

**ADDIS ABABA UNIVERSITY
COLLEGE OF HEALTH SCIENCES
SCHOOL OF PUBLIC HEALTH**



Survival and associated factors among cervical cancer patients in Black Lion Hospital, Addis Ababa, Ethiopia, 2008-2012, aretrospective longitudinal study.

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A THESIS SUBMITTED TO THE SCHOOL OF PUBLIC HEALTH, COLLEGE OF HEALTH SCIENCES, ADDIS ABABA UNIVERSITY IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF PUBLIC HEALTH.

February, 2014
Addis Ababa, Ethiopia.

Acknowledgements

I would like to pass my heartfelt gratitude to my advisor Dr. Adamu Addissie for his unreserved valuable support in advising and commenting the thesis work consistently throughout the period.

I also notice my out most appreciation to Dr Matheos Assefa, head of cancer treatment centre and Mr Timotiwos Genebo head of cancer registry at Black Lion hospital for giving me ground information.

I would like to thank Mr Messay Degife for his valuable technical support to accomplish the thesis work.

Finally my appreciation will go to Dr Eva and Mathias from University of Halle, Germany for their financial and technical support.

Acronyms

AA-	Africa America
AHR	Adjusted hazard ratio
ASIR	Age Specific Incidence Rate
ASMR	Age Specific Mortality Rate
BLH	Black Lion Hospital
BSc	Bachelor of Science
CI	Confidence Interval
EPI INFO	Epidemiological Information (software developed by CDC)
FIGO	International Federation of Gynecology and Obstetrics
GLOBOCAN	Global Burden of Cancer
HIV	Human immune virus
HPV	Human Papilloma Virus
IARC	International Agency for Research on Cancer
ICO	institute catalad'Oncologia
INCTR	International Network for Cancer Treatment and Research
LVSİ	Lymph-Vascular-Space-Invasion
MOH	Ministry of Health
NCDs	Non Communicable Diseases
RR	Relative Risk

RS	Relative survival
SCC	Squamous Cell Carcinoma
SES	Socioeconomic Status
SPSS	Statistical Package for Social Scientists
SR	Survival Rate
WHO	World health organization

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Abstract

Introduction: Cancer of the cervix is the second most common cancer among women worldwide and it is the most common cause of cancer deaths among women in developing countries. Cervical cancer ranks as the second most frequent cancer among women in Ethiopia. In spite of the high incidence and mortality rate, survival time among cervical cancer patients is not measured in our country. Thus, this study aimed at providing information on the survival time among cervical cancer patients and determining factors attributed to it in Black Lion Hospital, Addis Ababa, Ethiopia, 2013.

Objective- This study is aimed to assess a five year survival time and its predictors among cervical cancer patients in Black Lion Hospital, Addis Ababa, Ethiopia, from 2008-2012.

Methods- A retrospective longitudinal study in the cancer treatment center at Black Lion Hospital was conducted. All incident cases of cervical cancer (1391) registered during 2008-2012 in Black Lion Hospital were selected and followed retrospectively for the study of five year survival. Patient charts were reviewed and telephone interview made to generate survival rates from February to March, 2013. Survival table was used to estimate the probability values of survival after diagnosis of cervical cancer at different time intervals. Kaplan Meier survival curve together with log rank test was fitted to test for the presence of difference in survival among predictor variables. Cox regression was fitted to find out predictors of survival time. Backward Stepwise Multiple Cox regression was fitted at 5% level of significance to determine the net effect of each explanatory variable on time to death after diagnosis of cervical cancer.

Results- Overall survival was 32% at five years and 52% at three years. It is found that there is a difference in survival experience between categories of stage of cervical cancer, treatment modalities, age of patients, and place of residence. Being in stage IV cancer AHR 2.974(95%CI 1.303, 6.791), being operated AHR 0.488(95% CI 0.281, 0.848) and receiving palliative chemotherapy AHR 0.731(95% CI 0.534, 0.937) were predictors of survival time among cervical cancer patients.

Conclusion-The results of this study show a strong gradient in survival by stage and treatment, which underlines the key role of early detection and timely treatment of cervical cancer for reducing mortality.

1. Introduction

1.1 Background

Cancer is a major burden of disease worldwide. Each year, tens of millions of people are diagnosed with cancer around the world, and more than half of the patients eventually die from it(1). Based on the global burden of cancer 2008 estimates, about 12.7 million cancer cases and 7.6 million cancer deaths are estimated to have occurred in 2008; of these, 56% of the cases and 64% of the deaths occurred in the economically developing world(2). With significant improvement in treatment and prevention of cardiovascular diseases, cancer has or will soon become the number one killer in many parts of the world. As elderly people are most susceptible to cancer and population aging continues in many countries, cancer will remain a major health problem around the globe(3).

Cancer of the cervix uteri is the second most common cancer among women worldwide, with an estimated 529,409 new cases and 274,883 deaths in 2008. An estimated 12,170 cases and 4,220 deaths of invasive cervical cancer are expected in 2012. The crude incidence and mortality rate of cervical cancer in sub-Saharan African countries is estimated to be 24.4% and 22.9% respectively (3).

Only in the last few years have non communicable diseases, including cancer, received attention as public health issues in Ethiopia. The Federal Ministry of Health of Ethiopia recently created a task force to address the issue of non-communicable diseases. The taskforce design a strategic framework to prevent and control chronic non communicable diseases. One of the priority elements of the strategy is to reduce the incidence and mortality of cancer and improve the quality of life of cancer patients. Cancer control research and surveillance is also the other essential components of the strategy(4).

The age standardize incidence rate and mortality rate of cervical cancer in Ethiopia is 18.8 and 14% respectively. Cervical cancer ranks as the 2nd most frequent cancer among women in Ethiopia, and the 2nd most frequent cancer among women between 15 and 44 years of age. Data is not yet available on the human papilloma virus burden in the general population of Ethiopia(5).

HPV types 16 and 18 are responsible for about 70% of all cervical cancer cases worldwide. HPV is a necessary cause of cervical cancer, but it is not a sufficient cause. Other cofactors are necessary for progression from cervical HPV infection to cancer. Tobacco smoking, high parity, long-term contraceptive use, and co-infection with HIV have been identified as established cofactors(5).

Sexual intercourse is the primary route of transmission of genital HPV infection. HPV vaccines that prevent against HPV 16 and 18 infections are now available and have the potential to reduce the incidence of cervical and other ano-genital cancers. Successful cervical cancer prevention programs integrate screening with management of cervical pre-cancers.(6)

1.2 Statement of the problem

Cervical cancer is the second most common cancer and the fourth leading cause of Cancer related deaths among women worldwide. It is one of the registered Cancers with Increasing incidence trends in the US: 1999-2008(3).

Internationally, the burden of cervical cancer falls most heavily on developing nations. About 85% of the cases and 88% of the deaths due to cervical cancer occur in developing nations. Women in developing nations are at a 35% greater lifetime risk of developing cervical cancer than women in high-income countries. Although cervical cancer is most common in women older than 50 years, in developing nations, it is becoming increasingly prevalent among women during their reproductive years (age 15–49 years)(7).

Ethiopia has a population of 20.9 million women aged 15 and older who are at risk of developing cervical cancer. Each year an estimated 7619 women are diagnosed with cervical cancer; 6081 die from the disease. Crude incidence rates of cervical cancer in Ethiopian women per 100 000 population per year are estimated to be 23(8). The possible contributing factors are low level of awareness, cost, and limited access to screening services and lack of a national cancer registry(6). Hence, the intended study will determine survival time of patients with cervical cancer and its predictors which in turn enables to understand the quality of life of patients and the effectiveness of treatments.

1.3 Rationale

Studying survival of different cancers has important practical value for patients, providers, and researchers(9). Cancer patients may wish to know how their prognosis is changing over time, and what is their life expectancy based on the disease status. The proper understanding of prognosis may help both of the physicians and the patients decide on treatment options, balancing the personal values for quality versus quantity of life (10). Providers can make use of survival information to more objectively determine an appropriate frequency of follow-up visits and aggressiveness of surveillance testing based on patient's current risk profile. When designing Clinical trials, clinical researchers may also find it useful in helping to determine sufficient follow-up times for trial endpoints(11).

Cervical cancer is the most common cause of cancer deaths among women in developing countries (12). Cancer survival data is not widely available from countries in Africa, Asia, and Central America. There are few studies that are conducted regarding to HPV burden and screening in Ethiopia. There is also no data on the survival time and its determinants among cervical cancer patients despite the high burden and mortality. Hence, this study will assess the survival time among cervical cancer patients and its determinants at Black Lion hospital, Addis Ababa, Ethiopia, 2013.

