FIVE-YEAR SURVIVAL OF WOMEN DIAGNOSED WITH CERVICAL CANCER AT TIKUR ANBESSA SPECIALIZED HOSPITAL, ADDIS ABABA, ETHIOPIA; A RETROSPECTIVE COHORT STUDY.

Center for Innovative Drug Development and Therapeutic Trials for Africa (CDT-Africa)

By

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This is to certify that the thesis prepared by Olyad Mose, entitled *five-year survival status of women diagnosed with cervical cancer and treatment impact at Tikur Anbessa hospital, Addis Ababa, Ethiopia; a retrospective cohort study*. submitted in partial fulfillment of the requirements for the degree of Master of Clinical Trial Practice complies with the regulations of the University and meets the accepted standards with respect to originality and quality.

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ABSTRACT

Background: Worldwide, cancer of the cervix is one of the most common causes of cancer mortality among women, with about 288,000 deaths each year. While it is the second leading cause of cancer mortality among adult women globally, it is the most common cause of mortality in the economically emerging countries including in sub-Saharan Africa. The reason for this high mortality is likely to be the poor access to early detection or screening and treatment services. There is no sufficient Published data on the treatment outcome of cervical cancer in Ethiopia. This study would contribute to the evidence regarding the treatment outcome of cervical cancer.

Objectives: To assess the five-year survival among women who attended for treatment of cervical cancer.

Methods: A hospital based retrospective cohort study was conducted at the Oncology Department of Tikur Anbessa Specialized Hospital (TASH). Records of patients with a first diagnosis of cervical cancer were selected from a two-year medical records of cervical cancer patients who attended the oncology department of TASH from September 11/2012 to September 11/2014GC.Survival Outcome was evaluated over the subsequent five-year period until 2014GC. Because of the practical challenges of determining actual survival status, continuation in follow up (vs dropout from follow up) was used as a proxy indicator of survival. Descriptive statistics was employed to summarize basic sociodemographic and clinical variables. Kaplan-Meier and Cox-regression analysis was used to evaluate the potential role of various treatment modalities on survival outcome. Crude and adjusted Hazard ratios with 95% Confidence intervals were presented as measure of association. Statistical tests resulting in a p-value of less than 0.05 were considered statistically significant.

Results: Among 1008 cancer patients who were diagnosed and started Treatment at Tikur Anbessa Specialized Hospital Oncology Center during the two-year selection period ,418 had cervical cancer and were included in the current study. At the end of the five-year only 9.9% (40) had survived in follow-up. For the majority, stage at presentation was late. Patients who arrived with later stages (Stage-III) cervical cancer had lower follow-up survival probabilities compared with earlier stage [stage-0, (Carcinoma in situ)] **[**Adjusted Hazard Ratio=2.17; 95% -CI= 1.40,3.40**].**

Those who had received combination therapy (Radiotherapy, chemotherapy and surgery) have better survival probability than those who were treated with Radiotherapy and Chemotherapy alone [Adjusted HR= (0.29, 95%CI, 0.84, 2.20), (2.52,95%-CI,1.80,3.40), and (2.02,95%-CI,1.10,3.80)] respectively.

Conclusion and recommendation: The clinical factors identified as factors for survival in follow-up (e.g., stage at presentation) appear to justify using survival in follow-up as a proxy measure of survival. However,

this is extremely crude proxy. Thus, well planned prospective study of survival is needed. Nevertheless, if the crude assumption is correct, ensuring access to early diagnosis, and treatment is an urgent priority for improving survival of patient with cervical cancer in Ethiopia. There is a need of creating awareness, primary prevention by vaccination, and increasing early detection programs to increase early stages at presentation which gives more opportunity to appropriate treatment. Furthermore, expanding more treatment centers and implementation of advanced Technology like Linear accelerator, brachytherapy and PET-scan needs urgent attention.

KEY WORDS: Cervical cancer, Survival status; Early Detection; Delay in Treatment impact.

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List of Abbreviations and Acronyms.

BSC	Batcheler of science.
Cc	Cervical Cancer
CDT-Africa	Center for Drug Development and Therapeutic Trial for Africa
CIN	Carcinoma in situ
CRT	Chemotherapy
CT	Computerized Tomography
EMR	Electronic medical record.
FIGO	International Federation of Gynecology and Obstetrics
HIV	Human Immunodeficiency Virus
HPV	Human Papilloma virus
HR	Hazard Ratio
MD	Medical Doctor
MSc	Master of science
NCD	Non-Communicable Disease
OCP	Oral Contraceptive Pill
PaP-smear	Papineau's Smear
PET	Positron emoting tomography
RT	Radiotherapy
RX	Treatment
TASH	Tikur Anbessa Specialized hospital
WHO	World Health Organization

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1. INTRODUCTION

1.1 Background

Cancer is a leading cause of mortality both in developed and less developed countries; the burden is expected to rise across the world due to increased life expectancy of the population, especially in less developed countries, in which around 82% of the world's population lives. The espousal of lifestyle behaviors that are known to raise cancer risk, like smoking, poor diet, sedentary life, and reproductive changes (including lower parity and later age at first birth), have more increased cancer burden globally[1].According to GLOBOCAN estimates, about 14.1 million new cancer cases and 8.2 million mortality occurred in 2012 across the world. Over the years, the burden has shifted to less developed countries, which are currently responsible for around 57% of cases and 65% world wide of cancer mortality[1].

Worldwide, cancer of the cervix is one of the most common causes of cancer mortality among women, with about 288,000 deaths each year. Persistently, human papilloma virus (HPV)-infection is the leading factor for cervical cancer. Multiparity, increasing age ,human immunodeficiency virus (HIV),oral contraceptive pills (OCP), as well as cigarette smoking and low socioeconomic status are listed as the known risk factors for cervical cancer[2]. Population-based cervical cancer screening and testing programs have been highly effective in decreasing the frequency and mortality of cervical cancer[3].

Cervical Cancer is the fourth most common malignant tumor among women and seventh of overall neoplasms worldwide. The global annual incidence of cancer cases was predicted to be 528,000, and the annual number of Cervical Cancer- related mortality was estimated at 266,000 [4]. It is the second most common malignancy in women in developing countries Over half a million women are diagnosed each year with cervical cancer and more than half of these women die from their cancer worldwide[5].

Cervical cancer (CC) is the most leading cause of cancer related mortality in women in sub-Saharan Africa and other parts of the developing country, largely as a results of less access to early detection or screening and treatment services[6].

Cervical cancer detection has resulted in well-documented reduction in occurrence of new cases and cancer related death in the United States. Despite evidence showing that screening is effective in preventing invasive cervical cancer and cervical cancer related mortality, most women are not screened in practice. This is specifically true for women in countries with limited access to preventive health services and a usual source of care. More than half of all new cervical cancer cases are predicted to occur in those women who have never or rarely been tested[7].

Stage at diagnosis, which is based on the anatomic extent of a disease, is a major determinant of patients' outcomes. It is crucial in predicting patients' prognosis and to inform treatment decisions, as well as to assess the effect of public health interventions such as screening programs and educational or awareness campaigns, which aim to improve early- stage diagnosis[8].

The role of adjuvant chemotherapy followed by radical radiotherapy (RT) or chemoradiotherapy (CRT) in cervical cancer expects further confirmation. Research evidence showed that persistent human papilloma virus infection(HPV) DNA in exfoliated cell post-RT is a commonest biomarker of subclinical residual disease and thus contributes for the risk of recurrence[9].

Study established worldwide cancer survival rates for 10 common cancers and produced estimates of 5-year survival for more than 25 million patients in 67 countries and 279 cancer registries from 1995 to 2009. Globally, the 5-year net survival for cervical cancer varied from less than 40% to more than 70%. CONCORD-2 reported a slight decrease in the 5-year net survival for cervical cancer in the United States (from 64.2% in 1995-1999 to 62.8% in 2005-2009). Similar patterns were observed in other high-income countries[7].

The Role of human papilloma virus (HPV) in the disease of cervical cancer has been decisively recognized, and >90% of patients infected with HPV in their tumor cells. Besides, for patients with cervical cancer that are treated with radical RT or CRT, pretreatment HPV infection is related with good survival and lesser recurrence compared with HPV-negative tumor[9].

Treatment of cervical cancer depends on its stage at diagnosis, accessibility of Radiotherapy facility and ability of patient to afford for chemotherapy. Treatment could be surgical removal (radical hysterectomy with pelvic lymphadenectomy (Wertheim), Adjuvant, radical, and palliative radiotherapy and Chemotherapy).

There was a study done in Ethiopia 2014 Gc on Survival of 1,059 for cervical cancer patients in which 1-year and 2- year overall survival probabilities were 90.4% and 73.6% respectively.[10]

This study was however designed to assess the Five-year Survival Status of Women with cervical cancer attending adult oncology department of Tikur Anbessa specialized hospital (TASH), it also helps provide further information on recent outcome.

