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Survival Status and Associated Factors of Death Among Cervical Cancer Patients Attending at Tikur Anbesa Specialized Hospital, Addis Ababa, Ethiopia,2019.

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LISTS OF ACRONYMS AND ABBREVIATIONS

AIDS: Acquired Immune Deficiency Syndrome

AHR: Adjusted Hazard Ratio

CC: Cervical Cancer

CHR: Crude Hazard Ratio

CI: Confidence Interval

ETB: Ethiopian Birr

FIGO: International Federation of Gynecology and Obstetrics

HPV: Human Papillomavirus

ICC: Invasive Cervical Cancer

HR: Hazards Ratio

RT: Radiation Therapy

TASH: Tikur Anbesa Specialized Hospital

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ABSTRACT

Background: Cervical cancer is a cancer of uterine cervix caused by mostly sexually-acquired infection called Human papillomavirus (HPV). Death of cervical cancer varied 18-fold between different regions of the world. In developing countries, less than 50% of women with cervical cancer survive longer than 5 years. Thirty-five point nine new cases of cervical cancer are diagnosed and 22.6 die per 100,000 women annually in Ethiopia. **Objective**: The objective of this study was to asses survival status and associated factors of death among cervical cancer patients attending at Tikur Anbesa Specialized Hospital, Ethiopia,2019. **Methods and materials**: Institutional based retrospective cohort study was conducted from March to April 2019 at Tikur Anbesa Specialized Hospital oncology department (TASH). Data was collected from patient's chart using pre-tested and structured checklist prepared in English. Differences in survival among different variables was compared using the log-rank test. Variables with p-value <0.05 in multivariate analysis were considered as significantly associated to survival time. **Result:** The overall survival rate was 38.62% at five years. It is found that there were a significance differences in survival experience between categories of stage of cervical cancer, age of patients, comorbidity, substance use, base line anemia and treatment modalities. Being stage IV [AHR = 11.76; 95% CI (4.02-34.4)] ,being advanced age [AHR = 5.99; 95% CI (2.1-17.08)], being comorbid[AHR=1.58; 95%CI(1.14-2.19)], using substance[AHR=1.56;95% CI(1.09-2.22)] and being anemic [AHR=1.6;95% CI(1.11-2.36)] increased the risk of death. **Conclusion:** The five-year overall probability of survival rate among cervical cancer patient was 38.62.%, which is lower when compared with those of high- and middle-income countries. Significant factors of death after diagnosis of cervical cancer were; advanced FIGO stage, base line anemia, comorbidity, substance use, advanced age and treatment modality. **Recommendations:** Better to expand cervical cancer early screening programs and treatment facilities, give priority for comorbid and anemic patients, strengthen awareness in collaboration with public medias about cervical cancer prevention, screening and treatment options.

Key words: cervical cancer, survival status, Tikur Anbesa specialized hospital, Ethiopia

1.INTRODUCTION

1.1 Back ground of the study

Cancer describes a number of diseases that can affect various organs and parts of the body. Normally, cells multiply and die in an orderly fashion, helping us grow, replace worn tissue and heal wounds. If this process goes skewed and the cells get out of control, it creates a mass called a tumor or abnormal blood cells. In benign tumors, cells are confined to one area and cannot spread to other parts of the body, while malignant tumors consist of cancer cells that can spread through the bloodstream or lymphatic system (1).

Cancer of uterine cervix is caused by mostly sexually-acquired infection with Human papillomavirus (HPV) in which people are infected shortly after onset of sexual activity. Vaccination against Human papillomavirus in girls 9 to 13 years old integrated with regular screening in women above age 30 for precancerous lesions followed by adequate treatment are the main tools to prevent cervical cancer and increase survival rates (2).

Malignancy of uterine cervix affects women in the prime of their lives and causing premature and hopeless suffering and losing life in a critically significant part of the world's population, despite being one of the few cancers which can be prevented with simple testing (3).

The incidence of cervical cancer varied widely in different countries of the world with age-standardized rates ranging from 4.4 to 75.9 per 100 000 populations. About 85% of all new cases and 87% of all cervical cancer deaths occur in the less developed regions of the world (3).

Both the incidence and mortality rate of cervical cancer also generally increase with age, with a peak at the age group of 80-84 for both. The incidence rate is very low for women aged below 25 years and about 87% deaths occurred in the less developed regions of the world (4).

Each countries of Sub Saharan Africa should develop and implement justifiable preventive and screening programs using any of the available methods suitable and appropriate for their own setting. In addition, functional cancer registries are required to analyze the pattern of the disease so as to help in planning control programs. There is also a need to tackle some of the conditions that predispose to cervical cancer such as poverty, illiteracy, political instability and widespread underdevelopment(5).

In Ethiopia, about 35.9 new cases of cervical cancer are diagnosed and 22.6 die per 100,000 women annually. Factors that associated with cervical cancer were Human Papilloma Virus (HPV), cultural factors, Poverty, Coinfection and lack of awareness. Ethiopia has no standard policy or protocol for cervical cancer screening rather it is patchy resulting women typically present for cancer care at a late stage in the disease, where treatment is likely ineffective (6).

The study on pattern of cancer in Tikur Anbessa Specialized Hospital oncology center from 1998 to 2010 showed that among all cancer patients, only 10% of patients did come to the center in early stages (I and II). The most common cancers in female was gynecological cancers (47%) followed by breast carcinoma 26%. Cancer of uterine cervix was found the most common malignancies among all gynecological malignancies(7).

1.2 Statement of the problem

Cervical malignancy was the fourth most commonly diagnosed cancer in women in 2012, approximately 527,600 new cases worldwide. Every year more than 270 000 women die with cervical cancer, in which more than 85% of these deaths are in low and middle income countries(3, 8).

Mortality of cervical cancer varied 18-fold between the different regions of the world, with rates ranging from less than 2/100,000 in Western Asia, Western Europe and Australia greater than 20/100,000, in Melanesia (20.6), Middle Africa (22.2) and Eastern Africa (27.6). Similarly ,in less-developed countries ,less than 50% of women affected by cervical cancer survive longer than 5 years, while in developed countries the 5-year survival is about 66%(3, 9).

For black cervical cancer patients, 5-year survival rates were lower than 25% and large variation in survival from cervical cancer is observed even among developing countries due to variations in clinical stages of presentation and the availability and accessibility to diagnostic and treatment services according to the level of development of cancer related health services in different countries (10).

Treatment of cervical cancer in Africa is also hampered by the nonexistence of diagnostic and treatment services, healthcare set-ups and poor pathology services. Furthermore, there is a significant brain drain of trained healthcare workers in Africa that exacerbates the problem .By 2030, cervical cancer is expected to kill over 474,000 women per year, in which 95% of deaths are expected to be in low- and middle-income countries (8, 11).

Since cancer of the uterine cervix is still a problem in sub-Saharan Africa, intensive and focused effort towards the reduction in the burden of the disease is urgently needed and the strengthening of preventive, screening and therapeutic measures including education of the public on these aspects can bring the disease under control(5).

Ethiopia, with 16.5% cervical cancer is not the exception of low-income countries. Clients screened and diagnosed with cervical cancer and those who have multiple sexual partners had 40 times higher odd of cervical cancer than those with no multiple sexual partners.

Similarly, being human immune deficiency virus positive, sexually transmitted infection history and early age at initiation of sexual intercourse have statistically significantly associated with cervical cancer. About 35 cervical cancer cases were diagnosed for every 100,000 women, compared with only around 7 cases for every 100,000 women in North America and it is true in 2018 with an incidence of 6.6% and mortality of 7.5% in Ethiopia (9, 12)**.**

Without exception with many African countries, Ethiopia has a very limited cytological service, smears are only taken in a hospital or clinic setting and until very recently most had to be sent abroad for analysis. The prevalence of invasive cervical cancer in cervical cancer population was 15.6/1000 and risk factors were shown to be age over 35 ,parity over six ,very low income or subsistence economy, particularly in those from the rural areas and prostitution(13).

Histories showed that, of the nearly 22 million Ethiopian women above the age of 15, roughly 7,600 are diagnosed with cancer of uterine cervix and about 6,000 women die by the disease each year. These figures are probably significantly lower than the actual number of cases, given the low level of awareness, cost, and limited access to screening services and lack of a national cancer registry (14) .

Another evidences also showed that a single-visit visual inspection with acetic acid(VIA) screening at age 35 can reduce a woman's lifetime risk of cervical cancer by 25% and if she is screened again at age 40, her lifetime risk could be reduced by 65% (15).

Thirty-five point nine new cases of cervical cancer are diagnosed and 22.6 die from it per 100,000 women annually and many factors associated with it are Human Papilloma Virus (HPV), cultural factors like early marriage, poverty, coinfection and lack of awareness. There is an irregular and inconsistent cervical cancer screening although no standard policy and protocols. As a result, women typically present for cancer care at late stage in the disease, where treatment is likely ineffective(6).

2.LITERATURE REVIEW

2.1 Introduction

The aim of this literature review is to summarize what has already been existing knowledge base about cervical cancer survival and associated factors of death in developing and developed country, to discuss the impact of the research findings to clinical practice, and to identify gaps in cervical cancer patient's survival in Ethiopia. As a baseline, literatures have been reviewed and collected on overall survival status, socio demographic and individual level factors, pathologic and clinical factors and treatment factors, which have an impact on cervical cancer survival outcome.

2.2 Survival status of cervical cancer patients

A research conducted in Brazil on Five-year survival and associated factors in women treated for cervical cancer at a reference hospital showed that the overall survival rate was approximately 84% (16).

Another study done in India on the same topic reveal that the 5-year survival of stage IA patients was 95.1% and 5.3% for stage IV patients. In this study, all surgically treated stage IA patients, 94.1% of stage IB patients receiving intra cavity radiotherapy, 62% of stage IIB, 49% of stage III and 25% of stage IV patients receiving radiotherapy survived for 5 years (17).

