

Diagnosis and Risk Factors of Advanced Cancers in Ethiopia

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Background: Cancer is one of the leading causes of morbidity and mortality worldwide. Yet, limited is known about patterns of cancer and risk factors for advanced stage cancers in Ethiopia.

Methods: A cross-sectional study was conducted on 919 patients with biopsy-confirmed cancers at Tikur Anbessa Hospital in Ethiopia, 2010 to 2014. Pearson chi-square test, *t*-test, analysis of variance and multivariate logistic regression analyses were performed.

Results: The majority of the patients were females (72.4%). The commonest malignancies among males were bone and soft tissue (16.5%), colorectal (12.2%), and esophageal (9.1%). Among females, the most common cancers were cervical (39.7%), breast (18.3%), and ovarian (7.1%); of these, 41.7%, 59.0%, and 42.6% were diagnosed at advanced stages, respectively. Females had more advanced stage cancers at diagnosis than males (37.6% vs. 24.8%, $P < 0.01$). Among males, 46.7% of prostate and 29.0% of colorectal cancers were in advanced stages at the time of diagnosis. Delay in presentation from onset of symptoms was associated with advanced cancer among females (OR = 3.21; 95% CI = 1.69-6.10). Prostate cancer among males (OR = 5.22; 95% CI = 1.26-21.60) and breast cancer among females (OR = 1.93; 95% CI = 1.23-3.03) were more likely to be diagnosed at advanced stages.

Conclusions: Cancers with effective screening tests are common in Ethiopia and significant proportions of these were diagnosed at advanced stages, typically several months after onset of symptoms. Timely access to preventive care along with effective educational and screening strategies is needed in Ethiopia for early detection and treatment of common malignancies, such as cervical, breast and colorectal cancers.

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Key Words: Neoplasm staging, Neoplasms

INTRODUCTION

Non-communicable diseases are the leading causes of death globally, killing more people each year than all other causes combined. Of the 57 million deaths that occurred globally in 2008, 36 million were due to non-communicable diseases comprising mainly cardiovascular diseases, cancers, diabetes, and chronic lung diseases [1]. The combined burden of these diseases is rising fastest among the lower-income countries, populations, and communities [2]. Contrary to popular opinion, available data demonstrate that nearly 80% of deaths due to non-communicable diseases occur in low- and middle-income

countries [3]. In 2011, the World Health Organization [4] estimated that 34% of the Ethiopian population died from non-communicable diseases, with a national cardiovascular disease prevalence of 15%, cancer and chronic obstructive pulmonary disease prevalence of 4% each, and diabetes mellitus prevalence of 2%. Cancer is the second largest contributor to non-communicable disease deaths and causes a great deal of suffering worldwide [5].

Cancer is a leading cause of disease worldwide with estimated 14.1 million new cancer cases occurring in 2012 [6]. It is now the third leading cause of death worldwide with 8.2 million deaths in 2012 [6]. More than half of all cancer deaths each year are due to

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lung, stomach, liver, colorectal and female breast cancers [6]. These cancers accounted for more than 40% of all cases diagnosed worldwide. In men, lung cancer was the most common cancer (16.7% of all new cases in men). Breast cancer was by far the most common cancer diagnosed in women (25.2% of all new cases in women) [6]. By 2030, it is projected that 26 million new cancer cases and 17 million cancer deaths are expected to occur [7]. This represents an increase of 68% compared with 2012 (66% in low and medium human development index [HDI] countries and 56% in high and very high HDI countries) [6,8]. Moreover, the global distribution of cancer and types of cancer that predominate continues to change, especially in economically developing countries. Low- and middle-income countries accounted for about half (51%) of all cancers worldwide in 1975 [9]. This proportion increased to 55% in 2006 and is projected to reach 61% by 2050 [9]. The global increase in the cancer burden and its disproportionate impact on economically developing countries is being propelled by both demographic changes in the populations at risk and by temporal and geographic shifts in the distribution of major risk factors. Colorectal, lung, female breast and prostate cancers were the main contributors in most regions of the world, explaining 18% to 50% of the total healthy years lost [10]. These cancers are no longer largely confined to Western industrialized countries but are among the most common cancers worldwide. An estimated 169.3 million years of healthy life were lost globally because of cancer in 2008 and approximately 44% of cancer cases and 53% of cancer deaths occur in countries at a low or medium level of the HDI [11].