1.2 Statement of the problem.

Cervical cancer is the second most common cancer in females across the world. Each year more than 270 000 women die from it, and more than 85% of these deaths occur in low- and middle-income countries due to poor access to screening and treatment intervention[11]. Effective screening and treatment of pre-cancer for women aged 30 years and above can protect them from having cervical cancer. However only 22 countries, reported screening programs with coverage of 70% and above. screening incidence studies done in USA, reported that 83% of women aged 21 to 65 years are up-to-date with screening. This implies that approximately 1 in 5 women are not getting screened as recommended[12].Participation rate of most countries is below 50% and it is even less than 10% in some countries[13].

Survival rates from cervical cancer can be further improved by establishing effective cancer treatment programs[11].Improvement in cancer survival in several primary sites is related to the development of treatments and early detection[14]. Population-based cancer survival data, a key indicator for monitoring progress against cancer, are not widely available from countries in Africa, Asia, and Central America[15].

Cervical cancer mortality rate among women is correlated with the stage of the cancer at diagnosis. The chance of survival is high when cervical cancer is diagnosed in its early stage and treated[8][16]. Cervical cancer screening can detect cancer at an early stage when it is done correctly. Unfortunately, Ethiopia does not have routine screening scheme like many developing countries. Consequently, patients present at late stage, and this results in a significantly high morbidity and mortality. Late presentation of cancer patient mostly requires costly and advanced treatment methods and this put inadequately resourced health institutions in to challenges.

1.3 Significance of study

There is no sufficient Published data on the treatment outcome of cervical cancer in Ethiopia. Finding from the current study would help to understand treatment outcome of cervical cancer and factors associated with this outcome. This would in return help to improve the service provided to cervical cancer patients. The study would also highlight gaps in current knowledge and serve as basis for future studies

2 LITERATURE REVIEW

2.1 Introduction

Globally, cervical cancer is common, and became the second from all malignancies for women. It is the most common gynecologic tumor among women. Cancers stalk from disease with the human papillomavirus, even though other host reasons disturb neoplastic development following initial infection. As compared with other gynecologic malignancies, cervical cancer occurs in a younger resident among female. Thus, testing for this tumor with Pap smear sampling typically starts in youth or young adulthood[17].

Cervical cancer is the second most common and leading cause of mortality in female globally. This is mostly due to the extensive infection with high-risk group of human papillomaviruses (HPV) and decreased usage of or accessibility to Pap smear testing in many countries across the world. Approximately, 500,000 population of cervical cancer are expected globally, with around 240,000 mortality each year. Cancer occurrence is predominantly high in women living in Central and South America, the Caribbean, and southern and eastern Africa. Death rate is disproportionately high in Africa[18].

2.2 Epidemiology and Etiology of Cervical Cancer.

None communicable disease (NcD) is currently becoming accountable for the most of global mortality. and cancer is anticipated to rank as the leading cause of mortality and the solely most significant barrier to promoting life expectancy in every nation of the world in the 21st century[19]

Economically developed countries have expressively lower cervical cancer rates, and add only 3.6 percent of cancer incidence. This discrepancy in the incidence shows successes gained by cervical cancer screening programs in which Papanicolaou (Pap) smears are consistently found[17].

HPV is the primary neoplastic-initiating event in the vast majority of women with invasive cervical cancer. Other factors associated with cervical cancer include low socioeconomic status, cigar rate smoking, reproductive behavior (parity and oral contraceptive use), multiple sexual partners, early menarche and early initiation of sexual intercourse[20].

Result from Literature Review showed that, worldwide occurrence of Cervical cancer was a predictable to 528,000 women with of cervical cancer infection and 266,000 mortalities in 2012 and It is the fourth commonest cancer globally. In spite of effective screening program, cervical cancer increased to be a most community health problem.[21]. The best way of detecting a cervical cancer is to have regular testing with a Pap smear (test for human papilloma virus or HPV) Cystoscopy, proctoscopy, and examination under anesthesia. Imaging studies like (Chest X-ray, computerized tomography (CT),Intravenous Urography)[22].

The FIGO (International Federation of Gynecology and Obstetrics) tumor grading system is used commonly to stage, cervical cancer. Clinical stage is used based on the results of the doctor's physical examination, biopsies, radiologic test, and a few other tests that are done in some cases, like cystoscopy and proctoscopy[22]

HPV is expected to be responsible for – 100% of cervical cancer cases. HPV types 16 and 18 cause about 70% of all cervical cancers across the world. As of January 2008, two HPV vaccinations have been accepted for use in most part of the globe. Clinical trial results show that both vaccines (HPV 16 &18) are harmless and very fruitful[23].

According to 2015 guideline for cervical cancer in Ethiopia, community-based facility data collected by Tikur Anbessa specialized referral hospital from 1996 – 2008 indicated that approximately 30.3% of all cancers diagnosed in the hospital were cervical cancer. The expected program of cytology-based cervical cancer screening in Ethiopia is 1.6% in cities and their surroundings and 0.4% in country side areas[24]

Currently recommended approach to prevent and control cervical cancer is, vaccination against human papillomavirus (WHO 2018). Screening and treatment for pre-cancerous lesions, early diagnosis, treatment and palliative care of invasive cancer is recent recommended approach for woman with cervical cancer[13]

Based on reference from American cancer society, the methods for cervical cancer treatment are inhibition on two ways (reduce risk of precancer, regular screening with the pap), recognition (all females should have cervical cancer screening beginning at age 21) and treating with three common types (surgery, radiation, and chemotherapy). Cervical cancers that have disseminated outside the cervix are commonly treated with surgery or radiation, and then followed by chemotherapy[25].

Although cryotherapy is the treatment of choice when a lesion is identified through screening. Lesion is not eligible for cryotherapy and LEEP should be considered as an alternative treatment when the entire lesion or the junction between the squamous epithelium and the columnar epithelium of cervix is identified[26]

Patients who have good adherence to guideline have good Survival with supportive care, Brachytherapy to decrease toxic effect and economical support could also contribute for better survival outcome[6]

2.3 Survival and survivorship

Knowing survival rates gives an idea of what percentage of people with the same type and stage of cancer remain alive for certain amount of time (example, within 5 years) from the day they were diagnosed and started treatment [22]

Invasive cervical cancer can mostly be efficiently treated if screened at an early stage. The expected five-year net survival of cervical cancer is in the range of 60% to 70% in most developed nations. with accessible data. Between LMICs with obtainable survival data, five-year survival is 46% in India, 56% in Thailand, and 62% in Ecuador[27]**.**

In previous study conducted in Malesia, the average survival period was 65.8 months and the 5-year survival frequency were 71.1% as indicated by Kaplan Meier curve. In the same study, the general detected survival rates at 1, 3 and 5 years were 94.1%, 79.3% and 71.1% respectively. There was substantial variation in survival rates among women from diverse age groups. Females bellow 45 years old have a best 5-year survival period when compared with those 45 years old and above (85.2 vs 63.8%). In the multiple cox regression analysis, age group and ethnicity were significantly associated with the survival of women diagnosed with cervical cancer women[28].

Studies the outcome of Neoadjuvant chemotherapy in combination with radiotherapy or surgery showed that most cervical cancer malignancies are chemo responsive; in fact, 38% to 90% of

clinical responses, including complete re-missions, have been reported. Clinical trials using neoadjuvant chemotherapy followed by surgery reported that the reduction of tumor bulk could make radical surgery possible in a high percentage of cases previously considered inoperable[29]

In a survival cohort study done in the UK with a median follow-up time of 23 months there were 36/779 (4.6%) recurrences and 11/779 (1.4%) deaths. The majority of the recurrences occurred early in the follow-up period. mortality was not associated with route of surgery, there was an association between size of tumor, and the presence of lymph vascular space invasion. However, there was no association between grade or histological type of tumor and mortality[30].

Another study Relative five-year survival for cervical cancer in NSW increased from 64 per cent in 1972-1976 to 72 per cent in 1987-1991.All the increase occurred between 1972-1976 and 1977-1981. After adjusting for potential confounding variables the risk of death in five years due to cervical was reduced in the 0-39 years age group and increased in the older people(i.e. older than 64) [31]

According to the 2015 report of the Japan Society of Obstetrics and Gynecology, age of study participant, stage of cancer at presentation, Histologic type of tumor, and Treatment were significantly associated with survival[32].

In India, the overall 5-, 10- and 15-year pragmatic survival rates from cervical cancer were 51.0%, 36.3% and 30.0% respectively; the corresponding relative survival rates were 54.8%, 43.0% and 41.1% respectively relative survival rates were 54.8%, 43.0% and 41.1% respectively[33]

3 OBJECTIVES

3.1 General objective

To assess five-year survival among women diagnosed with cervical cancer who initiated treatment at Tikur Anbessa specialized Hospital Oncology Center.

3.2 Specific objectives

To describe survival for each treatment approach of women diagnosed with cervical cancer.

To estimate the proportion of deaths (measured through drop outs) over five-years of follow up among women diagnosed with cervical cancer and initiated treatment at Tikur Anbessa specialized Hospital Oncology Center

To identify factors associated with treatment outcome (Five-year survival) of women diagnosed with cervical cancer.