Identifying contributing factors of survival time among cervical cancer patients is very mandatory so as to reach on some recommendations to improve survival. Improvement in cancer survival is considered a valid indicator of the quality of care introduced to the patients. The data will be a key indicator for monitoring progress against cancer. Moreover, the study can be an input to policy makers, program managers, health professionals to decide based on evidence about cervical cancer and serves as a base line data for further studies, since it is a first of its kind in Ethiopia.

2. Literature review

2.1. Burden of Cervical cancer

In a recent analysis based on the 2008 worldwide estimates of cancer compiled by the International Agency for Research on Cancer (IARC), globally an estimated 530 000 women developed cancer and 275 000 women died of it. Worldwide, cervical cancer was the third most common cancer ranking after breast (1.38 million cases) and colorectal cancer (0.57 million cases). Eighty-six percent of all cervical cancers and 88% of all deaths caused by cervical cancer occurred within developing countries. The ASIR and ASMR were 18 and 10 per 100,000, respectively, in developing countries and 9 and 3 per 100,000, respectively, in more developed countries. In developing countries, 1.9% of women developed cervical cancer and 1.1% died of the disease, before the age of 75 years, in the absence of competing causes of death(12, 13).

In Africa, which has a population of 267.9 million women aged 15 years and older at risk of developing cervical cancer, approximately 80 000 women are diagnosed with cervical cancer each year, and just over 60 000 women die from the disease. However, cervical cancer incidence in Africa also varies considerably by region. The highest rates in Africa (ASIR >40 per 100 000) are all found in Eastern, Southern, or Western Africa(12, 13).

Based on the summary report of the information on human papillomavirus (HPV) and cervical cancer at the country-specific level by WHO/ICO Information Centre 2010, Ethiopia has a population of 20.90 million women ages 15 years and older who are at risk of developing cervical cancer. Current estimates indicate that every year 4648 women are diagnosed with cervical cancer and 3235 die from the disease. The crude and age standardize incidence rate is 11.5% and 18.8% per 100,000 population per year respectively. Cervical cancer ranks as the 2nd most frequent cancer among women in Ethiopia, The Prevalence of HPV 16 and/or HPV 18 among women with cervical cancer are 90.2%. But data is not yet available on the HPV burden in the general population of Ethiopia(5).

Based on the study conducted on the Prevalence of human papilloma virus infection in women in rural Ethiopia revealed, the overall prevalence of cervical HPV infection within the study population was 15.9%. Comparing age-standardized prevalence of all HPV

types to other countries and continents Ethiopia is second to Nigeria with 25.6%. Prevalence of HPV high risk infection was 13.2%. Age standardized rates amounted to 14.4% and 11.6%, respectively(14).

In a four years retrospective analysis of biopsy material from 475 women with postmenopausal bleeding in the department of pathology, Faculty of medicine, Addis Ababa University shows that malignant lesion of the genital tract were found in 60.8% of the cases. Cervical carcinoma was seen in 84.8% of the malignant lesions and it was responsible for 51.6% cases of all postmenopausal bleeding patients. Endometrial carcinoma was seen only in 10.7% of the malignant cases. In this study underlying cervical malignancy was found in approximately one of every two patients with postmenopausal bleeding(15).

In a retrospective molecular pathologic analysis for the distribution of Human Papilloma Virus in women with cervical histological abnormalities over five years period from the department of pathology of Gondar College of Medical Sciences, Gondar, Ethiopia revealed that Human papilloma virus was found in 263 of the 284-biopsy specimens (92.60%) and Human Papilloma Virus type 16 was identified to be the most frequent genotype accounting for more than 76% of all HPV species showing the burden of the disease is very high(16).

2.2. Literatures on survival time of Cervical cancer and associated factors

Cervical cancer is the most common cause of gynecologic cancer death globally with 274,000 deaths in 2008(17). Studies on survival time among cervical cancer patients have shown that stage of cancer at diagnosis, histological and morphological type of Cancer, age at diagnosis, treatment modality, co-morbid illness determine the survival time of cervical cancer. In developing countries, few studies have been conducted on cervical cancer survival time. Differences in survival time among cervical cancer patients have been reported in different countries and in different studies. Some of the literatures regarding to survival time and associated factors of cervical cancer are reviewed as follows.

A retrospective longitudinal study on the prognostic factors related to cervical cancer survival in Mexican women showed that 27.8% died from invasive cervical cancer at the end of the follow-up period (12.5 years). The overall survival rate was of 66.6%. The study also shows that age, histological type, tumor grade and clinic pattern do not show a difference in survival at 5 years ($P > 0.05$). Meanwhile survival is affected by those conditions that indicate a more advanced neoplastic process (stage IV SR=21.5%), The biggest tumor size (tumor > 6 cm SR=39.7%), lympho-vascular invasion (SR=27.7%) and therapeutic scheme combined with surgery, radiotherapy and chemotherapy (SR=55.1%) have a lower survival, meanwhile factors which may prevent illness advance such as the Papanicolaou smear show a higher survival (75.6%)(18).

A cohort study on Prognostic factors in adeno-carcinoma of the uterine cervix in Netherland shows a 5-year survival rates for stages I and II were, respectively, 79% and 37%. The 5-year survival rates for stages III and IV were less than 9%. Using univariate analysis stage and grade of cervical cancer were significant prognostic factors. Younger patients (age < 35 years) had a significantly better survival than older patients (> 65 years) ($P < 0.001$). Histological type (adeno-carcinoma vs. adeno-squamous vs. clear cell carcinoma) showed significant difference in survival ($P = 0.005$). The patients without lymph node metastases had a 5-year survival of 91% compared to 34% when positive lymph nodes were found. The survival was significantly better in patients undergoing primary surgical treatment in stages I and IIA when compared to primary radiation therapy ($P = 0.002$). Using multivariate analysis, only stage, grade and lymph node metastases remained significant independent predictors for survival. Longest survival was for patients with early stage disease, younger patients and after primary surgery. They found FIGO stage, grade and lymph node metastases of significant prognostic value for survival in cervical adeno-carcinoma(19).

A ten years retrospective follow up study conducted in cervical cancer patients from 11 German cancer registries revealed that a 64.7% rate of overall, age-adjusted five-year relative survival in 2002 – 2006. A strong age gradient was observed, with five-year relative survival (RS) decreasing from 81.7% in age group 15 – 49 years to 46.3% in age group 70 years. Prognosis furthermore strongly varied by stage, with age-adjusted

five-year RS reaching 84.6% for localized, 48.2% for regional, and 17.9% for distant stage. From 2002 to 2006, a significant improvement (4.7 percent units) in overall age-adjusted five-year RS was seen. The improvement was most pronounced for age groups 55 – 64 years (from 54.2 to 65.6%) and 65 – 74 years (from 50.0 to 58.1%). From the study it was concluded that prognosis of cervical cancer strongly varied by age and stage (20).

In a retrospective study done in 261 patients with cancer of the cervix registered in Uganda, in 1995–1997, Overall observed and relative survival at 3 years was 52.4 and 59.9%, respectively. Of these cases, one-quarter (63) had been treated in the radiotherapy department. These cases had better survival (82.6%) than non-treated patients (78.5%) after 1 year of follow-up, but there was no difference at 3 years. HIV status was not significantly related to prognosis. Stage is an important determinant of survival: cases with distant metastasis had a risk of death some three times that of patients with localized disease. Early detection and prompt treatment should improve overall survival from cervix cancer(21).

The survival experience of 284 patients with cancer of the cervix uteri registered by the population-based Zimbabwe National Cancer Registry in 1995–1997 revealed, Overall observed and relative survival at 3 years were 44.2% and 45.2%, respectively. Half of the cases (139) had been referred and treated in the radiotherapy department. Survival was significantly greater in the first 3 years for patients who received radiotherapy treatment compared to those that had not. Many cases presented late (distant metastasis), and extent of disease was an important determinant of survival; cases with metastases had a risk of death some 3 times that of patients with localized disease. The results demonstrate the importance of earlier diagnosis and availability of effective treatment(22)

A retrospective study done in Iranian cervical cancer patients showed a 3-year survival of 75.9 % (mean of 59.4 months). In first months, survival was the same in both pathology types, but because of the higher stages of squamous cell carcinomas in comparison with adeno-carcinomas, their overall rate was lower. Stage IIB and IIIB

survival rates were 90.9% and 30.8%, respectively, and rates with and without lymph node involvement were 64.8% and 80.1%. In patients who underwent surgery and chemo-radiation, the respective figures were 71.6% and 54.9%. 3-5 year survival of cervical cancer fluctuates in the range of 70 to 93%. The relationship with lymph node involvement is weak. Survival of women receiving chemotherapy was lower than after surgery(23). This finding showed an importance of diagnosis in primary stages and surgical resection of pelvic.

