

SAINT PAUL'S HOSPITAL MILLENIUM MEDICAL COLLEGE



SURVIVAL AND ITS DETERMINANTS AMONG PROSTATE CANCER PATIENTS IN TIKUR AMBESSA SPECIALIZED HOSPITAL ADDIS ABABA ETHIOPIA, RETROSPECTIVE COHORT STUDY

BY:

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MAJOR ADVISOR: MRS. SISAY TANIE (MSC, IN BIOSTATISTICS)

CO ADVISOR: MR. SAMSON ZEGEYE (MPH)

**RESEARCH PAPER SUBMITTED TO SPHMMC DEPARTMENT OF PUBLIC
HEALTH IN PARTIAL FULFILLMENT OF MPH IN FETP**

**MARCH 2018
ADDIS ABABA, ETHIOPIA**

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ST PAUL’S HOSPITAL MILLENNIUM MEDICAL COLLEGE DEPARTMENT OF PUBLIC
HEALTH GRADUATE STUDIES FINAL THESIS APPROVAL FORM

As member of the Board of Examiners of the final body of work with thesis open defense, we
certify that we have read and evaluated the body of work with thesis prepared by **Jemal Beksisa
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recommencement for the degree of Master of Public Health in Field Epidemiology.

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LIST OF ACCRONYMS

AACCR	Addis Ababa City Cancer Register
ADT	Androgen Deprivation Therapy
AHR	Adjusted Hazard Ratio
AJCC	American Joint Committee on Cancer
ASIRs	Aga Standardized Incidence Rate
ASR	Aga Standardized Rate
BMI	Body Mass Index
CHR	Cumulative Hazard Ratio
DALYs	Disability-Adjusted Life Year
DNA	Deoxyribonucleic Acid
DRE	Digital Rectal Examination
DT	Doubling Time
GBD	Global Burden of Disease
GLOBOCAN	Global Burden of Cancer Study
OR	Odd Ratio
PCSD	Prostate Cancer Specific Death
PSA	Prostate Specific Antigen
RR	Relative Risk
SDI	Socio Demographic Index
SPHMMC	Saint Paul's Hospital Millennium Medical College
SSA	Sub-Saharan Africa
TASH	Tikur Anbessa Specialized Hospital
TNM	Tumor Node Metastasis
YLDs	Years Lived with Disability
YLLs	Years of Life Lost

ABSTRACT

Background: Prostate cancer incidence rate is faster growing with higher mortality in developing countries than developed countries and it is the most common cancer disease among men in both developed and developing countries. It is the 2nd most common cancer among men in Ethiopia and is the 4th cause cancer death in men. Few studies are conducted regarding to prostate cancer burden in Ethiopia. There is scarcity of information on survival time and its determinants' among prostate cancer patients in the country. Hence, this study tried to estimate, survival and its determinants among prostate cancer patients, which in turn enables us to understand the survival of the patient.

Objective: is to assess survival and its determinants among prostate cancer patients diagnosed during 2012-2016 at Tikur Anbessa specialized hospital (TASH) Addis Ababa, Ethiopia.

Methods: prostate cancer patients diagnosed at oncology department of TASH were followed retrospectively by using retrospective cohort study design. All newly diagnosed cases during 2012-2016 were included in the study through obtaining their medical record numbers from cancer registry. Data extraction was performed by oncologic nurses from all retrieved patient charts by using checklist. The current event status was taken through phone call. Collected data were entered, cleaned and edited by Epi info version 7.1 and transferred to SPSS version 21 for analysis. Kaplan Meir survival analyses with log rank test were used to estimate probabilities of survival and to test for the presence of difference in survival among categories of covariates. Independent variables, which became significant during Bivariate Cox regression analysis at 20% level of significance was included in Cox proportional model for multivariable analysis. Independent variables whose p value were less than 0.05 during multivariable Cox regression analysis were considered as being the determinants of prostate cancer survival.

Result: The median survival time was 30.7 months with overall survival of 22% at 5-years and 57% at 2-years. The five year survival rates for stage I, II, III and IV were, 83%, 61%, 16% and 0% respectively. The group of prostate cancer patients with distant metastasize and non metastasized have a five year survival of 0% and 44% respectively. Prostate cancer patients who were treated with ADT have 27% survival at five years while those who did not treated with ADT have had 7% survival rates. The stage of cancer, metastasize status and ADT treatment categories of covariates have significant difference in survival with 0.0001, 0.001 and 0.03 p values. Then stage of cancer (AHR 6.9, CI: 1.81-26.7) and androgen deprivation therapy (AHR 0.48, CI: 0.23-0.99) become significant on the final Cox proportional hazard model.

Conclusions: The overall five year survival was 22% and covariates like stages of prostate cancer, distant metastatic status and ADT treatment modalities showed significant survival difference. Stages and ADT treatment modality were determinants of prostate cancer survival. In general our study shows poor survival or prognosis by late stage and treatments, indicating the key role of early detection and timely treatment for improving survival or reducing mortality from prostate cancer.

Key words: prostate cancer, survival, Ethiopia

1. INTRODUCTION

1.1 Background

Prostate is male sexual accessory gland located in front of the rectum surrounding the neck of the bladder and urethra. Its function is primarily to secrete prostatic secretions one component of seminal fluid that nourishes the sperm and its smooth muscles helps to expel semen during ejaculation. The prostatic secretion makes up 25% of seminal fluid and its major constituent is prostate specific antigen (PSA). PSA is glycoprotein produced by the prostate acinar cells and present in high concentrations in seminal fluid (0.5 - 2.0 mg/mL) but it has a much lower concentration in the blood (0 - 4 ng/mL). PSA is a widely used tumor marker since prostate cancer tissue releases approximately 10 times more PSA into serum than normal or benign prostatic hyperplasia tissue. Cancer is general term for diseases in which abnormal cells divide without control and can invade nearby tissues. Due to mutations in DNA, normal cells transformed into cancer cells that divide uncontrollably and disruption in maintenance of balance between proliferation and cell death happens. A cancer can be carcinoma that arises from epithelial tissues of the skin or lining cavity of organs or sarcoma that arise from mesenchymal tissue like bone, muscles and other connective tissues(1).

Prostatic adenocarcinoma is the most frequent form of prostate cancer and accounts for 90 to 95% of prostate cancer. It occurs in the epithelial cells lining the glandular organ of the prostate. In the early stages of prostate cancer, there are often no symptoms. Prostate cancer symptoms include frequent and difficulty in urination, blood in the urine, painful urination and difficulty of erection or painful ejaculation. If the cancer is advanced, it can spread to other organs, causing bone pain in the pelvis or ribs. Prostate tumors are only felt in a small percentage of cases during a digital rectal examination (DRE). Diagnosis of prostate cancer must be confirmed by a needle biopsy. According to American Joint Committee on Cancer(AJCC) Prostate cancer has 4 stages which uses TNM stage to evaluate extent of primary tumor (T), affected regional lymph node (N) and if it spread or metastases (M). In Stage I is only small non palpable part of prostate is affected, stage II if large part of prostate is affected, stage III if tumor involves beyond prostate and stage IV if it spread to far lymph nodes or organs. The Gleason Grading System is also grading prostate cancer where cancers are scored according to their appearance under a microscope. Gleason scores range from 2 to 10 where 10 has the poorest prognosis(2,3).

1.2 Statement of the problem

Cancer already constitutes a major public health burden globally. In 2015 alone, there were 17.5 million new cases and 8.7 million deaths from cancer worldwide and it was the second leading cause of death behind cardiovascular disease. Disability-Adjusted Life Year (DALYs) due to cancer were increased from 196.3 million in 2013 to 208.3 millions in 2015 globally. In 2013, Cancer caused 14.9 million incident cancer cases and 8.2 million cancer deaths. About 56% of incident cases, 62% of deaths, and 70% of DALYs occurred in developing countries. Between 1990 and 2013, absolute DALYs due to all cancers for both sexes increased by 29% globally, by 10% in developed countries, and by 40% in developing countries(4,5).

Worldwide, prostate cancer is rated the first most common cancer and fifth leading cause of cancer deaths among men, with over 1.6 million cases and 366,000 deaths estimated in 2015. Prostate cancer caused 6.3 million DALYs globally in 2015. It was the cancer with the highest incidence for men in 103 countries and the leading cause of cancer deaths for men in 29 countries. Between 1990 and 2013, Prostate cancer cases were increased by 217% globally, by 169% in developed countries, and by 361% in developing countries. Prostate cancer Age Standardized Incidence Rates (ASIR) are highest in Australia and Northern America (ASR 111.6 and 97.2 per 100,000, respectively), and in Western and Northern Europe (ASR 94.9 and 85 per 100,000), largely because the widespread practice of PSA testing and subsequent biopsy in those regions. Incidence rates are also relatively high in certain less developed regions such as the Caribbean (79.8), Southern Africa (61.7) and South America (60.1), but remain low in Asian populations, with estimated rates of (4.5-10.5). Prostate cancer incidence rates are still lower in developing countries than in developed countries, but because of a faster increase in rates in developing countries, the gap decreased between 1990 and 2013 from a 4-fold to a 3-fold difference(4–6).