4 METHODS

4.1 Study setting and period**.**

The study was conducted at oncology Department of Tikur Anbessa Specialized Hospital. Tikur Anbessa Specialized Hospital (TSH) was opened in 1972 and had since served as a teaching hospital hosting the school of medicine. With 700 bed capacity, TSH is the largest referral hospital in the country. The hospital was transferred to the School of Medicine by the Ministry of Health in 1988 and, with the establishment of the College of Health Sciences, the responsibility was transferred to the College. TSH offers specialized clinical services that are not available in other public or private institutions are rendered to the whole nation. The hospital, as per the information provided in the Addis Ababa University Website and updated in 2021 (http://WWW.aau.edu.et/chs/tikur-anbessa-specialized-hospital/background-of-tikur-anbessa-hospital/), has 200 doctors,379 nurses and 950 administrative staff.

The Hospital has fifteen Departments:(i.e., Internal medicine, Surgery, Gynecology and Obstetrics, Pediatrics, Radiology; Radiotherapy, Adult Oncology, Pediatric Oncology /Hematology, Nuclear Medicine, Psychiatry, Laboratory, Orthopedics and Pharmacy). The hospital, provides diagnostic, and treatment service for 400,000 patients per year. The oncology Department of TASH is the only Department providing Radiotherapy service for the country and has an outpatient department, which gives service to new and follow-up patients, and an in-patient's department, which has 19 beds.

Data was collected a Study participant who were diagnosed between September 11/2012 and September 11/2014GC were eligible. The outcome assessment was five years from the eligibility periods and was from 9/2/2020 GC to 8/4/2020 GC

4.2 Study design

The study was a hospital based retrospective cohort study.

4.3.1.4 Population

4.4 Source population

The source population constituted all patients with cervical cancer who attended oncology Department of TASH.

4.5 Study participants

The study participants constituted those whose records confirmed diagnosis of cervical cancer that was made for the first time during the two-year period from (September 11/2012 to September 11/2014GC).

4.6 Inclusion and exclusion criteria**.**

4.6.1 Inclusion

Medical charts of women diagnosed with cervical cancer and treated in the Oncology department of TASH from September 11/2012 and September 11/2014Gc.

Age ≥ 18 years.

First Diagnosed with cervical cancer from September 11/2012 and September 11/2014GC.

4.7 Sample size

The nature of the study has restricted the number of participants to be recruited. Thus, all cervical cancer patients who attended the oncology department of TASH from September 11/2012 and September 11/2014GC and fulfilled the inclusion criteria of the study were included in the study. As a result, there were Total of 1008 patients who visited the oncology unit of TASH from September 11/2012 and September 11/2014GC and 418 patients fulfilled the inclusion criteria and hence were included in the study.

4.8 Data entry and analysis.

The primary end point was Five-year survival status of women diagnosed with cervical cancer. Because of impossibility of obtaining survival status from records and by phone call, we used the drop out from follow up as proxy measure of mortality or at least as an indicator of a severe illness that prohibited the person from coming for follow up and likely to lead to death soon after the loss to follow up. Person time equaled the time from the date of pathologic diagnosis to death (drop out from follow-up) or to closing date for follow-up (8/4/2014GC), whichever came first. The data was entered into Epi info and transferred to the Statistical Package for the Social Sciences (SPSS) version 20.0 for analysis. Descriptive statistics was used to summarize study variables. Chi-Square was used to compare each treatment outcome. Logistic regression was used to analyze the associations between potential demographic and clinical risk factors such as age, parity, stage of disease, and type of treatment. and treatment outcome by using crude odds ratio (COR) and adjusted odds ratio (AOR) at 95% confidence level. Cox-regression and Kaplan-Meier were used to evaluate survival and compare Hazard Ratio (HR) between Treatment groups. A p-value of less than 0.05 was considered statistically significant.

4.9 Study variables

4.9.1 Independent variables.

- Demographic characteristics (age, Region)
- Clinical features of tumor (tumor size, nodal involvement and metastasis stage, histologic differentiation)
- Treatment approach. (Surgery only, chemotherapy, radiotherapy, or combination Therapy)
- Treatment modality (number of chemotherapy cycle, type of chemotherapy combination)
- Sexual characteristic of patients. (Multiple partners, single partner, never had sexual partner)
- Factors significantly associated with treatment outcome (Five-year survival) of women diagnosed with cervical cancer
- Contraceptive use
- History of smoking.

4.9.2 Dependent variables

- Five-year survival Status and time to death.

4.10 Data collection and technique.

A data collection format was used to extract the necessary information from medical records (Annex I) of study participants. Detailed baseline demographic and clinical information were extracted. This includes; age, marital status, parity, duration of illness, type of cancer, stage of illness, and treatment modalities. Follow up data focused on survival status. The data were collected by trained oncology nurses who were given a two-day training prior to data collection on how to use the data abstraction format to gather information from patients' medical records.

4.11 Data quality control.

To ensure quality of the data, pre-test was done on 5% of the study population to ensure the agreement of the data collection format with the need of the study. Any error found during the process of pre-test was corrected and modification made into the final version of the data abstraction format. The data collectors were trained for two days before the process of data collection. Supervision and checking made by the principal investigator to ensure completeness and consistency of the collected data. All collected data examined for completeness and consistency during data management, storage and analysis.

4.12 Ethical considerations.

Ethical clearance was obtained from the Scientific and ethics Review Committee (SERC) of CDT-Africa College of Health Sciences Addis Ababa University. Before the start of data collection, permission was obtained from oncology department of TASH. To ensure confidentiality, name and other identifiers of patients and health care professionals were not recorded on the data collection format. A waiver of informed consent was obtained from (SERC) of CDT-Africa.

5 RESULTS

5.1 Description of the Study Population

Between September 11/2012 and September 11/2014GC, a total of (1008) patients with cancer of the cervix uteri were registered at the Oncology department of TASH. Of those,418 were seen by the oncologist, diagnosed for the first time and radiotherapy/chemotherapy was planned for those enrolled in treatment. The remaining 590 patients were only seen by a physician once, and their charts with attached result and referrals from different health institute was found and they did not receive treatment. Therefore, not included in this analysis (Figure-1)

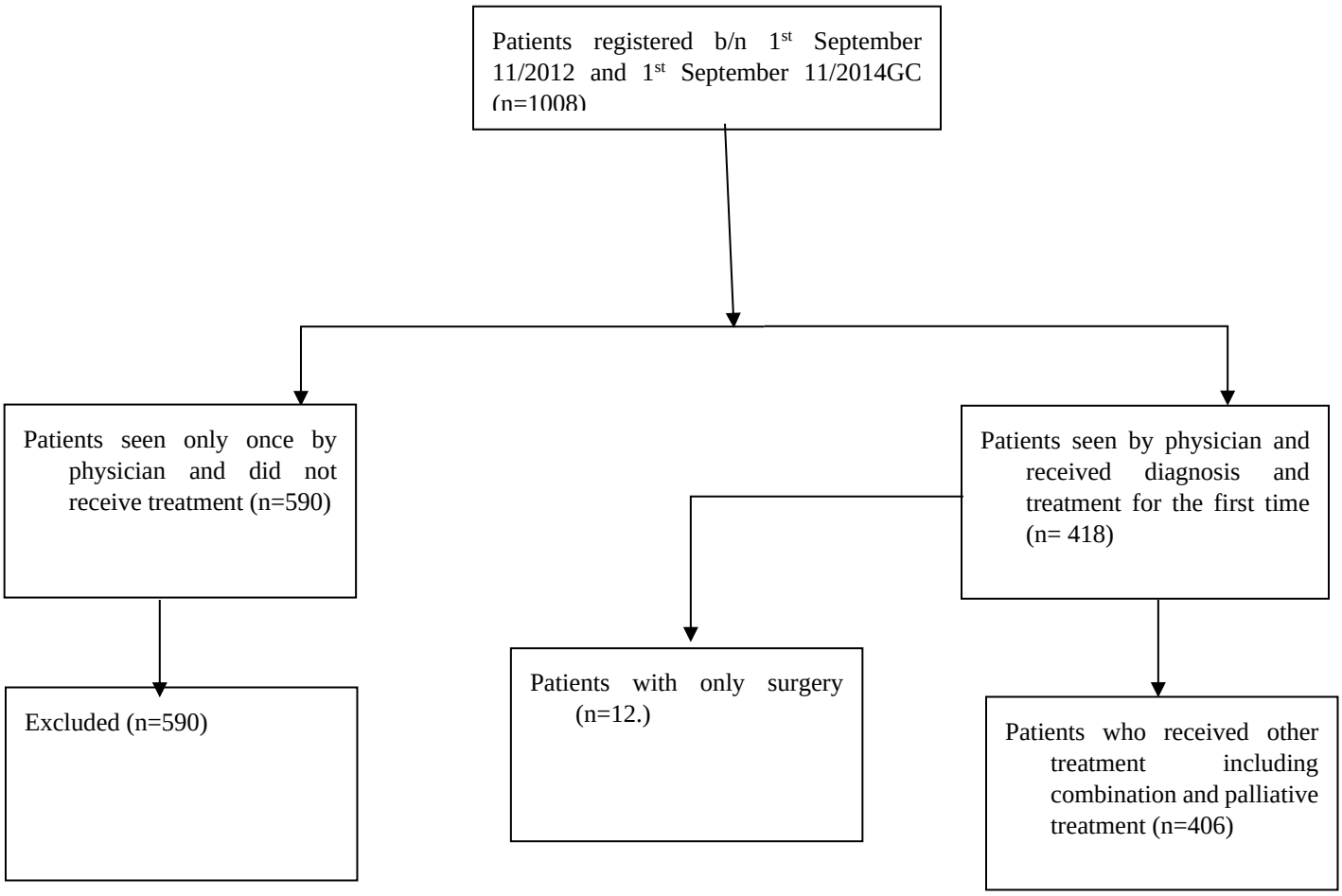

Figure-1: Participant flow Diagram

[Patients diagnosed with Cervical Cancer and included in this study are a subgroup of all patients who presented at the oncology department of Tikur Anbessa University Hospital, Addis Ababa].