A study conducted in Malaysia revealed overall five-year survival of 39.7% [95%CI: 30.7, 51.3] with a median survival time of 40.8 (95%CI: 34.0, 62.0) months. The log-rank test showed that there were survival differences between the groups for the following variables: stage at diagnosis ($p=0.005$); and primary treatment ($p=0.0242$). Patients who were diagnosed at the latest stage (III-IV) were found to have the lowest survival, 18.4% (95%CI: 6.75, 50.1), compared to stage I and II where the five-year survival was 54.7% (95%CI: 38.7, 77.2) and 40.8% (95%CI: 27.7, 60.3), respectively. The five-year survival was higher in patients who received surgery [52.6% (95%CI: 37.5, 73.6)] as a primary treatment compared to the non-surgical group [33.3% (95%CI: 22.9, 48.4)](24).

In Ethiopia studies are limited on assessing knowledge and attitude towards cervical cancer and cervical cancer screening; there is no data on the survival time of cervical cancer patients and factors attributed to it. Studying survival time and predictor variables in our country will help health professionals in cancer treatment centers to know the quality of care they provide. Prediction of prognosis will be based on evidence and local circumstances. It will also help to make some recommendations to improve the survival time of cervical cancer patients. Thus, this study will assess and contribute to the current knowledge about survival among cervical cancer patients and determinant factors at BLH, Addis Ababa, Ethiopia, 2013.

3. Objectives

3.1. General objective

To assess a five year survival time and its determinants among cervical cancer patients in Black Lion Hospital, Addis Ababa, Ethiopia, 2008-2012.

3.2. Specific objectives

1. To estimate the time to death of cervical cancer patients in BLH, AA, Ethiopia, 2008-2012.
2. To compare the survival time among categories of covariates of cervical cancer patients in BLH, AA, Ethiopia, 2008-2012.
3. To identify predictors of survival time in cervical cancer patients in BLH, AA, Ethiopia, 2008-2012.

4. Methodology

4.1. Study design

A health facility based, retrospective longitudinal study was employed.

4.2. Study area and period

This study was conducted in Black Lion Hospital which is found in Addis Ababa city, the capital of Ethiopia. BLH is a teaching, central tertiary generalized referral hospital with approximately 800 inpatients beds. It is the largest and best known public hospital which was built in the early 1960's(25).

The Black Lion Cancer treatment Center was established 17 years ago by Dr. Bogale Solomon who was at the time the only radiation and medical oncologist in the country.

The clinic is housed in a separate, newer building on hospital grounds and consists of three floors: the clinic with three examination rooms, physicians' offices, waiting room, pharmacy, and radiation vaults; a floor for the inpatient ward; and a floor for meeting rooms. The center has limited facilities for radiological diagnostics. There are currently four oncologists, one hematologist, three radiotherapists and 15 nurses working at the Cancer Center(25).

Black Lion Hospital aspires to become a center of excellence in the diagnosis, treatment and care of patients with cancer. With the support of Ethiopia's governmental institutions, None governmental organizations and international partners, including INCTR, the hospital is hoping to develop a comprehensive cancer care program, including cancer registry, early detection, prevention, standard treatment and palliative care(25).

Data was collected from January to march 2013. Cervical cancer patients enrolled from 2008-2012 time periods in radiotherapy center of BLH was followed. The starting point for retrospective follow-up was the time from first confirmed diagnosis of cervical cancer and the endpoint will be date of death, date of lost to follow up, date of last contact or the end date of follow-up period (December 30/2012).All charts of cervical cancer patients, diagnosed in between 2008-2012 at BLH were retrieved from local cancer registries. The record of all study participants was selected according to the eligibility

criteria. As there was no mortality data in the patient charts, there was a phone interview to all patients who have phone numbers to ascertain the current status of the patient. Patients who do not have phone number and whose current status is unknown, patients who didn't develop the outcome of interest (death) at the end of follow-up period, patients who were lost from follow-up, was considered as censored.

4.3. Study population

4.3.1. Source population

All cervical cancer patients in BLH who were diagnosed from January, 2008 to December, 2012.

4.3.2. Study population

All Cervical cancer patients in BLH who were diagnosed from January, 2008 to December, 2012 and who fulfill the eligibility criteria.

4.4. Inclusion and exclusion criteria

- All cervical cancer patients who were diagnosed and enrolled in BLH during the required time period (2008-2012) will be included.
- Incomplete patient charts regarding to important variables, patients who registered during the required period but their diagnosis is prior to that, for patients whose follow up time is less than a month and patients with a diagnosis of pre-cancer lesions were excluded from the study.

4.5. Sample size determination

All cervical cancer patients diagnosed between January 2008 to December 2012 and who fulfill the eligibility criteria was included in the study.

4.6. Variables of the study

3.7.1. Dependent (outcome) variable:

- The outcome variable is the survival time from the first confirmed diagnosis date of cervical cancer, to death.

3.7.2. Independent variables:

- Age of patient at diagnosis
- Stage of cancer at diagnosis
- Histological types of cancer
- Treatment modality
- Presence of co-morbid illness(HIV AIDS)
- Parity(total live birth)
- Marital status
- Place of residence

4.7. Data collection tools and procedures

Data collectors: Record review tool was prepared. Three BSc nurses working at the cancer treatment center extracted and collected the data.

Data collection procedure: Before collecting the data, the records to be reviewed (both baseline and follow up records) was identified by their medical record number. Then, the data collectors who were working at the cancer treatment center extracted and reviewed the charts. They also made a phone call to each patient to collect data on some variables.

Data quality: Training on record review was given to data collectors and supervisors for two days before data collection task and training guide was prepared to facilitate the training. The principal investigator supervised every aspect of the review and other supervisors (one BSc Nurse and data clerk) handled the task in the absence of the principal investigator. The Review checklist filled was gathered and checked for completeness by the principal investigator and supervisors on daily basis.

4.8. Data processing and analysis

Data was coded and then entered, cleaned, edited using EPI-info version 7 and transferred to SPSS 20 for analysis. Basic descriptive analyses were done. Survival table was used to estimate probabilities of survival after diagnosis of cervical cancer at different time intervals. Kaplan Meier survival curve together with log rank test was fit to test for the presence of difference in survival among categories of covariates. Cox regression was fitted to find out predictors of survival time.

For that, bivariate Cox regression was first be fitted and those independent variables which become significant on the bivariate regression at 20% level of significance was included in the multivariate analysis. Backward Stepwise Multiple Cox regression was fitted at 5% level of significance to determine the net effect of each explanatory variable on time to death after diagnosis of cervical cancer. The necessary assumptions for the model were checked by scheenfeld residual test. The results of these models are expressed as hazard ratios (HRs) with 95% CI.

4.9. Ethical consideration

An ethical clearance for the proposed study was obtained from the research ethical committee of school of public health, Addis Ababa University. Consent from medical director and cancer treatment center focal person of Black Lion Hospital was obtained. Verbal consent was obtained from patients before starting the phone interview. Confidentiality of the information was maintained throughout the study by excluding names as identification in the data extraction form and the data was used only for the purpose of the proposed study. In addition, health professionals from the cancer treatment center extract the data from medical records to keep the confidentiality.

5. Results

5.1. Socio Demographic Characteristics

There were 1495 patients diagnosed in Black Lion Hospital from 2008-2012. From among these, complete data were obtained for 1391 cases. Patient who was enrolled from January 2008 to September 2012 was followed for 5 years retrospectively. The median age was 50 years (inter quartile range IQR 40-57). Most of the women experience early marriage which accounts 1038(74.6%). 966(69.4%) women had 5 and more than 5 children. 834(60%) patients resides in rural parts of Ethiopia. Significant number of patients has multiple sexual partners that account 306(22%). The detail is presented in table 1.