The median survival time for cervical cancer in the study conducted in Malaysia was 65.8 months and the 5-year survival rate was 71.1% .The overall observed survival rates at 1, 3 and 5 years were 94.1%, 79.3% and 71.1% respectively and the log-rank test finding showed that there were significant differences in the 5-year survival rate among different ethnic groups(18).

A survival study of uterine cervix cancer patients in the North East India indicated that the 5-year overall survival was 40.7% and the median survival was 44 months .In this study, early stage and advanced stage patients had 47.7% and 29.4% 5-year overall survival($P = 0.002$)respectively, and HR for advanced stages was 1.8 (95% CI:1.2 to 2.7)(19).

A retrospective research conducted on cancer survival patients from a hospital-based cancer registry in China showed that the five-year survival of cervical patients taking treatment in the hospitals was 66.61% and younger patients had better prognosis and overall survival rate in Mysuru, India was found to be 48.1%, 38.7% were dead and 13.2% lost to follow up (20, 21) .

The study conducted on cervical cancer survival in a resource limited setting in North Central Nigeria indicated that the mean time to death for advanced disease was 6.9±7.0 months versus 23.7± 12.7 months for early disease (p-value 0.001) and there was a significantly higher proportion of death in those diagnosed at advanced stages compared to early stages (87.5 % versus 46.7 %, p-value 0.009).Death rate was significantly higher among women with advanced ICC (rate ratio=4.7, 95 % CI: 2.0_12.8, p-value 0.001) and those with baseline anemia (rate ratio=4.8, 95 % CI: 2.3–10.4, p-value 0.001). There was significantly lower death rate in this study for those who had chemo-radiation compared with those who did not (rate ratio=0.33, 95 % CI: 0.11, 0.81, p-value 0.007)(22).

A study in Kenya on analysis of factors contributing to the low survival of cervical cancer patients undergoing radiotherapy alarmed that the mean time to death after the start of treatment was about 15.1 months whereas the median survival was about 15 months. Median survival for FIGO Stage I was 21months while stages II, III, and IV were 18, 15 and 11 months respectively and the overall survival rate was less than 20%.Aretrospective study on determinants of survival among patients with cervical cancer reveled that overall five year survival rate was found to be 48.1%, 38.7% had lost their life and 13.2 % lost to follow up (23, 24).

The study conducted in Tikur Anbesa Specialized Hospital (TASH) on cervical cancer presentation and survival revealed that 17.3% cervical cancer patients died during the follow-up period and the median survival time was 38 months. Of the total deaths, 41(11%) and 31(22.3%) were HIV negative and HIV Positives while the median survival of HIV positives and HIV negative was 29 and 28 months respectively(25).

2.3 Associated factors of death among cervical cancer patients

Different studies on survival status and factors associated to death among cervical cancer patients have been shown that stage of cancer at diagnosis, histological grade and type, age at diagnosis, treatment modality, co-morbid illness, individual level and sociodemographic factors determine the survival time of cervical cancer.

Differences in survival time among cervical cancer patients have been reported in different countries and in different studies. Some of the literatures regarding factors associated to death among cervical cancer are reviewed as follows.

2.3.1. Sociodemographic and individual level factors

A research conducted on socioeconomic position and survival after cervical cancer among Danish women showed that mortality was higher in women with shorter rather than longer education (HR= 1.46;95%CI: 1.20–1.77), among those with lower rather than higher income (HR, 1.32; 1.07–1.63), among women age <60 years and without a partner rather than those who live together with partner (HR, 1.60; 1.29–1.98). Socioeconomic differences in survival were partly explained by cancer stage and less by comorbidity or smoking with adjusted HRs being 1.07; 0.96–1.19 for education and 1.15; 0.86–1.52 for income)(26).

A study in Kenya on analysis of factors contributing to the low survival of cervical cancer patients undergoing radiotherapy indicated that poor education, lack of cancer awareness coupled with an absence of regular screening programs, late patient presentation, sub-optimal diagnosis and treatments are major factors contributing to the alarmingly low survival rate of cervical cancer patients (23).

Another study conducted to identify determinants of survival of cervical cancer showed that age at diagnosis, education, performance status at presentation, staging ($p = 0.001$), parity, tobacco chewing ($p< 0.01$) and age at menopause ($p = 0.05$) were significantly associated with survival(24). Age at diagnosis (hazard ratio = 2.17, $p = 0.05$), performance status at presentation (hazard ratio = 0.21, $p = 0.001$), staging (hazard ratio = 0.55, $p = 0.001$) and treatment duration in weeks (hazard ratio = 1.96, $p < 0.01$) were the independent predictors of survival in the study conducted in Mysuru, India (21).

2.3.2. Pathological and clinical factors

A research done in the Northwest Russia on the incidence, mortality and determinants of survival from cervical cancer showed that one and 5-year survival was 77.4% (95% CI 75.4 to 79.4) and 60.0% (95% CI 54.6 to 61.5), respectively and Significant inverse association was observed between survival and stage of cancer. Patients with adenocarcinoma (HR=1.6, 95% CI 1.2 to 2.2), other histological types of cancer (HR=1.8, 95% CI 1.4 to 2.4) and those with undefined histologic type (HR=3.8, 95% CI 2.5 to 5.8) had shorter survival than patients with squamous cell carcinoma (27).

The five year cumulative survival afterward reappearance of cervical cancer was 34.3% and on multivariable analysis, pattern of reappearance ($p = 0.003$), symptom status ($p = 0.011$), age ($p = 0.035$), and white blood cell (WBC) count ($p = 0.017$) were independent prognostic factors for overall SAR from the study conducted in Thailand on clinical aspects and prognostic factors for survival in patients with recurrent cervical cancer after radical hysterectomy (28).

A research also conducted on incidence and survival rate of women with cervical cancer in the Greater Amsterdam area indicated as cases of adenocarcinoma of the uterine cervix are associated with a decreased survival rate compared to patients with squamous cell carcinoma. Decreased survival was related to tumor histology itself, since after correction for factors such as age, stage and lymph node status, the survival of adenocarcinoma patients was still lower compared with squamous cell carcinoma patients(29).

A research conducted in Brazil on five-year survival and associated factors in women treated for cervical cancer at a referral hospital reveled as disease stage ($p<0.01$), metastasis ($p<0.01$) and readmission ($p<0.01$) had significant influences on patient outcome, and the primary survival factors were associated with earlier stages of the disease(16).

Another study on comorbidity and cervical cancer survival of indigenous and non-indigenous Australian women indicated that presence of comorbidity lowered the survival rate by 4.6 times(HR=4.6,95%CI: 3.54–6.03)(30). The study on HIV infection and survival among women with cervical cancer in Botswana reveled as the three-year survival for the women with HIV was 35% (95% CI, 27% to 44%) and 48% (95% CI, 35% to 60%) for those without HIV.

In an adjusted analysis ,HIV infection significantly increased the risk for death among all women (hazardratio,1.95;95%CI,1.20to3.17)(30, 31).

The study conducted on cervical cancer survival in a resource limited setting in north central Nigeria indicated that unadjusted model showed a statistically higher hazard of death in patients with advanced disease (HR=3.9, 95 % CI: 1.7, 9.2, p-value 0.002),

and baseline anemia (HR=3.7, 95 % CI: 1.8, 7.5, p-value 0.001). Chemo-radiation showed a tendency towards reduced hazard of mortality (HR=0.45, 95 % CI: 0.19, 1.12, p-value 0.088). In the adjusted model ,stage at diagnosis, baseline anemia and chemo-radiation were independently associated with significant hazards of death after diagnosis of ICC (HR=3.3, 95 % CI: 1.2–8.9, p-value 0.021 and HR= 3.0, 95 % CI: 1.4, 6.4, p-value 0.006) respectively (22).

A retrospective cohort study conducted between September 2008 and September 2012 to examine the clinical characteristics and survival of CC patients registered at the radiotherapy center of TASH showed that HIV status, FIGO stage, co-morbidity and baseline anemia status and older CC patients had a two-fold higher risk of death than younger patients (HR=2.02, 95%CI: 1.01–4.05). CC patients with higher cancer stage (FIGO IIB-IIIA and recurrence) had a higher risk of death, with HR=2.60 (95%CI: 1.67–4.04) and HR=2.77 (95%CI: 1.35–5.68), respectively. Cervical cancer patients with anemia at baseline were more likely to die than no anemic patients with HR=1.65 (95%CI: 1.24–2.20) (25).

2.3.3. Treatment related factors

A research conducted on simultaneous chemotherapy and pelvic radiation treatment compared with pelvic radiation treatment alone as adjuvant treatment next to radical surgery in high-risk early-stage Cancer of the Cervix indicated that the patients who got both radiation and chemotherapy had an estimated 4-year progression-free survival rate of 80 percent, compared with 63 percent in women treated with radiation alone (P = .003) (32).

The estimated 4-year overall survival rates for these two groups in this study were 81 and 71 percent, respectively. Analysis of the women receiving chemotherapy found that higher numbers of completed chemotherapy cycles were associated with greater progression-free survival and overall survival rates (P = .03 for both)(32).

The study conducted in Florida to assess disparities in survival among women with invasive cervical cancer reveled that women who underwent surgical treatment had a 62% decreased risk of death compared with women who did not undergo surgery, whereas women who received radiation therapy had a 28% decreased risk of death compared with women who did not receive radiation therapy ($p < .001$) (33).

Another study done on cisplatin versus carboplatin; a comparative review of therapeutic management in solid malignancies reveled that early stage cervical cancer, use of cisplatin based chemoradiation as the gold standard of therapy in patients with locally advanced disease. Further, this research consolidated of chemoradiation vs RT alone favored chemoradiation with an absolute survival benefit of 12% at 5 years(34).

The study conducted in Ethiopia on the effect of adherence to radiotherapy on survival reveled that one-year overall survival (OS) after radical RT for FIGO stages IIA–IIIA was 89% for discontinuation (<72 Gy) and 96% for adherence (≥72 Gy; hazard ratio 1.3; 95%CL). One-year OS after nonradical RT for FIGO stages IIIB–IVA was 71% for discontinuation (<40 Gy) and 87% for adherence (44–50 Gy; HR, 3.1; 95% CI, 1.4–6.9) in this study and one-year OS for FIGO stages IIIB–IVB after one compared with two or more palliative single fractions of 10 Gy were 14% and 73% respectively (HR, 7.3; 95% CI, 3.3–16)(35).