5.2 Socio-demographic characteristics

The mean (SD) age of participant was 49.2 (11.9) yrs. with over half, two hundred twenty-seven (n=227; 56.3%) participants were in the age range 40-59 years. Three hundred and sixty-one (89.6%) were married,258 (64.0%) were Orthodox Christians, 117 (29.0%) had no formal education, and 112 (27.8%) were educated to the level of secondary school. In terms of their ethnicity, 143 (35.5%) were Oromo, 135 (33.5%) were Amhara. Most [n= 262 (65.0%)] were housewives (see Table 1).

Table:1: Distribution of socio-demographic characteristics of respondents who participated in the survey, women diagnosed with Cervical cancer at TASH, 2020, A.A., Ethiopia

Characteristics		Number	Percent
Age	25-39	88	21.8
	40-59	227	56.3
	>=60	88	21.8
Marital Status	Married	361	89.6
	Single	6	1.5
	divorced/separated	36	8.9
Ethnicity	Oromo	143	35.5
	Amhara	135	33.5
	Tigre	35	8.7
	Gurage	23	5.7
	SNNP	44	10.9
	Others*	23	5.7
Religion	orthodox	258	64.0
	Catholic	13	3.2
	Muslim	71	17.6
	protestant	61	15.1
Occupation	private business	53	13.2
	employed	88	21.8
	house wife	262	65.0
Educational	no formal education	117	29.0
status	Primary school	104	25.8
	secondary	112	27.8
	College and above	70	17.3

NB: SNNP, Southern nations and Nationalities People; TASH; Tikur Anbessa Specialized Hospital
* = Gambela, Benishangul.

5.3. Reproductive/gynecologic History

Concerning the sexual history of the study subjects, 361 (89.6%) had history of single partner; 48 (11.9%) had used contraceptive; (33 (8.4%) had used injectable contraceptives and 15 (3.7%) had used oral contraceptive pills. HIV status of nearly two-thirds (60.0%) was not recorded. In terms of histological differentiation of tumor cells, cells were well differentiated in 400 (99.3%) (Table 2).

Table:2: Reproductive history of respondents, TASH, 2020, A.A., Ethiopia.

Characteristics		Number	Percent
Sexual history	had history of multiple partner/mp/	42	10.4
	no history of mp but have history of single p	361	89.6
Contraceptive use	yes	48	11.9
	no	355	88.1
Contraceptive methods used	oral pills	15	3.7
	inject able	33	8.4
HIV status	+ve	44	10.9
	-ve	117	29.0
	unknown	242	60.0
Histological differentiation of tumors cell	well differentiated	400	99.3
	unknown	3	.7

5.3.1. FIGO staging system

Based on FIGO staging system, over half of the participants (58.3%, n=291) presented at diagnosis stage III. Over a quarter were in stage IIB (27.8%, n=112) (Figure 2).

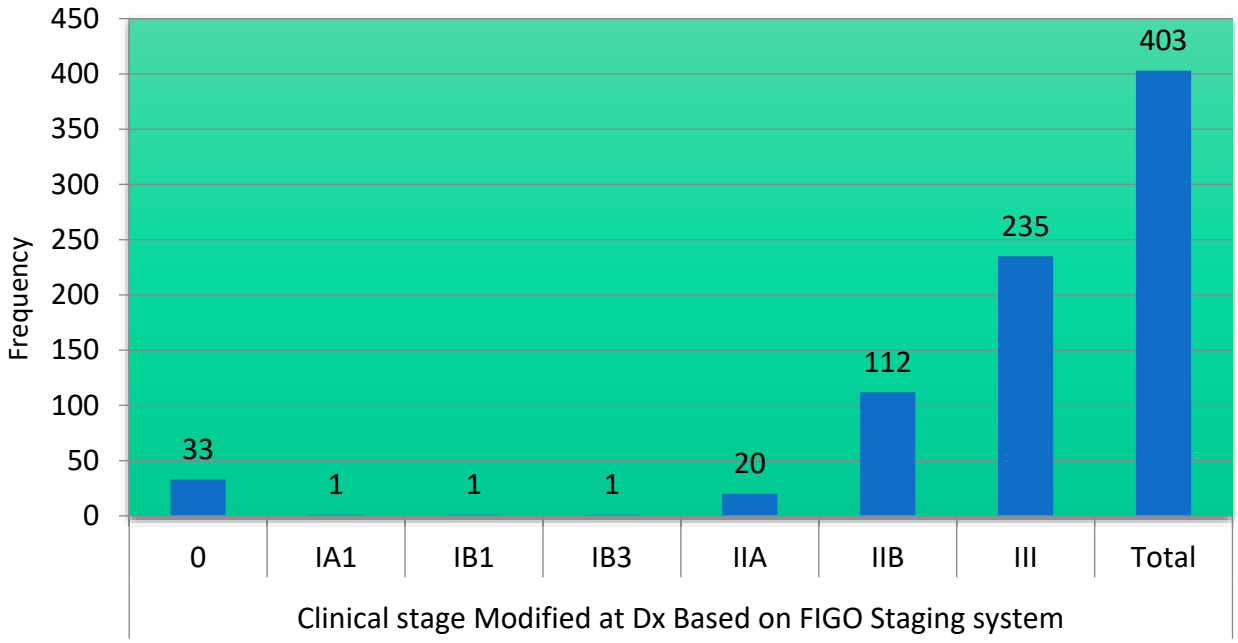

Figure-2: Clinical stage modified at diagnosis based on FIGO staging system among women diagnosed with Cervical cancer at TASH, 2020, A.A., Ethiopia.

NB-*TASH=Tikur Anbessa Specialized Hospital

-*Stage 0=Carcinoma in situ.

5.4. Treatment, complications, out Come and survival status (Fig-3 and Table-3).

Mode of treatment taken by 255 (63.3%) respondents was radiotherapy; followed by combination of radiotherapy plus chemo-therapy (n=78,19.4% (Fig. 3).

From the respondents treated by chemo therapy, 41 (10.2%) took Cisplastine+5-FU followed by Cisplatin 35 (8.7%). The cycle of chemo therapy taken was 6 (11.2%). Majority of respondents (n=342,84.9%) did not develop recurrence. Among the study participants, 40 (9.9%) were alive and 367 (91.1%) were lost to follow up, making difficult to know whether they are alive or not (table 3).