Table 1:- Baseline socio-demographic characteristics of cervical cancer patients in Black Lion Hospital, Addis Ababa, 2008-2012.

variables	Categories of variables	Vital status at last contact					
		censored		dead		Total	
		Count	Row N %	Count	Row N %	Count	Row N %
Age	20-29	34	85.0%	6	15.0%	40	2.88%
	30-39	174	78.0%	49	22.0%	223	16%
	40-49	330	78.4%	91	21.6%	421	30.3
	50-59	312	83.0%	64	17.0%	376	27%
	60 & above	259	78.2%	72	21.8%	331	23.8%
	Total	1109	79.7%	282	20.3%	1391	100%
Marital status	Unmarried	8	72.7%	3	27.3%	11	0.79%
	early marriage before18	814	78.4%	224	21.6%	1038	74.6%
	married after 18	68	78.2%	19	21.8%	87	6.3%
	Unknown	218	85.7%	36	14.3%	252	18.12%
	Total	1109	79.8	282	20.2	1391	100%
	Number of Sexual contacts	None	2	100.0%	0	0.0%	2
Sexual contacts	1	534	78.8%	143	21.2%	677	48.7%
	Few (two)	116	77.7%	33	22.3%	149	3.52%
	Multiple	248	81.0%	58	19.0%	306	22%
	Unknown	209	81.6%	48	18.4%	257	18.5%
	Total	1109	79.8%	282	20.2%	1391	100%
Place of residence	Rural	661	79.3%	173	20.7%	834	60%
	Urban	447	80.4%	109	19.6%	556	40%
	Unknown	1	100.0%	0	0.0%	1	0.1%
	Total	1109	79.72	282	20.27	1391	100%
No of children	Nulliparous	28	90.3%	3	9.7%	31	2.2%
	1-4 children	305	77.4%	89	22.6%	394	28.3%
	5 & above	776	80.3%	190	19.7%	966	69.4%
	Total	1109	79.7%	282	20.3%	1391	100%

5.2. Clinical and pathological characteristics

Most of the patients are diagnosed with stage II, stage III disease and histopathology of squamous cell carcinoma. There are 134 (9.6%) patients who undergone surgery and 206(14.8%) patients who received radical radiotherapy. HIV prevalence was 12.8% in this specific population. Table 2 depicts the clinical and pathological characteristics of cervical cancer patients.

Table2. Clinical and pathological characteristics of cervical cancer patients in Black Lion Hospital, Addis Ababa, 2008-2012.

Variables	Categories of variables	vital status at last contact				Total	
		censored		dead		Count	Row N %
		Count	Row N %	Count	Row N %		
Stage of cancer	stage 1	76	87.4%	11	12.6%	87	6.3%
	stage 2	459	78.9%	123	21.1%	582	41.8%
	stage 3	481	79.0%	128	21.0%	609	43.8%
	stage 4	88	81.5%	20	18.5%	108	7.8%
	Unknown	5	100.0%	0	0.0%	5	0.4%
	Total	1109	79.7%	282	20.3%	1391	100%
Histopathology	Squamous cell	1042	79.8%	264	20.2%	1306	94%
	adenocarcinoma	47	82.5%	10	17.5%	57	4.1%
	Adeno-squamous	11	73.3%	4	26.7%	15	1.1%
	others & unknown	9	69%	4	31%	13	0.9%
	Total	1109	79.7%	282	20.3%	1391	100%
Surgery as a primary Rx	no surgery	985	79.4%	255	20.6%	1240	89%
	Undergone surgery	115	85.8%	19	14.2%	134	9.6%
	Unknown	9	52.9%	8	47.1%	17	1.2%
	Total	1109	79.7%	282	20.3%	1391	100%
Chemotherapy	no chemo	986	80.3%	247	19.7%	1233	88.6%
	Concurrent radiochemo	89	84.8%	16	15.2%	105	7.5%
	Palliative	32	65.3%	17	34.7%	49	3.5%
	Adjuvant without RT	2	50%	2	50%	4	0.3%
	Total	1109	79.8%	282	20.2%	1391	100%
Radiotherapy	no radiotherapy	408	84.6%	74	15.4%	482	34.6%
	Radical radiotherapy	169	82%	37	18%	206	14.8%
	Adjuvant to surgery	32	94%	2	6%	34	2.4%
	Palliative Radiotherapy	497	74.6%	169	25.4%	666	47.9%
	Unknown	3	100%	0	0.0%	3	0.2%
	Total	1109	79.7%	282	20.3%	1391	100%
HIV sero-status	Negative	649	77.6%	187	22.4%	836	60%
	Positive	97	78.9%	26	21.1%	123	8.8%
	not screened	25	83.3%	5	16.7%	30	2.1%
	Unknown	338	84.2%	64	15.8%	402	28.9%
	Total	1109	79.8%	282	20.2%	1391	100%

5.3. Incidence of death during the follow-up

The median duration of follow-up was **13** months (IQR.60-1). Overall, there were **1657.33** person-years of observation or follow-up and **282** incident deaths were detected which makes the incidence rate of death among cervical cancer patients **17.01 per 100 person-years follow up**.

5.4. Survival from cervical cancer diagnosis to death

From a total of 1391 patients whose chart were reviewed **282** of them were found to be dead during the overall follow up period that is 60 months. Among these 47 and 48 were dead during the first and second six months of follow-up. The median survival time was **35** months. The overall survival rate was **32%** at 5-years and **52%** at 3-years. The probability of dying with in a one year period is **8%**; and in the next one year is **27%** etc. The table below shows the number of patients dead at each year and the cumulative probability of survival.

Table 3: Survival table for time to death for cervical cancer patients of Black Lion Hospital, Addis Ababa, 2008-2012.

No of patients	Interval start Time in months	Status		Cumulative Proportion Surviving at the Time		N of Cumulative Events	N of Remaining Cases
		dead	censored	Estimate	Std. Error		
449	6.000	48	401	0.966	0.005	48	1343
205	12.000	48	157	0.916	0.008	96	893
300	18.000	65	235	0.835	0.012	161	672
190	24.000	56	134	.728	0.017	217	381
134	30.000	37	97	.619	0.022	254	210
58	36.000	17	41	.526	0.028	271	96
30	42.000	6	24	.469	0.033	277	49
15	48.000	3	12	.412	0.042	280	22
1	54.000	0	1	.	.	280	9
9	60.000	2	7	.321	0.066	282	7

One can also see on the Kaplan Meir survival curve for time to death of cervical cancer patients, the probability of survival decreases as the follow-up time increases. Most patients terminate throughout 40 months of enrolment as indicated by the curve.

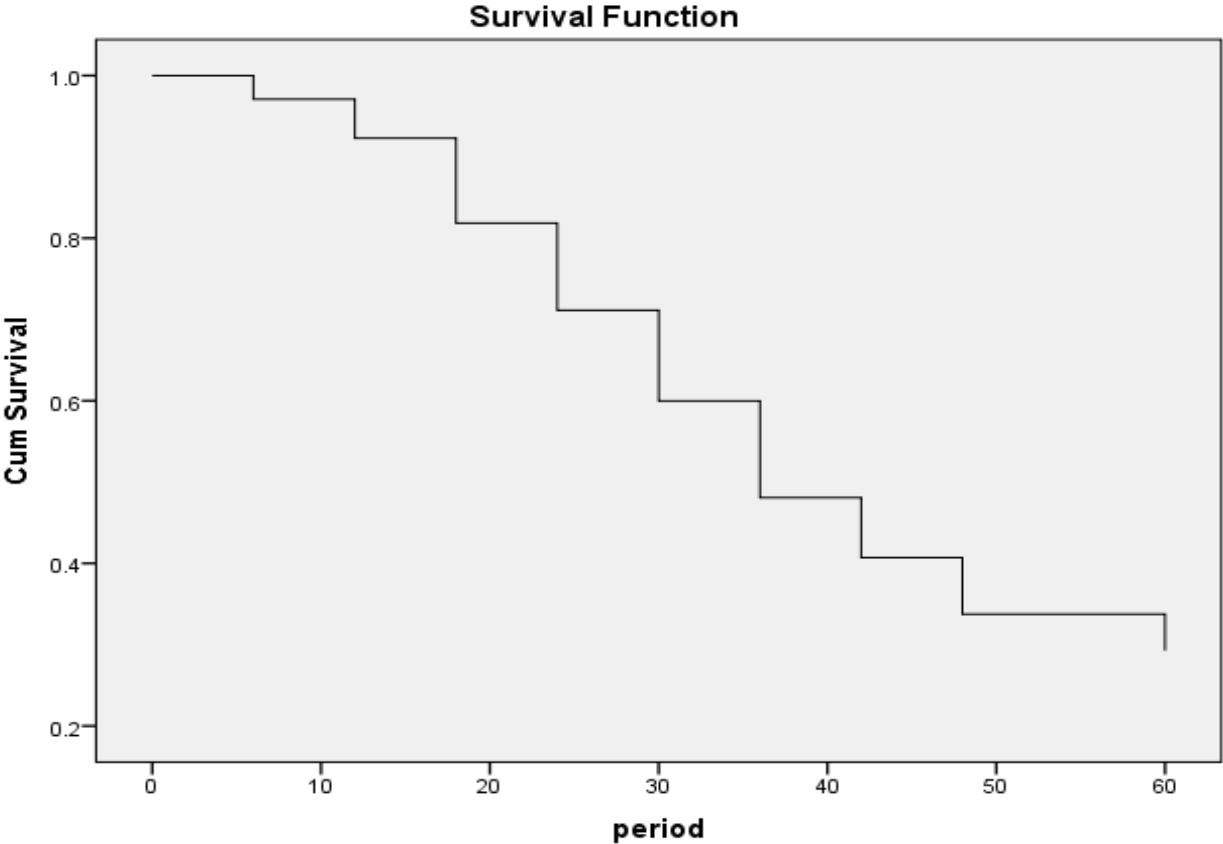


Fig 1: - Kaplan Meir survival curve for time to death among cervical cancer patients in Black Lion Hospital, Addis Ababa, 2008-2012.