2.4 Justification of the study

Although the increasing pattern of the disease, high incidence of death, advanced stage of diagnosis, and variation in survival rates of cervical cancer across the world, few is known about survival status and associated factors of death of cervical cancer in Ethiopia. Therefore, the need to asses survival status and associated factors of death among cervical cancer patients is very critical.

Despite, the government concern on the issue of non-communicable diseases with especial emphasis on cancer to reduce the incidence and mortality and different studies conducted on prevalence of cervical cancer, pattern of cervical cancer and factors on delay in diagnosis, almost none of them did touch the survival status and associated factors of cervical cancer.

Due to such reasons, the emphasis of this study was to identify survival status and major factors associated to time to death, outcomes of cervical cancer and the extent to which these disparities explained by many factors.

2.5 Significance of the study

The government of Ethiopia implemented a national strategic plan to reduce cancer incidence and mortality by 15%by 2020 through systematic and equitable implementation of evidence-based interventions for prevention, early detection, treatment, and palliation. The world cancer control initiative in low and middle income countries that reviewed current disease state ,health care situation and evaluation of disease control strategies also set priorities and allocate resources for national level strategy to reduce morbidity and mortality from cancer (36, 37).

This study will be an input to policy makers, program managers, health professionals in order to estimate survival rate of cervical cancer patients, to decide based on evidence about cervical cancer treatment and to support the plan of cancer control and prevention of the country's national cancer control program.

The rational of studying survival status and factors associated to it of cervical cancer patients will have practical vital value for patients, care providers, researchers and policy-makers in the Ministry of Health and the study will help both the individuals and society at large, to assess progress in cancer control, including the effect of early detection, diagnosis, and follow-up on cervical cancer outcomes.

This paper will also provide insight for nurses in cancer treatment centers to know the quality and effectiveness of care they providing. Furthermore, knowing cervical cancer survival outcome facilitates the initiation of personalized treatment, reduces unnecessary treatments, and more precise decision making for both clinicians and patients**.** This will promote nursing research, nursing education and clinical practice so as to provide evidence-based nursing care. Finally, this paper will also be a base line for future researchers who are interested in this area.

2.6 Conceptual framework

The conceptual framework shown below is set out from different literatures studied in many countries (20, 23, 24, 28) and adapted in the context of Ethiopia. It shows the effect of independent variables (Socio demographic& Individual level factors, pathologic and clinical factors and treatment related factors) on dependent variable (time to death).

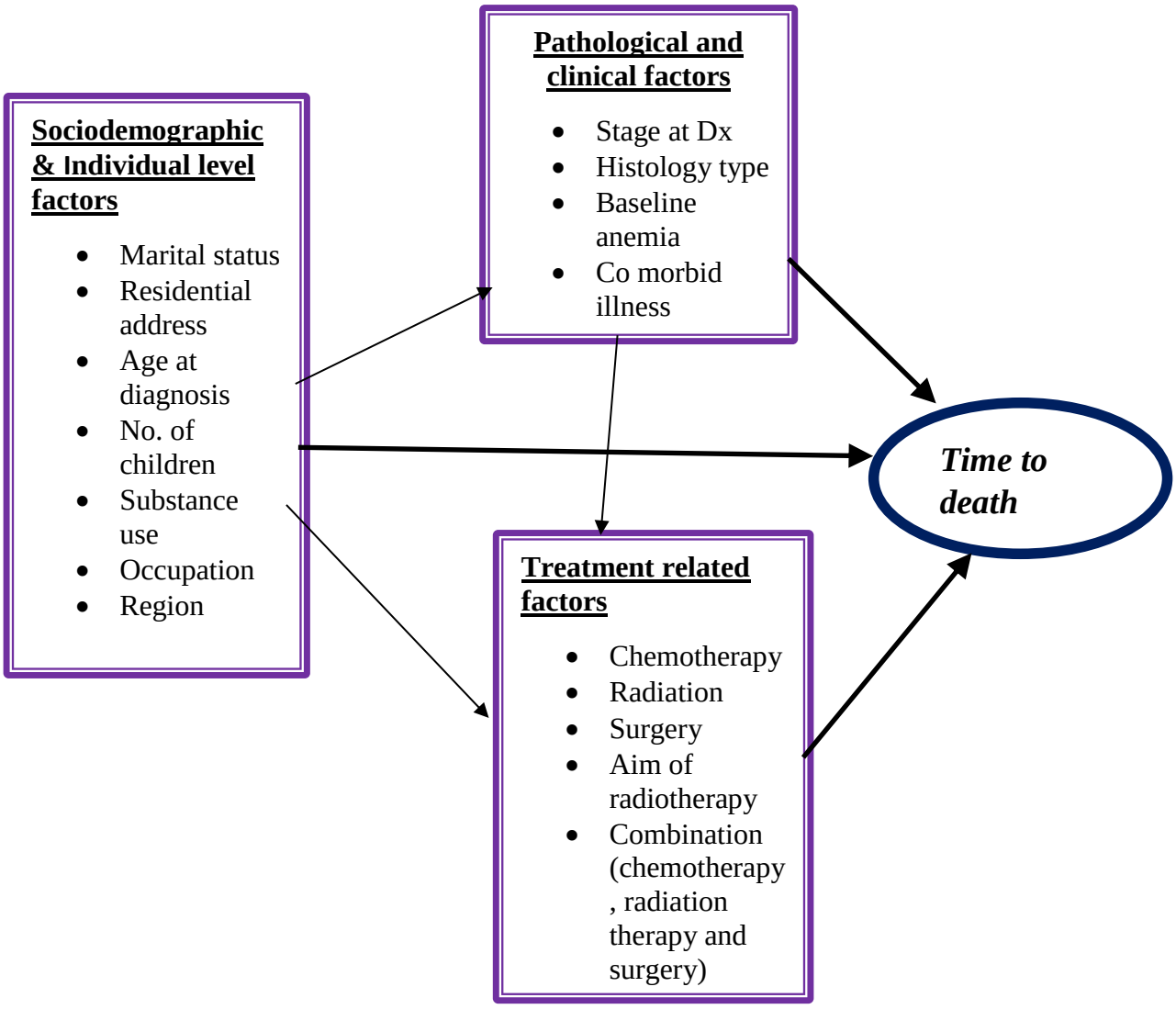

Figure 1: Conceptual framework for the assessment of survival status and associated factors of death among cervical cancer patients at Tikur Anbesa Specialized Hospital (TASH), Addis Ababa, Ethiopia, 2019(20, 23, 24, 28).

3.OBJECTIVES OF THE STUDY

3.1General objective

To asses survival status and associated factors of death among cervical cancer patients attending at Tikur Anbesa Specialized Hospital, Addis Ababa, Ethiopia

3.2 Specific objectives

1.To determine survival status of cervical cancer patients in Tikur Anbesa Specialized Hospital, Addis Ababa, Ethiopia.

2.To identify factors associated with death among cervical cancer patients attending Tikur Anbesa Specialized Hospital, Addis Ababa, Ethiopia,

4.METHODS AND MATERIALS

4.1 Study area and period

This study was conducted at the oncology department of Tikur Anbesa Specialized Hospital (TASH) Addis Ababa, Ethiopia. Addis Ababa is the capital city of Ethiopia, and the political capital of African union and other international organizations. Based on the central statistics agency description of census 2007, Addis Ababa city has a total population of 3,384,569(38). TASH is the biggest referral public hospital in Ethiopia established in 1972. It is the training center of health professionals including undergraduate and postgraduate medical students, dentists, nurses, pharmacists, laboratory technicians and others paramedics.

The hospital is staffed by many health professionals from various disciplines. It has total beds of 800 and the beds reserved for cancer care at oncology department are 20. The oncology department of the TASH is providing chemotherapy, radiation therapy, complain therapy and other supportive and palliative cares. It is the main center for cancer registry, early detection, prevention, standard treatment and palliative care in Addis Ababa and it is the only cancer center in the Ethiopia. This study was conducted from March to April 2019.

4.2 Study design

Institutional based retrospective cohort study was conducted.

4.3 Source population

All medical records of women diagnosed with cervical cancer in Tikur Anbesa Specialized Hospital attending the oncology department.

4.4. Study population

All medical records of cervical cancer patients who attended the oncology department of TASH from January 1,2014 to December 31,2016.

4.5 Sample population

All medical records of cervical cancer patients who attended the oncology department of TASH from January 1,2014 to December 31,2016 and who fulfill the inclusion criteria of the study.

4.6 Inclusion and exclusion criteria

4.6.1 Inclusion criteria

- All cervical cancer patients diagnosed and treated at TASH from January 1,2014 to December 31,2016

4.6.2 Exclusion criteria

- Patients whose medical charts are incomplete.
- Patients whose medical charts not found
- Patients who had been previous diagnosis of cervical cancer and registered during the data collection times.

4.7 Sample size determination

The sample size was all cervical cancer patient's medical records diagnosed and treated at TASH from January 1,2014 to December 31,2016.

4.8 Sampling procedure

Census sampling procedure was used and the procedure was as follows: at the beginning, profiles of all cervical cancer women on follow up between January 1,2014 to December 31,2016 in the TASH was assessed and 1227 patients' medical record numbers were found. Six hundred thirty-four (634) medical records which fulfilled the inclusion criteria were identified by data collectors from list of cervical cancer charts that are on cancer care follow up at TASH oncology department. Finally, data was collected from 634 patients' medical charts.

4.9 Study variables

Dependent variables: Time to death

Independent variables:

- **Sociodemographic and individual level factors:**
  - Marital status
  - Residential address
  - Age at diagnosis
  - Substance use
  - Number of children
  - Region
  - Occupation
  - Religion

- **Pathological and clinical factors**

- Stage at presentation
- Histology type
- Bassline anemia
- Comorbidity
- Types of comorbidity

- **Treatment related factors**

- Chemotherapy
- Radiation
- Surgery
- Aim of radiotherapy
- Combination of treatments

4.10. Operational definition

Event: Death of cervical cancer patients was an event of interest for this research.