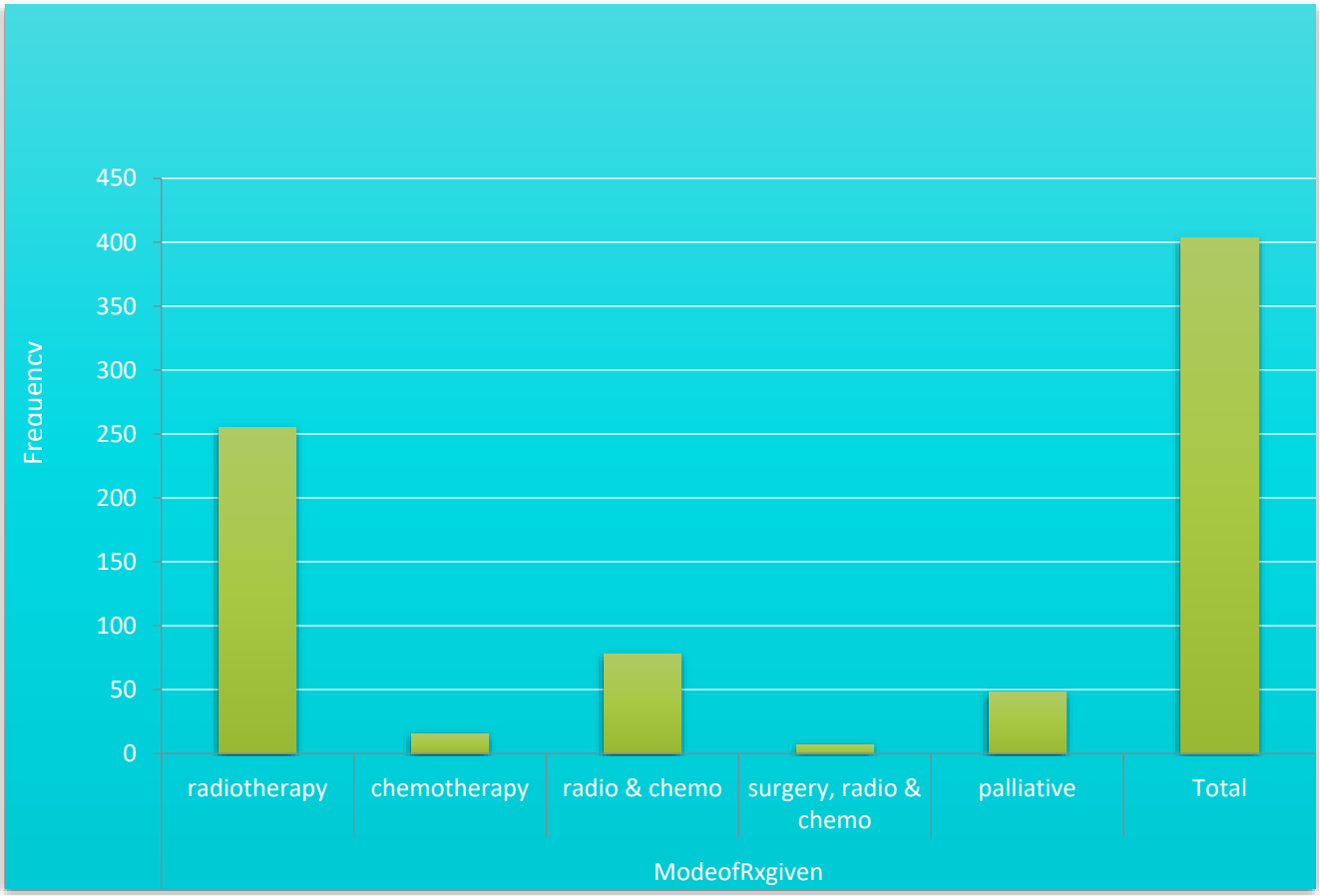

Figure-3: Mode of treatment given among women diagnosed with CC at TASH, 2020, A.A., Ethiopia.

Table:3: Chemo-therapy treatment, recurrence and survival status of respondents, TASH, 2020, A.A., Ethiopia.

Characteristics		Number	Percent
Type of chemotherapy Rx	5-fu	1	.2
	Cisplastine+5-FU	41	10.2
	Cisplatin	35	8.7
	Carboplastine+Paciltaxol	1	.2
	Carbotaxel	1	.2
	Cisplastine+Pasiltaxel	4	1.0
	TCA	8	2.0
Cycle of chemotherapy Rx	2-cycle	2	.5
	3-cycle	17	4.2
	4-cycle	10	2.5
	5-cycle	3	.7
	6-cycle	45	11.2
Recurrence	Yes	61	15.1
	No	342	84.9
Five-year survival status of the patient	Alive	36	8.9
	lost to follow up	367	91.1

5.5. Clinical factors associated with cervical cancer

Table 4: On Bivariate logistic regression model; marital status, occupation, educational status, Clinical stage Modified at Dx Based on FIGO Staging system, and mode of treatment were statistically significantly associated with five-year survival status of women diagnosed with cervical cancer. In the final model, the odds of five-year survival status of women diagnosed with cervical cancer are significantly associated with mode of treatment (Combination of surgery, chemotherapy and radiotherapy). Being married (COR, 0.40; 95% CI: 0.16, 0.99) was associated with reduced odds of survival as compared to divorced/separated women. Respondents that took radiotherapy, surgery, & chemotherapy AOR, 4.70,95% CI :(2.59,8.60): had increased odds of survival compared to those who took radiotherapy and chemotherapy, whereas, those who were Treated with only Radiotherapy: AOR, 0.37, 95% CI :(0.61,2.28) and those who treated with Chemotherapy alone AOR, 0.41, 95% CI:(0.34,4.77) have less chance of survival compared with those who took Radiotherapy and chemotherapy. The odds of being alive among house wives were 59% lower compared to those working in private business (AOR, 0.41; 95% CI: 0.18-0.97). Being educated to primary school were 95% (AOR, 0.05; 95% CI: 0.03-0.93) less likely to be alive than those educated to universities. However, variables like age, sexual Hx, contraceptive use, and Frequency of recurrence from day of Dx were not significantly (P>0.05) associated with Five-year survival.

Characteristics	Lost to Follow up	Alive	COR (95%-CI)	AOR (95%-CI)
Marital Status				
Married	329	32	**0.40(0.16,0.99) ***	.36(0.11,1.18)
Single	5	1	0.83(0.83,8.27)	3.90(0,27,5.60)
Divorced/Separated	29	7	1:00	1:00
Occupation				
Private Business	45	9	1:00	1:00
Employed	76	11	0.72(0.28,1.88)	.46(0.11,1.91)
House wife	242	20	**0.41(0.18,0.97) ***	.70(0.19,2.5.79)
Education				
No formal Education	108	9	0.43(0.16,1.012)	.18(0.32,1.01)
Primary School	99	5	**0.24(0.08,0.72) ***	.082(0.02,0.4.9)
Secondary School	98	14	0.69(0.29,1.60)	.36(0.10,1.32)
College and above	58	12	1:00	1:00
Sexual history				
Hx of Multiple Partners	40	2	1:00	1:00
No Multiple partners but have Single Partner	323	38	2.35(0.55,10.13)	.78(0.28,2.11)
Clinical Stage Based on FIGO Criteria				
0	24	9	1:00	1:00
IAI-IIA	20	3	0.4(0.09,1.68)	.48(0.81,2.92)
IIB	96	16	0.44(0.17,1.13)	.50(0.12,1.98)
III	223	12	**0.14(0.05,0.38) ***	.24(0.61,0.98)
Mode of Rx given				
Radiotherapy	244	11	0.14(0.63,0.31)	.37(0.61,2.28)
Chemotherapy	13	2	0.48(0.10,2.31)	0.42(0.34,4.77)
Radiotherapy &Chemotherapy	59	19	1:00	1:00
Surg, Radiotherapy &Chemotherapy	1	6	**8.63(2.11,16.40) ****	**4.7(2.60,18.60) ****
Palliative	46	2	0.13(0.03,0.61)	.48(0.46,4.52)

NB: *=significant, *p<0.05, **p<0.01 and ***p<0.001

Table:4: Clinical factors associated with cervical cancer of respondents, at TASH, 2020, A.A., Ethiopia.

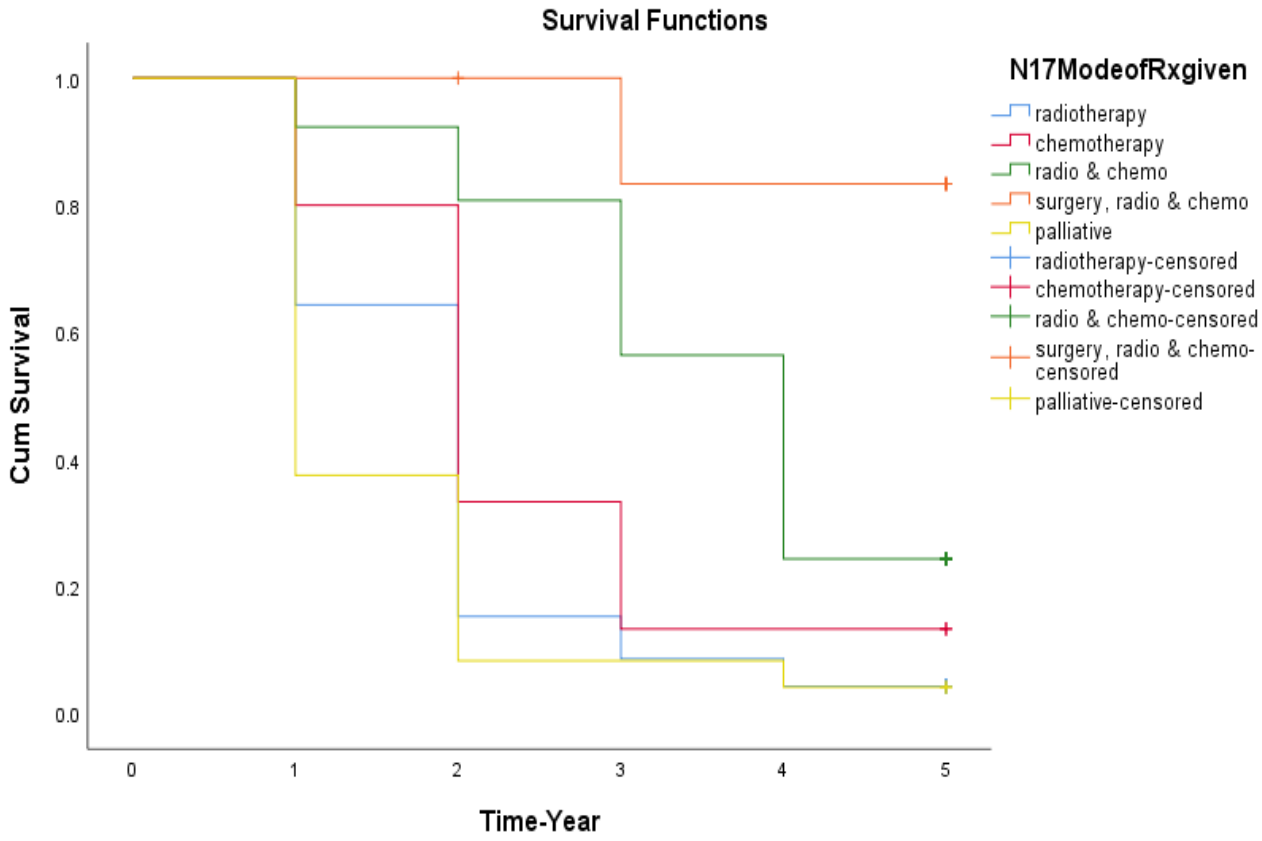

Figure-4: Kaplan-Meier for overall survival based on different treatment group.