Survival experience among different groups of cervical cancer patients

In this section hypothesis tests for the presence of statistically significant difference in survival time between different categories of covariates has been done. Then it is found that there is a difference in survival experience between categories of stage of cervical cancer, treatment modalities, age of patients, and place of residence. HIV sero-status and all other categories of covariate did not showed statistically significant difference in survival experience between them. The difference in survival experience among groups and covariates of cervical cancer patients is shown in table 4

Table4. Log-rank test for the presence of difference in survival experience between comparison groups and among categories of covariates.

Covariates	Difference in survival experience among covariates	P-value (pair wise comparison)	Chi-square
Stage of cervical Cancer	Stage 1 versus stage 2	0.013	6.21
	Stage 1 versus stage 3	0.0001	17.89
	Stage 1 versus stage 4	0.0001	18.09
Surgery as primary Rx	Undergone surgery Vs. No surgery	0.0001	17.63
Chemotherapy	No chemotherapy Vs. Concurrent chemo-radiotherapy	0.011	9.807
Radiotherapy	No Radiotherapy Vs. Radical Radiotherapy	0.0001	14.58
	No Radiotherapy Vs. Adjuvant to surgery	0.001	11.69
Age of patients	Age group 20-49 Vs. Age group 60+	0.038	4.69
Place of residence	Urban Vs. Rural	0.043	3.88

The five year survival rates for stage I and II were respectively, 81% and 33%. For stage III & IV, were 0%. Longer survival is seen in patients with early diagnosis, patients with the age group 20-29, patients who were treated with surgery. The following table shows a five year survival experience in different categories of covariates.

Table 5. The 5-year cervical cancer survival related to some independent variables

Variables	Five year survival (%)	Over all comparison p-value	chi-square
Stage of cancer		0.0001	35.44
Stage I	81%		
Stage II	33%		
Stage III	0%		
Radiotherapy		0.0001	25.16
No radiotherapy	19%		
Radical radiotherapy	53%		
Palliative	0.08		
Adjuvant to surgery	93%		
Primary Surgery		0.0001	29.79
Yes	69%		
No	15%		
Chemotherapy		0.001	20.96
No chemotherapy	20%		
Concurrent-radio-chemotherapy	60%		
Palliative(chemo only)	22%		
Adjuvant-without radiotherapy	27%		
Histology of tumor		0.031	9.38
Squamous cell carcinoma	73%		
Adenocarcinoma	70%		
Adeno-squamous	64%		

From the curve it can be seen patients with stage I & II diagnosis survived better than patients with late diagnosis that is stage III & IV.

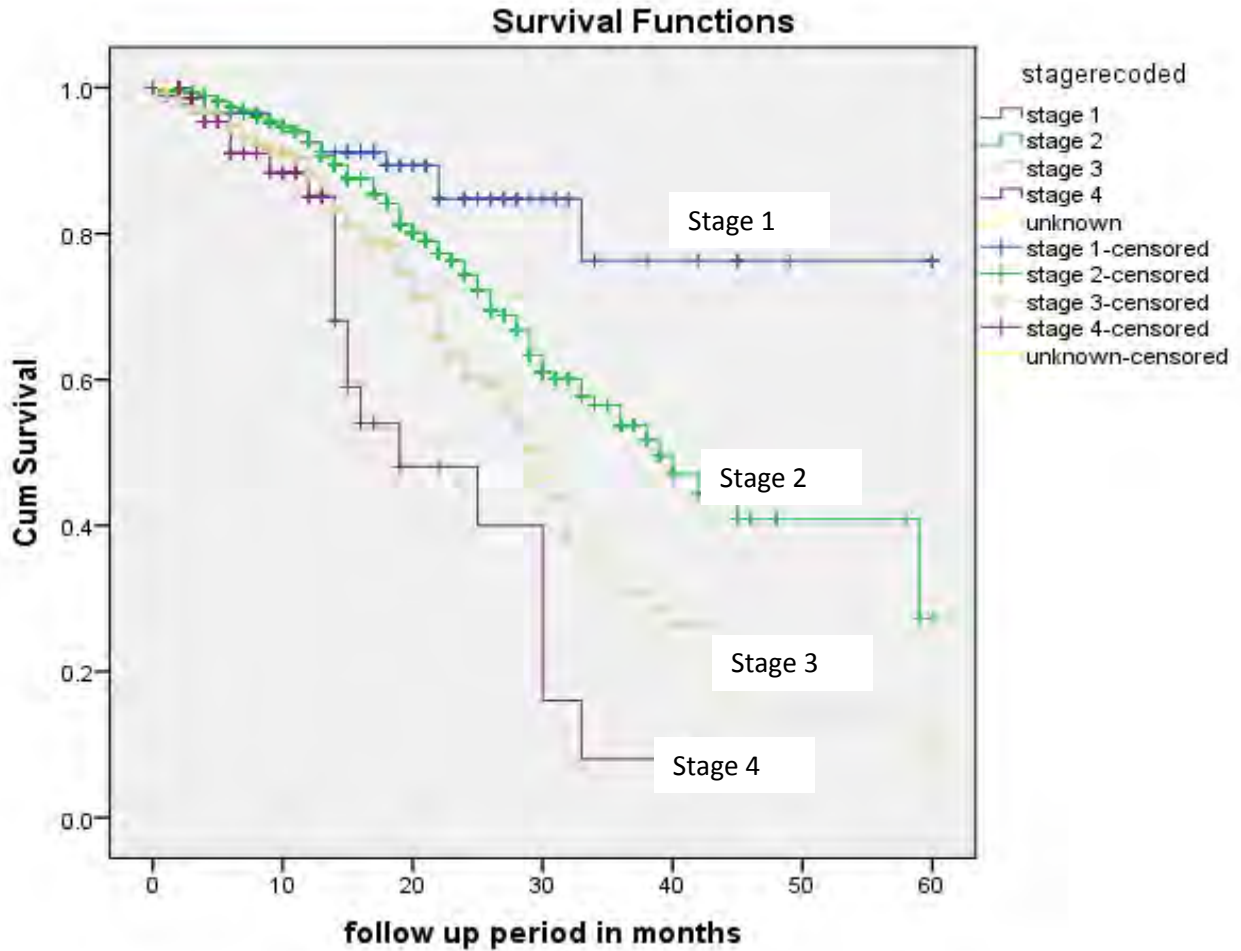


Fig 2:- Kaplan Meir survival curve for time to death in different stages of cervical cancer in Black Lion Hospital, Addis Ababa, 2008-2012.

One can see from the curve below that the survival of patients who undergone surgery is better than who didn't undergone surgery.