Censored: patients who loss follows up, not die up to the study period and those transfer to different care unit during the study.

Comorbidity: The presence of any conditions (mentioned in the Carlson comorbidity Index(39)) other than cervical cancer at diagnosis which was designated as "yes**"** in the checklist

Substance use: substance use in this research was defined as cervical cancer patients who used one, two or all of the three substances (cigar ate, chat and alcohol)(40)

Anemia: cervical cancer patient with hemoglobin levels below 12.0 g/dl was classified as anemic in this research(41)

Incomplete card: when one of the major independent variables that was not registered.

Entry date and closing date to follow-up: -The entry date was the starting date for calculation of survival status, and this was the first date of clear diagnosis of cervical cancer (January1st 2014 to December31st, 2016). Closing date was the ending date to follow up (December31st, 2018).

Survival status. In this research, survival status was defined as the outcome of patients which was classified into censored or death from patient clinical data file from scheduled or unscheduled return visits.

Time to death: time to death was calculated at the time between the date of clear diagnosis of cervical cancer to the date of death (in month).

Stage at diagnosis: The revised FIGO staging for carcinoma of the vulva, cervix, and endometrium was used in this study (42).

4.11 Data collection instrument

Data was collected from patient's charts using pre-tested and structured checklist prepared in English. The checklist consisted three parts: (1) sociodemographic and individual level factors, (2) Pathological and clinical factors and (3) Treatment related factors.

4.12 Data collection procedures

Two supervisors having second degree in oncology nursing and three data collectors having first degree in nursing were involved in the data collection process. After recruiting data collectors and supervisors, one-day intensive training was given to them before the actual work begin regarding the aim of the study, procedures including ways of collecting the data and clarify about the checklist.

4.13 Pre-test

Pretest study was conducted by considering 5% of the total sample size to test its consistency with actual data collection in the charts recorded during the study period. After pretest, the checklists were assessed for its clarity, length and completeness and the necessary corrections were done accordingly.

4.14 Data quality assurance procedures

The quality of data was assured by proper designing and pre-testing of the checklists in 5% of patient's charts and by giving training for the data collectors and supervisors before the actual data collection. Appropriate modifications were made after viewing the pre-test result and overall supervision was made by the principal investigator.

Every day after data collection, checklists were reviewed and checked for completeness, accuracy and clarity by the supervisors and principal investigator and the necessary feedback was offered to data collectors in the next morning.

4.15 Data processing & analysis

Data were coded and then entered, edited and cleaned using EPI-data 3.1 and exported to STATA14.2 statistical software for analysis. Frequencies, proportions and descriptive statistics was used to describe the study population in relation to relevant variables and was presented using tables and graphs. Kaplan Meier analyses with life table were used to identify the overall survival rates and median survival time. Differences in survival among different variables were compared using the log-rank test. Incidence rate of death was calculated for the entire study period. Subsequently, the number of mortalities within the follow up was divided by the total person time at risk on follow up and reported per 100 per person (PY). Before running the Cox regression model, assumption of proportional-hazard was performed. Cox-proportional hazard model assumption was checked using Schoenfeld residual test and variables having P-value >0.05 were considered as fulfilling the assumption.

Variables with a significance level below 0.2 in the bivariable Cox regression model were included in a multivariable Cox regression model analysis. Variables in multivariable Cox model with a p-value <0.05 were considered to have actual interference with the survival of the patients with 95%confidence interval.

4.16 Ethical considerations

Ethical approval for this study was obtained from the Institutional Review Boards of school of nursing and midwifery, Addis Ababa University. The study was conducted with and without individual informed consent because it relies on retrospective patient chart review except some variables that need phone call to the clients. Individual informed consent was taken for those variables that need phone call.

4.17 Dissemination of results

The result of this study will be presented to Addis Ababa University, College Of Health Science, school of nursing and midwifery. It will be submitted to Tikur Anbesa Specialized Hospital (TASH) department of oncology administration, Ministry of health and finally it will be published in peer review journals and it will also be presented at seminars and workshops

5. RESULT

5.1 Socio-demographic characteristics of the study participants

Between January 1st2014 to December 31st 2016, 1227 cervical cancer patients were enrolled to Tikur Anbesa Specialized Hospital from which 634 were eligible for this study. The median age of study participants was 50 months with SD ± 11.72. The minimum and maximum ages of patients were15 and 87 years respectively. Majority (56%) of participants were urban dwellers and most (32%) of the participants came from Oromia region. More than half (58.2%) of the study participants were Orthodox religion followers and 42.4% were house wives. Nearly one sixth (16.7%) use substance, about two third 64.2 % were married and 42% have more than three children (Table 1).

Table 1: Socio demographic characteristics of cervical cancer patients in TASH adult oncology department from 1st January 2014_December 31, 2018, Addis Ababa, Ethiopia 2019(n=634).

Covariates	**Code**	**Status at last contact**		**Total No (%)**
		Censored No (%)	Death No (%)	
Age	<30	55(93.2)	4(6.8)	59(9.3)
	30-39	100(84.0)	19(16.0)	119(18.8)
	40-49	118(72.0)	46(28.0)	164(25.9)
	50-59	101(65.2)	54(34.8)	155(24.4)
	≥60	74(54.0)	63(46.0)	137(21.6)
Residence	Urban	253(71.3)	102(28.7)	355(56)
	Rural	195(69.9)	84(30.1)	279(44)
Region	Amhara	104(64.6)	57(35.4)	161(25.4)
	Oromia	146(71.9)	57(28.1)	203(32)
	Tigray	14(60.9)	9(39.1)	23(3.6%)
	SNNP	41(68.3)	19(31.7)	60(9.5)
	Addis Ababa	127(76.0)	40(24.0)	167(26.3)
	Others	16(80.0)	4(20.0)	20(3.2)
Religion	Orthodox	257(69.6)	112(30.4)	369(58.2)
	Muslim	94(70.7)	39(29.3)	133(21)
	Protestant	87(73.1)	32(26.9)	119(18.8)
	Others	10(76.9)	3(23.1)	13(2.1)

Table 2: Socio demographic characteristics of cervical cancer patients in TASH adult oncology department from 1st January 2014_December 31, 2018, Addis Ababa, Ethiopia 2019(n=634) ……. continued.

Occupation	Gov't employee	63(74.1)	22(25.9)	85(13.4)
	Merchant	44(60.3)	29(39.7)	73(11.5)
	Farmer	77(65.8)	40(34.2)	117(18.5)
	house wife	197(73.2)	72(26.8)	269(42.4)
	Others	67(74.4)	23(25.6)	90(14.2)
Substance use	User	51(48.1)	55(51.9)	106(16.7)
	None user	397(75.2)	131(24.8)	528(83.3)
Children	no child	18(90)	2(10)	20(3.2)
	One	27(65.9)	14(34.1)	41(6.5)
	Two	64(69.6)	28(30.4)	92(14.5)
	Three	138(64.2)	77(35.8)	215(33.9)
	more than 3	201(75.6)	65(24.4)	266(42)
Marital status	Married	287(70.5)	120(29.5)	407(64.2)
	Single	22(71)	9(29)	31(4.9)
	Widowed	65(66.3)	33(33.7)	98(15.5)
	Divorced	74(75.5)	24(24.5)	98(15.5)

5.2 Clinical, histopathological and treatment characteristics

Majority (65.1%) of cervical cancer patients presented at advanced stages (III&IV), 574 (90.5%) participants had squamous cell carcinoma, nearly half (50.9%) were anemic during presentation. About one third (33.4%) had comorbidity and from those who had comorbidity, more than half (54.7%) were HIV positives. Majorities (50.3%) took radiation treatment only and from those who took chemotherapy treatment, 14.5% took only first cycle at last contact. Three hundred ninety (61.5%) of patients took palliative radiotherapy (Table 2&3).

Table 3: Clinical and histopathological characteristics of cervical cancer patients in TASH adult oncology department from 1st January 2014_December 31, 2018, Addis Ababa, Ethiopia,2019(n=634)

Covariates	Code	Status at last contact		Total No (%)
		Censored No (%)	Death No (%)	
FIGO stage	Stage I	59(93.7)	4(6.3)	63(9.9)
	Stage II	132(83.5)	26(16.5)	158(24.9)
	Stage III	184(72.2)	71(27.8)	255(40.2)
	Stage IV	73(46.2)	85(53.8)	158(24.9)
Histopathology	squamous cell	406(70.7)	168(29.3)	574(90.5)
	Adenocarcinoma	42(70.0)	18(30.0)	60(9.5)
Anemic status	Yes	184(57.0)	139(43.0)	323(50.9)
	No	264(84.9)	47(15.1)	311(49.1)
Comorbidity	Yes	117(55.2)	95(44.8)	214(33.4)
	No	331(78.4)	91(21.6)	422(66.6)
Types of comorbidity	HIV	56(47.5)	62(52.5)	118(55)
	Hypertension	29(59.2)	20(40.8)	49(23)
	Others	33(70.2)	14(29.8)	47(22)

Table 4:Treatment related characteristics of cervical cancer patients in TASH adult oncology department from 1st January 2014_December 31, 2018, Addis Ababa, Ethiopia,2019(n=634*)*

Covariate	Code	Status at last contact		Total No (%)
		Censored No (%)	Death No (%)	
Treatment initiated	Surgery and chemo	7(77.8)	2(22.2)	9(1.4)
	Chemotherapy only	13(81.3)	3(18.8)	16(2.5)
	Radiotherapy only	228(71.5)	91(28.5)	319(50.3)
	Chemo radiation only	142(66.7)	71(33.3)	213(33.6)
	surgery & radiation only	51(78.5)	14(21.5)	65(10.3)
	Surgery+chemo+radation	7(58.3)	5(41.7)	12(1.9)
Chemotherapy cycles	No chemo	235(70.6)	98(29.4)	333(52.5)
	First cycle	69(75)	23(25.0)	92(14.5)
	Second cycle	59(68.6)	27(31.4)	86(13.6)
	Third cycle	34(77.3)	10(22.7)	44(6.9)
	Fourth cycle	24(61.5)	15(38.5)	39(6.2)
	Others	27(67.5)	13(32.5)	40(6.3)
Aim of radiation treatment	Radical	178(82.8)	37(17.2)	215(33.9)
	no radiation	26(89.7)	3(10.3)	29(4.6)
	Palliative	244(62.6)	146(37.4)	390(61.5)

5.3 Incidence of death among cervical cancer patients during the follow-up time

A follow-up was conducted for five year on 634 cervical cancer patients yielding 1099.98 person years at risk. The median follows up time was 18.17 months. One hundred eighty-six (29.34%) [95%CI: 25.9-33] new death was observed in the total follow up time making the overall death incidence rate 16.9 (95%:CI: 14.64-19.52) per 100 person-years.