The estimated Kaplan-Meier curve above shows overall survival during Five year follow up time was high for combination Therapy (Chemotherapy, Radiotherapy and surgery) than (Chemotherapy and Radiotherapy). whereas it is low for only Chemotherapy or palliative care respectively.

NB- *ModeofRxgiven =Mode of Treatment given.

Fig, bellow shows, a Kaplan-Meier Survival for clinical stage at presentation based on Modified Figo criteria at which those individuals who present at early stage (IAI, IBI, IBII) have more chance of survival than those who present at late stage (IIB and III)].

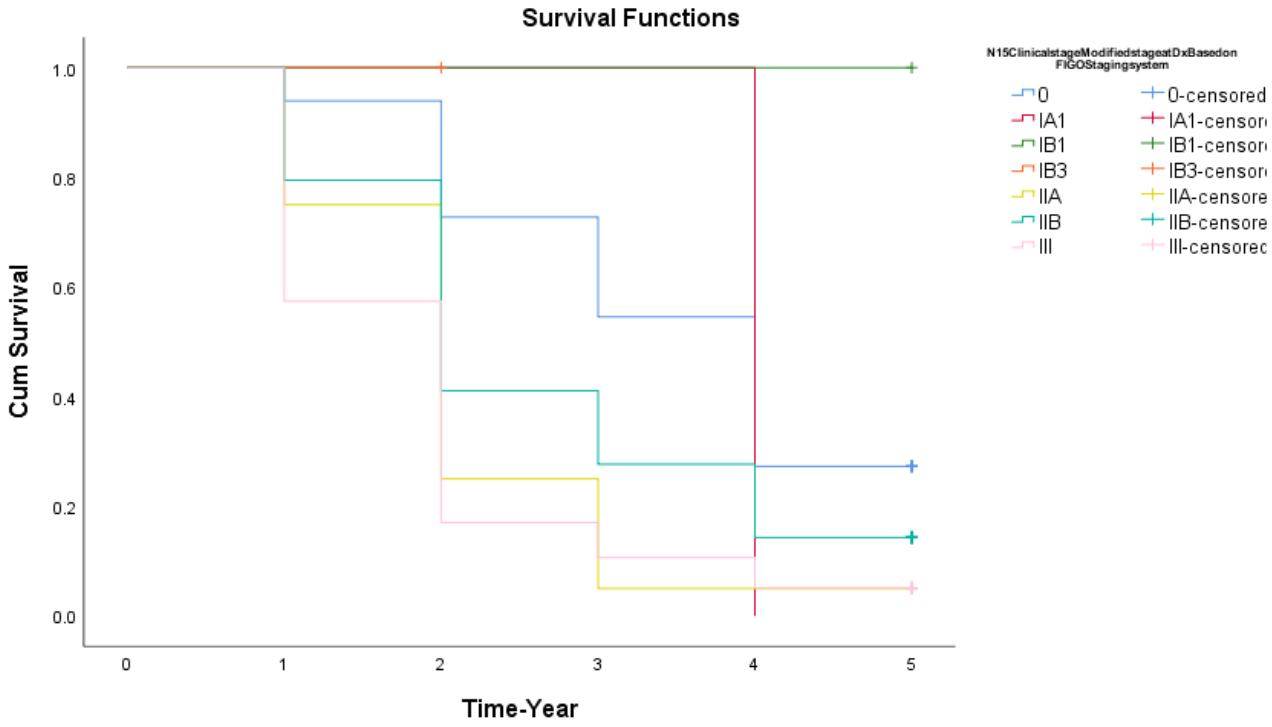

Figure-5: Kaplan-Meier for Survival of clinical stage at presentation based on Modified Figo Criteria.

Over Course of five-Year follow-up, this Fig of Cox-Regression model shows, out of 418 participants who took cancer treatment, there were 40 (9.9%) individuals were alive with 363 (89.4%) were censored, three cases with missing value. and no cases with negative time (those who lost follow up or died before they start treatment)

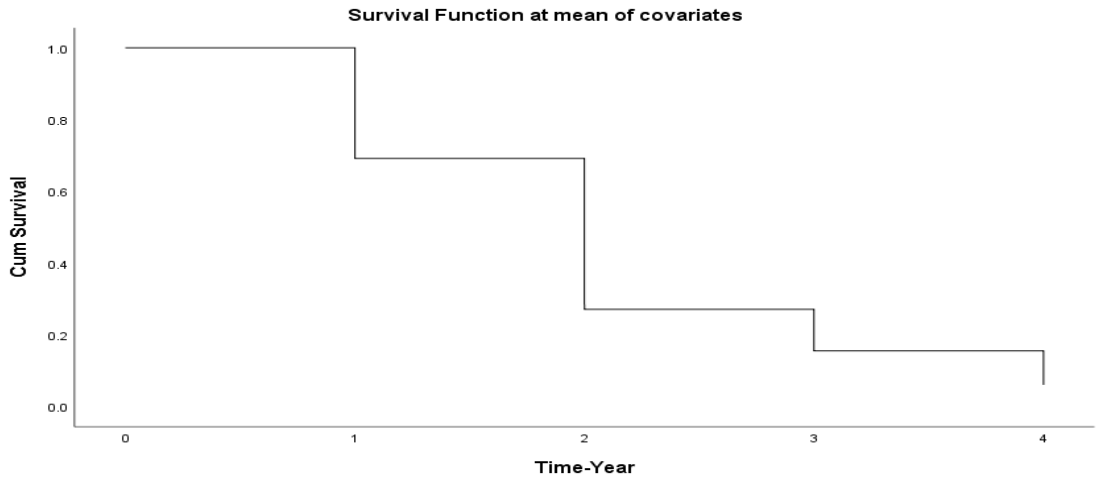

Figure 6: Fig of Survival Function of cervical cancer patients with Cox-Regression.

The above fig shows survival function of cox-Regression indicating individuals' chance of alive dropping downslope gradually as year of follow up increase.

.

Characteristics		Lost to Follow up	Alive	Crude-HR (95%-CI)	Adjusted-HR (95%-CI)
Age of Different group	25-39	83	5	0.94(0.70,1.30)	1.33(0.90,2.00)
	40-59	200	27	0.86(0.67,1.11)	1.04(0.74,1.47)
	>60	80	8	1:00	1:00
Marital Status	Married	329	32	1.06(0.73,1.60)	.98(0.67,1.47)
	Single	5	1	1.05(0.40, 2.70)	.67(0.25,1.80)
	Divorced /Separated	29	7	1:00	1:00
Occupation	Private	45	9	1:00	1:00
	Employed	76	11	1.20(0.80,1.70)	1.02(0.67, 1.56)
	House wife	242	20	**1.40(0.10, 1.90) ***	1.19(0.80,1.80)
Educational Status	No formal education	108	9	1.31(0.95,1.80)	1.35(0.78,2.30)
	Primary education	99	5	1.30(0.93,1.80)	1.35(0.80,2.30)
	Secondary education	98	14	1.03(0.70,1.40)	1.02(0.70,1.50)
	College & Above	58	12	1:00	1:00
Sexual History	Hx Of Multiple Partner	40	2	1:00	1:00
	No Multiple partners but has single partner.	323	38	1.30(0.95, 1.80)	.78(0.55,1.10)
Contraceptive use	Yes	39	9	1:00	1:00
	No	324	31	1.30(0.95,1.80)	1.05(0.74,0.50)
Clinical Stage Based on FIGO	0			1:00	1:00
Criteria	IAI-IIB	116	19	**1.60(1.03,2.50) ***	**1.68(1.00, 2.70) ***
	III	223	12	**2.44(1.60, 3.70) * * ***	**2.17(1.40,3.40) * * ***
Mode of Rx given	Radiotherapy	244	11	**2.50(1.90, 3.40) * * ***	**2.56(1.80,3.40) * * ***
	Chemotherapy	13	2	1.80(0.10, 3.30)	**2.02(1.10,3.80) ***
	Radiotherapy& Chemotherapy	59	19	1:00	1:00
	Radiotherapy, Chemotherapy &Surgery	1	6	0.20(0.02, 1.20)	.28(0.04, 2.20)
	Palliative therapy	46	2	**3.30(2.20, 5.00) * * ***	**2.78(1.80,40) * * ***
Recurrence and Duration	No	17		1:00	1:00
	6 months	33	3	2.30(0.80, 6.00)	.98(0.60,1.60)
	1 Year	4	1	2.40(0.80, 7.00)	1.16(0.80, 1.70)
	2 Year		2	2.60(0.90, 7.00)	.62(.22, 1.70)

NB: *=significant, *p<0.05, **p<0.01 and ***p<0.001

Table:5: Distribution of Cox-Regression Co-efficient for Hazard-Ratio of Clinical condition & Treatment significance for survival.