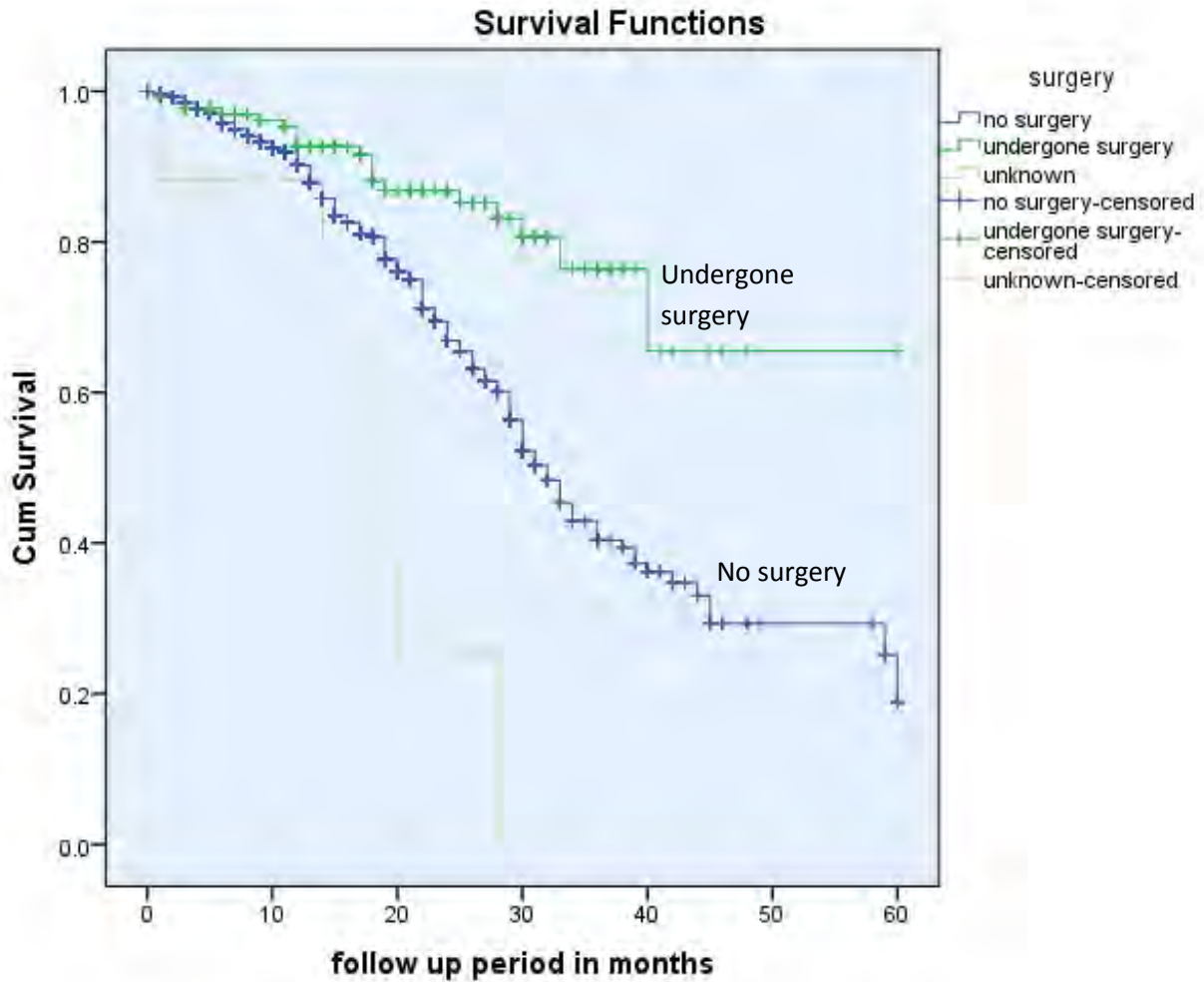


Fig 3:- Kaplan Meir survival curve for time to death among patients who undergone surgery and who didn't in Black Lion Hospital, Addis Ababa, 2008-2012.

5.5. Predictors of survival time among cervical cancer patients

In this part the independent variables are analyzed individually with the outcome variable and simple Cox regression is fit for all variables. Then the variables which become significant at $p < 20\%$ level of significance were included in the multiple Cox proportional hazard model. The proportionality of hazard assumption was checked using the Schoenfeld test.

From the bivariate Cox regression fit with all covariates; stage of cancer (p -value < 0.0001), chemotherapy (p -value < 0.0001), radiotherapy (p -value < 0.0001), surgery (p -value < 0.0001), marital status (p -value $= 0.168$), HIV sero-status (p -value < 0.190), place of residence (p -value < 0.136) and histology ($p = 0.037$) were found significant. The rest of the variables were not found to be significant at 20% level of significance and were not included in the second model.

The multiple Cox regression is therefore fitted by including the eight variables which were significant at 20% level of significance on the bivariate proportional hazard Cox regression analysis. Then stage of cancer, chemotherapy and surgery become significant on the final/parsimonious Cox proportional hazard model. The detail is shown in the table below.

Table 6:- Predictors of survival which are significant in the multiple Cox proportional hazards model among cervical cancer patients of black Lion Hospital, Addis Ababa, 2008-2012.

Variables	Categories of variables	Sig.	CHR	AHR	95.0% CI for Exp(B)	
					Lower	Upper
Stage of cervical cancer		0.006				
	Stage1			1.00		
	Stage 2	0.580	2.245	1.216	0.608	2.433
	Stage 3	0.202	3.707	1.604	0.776	3.314
	Stage 4	0.010	6.327	2.974	1.303	6.791
Surgery		0.021				
	No			1.00		
	Yes	0.011	0.370	0.488	0.281	0.848
Chemotherapy		0.016				
	No			1.00		
	Concurrent radio-chemotherapy	0.953	0.462	0.985	0.597	1.624
	Palliative chemo	0.610	0.941	3.911	0.937	16.326
	Adjuvant chemotherapy	0.002	0.601	0.731	0.534	0.937

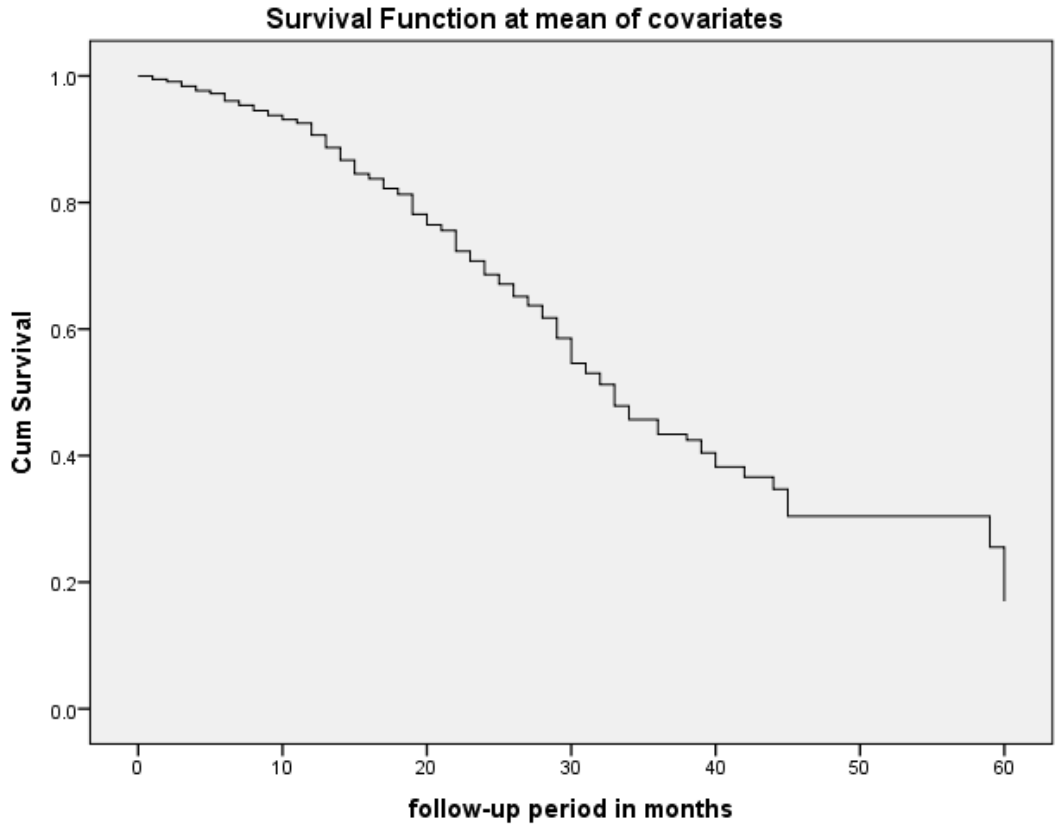


Fig 4:- Cox survival curve for time to death in different stages of cervical cancer patients of black lion hospital, Addis Ababa, 2008-2012.

6. Discussion

Assessing survival time of cancer patients has important implications for the level of development of health services and their efficiency to provide early diagnosis, treatment, and clinical follow-up care on cancer survival. It also represents the average prognosis of a cancer and is useful for assessing progress in cancer control(26).

This study estimates 5-year survival time among cervical cancer patients in Black Lion Hospital according to clinical staging, type of therapy, Pathology, age of patients and other factors.

Overall survival after 5 years among cervical cancer patients in the study was 32%. This is much lower from studies in Netherland, Germany and Mexico which is 60 %(19),64.7%(20) & 66.6 %(18)respectively. The wide availability and accessibility of screening programmers, early detection services, and cancer treatment facilities in these regions probably largely contributed to the high survival observed.

The three year survival in this study was 52%, which is similar with studies from Uganda and Zimbabwe that is 52% and 44% respectively. 3-year survival rate was 93% according to a study done in Tehran, Iranian patients(23). The observed differences in survival between countries seem to be largely a result of differences in the availability and accessibility of early diagnosis and treatment. The reason for the poor survival in this study may be due to the relatively advanced extent of disease, with most cases having regional spread at diagnosis. This could be due to the lack of screening programs to detect early stages of the disease or precancerous lesions in our country. This also could be due to patients may not get early treatment and follow up because there is limited availability of treatment facilities.