5.4 Overall Survival of cervical cancer patients during the follow-up time

In this study, 634 cervical cancer patients were followed for 60 months (five years). The median survival of this cohort was 37.03 (95%CI: 34.39to 43.67) months. The overall estimated survival rate after diagnosis of cervical cancer was 38.62% (95% CI: 31.15 to 46.02) at 60 months of follow up. The estimated cumulative survival was 92.11 %,75.29 %%, 52.92 %, 38.62 % and 38.62% at 12, 24, 36, 48 and 60 months respectively as shown in the following Kaplan Meir survival curve (Figure1).The curve also indicates that the probability of survival decreases as the follow-up time increases which is the typical characteristics of survival data analysis .As it is also shown on the KM survival curve, the highest rate of mortality was observed between 20 to 40 months.

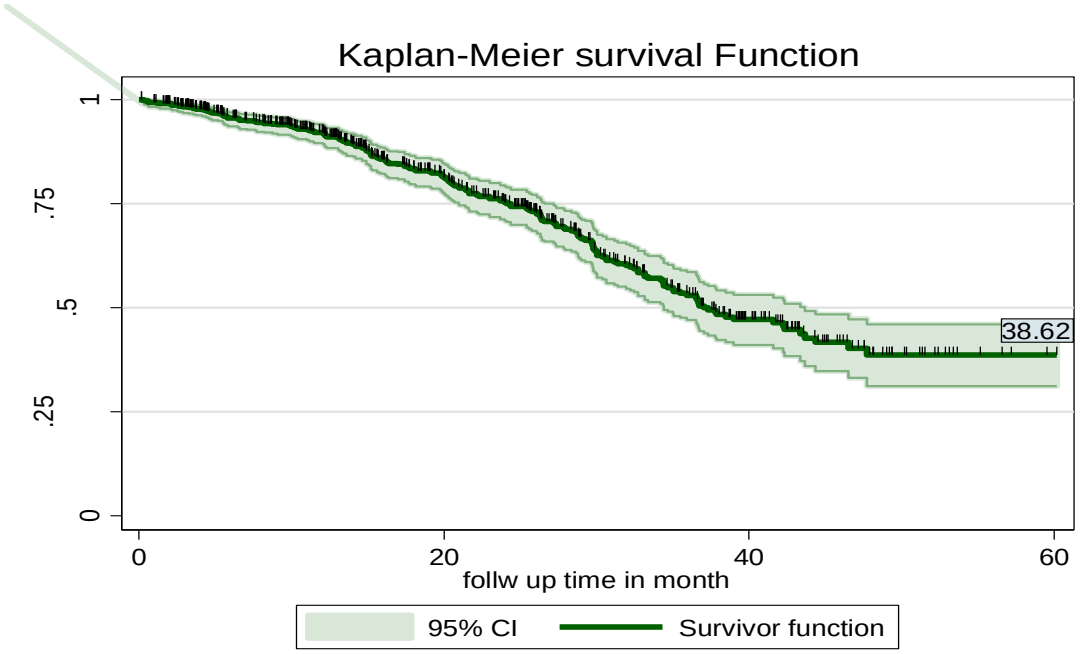

Figure 2:Overall Kaplan-Meier estimation of survival of cervical cancer patients followed at TASH from January 1st 2014 to December 31st 2018, Addis Ababa, Ethiopia, 2019(n=634),

5.5 Survival experience among different groups of cervical cancer patients

Log-rank test was performed to test equality of survival curves for the presence of any significant differences in survival time among various levels of the categorical variables considered in the study. Statistical difference in survival time between different categories of covariates was tested. It was found that there is a significant difference in survival experience between categories of stage of cervical cancer, substance use, age of patients, comorbidity, anemic status and aim of radiation therapy (RT) at p-value <0.05.

The median survival time for those who had FIGO stage I, II or III at baseline had a longer survival time than those in stage IV (28.87 months) (95% CI:21.6-34.37) at p= 0.00. The median survival time for those who are none substance users had a longer survival time (38.46 months; 95%CI: 35.93-47.7) than those who are substance users (32.2 months) (95% CI:20.5-37.77) at p value=0.001. For cervical cancer cases diagnosed at early stage (I&II), cumulative survival rate was 81.04% and 67.94% respectively and those cases diagnosed at advanced stage (III&IV) was 23.33% and 20.03% respectively. This finding clearly shows cervical cancer patients' mortality was highest for advanced stages at presentation. Other covariates did not show statistically significant difference in survival experience between them (Table 4 and figures 3,4,5 and 6).

Table 5: Median survival time, cumulative survival probability, significance and log rank test to different characteristics of patients during 5-year of follow-up of cervical cancer patients at TASH, Addis Ababa, Ethiopia,2019(n=634).

Covariates	Median survival time, In month (95% CL)	Overall 5-year Survival (%)	Log rank test	p–value
Age			39.87	0.000
<30	**	81.45		
30-39	**	56.51		
40-49	39 (31.93- 43.3)	41.42		
50-59	32.2 (27.37-38.46)	21.29		
≥60	30.37 (26.07-35)	22.30		
Substance			10.63	0.0011
User	32.2 (20.5-37.77)	31.57		
None User	38.46 (35.93-47.7)	39.62		
FIGO Stage			56.68	.000
I	**	81.04		
II	**	67.94		
III	35 (30.37-37.87)	23.33		
IV	28.87 (21.6-34.37)	20.03		
Anemic Status			27.05	0.000
Yes	31.4 (28.87-36.53)	30.26		
No	**	55.05		
Comorbidity			27.78	0.000
Yes	29.8 (26.33-33.17)	21.55		
No		51.80		
Aim RT			21.05	0.000
Radical	46.53 (34.4-51.52)	46.16		
Palliative	34.67 (30.03-37.3)	32.57		
No RT	**	82.8		

**values that hadn't median survival from the specific categorical variable in this research.

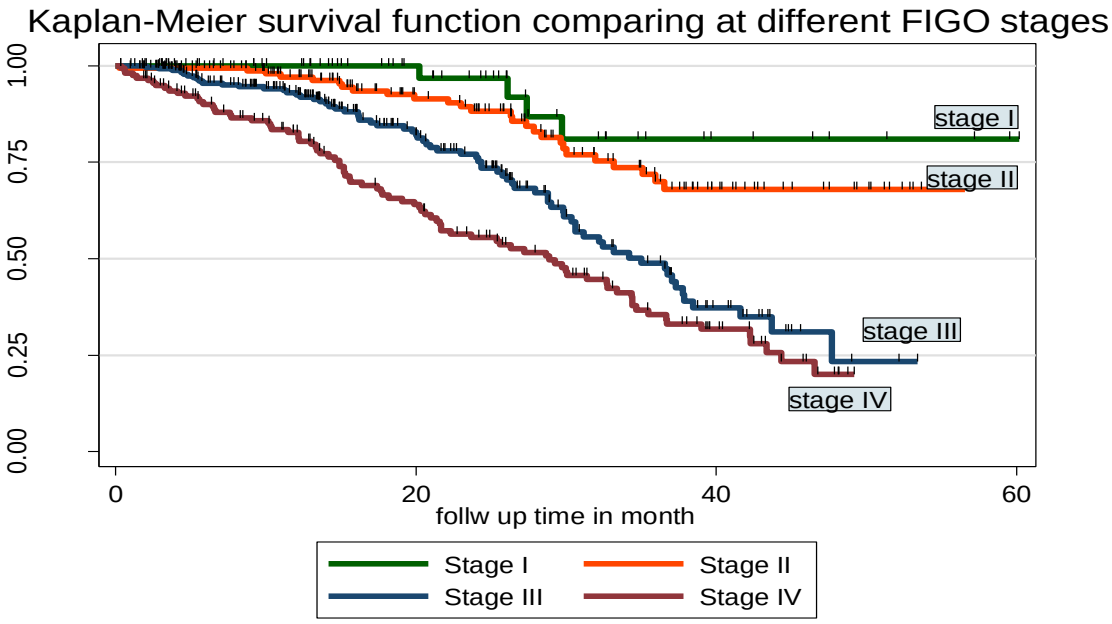

Figure 3:The Kaplan-Meier survival curves compare survival time of cervical cancer patients with different FIGO stages from January 1st 2014 to December 31st 2018 in TASH, Addis Ababa, Ethiopia(n=634).