The number of deaths from prostate cancer is larger in less developed regions (165,000) than in high developed regions (142,000). Mortality rates are generally high in populations of African descent (Caribbean, 29 per 100,000 and Sub-Saharan Africa, ASRs 19-24 per 100,000), intermediate in the Americas and Oceania, and very low in Asia (2.9 per 100,000). Prostate cancer incidence and mortality rates in Africa were reported to be 23.2 and 17.0 per 100,000, respectively in 2012(7). Reports show that higher incidence and mortality rates were observed in

eastern African region at 23.3 and 18.7 per 100,000, compared to the average rates in northern African regions 10.6 and 7 per 100,000 populations respectively. With continued urbanization, population growth and increasing life expectancies in Africa, its burden is still expected to increase. Similarly there is prevailing challenges like poor screening and diagnostics practices, treatment options, research and trainings, availability of population based cancer registration makes the burden prostate cancer in Africa to be underestimated or make difficult to know the exact burden of the disease(7–9). Reports from population based national cancer registry exploitation from neighbor countries like Sudan, Kenya and Uganda show that prostate cancer is the most incident cancer in men with 26.1, 9.4 and 37.1 per 100,000 population respectively(10).

In Ethiopia Prostate cancer is the 3rd cancer in incident and 8th cause of cancer death in both sexes next to breast and cervical cancer in 2015 (4). According to Addis Ababa city population based cancer registry (AACCR) report in 2011 to 2014, prostate cancer is the third incident (11%) cancer in males next to colorectal cancer and leukemia indicating. AACCR is the only population based cancer registry in the country established in 2011 at Tikur Anbessa Specialized Hospital (TASH) and registering cases from the city only. Despite this seemingly disproportionate burden and the prevailing challenges, it is still quite difficult to describe the burden of Prostate cancer in the country(10,11). Few studies are conducted regarding to prostate cancer burden in Ethiopia. There is no data on the survival time and factors associated with it among prostate cancer patients in the country. Hence, this study was tried to estimate 5-year survival and its determinants among prostate cancer patients, which in turn enables to understand the quality and effectiveness of care or treatments introduced and to improve the survival.

1.3 Significance of the study

Studying survival of different cancers has important practical value for patients, providers, and researchers. The result from this study may help prostate cancer patients wishing to know how their prognosis is changing over time, and what is their life expectancy based on the disease status. Inline to this 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. Also, health care 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. Identifying contributing factors of survival time among prostate cancer patients is very mandatory so as to reach on some recommendations to improve

survival especially policy makers may use this information. 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 prostate cancer and serves as a base line data for further studies.

2. LITERATURE REVIEW

2.1 Burden of Prostate cancer

In 2015 according to GBD report of cancer estimates, prostate cancer was the fourth most common cancer and globally 1.6 million men developed the disease while 366,000 died of it. ASIRs for men were the lowest in low middle SDI countries (17.6 per 100,000) and the highest in high SDI countries (123.6 per 100,000). Prostate cancer caused 4.8 million DALYs globally in 2013, with 57% occurring in developed countries, and 43% occurring in developing countries. The ASIRs per 100 000 increased by 69% globally (32.42 to 54.68), by 135% in developing countries (13.29 to 31.25), and by 63% in developed countries (61.51 to 100.29) between 1990 to 2013. Prostate cancer incidence rates are still lower in developing countries than in developed countries, but because of a faster increase in rates in developing countries, the gap decreased between 1990 and 2013 from a 4-fold to a 3-fold difference. Between 1990 and 2013, Prostate cancer cases were increased by 217% globally, by 169% in developed countries, and by 361% in developing countries. During the same timeframe, age-standardized DALY rates have decreased by 3% at the global level and by 9% in developed countries but have increased by 28% in developing countries(4–6).

Prostate cancer is the second most common cause of cancer death among men in the United States, with 33 720 fatalities in 2011. Prostate cancer incidence and mortality rates differ by race/ethnicity. In the United States, incidence and mortality rates are the highest among African-American men. African-American men have mortality rates 2.4 times greater than those of Caucasian men. Both incidence and mortality rates are lower among Asian/Pacific-Islanders, Native Americans and Hispanic men than among non-Hispanic whites. Part of the variation in incidence rates across populations can be explained by differences in screening practices, particularly screening with prostate-specific antigen, which often diagnoses a significant proportion of otherwise latent prostate cancer(7,12).

Prostate cancer incidence and mortality rates in Africa were reported to be 23.2 and 17.0 per 100,000, respectively in 2012. Study from 16 African countries stated that the overall pooled incidence in Africa was 21.95 per 100,000 populations, with the highest incidence was 39.0 per 100,000 population estimated in people aged 70 years and above. Prostate cancer incidence and mortality rates were lower in northern Africa at 10.6 and 7.0 per 100,000, compared to the

average rates in Sub-Saharan Africa (SSA) with 34.3 and 22.1 per 100,000, respectively. Some of these variations have been attributed to the relatively higher poverty levels, dietary differences, genetic differences and the presence of infectious diseases in SSA(6,8,9). Similarly, reports from population based national cancer registry exploitation from Sudan, Kenya and Uganda show that prostate cancer is the most incident cancer in men with 26.1, 9.4 and 37.1 cases per 100,000 populations respectively(10). In Ethiopia the review of Addis Ababa cancer registry in 2014 shows that prostate cancer is the third most common cancer in males. According to GBD cancer estimate reports of 2015, in Ethiopia, Prostate cancer is the 3rd cancer in incident in both sexes next to breast and cervical cancer and it is the most common cancer in males. It is the 8th cause of cancer death in both sexes. Ethiopia there is no population based cancer registry except Addis Ababa cancer registry that was started in 2011 which is avail only in capital city and poor screening, research, diagnosis, treatment and data handling were the challenges to know the exact burden of the disease in the country. Compared to Europe and the Americas, Africa seemed to have lower prostate cancer incidence in general. Prostate cancer incidence in African nations could be underestimated due to the lack of population-based cancer surveillance and poor cancer screening practices. However the incident rate of prostate cancer case and Prostate cancer death is highly increasing in Africa due to population aging , an adoption of cancer-associated lifestyle(smoking, physical inactivity, “westernized” diets), few options of cancer treatment and diagnostic facilities(4,9–11).

2.2 Survival and Associated factors of Prostate cancer

Established risk factors for total prostate cancer risk are few and include older age, race, family history and gene changes. Prostate cancer rarely is diagnosed among men before the age of 40 years, and mortality is relatively rare before the age of 50 years. Men with a family history of prostate cancer are at increased risk of prostate cancer diagnosis and mortality. The risk of death from prostate cancer is approximately twofold higher for men with a father or a brother who died of prostate cancer, compared to men with prostate cancer who do not have a positive family history(12,13). Also study showed that prostate cancer incidence and mortality were associated with balding men, presence of diabetes, aspirin usage, PSA levels ≥ 10 , obesity or high BMI, smoking habit, chemical exposures and inflammation of prostate(14,15). They increase risk of developing advanced stage prostate cancer, higher rates of recurrence and cancer-specific