Most of cases were diagnosed at advanced stage (stage II, III), rather than as pre-cancers or early cancers. Women with early cervical cancers and pre-cancers usually have no symptoms. Symptoms often do not begin until the cancer becomes invasive and grows into nearby tissue. Besides it is not common to undergone for a women routine cervical cancer screening in our country.

Since patients at late stage may die at home before reaching health facilities, less number of stage IV patients was diagnosed in this study.

Overall survival after 5-years for stage I, II & III was 81%, 33% and 0% respectively. Better survival was observed in patients with early stages of the diseases. This is similar with the study conducted in Netherlands that reveals a 5-year survival rates for stages I, II & III were, respectively, 79% , 37% & less than 9%(19). This finding is also in line with the study conducted in Malaysia(24). Early detection and treatment greatly improves the survival time of cervical cancer patients.

In the long rank test it is found that there is a significant difference in survival experience between categories of stage of cervical cancer, treatment modalities, age of patients, and place of residence. Patients with stage I diagnosis had a significantly better survival than stage IV disease ($P < 0.0001$). Survival declined steadily with advancing stage of disease at diagnosis. This is consistent with study in Netherland(19). Five year survival rate in operated cases was 69%, according to the study in Iranian patients the survival rate was 70%. The five-year survival was higher in patients who received surgery than who didn't receive surgery as a primary treatment ($p=0.0001$). This finding is consistent with the study in Malaysia and Iran(23, 24). Though it was not statistically significant there was a difference in survival experience in histological types of tumor. Less survival was observed in patients having adeno-squamous followed by adeno-carcinoma. This finding is consistent with the study conducted in Germany(23). Among the cases for which HIV status was known, there was no statistical difference in survival at five years ($p=0.853$). This result is consistent with the study in Uganda(21).

In the Cox proportional hazard model stage of cancer, surgery and chemotherapy were statistically significant. There was a significant relationship between survival and stage of cancer. Stage IV Patients are 2.97 times as likely as to be dead at any time than stage I patients AHR, 2.97(95%CI, 1.303, 6.791). This finding is in agreement with study conducted in Uganda and Zimbabwe in which stage was an important determinant of

survival (21, 22). Stage is an important predictor of survival from cervix cancer, and the most significant influence on outcome in the present study.

Patients who undergone surgery are also significantly associated with reduced incidence of death HR, 0.49(95% CI, 0.281, 0.848). That is women who were operated had 51% more chance of surviving than those who didn't undergone surgery at any time. This finding is also in line with study conducted in Netherlands which identified primary surgery as a predictor of survival (19). This can be due to the options for treating a patient with cervical cancer depends on the stage of disease and surgery is indicated for patients with early stage and most of the surgery cases were treated with some curative intent. Patients with early stage diagnosis survived better. So, this is not only related with the surgery they undergone but also with the stage of their first diagnosis.

Adjuvant Chemotherapy was also predictors of survival that becomes statistically significant in the cox proportional hazard model. Receiving adjuvant chemotherapy is significantly associated with reduced incidence of death, AHR 0.731(95%CI, 0.534,0.937). Cases without adjuvant chemotherapy has 27% more chance of death than that of patients who was treated. This result is consistent with the study in Uganda and Zimbabwe that demonstrates the availability of effective and prompt treatment improved survival from cervical cancer (21, 22). Additional studies appear to confirm a positive impact of adjuvant treatment. Concurrent chemo-radiotherapy and palliative chemotherapy were not statistically significant as a predictor of survival; this can be due to the indications like advanced stage of cancer for this treatments.

7. Strength and limitation of the study

The strength of the study is use of analytical methods which can account for censored data and the use of large sample size, this will minimize sampling error. Furthermore, this study provided most up-to-date and comprehensive survival estimates of cervical cancer and it is a first of its kind in our country.

The limitations of this study are, since it is retrospective study and based on records, availability of data for all variables are difficult and some of information was missed. Some cards/charts are not found. However, since it doesn't exceed 10 % of the total study population, it doesn't affect the result of the study. The ascertainment and the cause of death is based on phone interview and not based on mortality data may lead to over or under detection of death as a result outcome ascertainment bias. There were significant number of lost to follow up and patients without phone numbers, as a result tracing of patients was difficult and censored data was higher in number. People with cancer may die from things other than cancer, and these rates don't take that into account.

8. Conclusion

Overall survival after five years was 34%. There were differences in survival experience between categories of covariates like among stages of cervical cancer, treatment modalities, age group of patients, and between categories of place of residence.

Predictor variables which were significantly associated with time to death of cervical cancer patients were stages of cervical cancer, being treated with surgery and adjuvant chemotherapy.

The results of this study show a strong gradient in survival by stage and treatment, which underlines the key role of early detection and timely treatment of cervical cancer for reducing mortality from cervical cancer.

9. Recommendation

The following recommendations are made from this study.

FMOH

- Improvement in comprehensive cervical cancer control program including prevention, early detection, treatment & palliative care is mandatory
- The need to expand cervical cancer screening programs (HPV testing & PAP smear)
- To create awareness in collaboration with public medias about cervical cancer prevention, screening and treatment is crucial

BLACK LION HOSPITAL

- The need to improve public and professional awareness, early detection and prompt treatment using feasible and effective regimens,
- To include detailed patient characteristics in the cancer registry data is important.

RESEARCHERS

- Further studies on survival time among cervical cancer patients that can address the limitations of this study and devise strategies to improve completeness by use of complementary active methods.

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Annexes

Annexes I: Data extraction form

Table 7: - data extraction form for the Assessment of survival time and associated factors among cervical cancer patients at BLH, AA Ethiopia, 2008-2012.

Part I: Socio demographic characteristic			Remark
1.	Medical record number(MRN)	_____	
2.	Age	_____years	
3.	Place of residence	Urban(regional town, zonal town, district town)-----1 Rural -----2	
4.	Marital status	Single -----1 Married -----2 Widowed-- -----3 Divorced -----4	
5.	Parity(number of live birth)	_____	

Part two:- Medical History			
1.	Patient age at diagnosis	_____years	
2.	Date of diagnosis	____/____/____	
3.	Date of starting treatment	____/____/____	
4.	Stage of cancer at diagnosis	1. Stage I 2. Stage II 3. Stage III 4. Stage IV 5. Unknown	
5.	Histological grades of cancer	1. well differentiated 2. moderately differentiated 3. poorly differentiated 4. undifferentiated	
6.	Histological types of cancer	1.squamous cell carcinoma 2.adenocarcinoma 3.adenosquamous cell carcinoma 4.unknown	

7.	Treatment modality	1. surgical treatment (yes / no) 2. chemotherapy (yes / no) 3. radiotherapy (yes / no) 4. none 5. unknown	
8.	HIV status	1. HIV negative 2. HIV positive 3. Not screened 4. unknown	
9.	Date of last contact	___ / ___ / ___	
10.	Status of the patient during last contact	1. Alive 2. Dead	
11.	Current status of the patient	3. Alive 4. Dead	
12.	If alive, functional status of the patient	1. Working 2. Ambulatory 3. Bed ridden	
13.	If dead, date of death If lost to follow up, date of lost to follow up	___ / ___ / ___ ___ / ___ / ___	