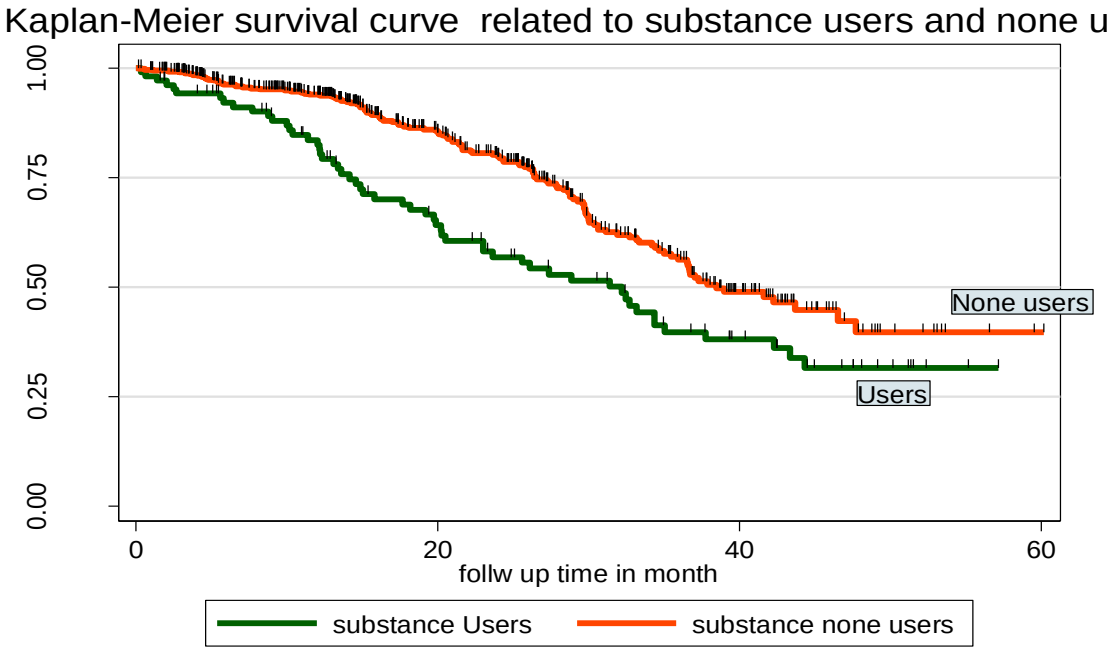

Figure 4:The Kaplan-Meier survival curves compare survival time of cervical cancer patients related to substance users and none users in TASH, Addis Ababa, Ethiopia, 2019(n=634).

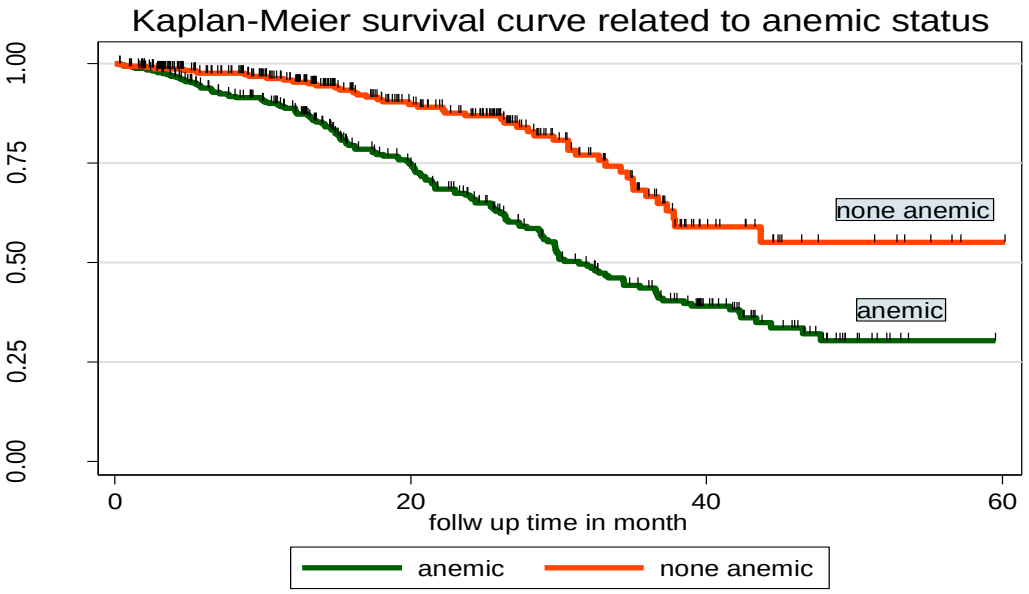

Figure 5:The Kaplan-Meier survival curves comparing survival time of cervical cancer patients related to anemic status in TASH from January 1st 2014 to December 31st 2018, Addis Ababa, Ethiopia ,2019(n=634)

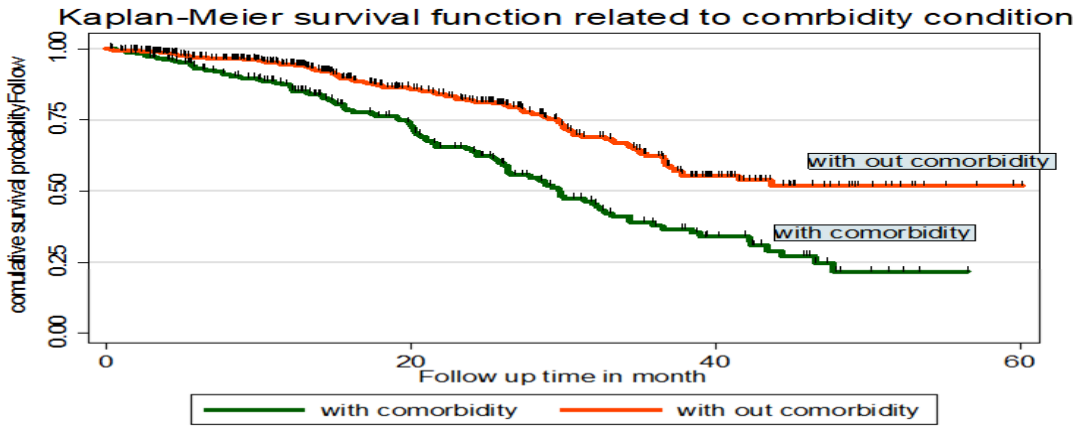

Figure 6:The Kaplan-Meier survival curves comparing survival time of cervical cancer patients related comorbidity status at TASH, from January 1st 2014 to December 31st 2018, Addis Ababa, Ethiopia,2019(n=634).

5.6 Testing overall Cox model fitness

The figure below implies as Cox regression model fitted the data i.e. the estimated cumulative hazard for each individual at the time of their death or censoring is like a censored sample from a unit exponential. This is called the generalized or Cox-Snell residual test. Hence, the output shows cox–Snell residuals satisfied the overall model fitness test.

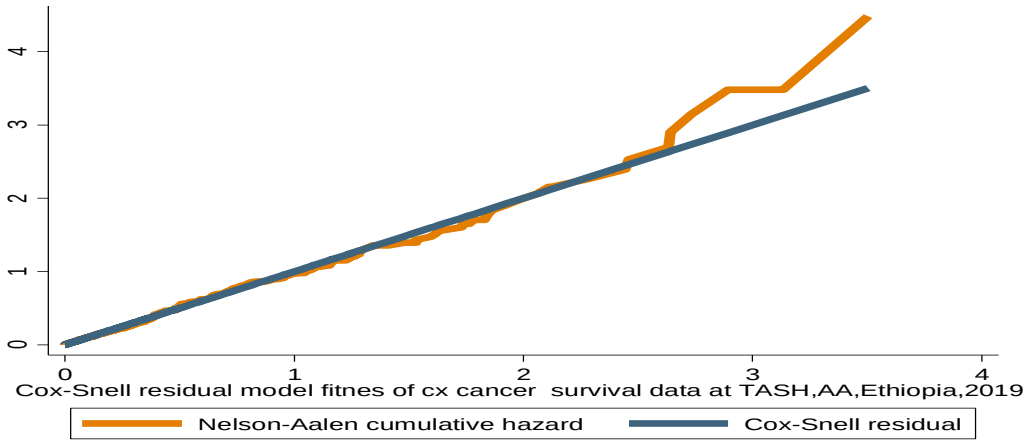

Figure 7:Cox-Snell residual Nelson -Aalen cumulative hazard graph on cervical cancer patients in TASH from January 1st 2014 to December 31st 2018, Addis Ababa, Ethiopia,2019(n=634).

5.7 Factors associated with survival time among cervical cancer patients

The independent variables were analyzed individually with the outcome variable and those variables fitted at p-<0.2 were included in the multivariate Cox regression model. The proportionality of hazard assumption was checked using the Schoenfeld residual test and it satisfied at p-> 0.05 of independent factors.

Age group, occupation, number of children, substance, FIGO stage, comorbidity, anemic status, treatment, cycles of chemotherapy and aim of radiation therapy were fitted in bivariate analysis at p-<0.2. In multivariate analysis, age (50-59 and ≥60), substance use, FIGO stage, comorbidity, anemic status and treatment (surgery plus radiation) were significantly associated to the outcome variable at p-<0.05.

The result of multivariable analysis revealed that women with FIGO stages IV and stage III were11.76 times [AHR=11.76,95%CI (CI:4.02-34.4)]and 7.4 times [AHR=7.4,95%CI(2.55-21.7)] respectively at high risk to die as compared to those with early FIGO stage I as a reference. Those women with advanced age (≥60) were 5.99 times [AHR=5.99,95%CI (2.1-17.08)] at high risk to die than those with early age (≤30).

Patients who used substance were 1.56 times [AHR=1.56,95% (CI: 1.09-2.22)] at high risk to die than those who were none substance users. Similarly, cervical cancer patients who have comorbidity were 1.58 times [AHR=1.58,95%CI (1.14-2.19)] at higher hazard to develop the event than those who haven't comorbidity and patients who were anemic were 1.6 times [AHR=1.6,95%CI (1.11-2.36)] at high risk to die than with those without anemia. Patients who were treated with surgery and radiation were 0.70 times [AHR=0.30,95%CI (0.10-0.93)] at lower risk to die than those patients treated with combination of chemotherapy, surgery and radiation therapy (Table 5).

Table 6:Results of the bivariable and multivariable cox regression analysis of cervical cancer patients at Tikur Anbesa Specialized Hospital, Addis Ababa, Ethiopia, from January 1st 2014 to December 31st 2018,2019 (n=634).