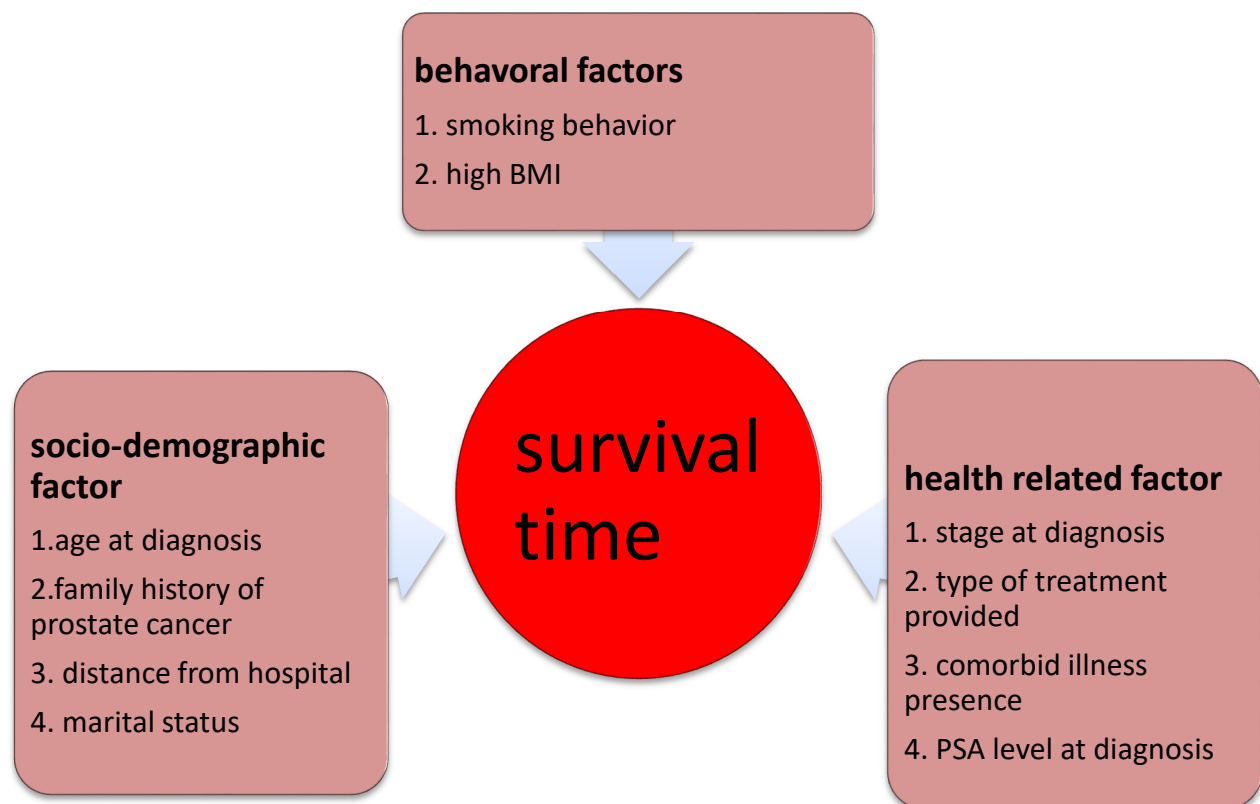
mortality after diagnosis. However foods like vitamin E, selenium, coffee, zinc and drugs (aspirin, 5 alpha reductase inhibitors) reduces the risk of getting prostate cancer(16).

The cohort study conducted in Brazil state that, the five-year survival rates were 87.8%. The five-year survival for patients with pretreatment PSA <40 ng/mL was 91.2% and for patients with ≥ 40 ng/mL was 70.1%. The five-year survival rate for Gleason score 5 or 6 was 87.3%. The five-year survival of patients with tumor stage B1 and B2 was 98.1% and 81.7%, respectively. Patients treated with radiation therapy had lower 5-year survival rates than those treated with radical prostatectomy of 79.8% and 96.5% respectively. The poorest prognosis was seen among those aged 70 years or more who showed a risk of dying from cancer almost four times higher than that of patients aged 50 to 59 years. The effect of stage B2 became significant, indicating a risk almost three times higher of dying from prostate cancer for each year of follow-up compared to that of patients with tumors classified as stage B1. Patients with moderately differentiated tumors had a 58% lower risk of dying from prostate cancer than patients with poorly differentiated tumors. Patients with pretreatment PSA levels ≥ 40 ng/mL were almost four times more likely of dying than patients with lower PSA levels(17).

According to study conducted in Harvard University to identify predictors of time to prostate cancer specific death (PCSD) after radiation therapy (RT) on 381PCa patients. Pretreatment identified risk (low, intermediate and high risk) based on their Gleason score and PSA level and post treatment factors for 94 patients who developed PSA failure included time to PSA failure, post treatment PSA doubling time (DT) and timing of salvage hormonal therapy. In Pretreatment Prognostic Factors, the 10-year estimates of PCS survival were (100% v 94% v 55%; $P .005$) for low, intermediate and high risk groups respectively. The relative risk (RR) of death caused by prostate cancer was 6 (95% CI, 2.5 to 10) for high-risk compared with low- or intermediate-risk patients. For Post treatment Prognostic Factors, men with a short PSA DT (ie, ≤ 12 months), estimates of PCSD and all-cause death after PSA failure were nearly identical. Specifically, the 5-year estimate of PCSD after PSA failure was 52%. The RR of PCSD and all cause death was 5.1 (95% CI, 2 to 8.9; $p=0.03$) and 2.2 (95% CI, 1.2 to 4; $p=0.05$) for patients, respectively, with a PSA DT ≤ 12 compared with more than 12 months. Patients who began salvage hormonal therapy when the bone scan was positive versus negative had an RR of 12 (95% CI, 6.2 to 18; $p=0.0006$) and 9.1 (95% CI, 4 to 14.3; $p=0.0001$) for PCSD and all-cause death, respectively(18).

The study reviewing prostate cancer patients managed in the University of Maiduguri teaching hospital (UMTH), Nigeria shows that age ranged from 42- 90 years with peak age group of 60 – 69 years. The 2 year and 5 year survival were 71% and 27% respectively. Carcinoma of the prostate is common and patients present late with advanced disease and complications(19). According to a five year retrospective cohort study conducted in Sudan, the 5-years survival rate was 91.6% for patients who diagnosed in grade 1 of the disease, 76.5% in grade 2, 24%in grade 3 and 7.5% in grade 4(20). The study found that there were many factors affected the survival rate in Sudanese population such as treatment type and diagnosis date. The observed, corrected and relative 5-years survival rate of cancer in Sudan are 40.5%, 52% and 47% respectively. A nine year prostate cancer survival analysis in Ghana shows that 13.6% of the patients diagnosed at the age of 68 died with the prostate cancer when the cancer has developed into stage three. Only the stage of cancer at which a patient was diagnosed contributed to the survival or hazard of a patient, p-value < 0.05(21).

Conceptual Frame work of the study



3. OBJECTIVES

3.1 General Objectives

To assess survival and its determinants among prostate cancer patients diagnosed during 2012-2016 at Tikur Anbessa Specialized hospital, Addis Ababa, Ethiopia

3.1 Specific Objectives

- To estimate the time to death of prostate cancer patients in TASH ,AA,Ethiopia,2012-2016
- To compare the survival among categories of covariates of prostate cancer patients in TASH, AA, Ethiopia, 2012-2016
- To identify determinants of survival in prostate cancer patients in TASH, AA, Ethiopia ,2012-2016

4. METHODS AND MATERIALS

4.1 Study Area and Period

The study was conducted in Tikur Anbessa Specialized Hospital (TASH), which is found in Addis Ababa city, the capital of Ethiopia. TASH is a teaching, central tertiary generalized referral hospital with approximately 800 in patient's beds. TASH Cancer treatment Center (radiotherapy center) is the only cancer referral center of the country. This radiotherapy center is housed in a separate, newer building on hospital grounds and consists of three floors. With the support of Federal Minister of Health, None governmental organizations and international partners, TASH had developed Addis Ababa Population Based Cancer Registry(AAPBCR) at radiotherapy center in 2011. AAPBCR is the first population based cancer registry of the country and cancer cases that were stayed in Addis Ababa city at least for six months were considered as dwellers of the city to be registered by this program. The main sources for population based cancer registry (PBCR) in Addis Ababa city are Hospitals (from different departments and radiotherapy center), higher diagnostic Clinics and Diagnostic Laboratory with pathology services.

The starting point for retrospective follow-up was the time from first confirmed diagnosis of prostate cancer and the endpoint was date of death, date of lost to follow up, date of last contact or the end date of follow-up period (December 30/2016). The study period for this study was from to October 20-December 30/2017.

4.2 Study Design

A retrospective cohort study design was employed to assess survival of prostate cancer in TASH.

4.3 Study Populations

4.3.1 Source populations

All prostate cancer patients in TASH who were newly diagnosed from January 2012 to December 2016

4.3.2 Study populations

All prostate cancer patients in TASH who were newly diagnosed from January 2012 to December 2016 and who fulfill the eligibility criteria

4.4 Inclusion and Exclusion Criteria

All prostate cancer patients who were newly diagnosed in TASH during the required time (2012-2016) and whose charts are available were included. Patients who registered during the required period but their diagnosis were prior to that were excluded from the study. Incomplete charts or charts having neither of histopathology or PSA level report and cancer stage report were also excluded.

4.5 Sample Size Determination and Sampling Procedure

All incident cases of prostate cancer patients diagnosed between January 2012 to December 2016 and who fulfill the eligibility criteria were included in the study.

The chart number (medical record number) of all prostate cancer patients diagnosed during 2012- 2016 at oncology department of TASH was obtained from Addis Ababa Population Based Cancer Registry and local cancer registry. Then the charts of all prostate cancer patients reported were retrieved using this medical record number. From 171 prostate cancer cases registered during the period, the charts of 149 cases were retrieved. From this 12 incomplete charts (no report of histopathology, PSA level and cancer stage) were excluded from the study. Finally the records from 137 retrieved charts were extracted.