Distribution of Cox-Regression Co-efficient for Hazard-Ratio shows, participants who were diagnosed at earlier stage (stage-0) have high chance of survival when compared with those who presented at late stage(stage-III), [Adjusted HR=2.17; 95% CI= 1.40, 3.40].

On the other hand, Participants who were Treated with Radiotherapy [Adjusted HR=2.52,95%-CI,1.80,3.40] and Chemotherapy [Adjusted HR=2.02,95%-CI,1.10,3.80] alone were less likely for overall Five-year Survival when compared with individuals who treated with both Radiotherapy and Chemotherapy. And also, overall, five-year survival increases for those who treated with Radiotherapy, chemotherapy and surgery [Adjusted HR=0.28, 95%CI, 0.84, 2.20] when compared with those who were treated with Radiotherapy and Chemotherapy [Table-5 above].

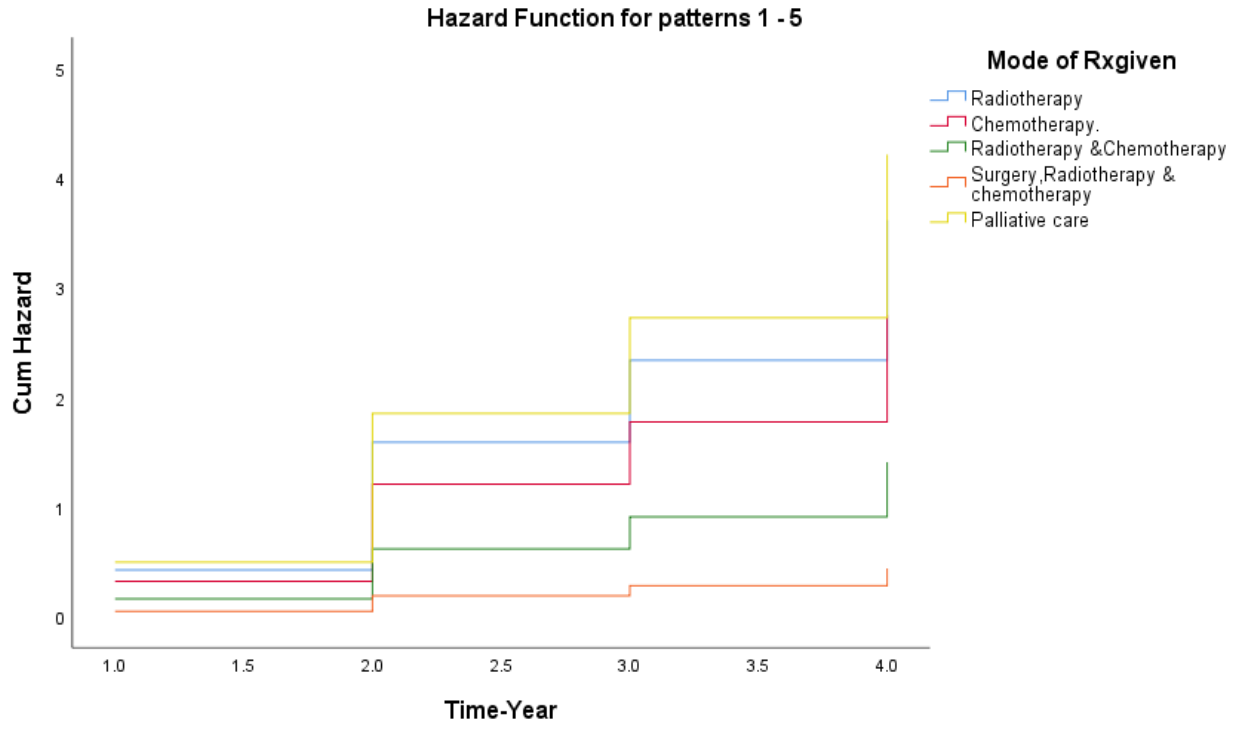

Figure7: [Shows Distribution of Cox-Regression Co-efficient for Hazard-Ratio indicating how risk of death is high between different group of treatment approach.]

6. DISCUSSION

This study is one of the very few studies done in Ethiopia as well as sub-Saharan African countries assessing survival status of patients diagnosed with cervical cancer and Treatment impact. However, from the outset, it is important to address the key limitations of the study so that the discussion put forward are understood in the context of those limitations. These limitations are also highlighted under the limitation section below.

The major limitation is related to the definition of outcome. The initial interest of the study was to evaluate survival status of patients with cervical cancer. However, we found out that, based on previous experience and our initial exploration, recontacting the patients was not possible. Therefore, instead of actual death, which was not possible to obtain, we used to drop out from follow up as a relevant proxy of survival. This consideration was supported by two facts. First, patients often arrived in late stage of illness, a stage generally associated with poor survival and was also shown to be was associated with high drop out in this study. Secondly, there is no hospice service with in the hospital or elsewhere. Terminal care is undertaken with in a home environment. Not returning from home for follow up may suggest the occurrence of death. Moreover, with in this study sample, patients who received palliative care were more likely to be lost to follow up in the first instance strengthening the assumption that patients who did not return for follow up may be because they have passed away or were critically sick and would not have survived for longer. However, even if the assumption were true, precise date of event was not available. Thus, the survival graphs were affected by shared outcome intervals.

The other limitation was that participants were recruited from a hospital that provide advanced care for patients who are likely to have advanced cancer. Therefore, the study is not representative of patients with cervical cancer or even those attending hospital for care.

Demographic characteristics of participants.

Most of the participants (n=227;(56.3%) were between age of 40-59 year with a mean age of 49.2 (SD+11.9) yrs. Virtually all (n=361;(89.6%) were married. The study also showed that many patients were from Amhara and Oromia region. This can be explained by large number of populations from both ethnic group and the fact that people from nearby regions have easy access to TASH for diagnosis and treatment.

Treatment Characteristics

From a total of 1008 patients recorded over two years, only four hundred Eighteen were started on various treatment modalities while the rest (590) were only seen for first time by physician and were not given treatment and were excluded from study. The reason for these patients not receiving treatment is not clear but over 50% of participants not receiving treatment and being excluded does introduce bias. Several possibilities related to personal and service delivery issues. for example, the limited access for service and long waiting list, and the poor access to Radiotherapy and/or Chemotherapy, may have discouraged patients and they may have simply dropped out of care before being offered the treatments.

Treatment of cervical cancer depends on stage at diagnosis, accessibility of Radiotherapy facility, and ability of patients to afford for chemotherapy. Over all, treatment could be, Surgical removal (radical hysterectomy with pelvic lymphadenectomy (Wertheim, adjuvant, radical and palliative radiotherapy and chemotherapy will be applied. Studies the outcome of neoadjuvant chemotherapy in combination radiotherapy or surgery showed that most cervical cancer malignancies are chemotherapy responsive; in fact,38% to 90% of clinical responses, including complete re-missions, have been reported. Clinical trials using neoadjuvant chemotherapy followed by surgery reported that the reduction of tumor bulk could make radical surgery possible in high percentage of cases previously considered inoperable (29)

Survival Characteristics

Compared with other studies from Africa, our finding of a survival of 9.9% (95%-CI) over five years is lower. The general report of five-year survival from African studies is 13%-22%. According to a study done in Uganda, a population-based cancer Registry shows a 5-year standard relative survival conducted between 1993 and 1997 was 19% [34]. Another study conducted in Gambia and Uganda indicated a 5-year over all relative survival rate of 22% and 13% respectively [35].Nevertheless, the rate was lower in our sample. This could be because of the proxy measure of survival that we used. The dropout rate from follow-up is likely to exaggerate death and thus underestimate survival. Other factors, such as access to early detection and various treatment, such as radiotherapy and chemotherapy may also be important. For example, Tikur Anbessa specialized Hospital is the only Hospital which has radiotherapy service in the country. Thus, limiting the number of patients who would be able to access the service in good time.

The survival figure in our study is much smaller compared with studies reported from developed countries. The expected five-year net survival of cervical cancer is in the range of 60% to 70% in most developed nations. The 5-year net survival for cervical cancer in the United States was reported to be 64.2% in 1995-1999 with comparable, albeit slightly lower, 62.8% in 2005-2009.Similar patterns were observed in other high-income countries [7].With accessible data between LMICs with obtainable survival data, five-year survival is 46% in India, 56% in Thailand, and 62% in Ecuador [27]**.** In India, the overall 5-, 10- and 15-year pragmatic survival rates from cervical cancer were 51.0%, 36.3% and 30.0% respectively; the corresponding relative survival rates were 54.8%, 43.0% and 41.1% respectively relative survival rates were 54.8%, 43.0% and 41.1% respectively [33]. Another study done in 5,619 patients receiving external beam radiotherapy followed by high-dose brachytherapy as reported in original publications between 1985 and 1997. Over all 5-year survival probabilities were higher than our findings: 85%, 68%, and 47% [36].This could be due to Lack of advanced Radiotherapy interventions like brachytherapy, Linear accelerator and a PET scan.