Form completed by _____ Sign _____

Date form completed ___ / ___ / ___

Name of supervisor _____ sign _____

Annex II. Conceptual framework

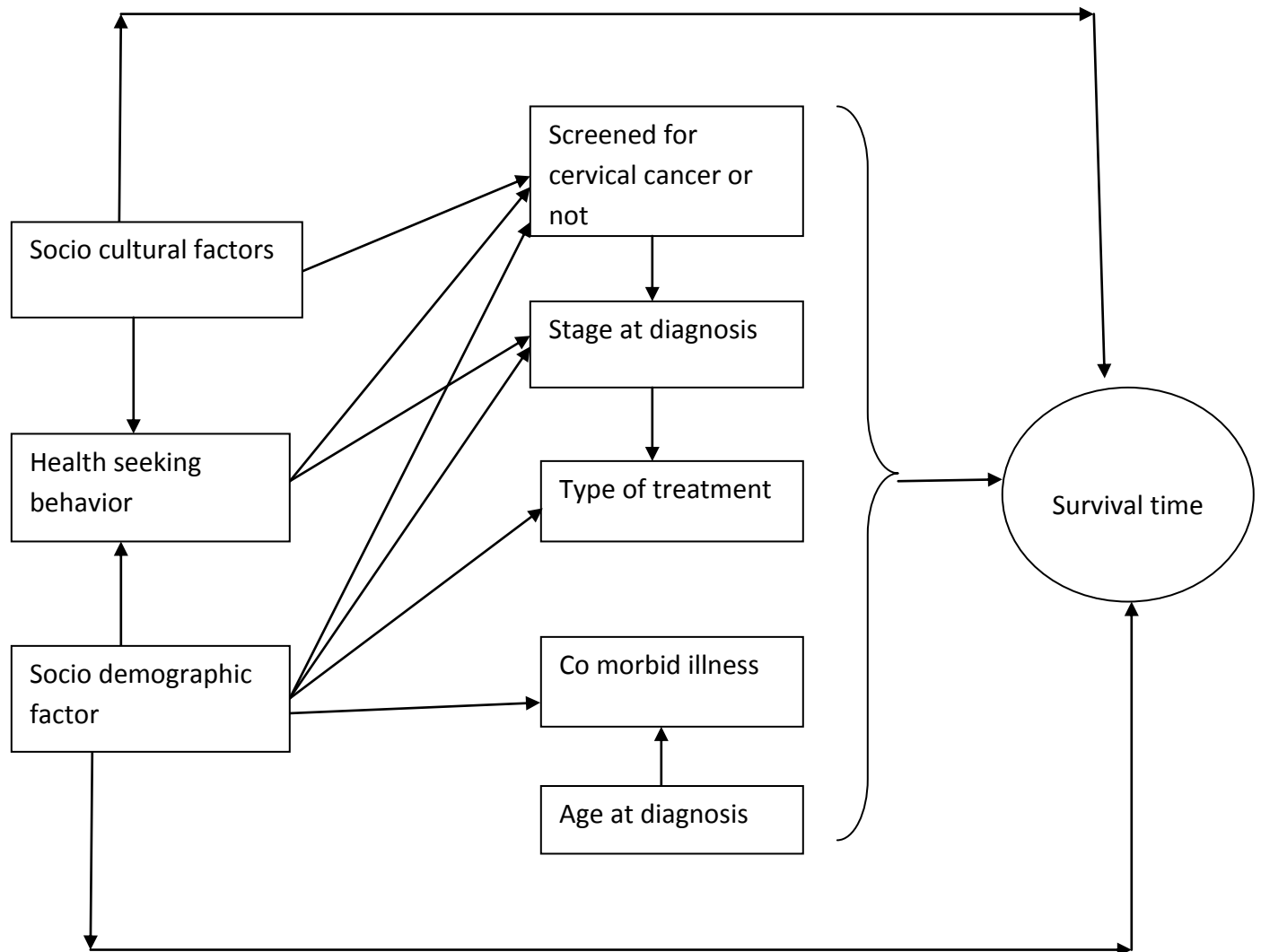


Figure 5. Conceptual frame work for the Assessment of survival time and associated factors among cervical cancer patients at BLH, AA Ethiopia, 2008-2012.

Annex III: Information Sheet

Title of the Research Project: Assessment of survival time and associated factors among cervical cancer patients at Black Lion Hospital, AA, Ethiopia, 2013, a retrospective longitudinal study.

Name of Principal Investigator: Tigist Yesuf

Name of the Organization: Addis Ababa University, College Of Medicine and Health Sciences.

Name of the Sponsor: Self sponsor

Introduction: This information sheet and consent form was prepared for Black Lion Hospital, cancer treatment center. The aim of the form was to make the above concerned office clear about the purpose of the research work, data collection procedures and get permission to undertake the research.

Purpose of the Research Project: The main aim of this research was to assess a five years survival time and associated factors among cervical cancer patients at Black Lion hospital, AA, Ethiopia, 2013.

Procedure: In order to come up with the above mentioned findings, total document of program clients enrolled during 2008-2012 was selected and followed up-to Dec 30, 2012 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: By participating in this research project, there is totally no risk that comes to one whom document is reviewed and phone called whereas doing these is of great importance to the research project; which is in turn important for overall planning and improvement of the program.

Benefits: The research have no direct benefit for one whose document/record is included in this research. But the indirect benefit of the research for the participant and all other clients in the program is clear. This is because if program planners are preparing predicted plan there is a benefit for patient in the program of getting appropriate care and treatment services.

Of all, the Research work has a paramount direct benefit for health care planners and managers, especially for those on cancer prevention and treatment planning and management.

Confidentiality: To keep the confidentiality of the records of the patients, the record was extracted by two trained cancer treatment center staffs using randomly selected card numbers. Then, two oncologic nurses (data collectors) reviewed the selected charts and they made a phone interview. The information collected from this research project was kept strictly confidential and information reviewed about the patients by this study was stored in a file, without name i.e. investigators use number codes to the record during the review. The information gathered was not accessible to anyone except the principal investigator and was kept locked with password and appropriate locks.

Person to contact: This research project was reviewed and approved by the institutional review board of college of medicine and health sciences, 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.

1. Dr. Adamu Addissie (MD,MPH, MA),Assistant professor: Addis Ababa University, college of medicine and health sciences, school of public health. Tel: 0911404954

2. Tigist Yesuf : Addis Ababa, Kolfe Keranio Sub city health office. Tel: 0911376492

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.

Annex IV. Consent form (English version)

My name is _____ i am working with Tigist Yesuf who is doing a research as partial fulfillment for the requirement of MPH at Addis Ababa University. This study is intended to assess the survival time and associated factors among cervical cancer patients in Black Lion Hospital.

The study is aimed to fulfill the information gap and provide evidence for program planners, implementers and decision makers at different levels by enabling them to access a baseline data. It also assists in the development of a system for improving the survival of cervical cancer patients.

The information will be collected through reviewing secondary data in the cancer treatment center and by interviewing patients through phone. We are asking you for a little of your time to help in this study. All the information will be numbered and coded; names will not be used throughout the research process.

Your answers to any of the questions will not be given to anyone else and no reports of the study will ever identify you. The interview is voluntary. Your participation, non-participation or refusal to answer questions will have no effect on services that you or any member of your family may receive from the health service provider.

Are you willing to participate in the study?

1. Yes

2. No

Annex V. ፈቃደኝነትን መጠየቅያ ቅጽ (consent form, Amharic version)

ስሜ ----- ይባላል።

በአሁኑ ሰአት በአዲስ አበባ ዩኒቨርሲቲ ለሁለተኛ ዲግሪዎቻቸው የመመሪቂያ ፅሁፋቸውን ከሚያዘጋጁት ከወ/ሪት ትእግስት የሱፍ ጋር በመሆን የማህጸን በር ካንሰር ህመማቸውን በሚመለከት በጥቁር እንበሳ ሆስፒታል መረጃ በመስጠት ላይ እገኛለሁ።

ጥናቱ ለፕሮግራም አውጭዎች፣ አስፈጻሚዎች እንዲሁም ለውሳኔ ሰጪዎች መረጃ በመስጠት የህመማችን የጤና ሁኔታ ለማሻሻል ጉልህ አስተዋጾ ያደርጋል።

መረጃው የሚሰበሰበው በካንሰር ህክምና ማእከል ከሚገኘው የህመማችን ማህደርና ለህመማችን ስልክ ደውሎ በማነጋገር ነው። የሚሰጡት መረጃ ሚስጥራዊነት እጅግ የተጠበቀ ሲሆን ስምዎችም ሆነ ሌላ የእርሶን ማንነት የሚገልፅ በዚህ ጥናት ሂደት ውስጥ የማንጠቀም መሆኑንና መረጃውንም ለሌላ ወገን አሳልፈን እንደማንሰጥ ላረጋግጥልዎት እወዳለሁ።

ቃለ ምልልሱ በፈቃደኝነት ላይ የተመሰረተ ሲሆን በዚህ ጥናት ውስጥ የመሳተፍ ወይም ያለመሳተፍ እንዲሁም ቃለምልልሱን በማንኛውም ሰአት የማስቆም መብትዎ የተጠበቀ ነው። ይህም በመሆኑ በእርሶም ሆነ በቤተሰብዎ ላይ ከሆስፒታሉ በሚያገኙት አገልግሎት ላይ ምንም ዓይነት ተፅእኖ እንደሌለው በድጋሚ ልገልፅልዎት እወዳለሁ።

ለጥናቱ መረጃ ለመስጠት ፍቃደኛ ነዎት?

- 1. አዎን
- 2. አይደለሁም

Annex-V: Assurance of investigator

I, the undersigned senior MPH candidate agree to accept responsibility for the scientific, ethical and technical conduct of the research project and for provision of required progress reports as per terms and conditions of the research and publications office of the Addis Ababa University.

Name of the Investigator: Tigist yesuf

Signature _____ Date ____/____/____

Approval of the advisor

Advisor:

Name: Dr. Adamu Addissie (MD, MPH, MA), Assistant professor

Signature _____

Date ____/____/____