4.6 Variables

4.6.1 Dependent/Outcome Variables

- Time to death of prostate cancer patients

4.6.2 Independent variables /Covariates

- Age of patients at diagnosis
- Stage of cancer at diagnosis
- Gleason score at diagnose
- PSA level at diagnose
- Histological types and grade of prostate cancer

- Treatment type
- Place of residence
- Family history of prostate cancer,
- smoking
- Hypertension, Diabetes and HIV infection co morbidities

4.7 Operational Definition

Time to death – is the survival of prostate cancer patients from the first confirmed date of diagnosis to death of patients

Event – is death of prostate cancer patients who are under the study due to prostate cancer

Censoring – is prostate cancer patients who are under the study and who have incomplete information on time to death due to the cancer. Prostate cancer patients who do not develop death, who were lost to follow up before developing event, who were died due to other cause unrelated to prostate cancer and patients who have no phone number and whose current status is unknown, to know their event status were considered as censored individual.

4.8 Data Collection Tools and Procedures

4.8.1 Data Collection Tools

Record review checklist was prepared in English language based on available information on patient charts and through referring some important variables from literatures on related topics.

4.8.2 Data Collection Procedure

Prostate cancer patients those diagnosed and enrolled from 2012-2016 periods at TASH were followed retrospectively through retrieving their charts from cancer registries of the hospital. Two oncologic nurses who are working at the cancer treatment center were extracted the data. Before data collection started the charts of all prostate cancer patients were identified and retrieved by their medical registration number from central card room and radiotherapy center of the hospital. Then data collectors reviewed the records (both baseline and follow up) of the patient from their charts. As there were no mortality data in the patient charts, there was phone interviewing to all patients who have phone numbers to ascertain their current event status, date of death if died, presence of other co morbidity like hypertension or diabetes and other data mainly not found from the chart. Patients with unknown current event status and who

do not have phone number (lost from follow-up) or who didn't develop the outcome of interest (death) at the end of follow-up period were considered as censored cases.

4.9 Data Quality Assurance

Discussions were made with oncologic nurses (data collectors) regarding to data collection checklists, objective of the study and how to maintain the quality of data for data for one day before data collection was started. The review checklist filled were collected daily and checked for completeness by principal investigator.

4.10 Data Processing and Analysis

Data were coded and then entered, cleaned, edited using Epi info version 7.1 and transferred to SPSS version 21 for analysis. Basic descriptive analysis like mean, median and frequency were done. Kaplan Meier method of estimating survival time was performed to estimate the survival. Kaplan Meier curve together with Log rank test was used to test for the presence of difference in survival among categories of covariates (groups of prostate cancer patients'). For the Bivariate analysis, Cox regression was performed and the independent variables, which became significant at 20% level of significance, were included in final Cox proportional model for multivariable analysis. The multiple Cox regression was therefore fitted for eight variables after checking for the presence of multicollinearity and proportional hazard assumption fulfillment. Accordingly Co linearity were seen between the variable bone metastasize and distant metastasize showed, therefore bone metastasize were excluded from final model. All variables included in the final model have p value of greater than 0.05 during partial residual schoenfeld test done for checking proportionality of hazard assumption. The result of the model was expressed as adjusted hazard ratios (AHRs) with 95 %CI to determine the net effect each explanatory variable on time to death after diagnosis of prostate cancer.

4.11 Ethical Considerations

An ethical clearance for the proposed study was obtained from the research and ethical committee of Public Health Department of SPHMMC. Permission from medical director and focal person of cancer treatment center of Tikur Anbessa specialized Hospital was obtained. Verbal consent was also obtained from patients before starting phone call interview which were done by data collectors. Confidentiality of the information maintained throughout the study by

anonymously excluding patient names as identification from data extraction form and it is used for the purpose of the proposed study only. In additions, health professionals (oncologic nurses) from the cancer treatment center extracted the data from patient to keep confidentiality.

4.12 Dissemination of Result

The result of the study will be presented to SPHMMC Department of Public Health. It will be communicated to TASH Oncology department and to other stake holders. In addition it will be presented on different conference and seminars. Finally, an attempt will be made to publish the paper in reputable journal

5. RESULT

From 171 patients diagnosed in Tikur Anbessa Specialized Hospital between 2012 and 2016, complete data were obtained for 137 cases. The minimum and maximum age of cases was 43 and 91 years with median age of 68 years (IQR 15). About 50 (36.5%) of cases were found in 61-70 years age category. Nearly two-third (59.1%) of cases are residents of Addis Ababa city followed by Oromia region (24.1%) (table 1).

Table 1 Socio-demographic characteristics of prostate cancer patients in Tikur Anbessa Specialized Hospital, Addis Ababa, 2012 – 2016

variables	categories of variables	Outcome status at last contact					
		censored		dead		Total	
		N	%	N	%	N	%
Age category	<= 50 yrs	5	83.3	1	17	6	4.4
	51-60 yrs	18	58.1	13	42	31	22.6
	61-70 yrs	31	62	19	38	50	36.5
	71-80 yrs	24	55.8	19	44	43	31.4
	>= 81 yrs	4	57.1	3	43	7	5.1
marital status	married	59	60.8%	38	39.2%	97	70.3
	widower	8	50%	8	50%	16	11.7
	divorced	5	72.4%	2	27.6%	7	5.1
	unknown	10	58.8%	7	41.2%	17	12.4
region	Addis Ababa	45	55.6%	36	44.4%	81	59.1
	Oromia	20	60.6%	13	39.4%	33	24.1
	SNNPR	9	90.0%	1	10.0%	10	7.3
	Amhara	6	75.0%	2	25.0%	8	5.8
	Somalia	0	0.0%	2	100.0%	2	1.5
	Gambella	0	0.0%	1	100.0%	1	0.7
	Harar	1	100.0%	0	0.0%	1	0.7
	Tigray	1	100.0%	0	0.0%	1	0.7

Clinical and Pathological Characteristics

The tumor marker test (pre treatment serum PSA level) were performed in 116 (85%) patients, of which about 105 (90%) have a PSA level above 4 ng/ml. Histopathology test were performed for 92 (67.2%) of the cases and imaging test for 121 (88%). From the cases having histopathology test report, about 89 (96.7%) have adenocarcinoma cancer cell type with 50 (54.3%) having poorly or undifferentiated prostate cancer cell. Majority of cases 86 (62.8%) were diagnosed with stage four followed by stage three 19(13.95%) (Table2).

The number of cases diagnosed with distant metastasize were 81 (59.1%). Of which bone metastasize were reported in 70 (86%) of cases followed by lymph nodes 13 (16%), liver 6(7.4%) and 2 (2.4%) lung involvement. The prevalence of chronic co morbidities like hypertension, diabetes mellitus and HIV infection in our study population were 13.9%, 10.9% and 2.9% respectively. About 19% of the cases have history of smoking. Most of cases 112 (81.8%) were treated with Androgen Deprivation Therapy (ADT), 103 (75.2%) with radiotherapy, 69 (50.4%) with surgery and 37 (27%) with combination of ADT + radiotherapy + surgery (table 2). Only 7 (5%) of cases were treated with chemotherapy.

Table 2 Clinical and pathological characteristics of prostate cancer patients in Tikur Anbessa Specialized Hospital, Addis Ababa, 2012 to 2016

Variables	Outcome status at last contact					
	censored		dead		Total	
	N	%	N	%	N	%
Serum PSA level						
0-4 ng/ml	7	58.3	5	41.7	12	8.8
4.1-10 ng/ml	7	77.8	2	22.2	9	6.6
10.1-20 ng/ml	4	80.0	1	20.0	5	3.6
above 20.1 ng/ml	51	56.0	40	44.0	91	66.4
unknown	13	65.0	7	35.0	20	14.6
Stage at diagnosis						
stage IV	43	50.0	43	50.0	86	62.8
stage III	11	57.9	8	42.1	19	13.9
stage II	11	84.6	2	15.4	13	9.5
stage I	9	90.0	1	10.0	10	7.3
unknown	8	88.9	1	11.1	9	6.6
Histologic grade						
well differentiated (Gs 2-4)	14	77.8	4	22.2	18	13.1
Moderately differentiated (Gs 5-6)	15	68.2	7	31.8	22	16.1
Poorly/undifferentiated (Gs 7-10)	26	52.0	24	48.0	50	36.5
unknown	27	57.4	20	42.6	47	34.3
Distant metastasis						
yes	42	51.9	39	48.1	81	59.1
No	40	71.4	16	28.6	56	40.9
Bone metastasize						
Yes	37	52.9	33	47.1	70	51.1
No	45	67.2	22	32.8	67	48.9
Lymph node involvement						
Yes	5	38.5	8	61.5	13	9.4
no	77	62.1	47	37.9	124	90.6
Hypertension						

yes	12	63.2	7	36.8	19	13.9
no	56	54.4	47	45.6	103	75.2
unknown	14	93.3	1	6.7	15	10.9
Diabetes						
yes	12	80.0	3	20.0	15	10.9
no	59	53.6	51	46.4	110	80.3
unknown	11	91.7	1	8.3	12	8.8
Smoking status						
yes	16	61.5	10	38.5	26	19.0
no	51	53.1	45	46.9	96	70.1
unknown	15	100.	0	0.0	15	10.9
Chemotherapy						
yes	5	71.4	2	28.6	7	5.1
no	77	59.2	53	40.8	130	94.9
Surgery						
yes	42	60.9	27	39.1	69	50.4
no	40	58.8	28	41.2	68	49.6
ADT						
yes	74	66.1	38	33.9	112	81.8
no	8	32.0	17	68.0	25	18.2
Radiotherapy						
yes	56	54.4	47	45.6	103	75.2
no	26	76.5	8	23.5	34	24.8
Combination of surgery, Radiotherapy and ADT						
yes	26	70.3	11	29.7	37	27.0
no	56	56.0	44	44.0	100	73.0