Covariates	Bivariable		Multivariable	
	p-value	CHR (95% CI)	p -value	AHR (95% CI)
Age				
<30		1		1
30-39	0.095*	2.5(0.85-7.4)	0.317	1.76(0.58-5.28)
40-49	0.003*	4.9(1.7-13.3)	0.103	2.4(0.84-6.94)
50-59	0.000*	6.6(2.39-18.4)	0.002**	5.4(1.91-15.31)
≥60	0.000*	7.97(2.89-21.97)	0.001**	5.99(2.1-17.08)
Occupation				
Government employee		1		1
Merchant	0.024*	1.9(1.09-3.31)	0.058	1.74(0.98-3.11)
Farmer	0.154*	1.5(0.86-2.46)	0.189	1.4(0.83-2.5)
House wife	0.664	1.1(0.69-1.79)	0.677	1.11(0.66-1.87)
Others	0.926	1.03(0.57-1.84)	0.381	0.75(0.40-1.42)
substance use				
User	0.001*	1.7(1.23-2.224)	0.013**	1.56(1.09-2.22)
None user		1		1
No. of children				
No child		1		1
One	0.026*	5.4(1.23-23.78)	0.119	6.25(0.35-28.9)
Two	0.081*	3.6(0.85-15.08)	0.173	3.9(0.88-16.66)
Three	0.055*	3.9(0.97-16.11)	0.111	3.24(0.76-13.8)
More than three	0.040*	4.4(1.07-17.9)	0.098	3.43(0.79-14.8)
FIGO stage				
Stage I		1		1
Stage II	0.160*	2.13(0.74-6.1)	0.007**	4.6(1.53-13.94)
Stage III	.001*	5.24(1.91-14.36)	0.000**	7.4(2.55-21.7)
Stage IV	.000*	8.14(2.98-22.18)	0.000**	11.76(4.02-34.4)
Anemic status				
Yes	0.000*	2.35(1.68-3.27)	0.011**	1.6(1.11-2.36)
No		1		1
Comorbidity				
Yes	0.000*	2.13(1.59-2.83)	0.006**	1.58(1.14-2.19)
No		1		1

Table 7:Results of the variable and multivariable cox regression analysis of cervical cancer patients at Tikur Anbesa Specialized Hospital, Addis Ababa, Ethiopia, from January 1st 2014 to December 31st 2018,2019 (n=634) ……Continued.

Treatment				
Surgery &chemo	0.261	0.39(0.07-2.01)	0.792	0.78(0.13-4.8)
Chemotherapy	0.528	0.63(0.15-2.64)	0.942	1.06(0.20-5.62)
Radiotherapy	0.318	0.63(0.26-1.56)	0.271	0.49(0.13-1.74)
Chemo radiation	0.505	0.73(0.29-1.82)	0.092	0.42(0.16-1.15)
Surgery& radiation	0.064*	0.37(0.14-1.06)	0.037**	0.30(0.10-0.93)
Combination of three modalities		1		1
Cycle of chemotherapy				
No chemo	0.113*	0.63(0.35-1.12)	0.160	0.52(0.21-1.3)
First	0.009*	0.40(0.20-0.80)	0.056	0.49(0.24-0.98)
Second	0.154*	0.62(0.32-1.2)	0.196	0.63(0.31-1.27)
Third	0.808	0.90(0.39-2.06)	0.727	0.85(0.35-2.08)
Fourth	0.978	0.98(0.47-2.08)	0.772	1.13(0.51-2.5)
Others		1		1
Aim of Radiation therapy				
Radical		1	1	
No RT	0.357	0.58(0.177-1.87)	0.477	0.61(0.15-2.41)
Palliative	0.000*	2.1(1.45-2.99)	0.246	1.26(0.85-1.88)

CI; confidence interval, AHR; adjusted Hazard ratio, CHR: crude hazard ratio, *indicates that the variables significantly associated with the outcome bivariable analysis at 95% level of significant ($P < 0.05$). ** indicates that the variables significantly associated with the outcome at multivariable analysis 95% level of significant ($P < 0.05$).

5.8 Testing proportional hazard assumption

A Cox regression model was used to examine the effects of sociodemographic, clinical and treatment characteristics of patients on time to death. Schoenfeld residuals test was conducted to assess the proportional hazard (PH) assumptions of the Cox model for given factor variables. The findings indicated that all variables included in the model including global PH assumption test were satisfying PH assumptions (p-value>0.05) (Table 6).

Table 8: Schoenfeld residuals test assessing proportional hazards Assumption

Variables	**rho***	**chi2**	**df****	**Prob>chi2**
Age	0.15209	2.31	1	0.1286
Residence	-0.08591	0.77	1	0.3796
Region	0.00039	0.00	1	0.9969
Religion	0.12867	1.87	1	0.1712
type of Comorbidity	-0.08197	0.82	1	0.3649
Occupation	0.07656	0.52	1	0.4692
Substance	0.16514	3.01	1	0.0829
No. of child	3.01	0.15	1	0.7000
Marital status	-0.03520	0.15	1	0.7002
FIGO stage	0.07530	0.46	1	0.4966
Histopathology	0.4966	0.4966	1	0.0648
Anemia	0.15896	3.02	1	0.0821
Comorbidity	-0.16739	0.06	1	0.8067
Treatment	-0.03239	0.10	1	0.7501
Chemo cycle	-0.07474	0.52	1	0.4699
Aim of RT	-0.15546	3.14	1	0.0762
Global test		18.98	16	0.2695

*The correlation coefficient between the residuals and time.

**Degree of freedom

6.DISCUSSION

This study targeted to asses survival status and associated factors of death among cervical cancer patients at Tikur Anbesa Specialized Hospital, Addis Ababa Ethiopia,2019. Age at diagnosis**,** FIGO stage, comorbidity, anemia, substance use and treatment modality were significant factors that influenced survival of cervical cancer patients.

In this study, about 38.6% cervical cancer patients could survive at least five years after diagnosis of cervical cancer. This is significantly lower than the researches conducted in Brazil which were 84% (16), India 62%(17), Malaysia 71.1%(18) ,China 66.61%(20) ,Northwest Russia 60.0%(27) ,Mysuru (India) 48.1% (21), but in line with the study conducted in North East India 40.7%(19).

About 92%,75%%, 53 %, 39 % and 38.6% of women with cervical cancer could survive at least one, two, three, four and five years respectively in the current study. This is lower than the study conducted in Malaysia which was 94.1%, 79.3% and 71.1% at one, three and five years respectively (17).

The discrepancy of the results might be due to difference in sample size of participants, difference in the study period as there could be changes in treatment modality, differences on health care policy related to cervical cancer, differences in treatment modalities and availability of health-related infrastructures that support early detection and treatment of the cervical cancer.

Nearly 88% of cervical cancer patients who took palliative radiation therapy and 97% of those who took radical radiation therapy survived at least one year from this research finding. The current result is in agreement with study conducted on the effect of adherence of radiation therapy for one-year survival in Ethiopia which was 96% for radical therapy and 87% for those who took none radical radiation therapy (35).This agreement may be due to the similarity of study setting, similarity of treatment modalities and roughly the same sample sizes of study participants.

Fifty percent chance of surviving of an individual woman with cervical cancer participated in this study was about 37 months over 60 months. This finding is higher than a study conducted in Kenya which was 15 months (23),but lower than Malesia 65.8 months (17) and North East India 44 months (19).

The above median survival time dissimilarities may be due to study period variation, the stage and overall condition of patients during presentation, variations of waiting time for treatment after confirmed cervical cancer diagnosis and cancer care policy differences.

However, the median survival time result of this study is in agreement with the study conducted in Ethiopia ,that was 38 months (25).

This similarity will be due to the similarity of study settings, cancer care policy of the country Ethiopia which is unchanged till, the stage of the disease at presentation, and overall care of cervical cancer patients in Tikur Anbesa Specialized Hospital oncology department.

About 29 of cervical cancer patients per 100 died during the study period in this study. This is lower than studies conducted in India (38.7/100) but higher than Ethiopia (about 17/100) (21, 25).The disagreement in the same setting(Ethiopia)may be due to the differences of waiting time from the real diagnosis to starting time of treatment; i.e. During the current study time (2014 to 2018), cervical cancer patients after confirmed diagnosis are obligated to wait 6 to 12 months in average to get treatment of free payment but in average one week to one month waiting time duration in the past study period (2008 to2012).The disagreements with India may be sample size differences, health care policy differences of the countries' and treatment adherences differences of the study participants .

In the present study, age at diagnosis was found to be a significant factor of death among cervical cancer patients. Patients with advanced age (≥60 and 50-59) during presentation were about 6 and 5.4 times at high risk to die than those with early age (≤30) as a reference respectively. This finding is supported by the studies conducted in Danish (HR, 1.60; 1.29–1.98) and Mysuru (HR= 2.17, p = 0.05) (21, 26). This agreement will be due to the fact that the death of cervical cancer increases as the age of women with this disease increases(4).

Stage at presentation was the contributing factor for low survival of cervical cancer patients in this study. Women with FIGO stage IV and III were about 12 and 7.4 times at high risk to die as compared to those with early clinical stage I respectively.

This finding is in line with the studies conducted at north west Russia (HR=3.8, 95% CI 2.5 to 5.8) (27), Nigeria (HR=3.3, 95 % CI: 1.2–8.9)(22) , Ethiopia (HR=2.60 (95%CI: 1.67–4.04) (25) and North East India (HR =1.8 ,95% CI:1.2 to 2.7)(19).

The similarity of these findings may be due to the reason that as the cancer stage increases, metastasis will also increase, which leads to compromising of patient's immunity to resist other infections, difficulty of treating such complicated metastasis cases and these factors in aggregate increases the probability of dying (42).

Patients who were anemic in this study were 1.6 times at high risk to die than with those patients without anemia. This result is supported by the studies conducted at Nigeria (HR= 3.0, 95 % CI: 1.4, 6.4) (22) and Ethiopia (HR=1.65 (95%CI: 1.24–2.20) (25). This agreement could be due to the fact that low level of hemoglobin in the blood can lead to oxygen starvation of both cancerous and normal cells that consequently results unprogrammed cell death. This unprogrammed cell death could lead to tumor lysis syndrome which is acute and fatal in case of cancerous cells. Another possible reason will be health care professional's knowledge level at health centers and primary hospitals, lack of training about cervical cancer, and health seeking behavior of cervical cancer patients at early stage.