Stage at presentation is another important factor for relative survival of women with cervical cancer. Based on a study done in Kuwait net survival at early stage was 36.2% [8]. Overall, the 5-year survival status was 92%. The Kaplan Meier survival by FIGO stage were 94% for stage IBI, 85% for stage IBII and 89% for stage IIA [37]. A report from Gynecologic Oncology, the Japan Society of Obstetrics and Gynecology also shows Patient Annual Report for 2012, stage I accounted for 55.4%, stage II for 23.0%, stage III for 11.0% and stage IV for 10.6% of all patients with cervical cancer [37].But In our case, Bivariate logistic regression model and Kaplan-Meier survival; shows most patients (58.3%) presented at late Clinical stage Based on Modified FIGO Staging system (stage III and above),this can also another reason for low survival.

The main approaches for prevention and control of cervical cancer according to WHO (2018) involves, vaccination against human papillomavirus, screening and treatment for pre-cancerous lesions and diagnosis, treatment and palliative care of invasive cancer.[13].In our case, there was no sufficient data about HPV screening and vaccination.

In our study, the odds of five-year survival status of women diagnosed with cervical cancer and Kaplan-Meier survival curve were, significantly associated with mode of treatment. The odds of survival among respondents taking radiotherapy, surgery, and chemotherapy; as well as those

taking, radiotherapy and chemotherapy were about seven and half times, and 28 and half times more likely to be alive compared to those taking palliative mode of Rx. (AOR, 7.41, 95% CI: 1.42-38.58) and (AOR, 28.56, 95% CI: 19.42-42.91), respectively.

The Hazard of overall five-year Survival also shows, participants who were treated with Radiotherapy [Adjusted HR=2.515,95%-CI,1.8,3.4**]** and, Chemotherapy [Adjusted HR=2.016,95%-CI,1.1,3.8] alone were less likely for overall Five-year Survival when compared with those who treated with Radiotherapy and Chemotherapy. And individuals who treated with Radiotherapy, Chemotherapy and surgery [Adjusted HR=0.287, 95%CI, 0.84, 2.2] have high likely overall survival when compared with those who were treated with Radiotherapy and Chemotherapy.

Adherence to Treatment indicates one of contributing factors for optimum survival and better supportive care of patients with survival, but in our case, majority of study participants (363=89.4%) were not adhered to treatment due to several factors ,this supports study done in Ethiopia how adherence to treatment for cancer patient have optimum outcome [6]

7 LIMITATIONS OF THE STUDY

As indicated above, there was no clinical information on more than half of our study population (590) who were not involved in any treatment. While, this information was available from the chart, other characteristics were not available. we do not know why these participants did not receive treatment although we assumed that long waiting list, economic reasons, distance from treatment center would be important reason. Whatever the reason for this, the fact that over half of the patients who attended did not receive care is likely to introduce selection bias and also affect generalizability of the study. Second limitation of this study was lack of outcome data with regard to survival. This made it difficult to draw a clear conclusion as what happened to those who did not complete their follow up schedule. We equated drop out from follow-up with non- survival. This is very likely to underestimate survival and overestimate mortality. However, we used this as a pragmatic alternative when we knew it was not possible to make confirmatory phone calls. We concluded confirmatory phone calls was not possible either because of the lack of contact numbers or experience of other colleagues who tried to contact surviving family members. From this experience, we deduced that phone calls may not be received well by family members. The documentation in patients' chart was also poor and it was impossible to get sufficient information on values like End-date of follow up. Total dose of radiation was also not clearly documented, archiving of charts was manual and misplacing of file was common. Poisson regression was not used for analysis because during data collection we

couldn't manage exact end date on charts, and phone interview was not allowed from IRB. We also could not Retrieve one-month chart, this could be another drawback. Third, radiotherapy did not include the application of brachytherapy, Linear Accelerator and PET-scan. This is known to be a suboptimal standard of treatment. It could be explained by resource limitation. since we had no precise data, we used only indicative data to make conclusion. Fourth being only one treatment center giving radiotherapy service for around 114.5 mill population, generalization of cervical cancer survival for this number is Limited.

8 CONCLUSIONS

Under this study, from 1008 we included 418 cervical cancer patients who were diagnosed and started Treatment at Tikur Anbessa hospital oncology center between September 11/2012 and September 11/2014Gc.we found over all Five-year survival was low (9.9%) when compared with high income and middle-income countries. Stage at presentation is late, and the disease progresses during waiting times. Later stages showed lower survival probabilities compared with earlier stages. combination therapy (Radiotherapy, chemotherapy and surgery) has good survival probability than single therapy.

RECOMMENDATIONS

There is a need for creating awareness, primary prevention by vaccination, and early detection programs to increase early stages at presentation. Furthermore, expanding more treatment centers and implementation of advanced Technology like Linear accelerator, brachytherapy and PET-scan needs urgent decision. Lastly, Modern way of chart handling with EMR is also recommended to avoid misplacement and enhance a good patient record. This study helps as a bench mark with indicative evidence; but further, short- or long-term prospective study is also recommended for better scientific evidence.

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Appendix(I)

Data Collection format checklist.

A: Sociodemographic Data:

1. Age (years) _____
2. Marital status:
   1) Married ( )
   2) Single ( )
   3) Divorced / separated ( )
   4) Widowed ( )

3. Ethnicity (tribe)_____

4. Home residence _____ phone number _____

5.Card number_____

6. Religion:

   1) Orthodox ( )

   2) catholic ()

   3) Muslim ( )

   4) Protestant ( )

   5) Other specify _____

7. Occupation:

   1) Peasant

   2) Private Business

   3) Employed

   4) House wife

8.Educational status.

1) No formal Education ( )

2) Primary school (grade) ( )

3) Secondary education ( )

4) College ( )

5) University ( )

6) Other specify _____

B: Reproductive/Gynecologic History

9.Sexual History

1) had history of multiple partner

2) No history of multiple but have history of having single partner

3) Never had sexual partner

10.contraceptive use

1) Yes

2) No

11. If yes, Which method?

1) Condoms

2) Oral pills

3) Injectable

4) IUD

5) Norplant's

6) Tubal ligation

7) Others specify_____

12. HIV status:

1) Positive

2) Negative

3) Unknown

13.screening for HPV

1) yes

2) No

14. Histological differentiation of tumor cell?

1) Well differentiated

2) Poorly differentiated

3) None identified

4) unknown

15. Clinical stage – modified Stage at diagnosis (Based on FIGO staging system.)

1) 0

2) IA1

3) IA2

4) IB1

5) IB2

6) IB3

7) IIA

8) IIB

9) III

16. Date that treatment was initiated_____/_____/_____

17. Mode of treatment given and their duration of treatment:

1) Only surgery_____ Duration_____

2) Radiotherapy _____Duration_____

3) Chemotherapy_____ Duration_____

4) Radiotherapy & Chemotherapy _____ Duration_____

5) Surgery, Radiotherapy & chemotherapy_____ Duration_____

6) Palliative care _____Duration_____

18. If chemotherapy,

    1.) Type of chemotherapy_____

    2) Number of cycles of chemotherapy_____

19. If radiotherapy total dose of irradiation _____

20. If surgery was done the type of surgery:

    1) Radical Hysterectomy

    2) Cryosurgery

    3) Laser surgery

    4) Conization.

C: Treatment, Follow up, Complications, AND Outcome.

21. Radiation complications during radiotherapy:

    1) Hematological

    2) Cutaneous

    3) Neurological

    4) Others Specify_____

22. Recurrence

    1) Yes

    2) NO

23. If yes, site of Recurrence or metastasis

    1) Lung

    2) RES (liver, spleen)

    3) Bone

    4) Brain

    5) lymph node

24.If yes after how long from day of diagnosis does Recurrence occur?

1) 6month

2) 1year

3) 2year

4)3year

5)4year

6)5year

25.How did Metastasis or recurrence confirmed?

1) X-Ray Examination

2) U/s Examination

3) CT scan

4) clinical Diagnosis

5) unknown

26.Number of follow up during cores of Treatment.at first year.

1) Not at all

2) One

3) Two

5) Three

6) More than.

27.Number of follow up during cores of Treatment.at second year.

1) Not at all

2) One

3) Two

4) Three

5) More than Three.

28.Number of follow up during cores of Treatment.at third year.

1) Not at all

2) One

3) Two

4) Three

5) More than Three.

29.Number of follow up during cores of Treatment.at fourth year.

1) Not at all

2) One

3) Two

4) Three

5) More than Three.

30.Five-year survival status of the patient?

1) Alive

2) Dead

3) Recurrence

4) lost to follow up

31. If dead when?

1) <1year

2) <2year

3)<3year

4)<4year

32 If recurrence/metastasis, when did it occur?

1) <1year

2) <2year

3)<3year

4)<4year

33.If Death, what was the immediate cause of Death?

1) Due to Cervical cancer

2) Treatment complication

3) Other Medical cause.

34.History of smoking.

1) yes

2) No

35. If other medical cause, mention_____