Gs=Gleason score

Survival from Time of Diagnose to Death

From a total of 137 patients **55** of them were found to be dead during the 5 year follow up period. The minimum and maximum time that cases were followed is 1 and 59 months respectively. The mean and median survival time was 30.7 and 28 months respectively. The overall survival rate was 22% at 5-years and 57% at 2-years. One can also see on the Kaplan Meir survival curve for time to death of prostate cancer patients from the graph below (figure1).

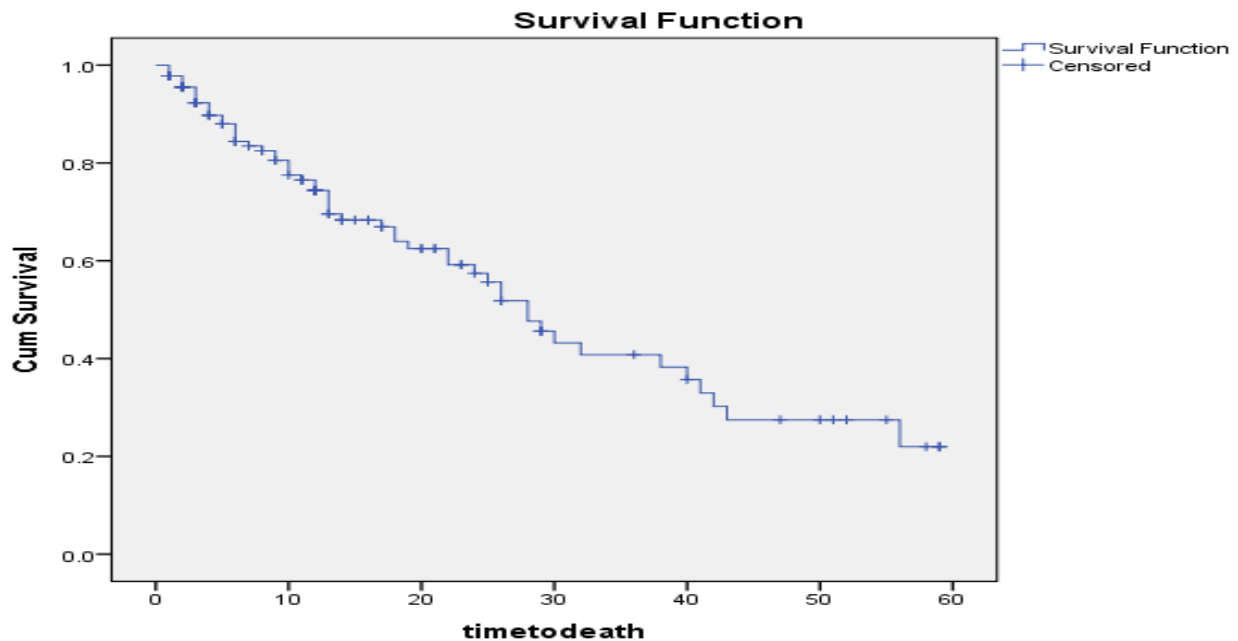


Figure 1 Kaplan Meir survival curve for time to death among prostate cancer patients in Tikur Anbessa Specialized Hospital, Addis Ababa, 2012 to 2016.

Survival experience among different groups of prostate cancer cases

The tests for the presence of statistically significant difference in survival time between different categories of covariates were done by using log rank test. There is a difference in survival experience between categories of stage of prostate cancer, distant metastasize status of cancer, bone metastasize, Androgen Deprivation Therapy (ADT), serum PSA level and radiotherapy treatment modalities. All other categories of covariate did not showed statistically significant difference in survival experience between them. The difference in survival among categories of covariates of prostate cancer patients with the pair wise log rank test is shown in table 3 below.

Table 3 Log-rank test for difference in survival among categories of covariates for prostate cancer patients in Black Lion Hospital, Addis Ababa, 2012 to 2016

covariates	Difference in survival experience among groups	Chi-square	P-value(pair wise comparison)
Stage of cancer	stage I versus stage II	2.5	0.113
	stage I versus stage III	7.18	0.008
	stage I versus stage IV	14.1	0.0001
	stage I&II versus stage III&IV	18.832	0.001
Serum PSA level	< 20ng/ml versus $\geq$ 20ng/ml	1.5	0.20
	<20ng/ml versus unknown	4.7	0.03
Distant Metastasis status	Metastasis versus non metastasized	12.95	0.001
Bone metastasis	bone metastasized versus non metastasized	10	0.002
Androgen Deprivation Therapy	Treated with ADT versus not treated with ADT	4.6	0.031
Radiotherapy	Treated with combination of radiotherapy , surgery and ADT versus radiotherapy only	4.4	0.036

The five year survival rates for stage I, II, III and IV of prostate cancer were, 83%, 61%, 16% and 0% respectively. This stage of prostate cancer showed survival difference with overall (log-rank test $p=0.0001$) (figure 2).

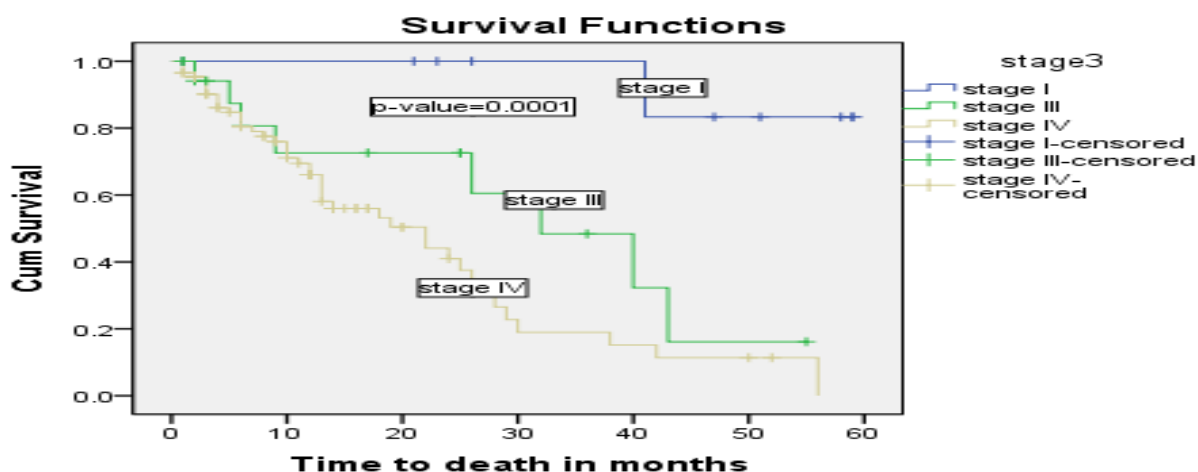


Figure 2 Kaplan Meir survival curve for time to death among categories of stages of prostate cancer patients in Tikur Anbessa Specialized Hospital, Addis Ababa, 2012-2016.

Similarly patients having serum PSA level less than 20 ng/ml during diagnose in comparisons to those having above 20 ng/ml and unknown have better five year survival with (log-rank test $p=0.048$) (figure 3). The five year survival is 25%, 19% and 0 in patients with <20mg/ml, >20mg/ml and unknown PSA levels respectively.

