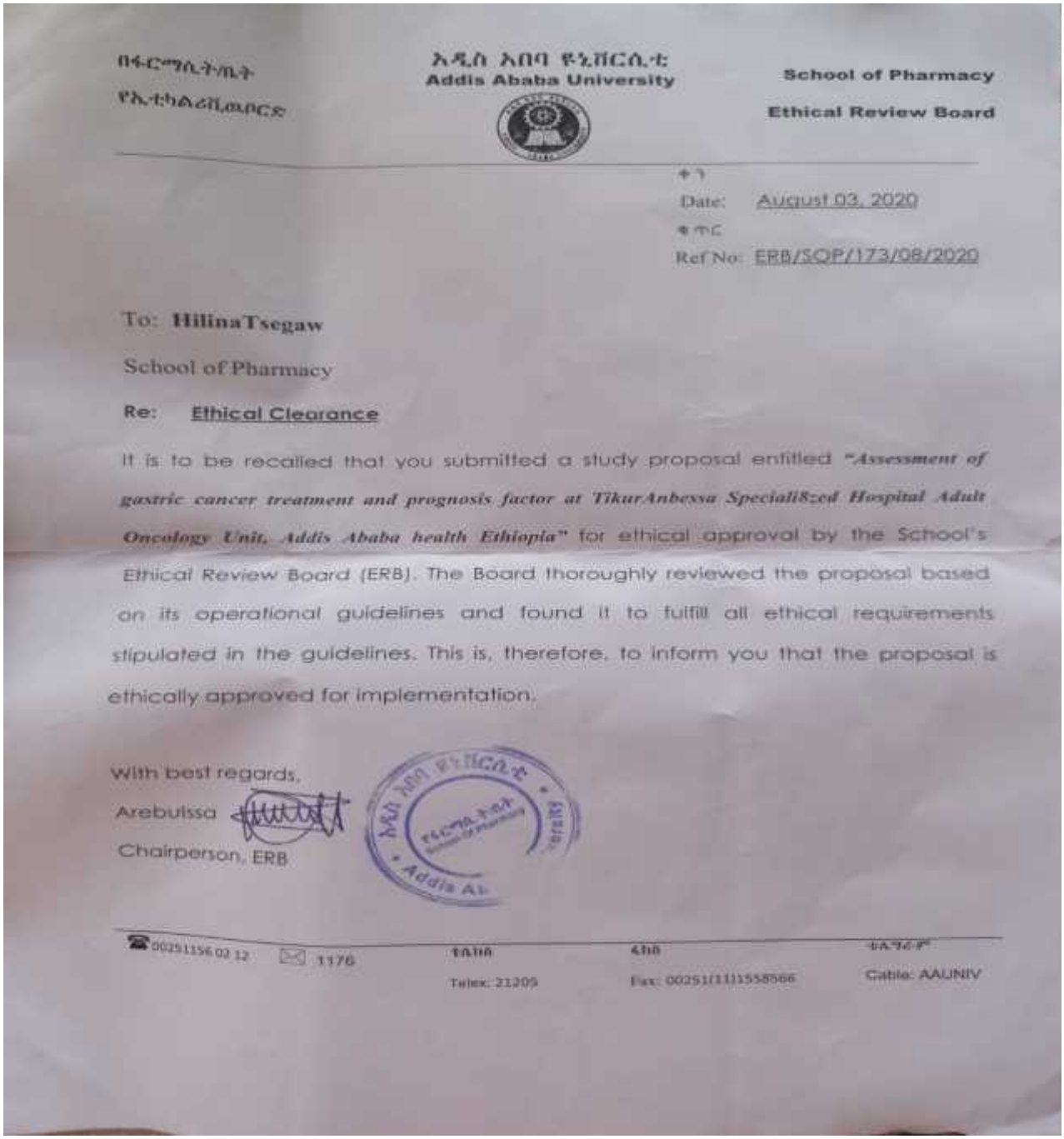
በሂሊናዐጋውበክሊኒካልፋርማሲትበጥቁርአንበሳስፔሻላይዝድሆስፒታልየአዋቂዎችኦንኮሎጂክፍልበጨጓራካንሰርላለባቸውታማ ሚዎችየህክምናውጤቶቹእናፕሮግኖስቲክምክንያቶችለመዳንጥናትእያደረግኩስለሆነነው።እናጥቂትደቂቃዎችንልጠይቅዎት??

እናያቀረቡትመረጃበጥናቱውስጥብቻጥቅምላይይውላል.ለጥናቱአስፈላጊየሆነውመረጃከህክምናዎይወሰዳል።
ጥናቱየሚካሄደውየሕክምናመዛግብትዎንበመገምገምብቻስለሆነ፣
ሚስጥራዊነቱእስከሚጠበቅድረስምንምዓይነትጉዳትአያስከትልም።ፈቃድሲሰጡመረጃውይወሰዳል፣
ተሳትፎሙሉበሙሉበፈቃደኝነትነው።
የእርስዎስምእናሌሎችየግልመለያዎችበመረጃመሰብሰቢያቅጽላይአይመዘገቡምእናእርስዎየሚሰጡንመረጃበሚስጥርይጠበቃልእና ለዚህጥናትዓላማብቻጥቅምላይይውላል።
በሕክምናመዝገብላይያለዎትመረጃለዚህጥናትጥቅምላይእንዲውልላለመፍቀድሙሉመብትአለዎት።
ነገርግንየሚወሰደውመረጃለጥናቱበጣምጠቃሚይሆናል.መረጃውከመዝገቦችዎውስጥእንዲወሰድካልፈቀዱምንምአይነትችግርአይ ገጥምዎትምእናእንዲሁምከሆስፒታልምንምአይነትየህክምናአገልግሎትእንዳያገኙአይከለከሉም.ስለዚህጥናትማንኛውምአይነትጥ ያቄካሎትእኔንወይምዋናውንመርማሪወይዘሪትሒሊናጳጋው፡በስልክቁጥር 0921303173 ኢሜል፡ Hilinats30@gmal.comመጠየቅይችላሉ።

መረጃዎትንለዚህጥናትእንዲውልለመፍቀድፍቃደኛነዎት?1.አዎ 2. የለም

የቃለመጠይቁኢድራጊፊርማይህምምላሽሰጪውበጥናቱለመሳተፍ (በቃል) መስማማቱንያሳያል

11.4 Annex III: Ethical clearance



በፋርማሲትሜት
የኢተከልሪቪውቦርድ

አዲስ አበባ ዩኒቨርሲቲ
Addis Ababa University

School of Pharmacy
Ethical Review Board

ቀን
Date: August 03, 2020
ቁጥር
Ref No: ERB/SOP/173/08/2020

To: HilinaTsegaw

School of Pharmacy

Re: Ethical Clearance

It is to be recalled that you submitted a study proposal entitled *"Assessment of gastric cancer treatment and prognosis factor at TikurAnbessa Specialized Hospital Adult Oncology Unit, Addis Ababa health Ethiopia"* for ethical approval by the School's Ethical Review Board (ERB). The Board thoroughly reviewed the proposal based on its operational guidelines and found it to fulfill all ethical requirements stipulated in the guidelines. This is, therefore, to inform you that the proposal is ethically approved for implementation.

With best regards,

Arebulssa

Chairperson, ERB

ስልክ 00251156 02 12 ፖ.ሳ.ቁ 1176 ቴሌክስ Telex: 21209 ፋክስ Fax: 00251(1)1558566 ቴሌግራም Cable: AAUNIV