Comorbidity was another significant factor contributing for lower survival of cervical cancer patients in the current study. In the lists of comorbidities, HIV/AIDS was most prevalent (55%). Therefore, HIV may contribute higher part of risks to die in this research.

Cervical cancer patients who had comorbidity were 1.58 times at high risk to develop the event than those who haven't comorbidity in this study. This is in agreement with the studies conducted in Australian [HR=4.6,95%(CI: 3.54–6.03)](30) and Ethiopia [HR=2.02, 95%CI: 1.01–4.05) (25). The study on HIV infection and survival among women with cervical cancer in Botswana indicated that HIV infection significantly increased the risk for death among all women with cervical cancer [HR=1.95;95%CI(1.20to3.17)](31) and this also strengthen the current study result. The rational of these similarities may be due to the fact of Carlson comorbidity index which states as the presence of comorbidity leads to shortening of the lives of patients based on the severity of each comorbidity(38).

Another significant finding in this research that lowered survival probability was substance use (Chat chewing, alcohol drinking and cigarette smoking). Patients who used substance in this study were 1.56 times at higher risk to die than those who don't used substances. This result is new i.e. there is no any updated research conducted on this issue, based on our level of searching ability of articles.

The result of this study may be due to substances which were used by the patients weekend their immunity which leads to be attached by other infectious diseases that lower survival.

Patients who were treated with the combination of surgery and radiation therapy in this study developed the event about 70% lower than patients who treated with the combination of surgery, radiation therapy and chemotherapy. This lower risk of developing the event may be due to the absence of chemotherapy side effects that kill normal cells. But this finding is not supported by the study done on simultaneous chemotherapy and pelvic radiation treatment compared with pelvic radiation treatment alone as adjuvant treatment of Cancer of the Cervix which revealed as patients who got both radiation and chemotherapy had an estimated 4-year progression-free survival rate of 80 percent (P = .003) but 63 percent for those who took radiation only(32) and the study done in north central Nigeria reveled as patients who got chemoradiation treatment survived more than who did not get the such treatment regimen(22).

In general, there are differences in cervical cancer survival rate, median survival time, effects of covariates on survival among different countries. But it is not easy to interpret the dissimilarities. This perhaps could be due to advanced stage at diagnosis, lack of early screening programs, limited treatment facilities, treatment compliance of patients and financial problems. Another explanation could be there is only one cancer treatment facility located at the capital city in Ethiopia which can affect cost effective cancer treatment delivery in the country. Hence, most cancer patients were referred to the central level that could result delay in diagnosis and treatment. Additional possible explanation for variations in survival could be due to different methodologies applied in each of the studies as well as differences in local cancer care policies.

6.2. Limitations and Strength of the study

6.2.1. Limitations of the study

This study has some limitations. First, cause specific (relative) survival was not determined due to lack of data on specific cause of death, this may over estimate cervical cancer related mortality rate. Information on sociodemographic factors, such as educational level, history of abortion, age at first marriage, age at first sex, history of cervical cancer recurrence and family history of cervical cancer were not recorded and not included in this study.

Moreover, the data were collected on patients registered from January one 2014 to December thirty one 2016 that may not reflect current utilization of advanced treatment modalities for cervical cancer treatment, which could affect the opportunity to improve survival rate.

6.2.2 Strength of the study

Despite the above possible limitations, the study has the following strengths: the study will give an insight for future researchers especially those who are interested for prospective follow up study, the study left two-years for follow up period in addition to three years entry periods which probably increased the number of events and data were collected by Nurses who were trained on cancer care and this has an important role in the quality of the data.

7. CONCLUSION AND RECOMMENDATIONS

7.2. Conclusion

The five-year overall probability of survival rate among cervical cancer patient was 38.62%, which is lower when compared with those of high- and middle-income countries. Significant factors of death after diagnosis of cervical cancer were; advanced FIGO stage, bassline anemia, comorbidity, substance use, advanced age and treatment modality.

7.3 Recommendations

Based on this study finding, the following recommendations could be forwarded with respective bodies: -

To federal minister of health: Better to expand cervical cancer early screening programs and cervical cancer treatment facilities and better to create awareness in collaboration with public medias about cervical cancer prevention, screening, treatment options and early symptoms.

To Tikur Anbesa Specialized Hospitals: Could give special emphasize to those who are anemic, having comorbidity at the time of diagnosis, aged and advanced stage patients, substance users. and enhance treatment using feasible and effective regimens. The healthcare providers could enhance the awareness of early sign and symptoms of cervical cancer and encouraging women to seek clinical help at early times.

To Future researchers: Further studies on survival status and associated factors among cervical cancer patients that can address the limitations of this study and create strategies to improve completeness by use of prospective design. Further prospective follow up study could be conducted by incorporating important predictors of mortality like financial problems, treatment adherence, societal and health system related factors.

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9.ANEXES

A: Assurance of principal investigator

I undersigned here agrees to accept responsibility for scientific ethical and technical conduct of the research project and for provision of required progress reports as per terms and the condition of the research publication office in effect at the time of the grant is forwarded as the result of this application.

Name of the Investigator: Mulugeta Wassie (BSN): Signature _____ Date _____

B: Information sheet

Title of the Research proposal: Survival status and associated factors of death among cervical cancer patients in Tikur Anbesa Specialized Hospital Adult Oncology Unit, Addis Ababa, Ethiopia,2019.

Name of Investigator: Mulugeta Wassie (BSN)

Name of the Organization: Addis Ababa University, College of Health science, school of Nursing and midwifery.

Name of the Sponsor: Addis Ababa University

Introduction: this information sheet is prepared for Tikur Anbesa Specialized Hospital, oncology unit Addis Ababa, Ethiopia. The aim of the form is to make the above concerned office clear about the purpose of research, data collection procedures and get permission to conduct the research.

Purpose of the Research thesis: To assess survival status and associated factors of death among cervical cancer patients on follow up at Tikur Anbesa Specialized Hospital adult oncology unit, Addis Ababa, Ethiopia, 2019.

Procedure: In order to achieve the above objective, information, which is necessary for the study will be taken from cervical cancer medical record follow up forms, chemotherapy intake forms, radiation therapy chart and medical history sheet. In order to come up with the above-mentioned findings, total document of clients enrolled during January 1st 2014 to December 31th 2016 will be selected and followed up and a review of the required information from the

records will be made by using the checklist. There will be a phone call to patients to collect information on some variables.

Risk and /or Discomfort: Since the study will be conducted by taking appropriate information from medical chart, it will not inflict any harm on the patients. But in case of phone calling to get appropriate information in some variables, individual informed consent will be taken.

The name or any other identifying information will not be recorded on the questionnaire and all information taken from the chart will be kept strictly confidential and in a safe place. The information extracted will be kept secured by locked in to locker by key. After the data will be entered in to the computer by password, the information retrieved will only be used for the study purpose.

Benefits: the research has no direct benefit for those whose document/ record is included in this research. However, the indirect benefit of the research for the participant and other clients in the program is clear. This is because if program planners are preparing predicted plan, there is a benefit for clients in the program of getting appropriate care and treatment services for the cervical cancer patients. Of all, the research work has a paramount direct benefit for health care planners and managers, especially for those on cervical cancer program planning and management**.**

Confidentiality: To ensure confidentiality the data on the chart will be collected by those individuals who are working in oncology unit nurses and information will be collected without the name of the clients. The information collected from this research project will be kept confidential and will be stored in a file. In addition, it will not be revealed to anyone except the investigator and it will be kept in key and locked system with computer password.

Person to contact: This research project will be reviewed and approved by the institutional review board of college of health sciences, school of nursing and midwifery, Addis Ababa University. If in case you want to know more information about the research and its undertakings, you can contact the committee through the address below.

- Mulugeta Wassie (BSN): University of Gondar. Tel:0927638081 **E-mail:** mulugeta2113@gmail.com.

Permission: Lastly but not least, you are kindly requested to permit and forward your permission to concerned body in your organization so that the researchers can get cooperation from the data clerks and other responsible bodies in place.

C: Data extraction form

Table 9:Data extraction form for the Assessment of survival status and associated factors of death among cervical cancer patients at TASH adult oncology department, Addis Ababa, Ethiopia,2019.

Part I: Socio demographic characteristics			
S.No	**Variable Category**	Code	Remark
1	Participant phone Number	----------	
2	Entry date	----------	
3	Leaving date	----------	
4	Age of patient	----------	
5.	Residence of patients	1.urban 2.rural	
6	Region	1. Amhara 2. Oromia 3. Tigray 4.SNNP 5. Addis Ababa 6.Others (specify…...)	
7	Religion	1.orthodox 2.muslim 3.protestant 4.others (specify….)	
8	Occupation	1. Government employee 2. Merchant 3. Farmer 4. Student 5. Private employee 6. Daily laborer	

		7.unknown	
9	Substance use	1.user 2.non user	
10	Number of children	1.no child 2.one 3.Two 4.three 5. more than three	
11.	Marital status of women	1.Married 2.Single 3.Widowed 4.Divorced	
Part two: - clinical and histopathological variables			
12	Status	1.death 0.censord	
13	Stage of the diseases	1.stage 0 2.Stage I 3.Stage IA 4.Stage IB 5.Stage II 6.Stage IIA 7.Stage IIB 8.Stage III 9.Stage IIIA 10.Stage IV 11.Stage IVA 12.Stage IVB	

14	Histopathological Report	1.squamous cell carcinoma 2.adenocarcinoma 3.others (specify….)	
15	Baseline anemia	1.yes 2.no	
16	Comorbidity	1.yes (specify…...) 2.No	

Part three: - Treatment related variable			
17	Starting date of treatment	----------	
18	type of treatment initiated	1.Surgery 2.chemotherapy 3.radiotherapy 4.Chemo radiation 5. Surgery+chemo+radation	
19	number of cycles the patient took chemotherapy	1.No chemo 2.First cycle 3.Second cycle 4.Third cycle 5.Fourth cycle 6.others (specify……)	
20	Aim of radiotherapy	1.Radical 2.No RT 3.Palliative	