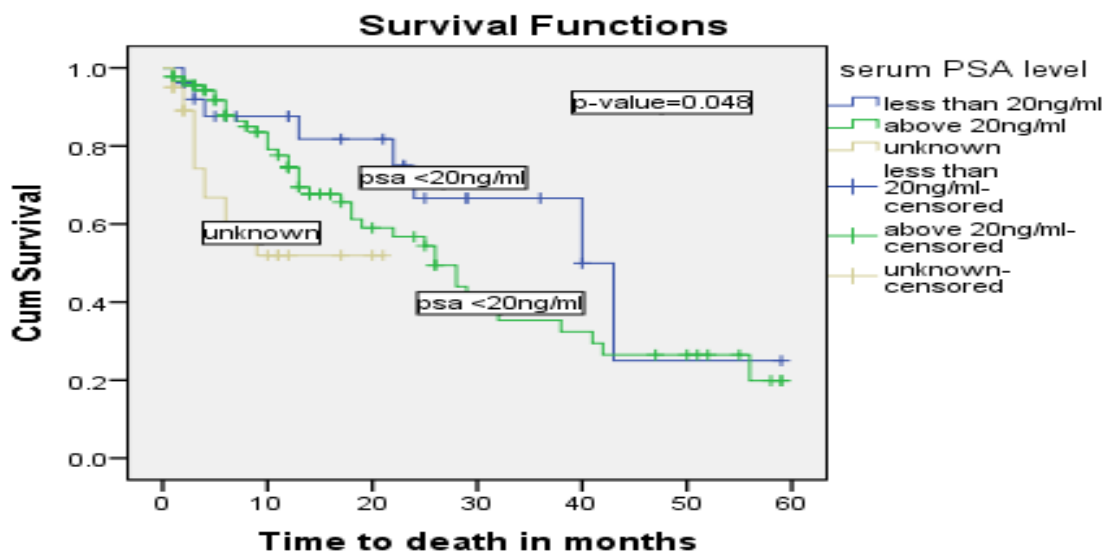


Figure 3 Kaplan Meir survival curve for time to death by level of serum PSA among prostate cancer patients in Tikur Anbessa Specialized Hospital, Addis Ababa, 2012-2016

The group of prostate cancer patients having distant metastasize at the time of diagnose were experienced 40% and 0% survival for two and five years respectively, while for those with no distant metastasize the two and five year survival were 67% and 44% respectively with (log rank test, $p=0.001$) (figure 4).

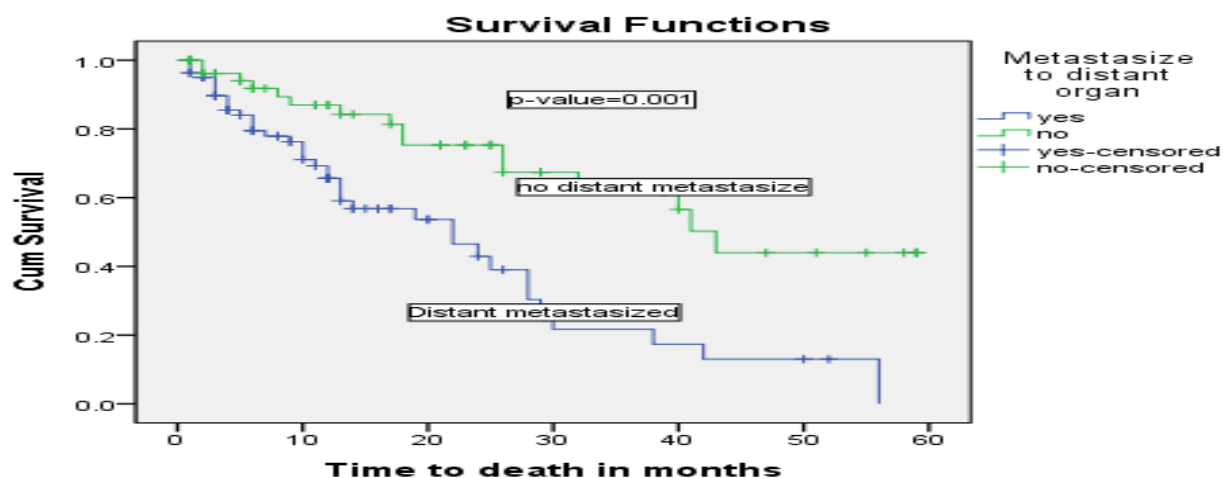


Figure 4 Kaplan Meir survival curve for time to death among categories of prostate cancer patients with distant metastatic status in Tikur Anbessa Specialized Hospital, Addis Ababa, 2012 to 2016.

Similarly group prostate cancer patients who were treated with ADT (either of orchieodectomy or other ADT drugs) were experienced 58% and 27% survival at two and five years respectively, and those who did not treated with ADT have had 49% and 7% survival rates at two and five year (figure 5).

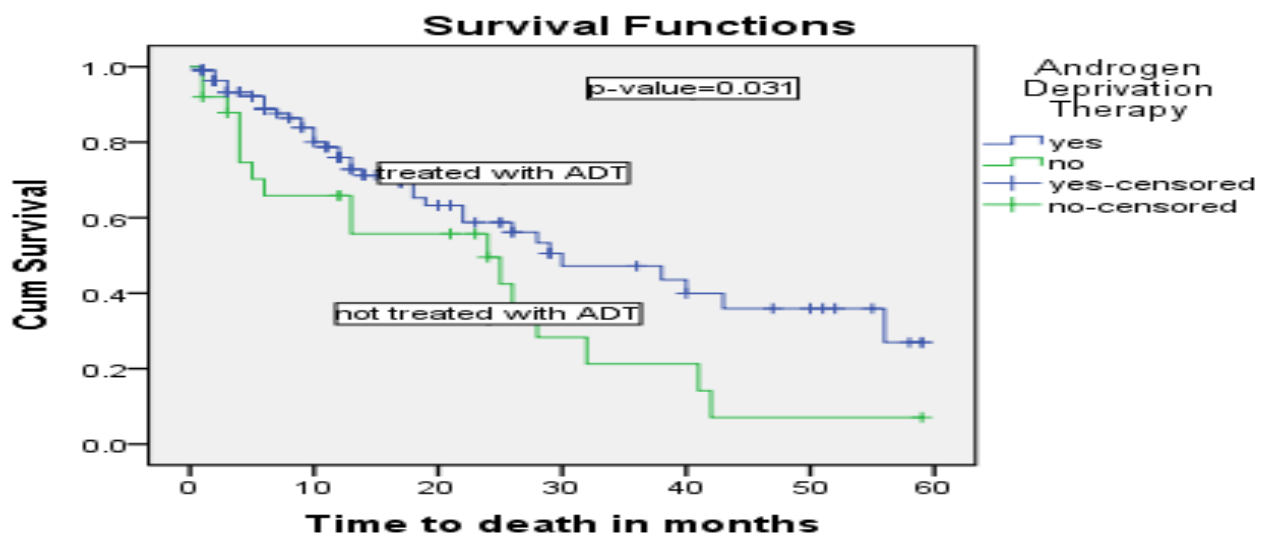


Figure 5 Kaplan Meir survival curve for time to death among categories of prostate cancer patients with ADT treatment modality in Tikur Anbessa Specialized Hospital, Addis Ababa, 2012-2016.

In general longer survival is seen in patients with early diagnosis, PSA level less than 20ng/ml, without distant metastasize, no bone involvement and treated with ADT with log-rank test pooled over strata p-values of 0.0001, 0.048, 0.001, 0.002 and 0.031 respectively.

Determinants of survival time among prostate cancer cases

During Bivariate co regression analysis eight variables were significant at p-value of 0.2. These variables are: poorly differentiated Histologic grade (CHR=2.2, P=0.13), serum PSA >20ng/ml (CHR=1.6, P=0.06), cancer stage III & IV (CHR=7.8, P=0.001), distant metastasize cancer (CHR=2.8, P=0.001), bone metastasize (CHR=2.4, P=0.002), lymph node metastasize cancer (CHR=1.8, P=0.11), ADT treatment (CHR=0.5, P=0.035) and combination therapy of ADT, surgery & radiotherapy (CHR=0.6, P=0.13) (table 4).

Table 4 Bivariate Cox regression analysis describing possible determinants of prostate cancer survival at Tikur Anbessa Specialized Hospital, Addis Ababa, 2012-2016

VARIABLES	outcome status		CHR (95% CI)	p-value
	Censored n (%)	Dead n (%)		
Age category				
<= 50 yrs	5(83.3)	1(17)	1	0.75
51-60 yrs	18(58.1)	13(42)	3.1(0.40, 23.8)	0.27
61-70 yrs	31(62)	19(38)	3.5(0.47, 27.10)	0.21
71-80 yrs	24(55.8)	19(44)	3.2(0.43, 24.6)	0.25
>= 81 yrs	4(57.1)	3(43)	4.6(0.47, 45.7)	0.18
Histologic grade				
well differentiated (Gs 2-4)	14(77.8)	4(22.2)	1	0.18
Moderately differentiated (Gs 5-6)	15(68.2)	7(31.8)	1.0(0.30, 3.6)	0.92
Poorly/undifferentiated (Gs 7-10)	26(52)	24(48)	2.2(0.77, 6.4)	0.13
unknown	27(57.4)	20(42.6)	2.1(0.71, 6.1)	0.17
serum PSA level				
less than 20ng/ml	18(69.2)	8(30.8)	1	0.06
above 20ng/ml	51(56)	40(44)	1.6(0.74, 3.4)	0.22
unknown	13(65)	7(35)	3.5(1.5, 9.9)	0.019
Staging				
stage III & IV	54(51.4)	51(48.6)	7.8(2.3, 25.6)	0.001
stage I & II	20(87)	3(13)	1	
Distant metastasis				
yes	42(51.9)	39(48.1)	2.8(1.5, 5.1)	0.001
No	40(71.4)	16(28.6)	1	
Bone metastasize				
Yes	37(52.9)	33(47.1)	2.4(1.3, 4.3)	0.002
No	45(67.2)	22(32.8)	1	
Lymph node involvement				
Yes	5(38.5)	8(61.5)	1.8(0.85, 3.8)	0.118
no	77(62.1)	47(37.9)	1	
Hypertension				
yes	12(63.2)	7(36.8)	2.9(0.3, 24.3)	0.36
no	56(54.4)	47(45.6)	3.8(0.52, 27.7)	0.31
unknown	14(93.3)	1(6.7)	1	0.18
Diabetes				
yes	12(80)	3(20)	1.5(0.15, 14.6)	0.42
no	59(53.6)	51(46.4)	2.6(0.35, 19.18)	0.72
unknown	11(91.7)	1(8.3)	1	0.34
Chemotherapy				
yes	5(71.4)	2(28.6)	0.17(0.09, 1.5)	0.37

no	77(59.2)	53(40.8)	1	
Surgery				
yes	42(60.9)	27(39.1)	0.79(0.46, 1.3)	0.40
no	40(58.8)	28(41.2)	1	
ADT				
yes	74(66.1)	38(33.9)	0.5(0.3, 0.95)	0.035
no	8(32)	17(68)	1	
Radiotherapy				
yes	56(54.4)	47(45.6)	1.6(0.7, 3.4)	0.22
no	26(76.5)	8(23.5)	1	
Combination of surgery, Radiotherapy and ADT				
yes	26(70.3)	11(29.7)	0.6(0.3, 1.16)	0.13
no	56(56)	44(44)	1	

During multivariable Cox regression analysis seven variables were those significant during Bivariate and age variable were included and only two variables became significant at level of p-value 0.05. These are stage of prostate cancer (AHR 6.9, CI: 1.81-26.7) and androgen deprivation therapy (AHR 0.48, CI: 0.22-0.99) become significant on the final Cox proportional hazard model (table 5).

Table 5 variables included in the multiple Cox proportional hazards model among prostate cancer patients at Tikur Anbessa Specialized Hospital, Addis Ababa, 2012-2016

Variables	Outcome status		CHR(95% CI)	AHR(95% CI)	p-value
	Censored n (%)	Dead n (%)			
age category					
<= 50 yrs	5(83.3)	1(17)	1	1	0.31
51-60 yrs	18(58.1)	13(42)	3.1(0.40, 23.8)	5.7(0.58, 56.6)	0.13
61-70 yrs	31(62)	19(38)	3.5(0.47, 27.10)	9.55(1.0, 88.67)	0.04
71-80 yrs	24(55.8)	19(44)	3.2(0.43, 24.6)	7.07(0.7, 66.2)	0.08
>= 81 yrs	4(57.1)	3(43)	4.6(0.47, 45.7)	6.4(0.5, 75.4)	0.14
histological grade					
well differentiated(Gs 2-4)	14(77.8)	4(22.2)	1	1	0.64
Moderately differentiated(Gs 5-6)	15(68.2)	7(31.8)	1.0(0.30, 3.6)	0.68(0.17, 2.7)	0.59
Poorly/undifferentiated(Gs 7-10)	26(52)	24(48)	2.2(0.77, 6.4)	1.24(0.39, 3.9)	0.7
unknown	27(57.4)	20(42.6)	2.1(0.71, 6.1)	0.97(0.28, 3.3)	0.97
serum PSA level					
<= 20 ng/ml	18(69.2)	8(30.8)	1	1	0.08
>20 ng/ml	51(56)	40(44)	1.6(0.74, 3.4)	1.03(0.42, 2.48)	0.94
unknown	13(65)	7(35)	3.5(1.5, 9.9)	3.08(0.9, 10.5)	0.07
stage					
stage III & IV	54(51.4)	51(48.6)	7.8(2.3, 25.6)	6.96(1.81, 26.7)*	0.005
stage I & II	20(87)	3(13)	1	1	
distant metastasize					
yes	42(51.9)	39(48.1)	2.8(1.5, 5.1)	1.14(0.53, 2.4)	0.73
no	40(71.4)	16(28.6)	1	1	
limp node metastasize					
yes	5(38.5)	8(61.5)	1.8(0.85, 3.8)	1.69(0.63, 4.5)	0.29
no	77(62.1)	47(37.9)	1	1	
ADT treatment					
yes	74(66.1)	38(33.9)	0.5(0.3, 0.95)	0.48(0.23, 0.99)*	0.049
no	8(32)	17(68)	1	1	
Surgery + ADT + radiotherapy					
yes	26(70.3)	11(29.7)	0.6(0.3, 1.16)	0.61(0.26, 1.39)	0.24
no	56(56)	44(44)	1	1	

* indicates significant variables at level of p value 0.05

6. DISCUSSION

Our study tried to assess survival of prostate cancer patients generally and among groups with its determinants for cases diagnosed at TASH. The overall five year survival was 22% which mean the percentage of prostate cancer patients who lived at least five year after they were diagnosed irrespective of their stage and treatments undergone. This result is almost similar with the studies in Nigeria 26% and in Sudan 36.5%(19,20). The survival for stage I-IV was 83%, 61%, 16%, and 0% respectively. This indicates that better survival was observed in patients with early stages of the diseases (stage I & II) than advanced stages (stage III & IV). This finding is supported with the study conducted in Sudan and Ghana(20,21)

The overall survival in early stage, advanced stage, non metastatic and distant metastatic cases in our study was lower compared to the studies in the western countries(2,17,18,22). In our study the five year survival for early stage (stage I &II) were 83% and 61% which is lower compared to the studies in Brazil on localized prostate cancer patients (stage I, II & III) having the five-year survival rates of 87.8% and 100% in USA(17,18).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 advanced stage with distant spread at diagnosis. Most of cases were diagnosed at advanced stage (stage III & IV) with distant metastasize mostly involving the bone (86%), followed by lymph nodes rather than as precancerous or early cancers. This could be due to the lack of screening programs or confirmatory test to detect early stages of the disease in our country and prostate cancer that it doesn't have symptoms until it become invasive so results higher numbers of cases with advanced stage with poor survival. The other reason for the difference could be attributed due to high availability and accessibility of screening programmers, early detection services, and cancer treatment facilities in the western (developed) countries. Early detection and treatment greatly improves the survival time of prostate cancer patients.

In this study there is a significant difference in survival experience between categories of stage of prostate cancer, distant metastasize status, bone metastasize, PSA levels and ADT treatment modalities. Patients with stage I diagnosis had a significantly better survival than stage III & IV disease (log-rank test, $p=0.0001$). Also the merged clinical stage I and II (early stage) have a

significantly better survival than those of having advanced stage (stage III & IV) patients (log-rank test, $P=0.001$). Survival declined steadily with advancing stage of disease at diagnosis. This is consistent with the study in Ghana in which stages of prostate cancer shows survival difference at (log-rank test, $p=0.0004$) (21). Patients with distant metastatic (stage IV patients with distant organ involved) had significantly lower survival than those who have localized or regional prostate cancer (stage I-III and stage IV with no distant spread) with (log rank test, $p=0.001$). This result is similar with the findings in eastern regions of Sweden conducted on national cancer registry showing that there is significant survival difference among M category stage (M0 & M1) of prostate cancer and cases with M0 category showed better survival than those with M1 category(22). Similarly patients with bone metastatic at time of diagnose compared to those with no bone involvement showed significant survival difference at (log-rank test, $p=0.002$). This result is supported with the study conducted in Indonesia among bone metastatic prostate cancer patients comparing their survival based on their bone scan index measurement shows cases with high bone scan index value have showed survival difference at (log-rank test, $p=0.004$) (23). Probably presence of high proportion of cases with bone metastasize (86%) in or study may have contributed.

In our study a group of patients who were treated with ADT have had significantly better survival than those who were not treated with ADT (treated with other treatment modality) (log-rank test $p=0.031$). This could be due to that ADT was the most effective therapeutic options provided for advanced or metastatic cases and in our study since most of cases have metastatic cancer disease and thus most of patients (82%) provided these treatment modalities than surgery and radiotherapy. ADT is hormone therapy that is used to reduce levels of male hormone that can be bilateral orchiectomy or other anti androgen drugs. We considered any patient who have taken either one or combination of the drug as treated with ADT and those haven't taken any type of ADT as not treated with ADT. Radiotherapy and surgical prostatectomy are the treatment modalities preferred for patients with non advanced stage of cancer (2). Radiotherapy only treated cases had showed poor survival compared to combination of ADT, surgery and radiotherapy treated groups (log-rank test, $p=0.036$) in this study may strengthen the above idea. The study conducted in Japan on metastatic prostate cancer patients treated with combination of ADT have shown better survival than those treated with single ADT treatment with (log-rank test, $P=0.034$). Similarly patients having serum PSA level less than 20 ng/ml during diagnose in comparisons to those having above 20 ng/ml and unknown have better five year survival with

(log-rank test $p=0.048$). This implies that cases having less than 20ng/ml PSA showed better survival. In clinical practice, a PSA level of 20 ng/ml is used as the cutoff value for advanced Prostate cancer and PSA 4 ng/ml is used as cutoff point for prostate cancer diagnosis((2,26)). This justify that cases with advanced stage have poor survival as discussed in the above paragraph.

In the Cox proportional hazard model stage of cancer and ADT treatment modality were statistically significant. Accordingly, stage III & IV (advanced stage) Patients are 6.9 times as likely as to be dead at any time than stage I & II (early stage) patients with (AHR 6.9, 95% CI, 1.81-26.7). This means that cases with advanced stage after adjusted with age, treatment and other clinical patterns identified as prognostic factors, it is the determinant for survival of prostate cancer patients. This result is supported with the findings in Sweden and USA shows that cases with higher T category have poor survival (18,22). Patients who were treated with ADT are also significantly associated with reduced incidence of death (AHR, 0.48, 95% CI, 0.23- 0.99). That is patients who were treated with ADT had 52% more chance of surviving than those who didn't taken ADT at any time. This indicates that generally ADT treatment provision has showed better survival without considering whether it was given in combination or singly. This could be due to that most cases in our study are those who need ADT than other treatments since there were high cases with metastatic disease. The study In Japan and Italy support this result in which cases of having metastatic stage treated with combination of ADT treatment showed significantly associated with a favorable overall survival compared with single ADT with (hazard ratios 0.66 and 0.15, respectively) (24,25). In our study PSA level, histological grade/Gleason score and age at diagnose were not identified as having significant effect on prostate cancer survival as seen in other studies. This could be due to that the nature of the study retrospective (record review) thus incomplete data (for Gleason score or tumor grade). The other reason could be that we have included all cases without considering extent of the disease (local/distant, early/advanced stage) that may have great variation on records since we have small number of cases. Distant metastatic variable were significantly associated survival during Bivariate Cox-regression and became non significant during multivariable Cox regression.

7. STRENGTH AND LIMITATIONS OF THE STUDY

One of the strength of the study is that use of analytical methods (survival analysis) allowing simultaneous analysis of progress for different durations of follow-up which give consideration for times to event analysis through accounting for censored data. Additionally inclusion of all study participants in our study may decrease the probability of sampling errors.

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 (incomplete chart). Some cards/charts are not found. However, for more than 80% of the study participants, their charts were found so it may not affect the result of the study. The ascertainment and the cause of death are based on phone interview from their family or care takers. This may lead to under or over detection of deaths due to prostate cancer, which may cause outcome ascertainment bias.

8. CONCLUSIONS

This study revealed that, overall five year survival of prostate cancer patients was 22% with different survival experience among different groups at different time. There is a significant survival differences among categories of stage of prostate cancer covariate, distant metastatic status covariates, bone involvement, PSA level and among different treatment modality covariates. ADT treatment modality and stage of prostate cancer were the determinants of survival which are significantly associated with time to death (survival) of prostate cancer patients in our study. In general our study shows poor survival or prognosis by late stage and treatments, indicating the key role of early detection and timely treatment for improving survival or reducing mortality from prostate cancer.

9. RECOMMENDATIONS

Improving and integrating of prostate cancer control program including prevention, early detection and treatment with other cancer control program is mandatory. Also expanding and availing prostate cancer screening programs (PSA tumor marker test) in different levels of health facilities and creating public awareness in collaboration with public Medias about prostate cancer is needed at the level of governmental and nongovernmental organizations working on cancer control program including FMOH.

Creating public and professional awareness in early detection and using feasible and effective treatment regimen is recommended in all service providing facilities. Also including detailed patient characteristics on their chart or cancer registry and proper handling of the patient chart is needed in health facilities. Further studies on survival time among prostate cancer patients with large sample size, considering different level of extent the cancer and different research methods that overcome the limitations of this study are needed.

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11. ANNEX

Annex I: Data Extraction Tool

Table 6 Data extraction form for the Assessment of survival time and associated factors among prostate cancer patients at BLH, AA Ethiopia, 2012-2016.

Part I: Socio demographic characteristic.	
1. Medical record number(MRN)	_____
2. Age in years	_____
3. Place of residence	1.urban (if regional, zonal or district(woreda) town) 2. rural
4. name of place and distance from Addis Ababa in kilometers	1. _____ (woreda name for rural) 2. _____ Km
5. Marital status	1. Single 2.Married 3.Widowed 4. Divorced
Part II:- Medical History	
1. Patient age at diagnosis in years	_____
2. Basis for diagnosis	1. Clinical only 2. Tumor marker (PSA) 3.Imaging test/x-ray(CT scan or MRI) 4. Biopsy (histopathology) 5. Transrectal Ultrasound (TRUS) 6. unknown
3. Date of diagnosis	____/____/____ (DD/MM/YEAR)
4. serum PSA level at time of diagnose	1.____(ng/mL) 2.not done
5. gleasonscore at time of diagnose	1.____ 2.not done
6. Stage of cancer at diagnosis	1. Stage I 2. Stage II 3. Stage III 4. Stage IV 5. Unknown
7. Histological grades of prostate cancer	1. Well differentiated 2. Moderately differentiated 3. Poorly differentiated 4. Undifferentiated 5.unknown
8. Histological types of cancer cell	1. adenocarcinoma 2.squamous cell carcinoma 3.adenosquamous cell carcinoma

	4.others	5.unknown
9. Date of starting treatment	____/____/____ (DD/MM/YEAR)	
10. Treatment type provided	1. surgical treatment (yes / no)	
	2. chemotherapy (yes / no)	
	3. hormonal therapy (yes/ no)	
	4. radiotherapy (yes / no)	
	5. none	
	6. unknown	
11. smoking behavior of case at time of diagnosis	1.yes	
	2. no	
	3. Not screened	
	4. unknown	
12. body mass index(BMI) status of case at time of diagnose	1. weight____(Kg)	
	2. height____(m)	
	3.BMI_____	
	4. Not screened	
13. family history of prostate cancer	1.yes	
	2. no	
	3. Not screened	
	4. unknown	
14. HIV infection status of the case	1. HIV negative	
	2. HIV positive	
	3. Not screened	
	4. unknown	
15. presence of other chronic co morbidities	diabetes mellitus 1. yes 2. no	
	Hypertension 1. yes 2. no	
16. Date of last contact	____/____/____ (DD/MM/YEAR)	
17. Status of the patient during last contact	1. Alive	
	2. Dead	
18. Current status of the patient	1. Alive	
	2. Dead	
19. If alive, functional status of the patient	1. Working	
	2. Ambulatory	
	3. Bed ridden	
20. If dead, date of death	____/____/____(DD/MM/YEAR)	
21.If lost to follow up, date of lost to follow up	____/____/____(DD/MM/YEAR)	

Annex II. Biography of the Principal Investigator

My name is Jemal Beksisa Shuramu. I was born on October 29/1989 G.C in Alge, Ilu Ababor zone, Western Oromia, Ethiopia. I attended my primary education at Dupha Elementary School and my high school at Alge Secondary School.

Then I had joined Hawassa University in 2008 and graduated with Junior Public Health profession in 2011G.C. Since that I was worked in chefe health center, east Showa zone, Oromia regional state and in Yeka sub city Woreda 13 health center, Addis Ababa city Administration at different departments for about five years. I had worked in health centers as a coordinator for diseases prevention and control core process, as Health Officer giving health care service at adult and pediatric departments and as disease surveillance focal person. By the year of 2015 I started to study my post graduate study of master of public health in Field Epidemiology at Saint Paul's Hospital Millennium Medical College.