In sub-Saharan Africa, cancer burden is predicted to increase by 85% by 2030 due to the increase in life expectancy, changes in diet and lifestyle and lower burden of communicable diseases [5]. According to the International Agency for Research on Cancer, about 715,000 new cancer cases and 542,000 cancer deaths occurred in 2008 in Africa. These numbers are projected to nearly double (1.28 million new cancer cases and 970,000 cancer deaths) by 2030 simply due to the aging and growth of the population [12]. With the potential to be even higher because of the adoption of behaviors and lifestyles associated with economic development, such as smoking, unhealthy diet, and physical inactivity [13].

Despite this growing burden, cancer continues to receive low public health priority in Africa, largely because of limited resources and other pressing public health problems, including communicable diseases, such as acquired immune deficiency syndrome (AIDS)/human immunodeficiency virus (HIV) infection, malaria, and tuberculosis [14]. It may also be in part due to a lack of awareness about the magnitude of the current and future

cancer burden among policy makers, healthcare providers, the general public, and international private or public health agencies [14].

Ethiopia is home to a growing population of more than 105 million people and is the second most populous country in Africa and is expected to become the ninth most populous country in the world by 2050, with an estimated parallel rise in cancer burden [15]. In Ethiopia, cancer is estimated to account for about 5.8% of total national mortality [16]. Although population-based data do not exist in the country except for Addis Ababa, it is estimated that the annual incidence of cancer is around 60,960 cases and the annual mortality is over 44,000 [16]. For people under the age of 75 years, the risk of being diagnosed with cancer is 11.3% and the risk of dying from the disease is 9.4% a five year prevalence for 2003 to 2008 was 224.2 per 100,000 people [17]. The most prevalent cancers in Ethiopia among the adult population are breast cancer (30.2%), cancer of the cervix (13.4%), and colorectal cancer (5.7%). About two-thirds of reported annual cancer deaths occur among women [16]. Based on 2013 data from the Addis Ababa Cancer Registry, breast cancer accounted for 31.4%, cervical cancer for 14.3% and ovarian cancer for 6.3% of all cancer cases [18]. According to a qualitative study at the only oncology center in the country at Tikur Anbessa Specialized Hospital, limited patient awareness along with lack of resources contribute to diagnoses of cancers at advanced stages, which lead to poor patient outcomes [19]. However, patterns of cancer, their stages and risk factors for advanced cancers have not been well studied and documented in Ethiopia, as prior studies have largely focused on communicable diseases, such as AIDS/HIV, malaria, and tuberculosis [20]. To fill this substantial gap, this study examines patterns of cancer occurrence and stages of cancer at diagnosis, and risk factors associated with advanced stage cancers among patients at Tikur Anbessa Hospital from 2010 to 2014.

MATERIALS AND METHODS

1. Study design and setting

A hospital-based retrospective cross-sectional study was conducted based on medical record review of selected patients at Tikur Anbessa Hospital in Addis Ababa, Ethiopia. Tikur Anbessa Hospital is Ethiopia's highest tertiary level referral and teaching hospital, and the nation's sole cancer referral center. It is staffed with the nation's most senior specialists and faculty from Addis Ababa University. Tikur Anbessa Hospital is a training center for undergraduate and postgraduate medical students, dentists, nurses, pharmacists, and public health specialists. The hospital

serves approximately 370,000 to 400,000 patients a year and the emergency department sees around 80,000 patients a year. This study was conducted at pathology department of the school of medicine at Tikur Anbessa Hospital. Before starting data collection ethical approval letter was obtained for data collection from Jimma University (Ethical clearance letter number RPGC/3061/2015).

2. Study population

The inclusion criteria were all sampled patients who were diagnosed to have cancer by biopsy at Tikur Anbessa Hospital pathology department between January 1st, 2010 and December 15th, 2014. The exclusion criteria were inconsistency of data among all of the three data sources (biopsy logbook, the physician biopsy request forms and patient cards), if data was not found in all of the three data sources, if the data of a patient was recorded in previous records and if the result of the diagnosis was non-cancerous or a benign lesion.

3. Sampling procedures

All samples are given biopsy numbers in the biopsy logbook by calendar year, starting in January and ending in December. The samples were selected by stratified sampling technique considering each of the study years as strata and calculating the samples to be selected from each stratum to be proportional to their size. These samples from each stratum were then included in the study using simple random sampling method using randomly generated numbers.

4. Sample size calculation

Sample size is calculated using formula for single and finite population.

$$Nf = N \frac{(Z_{\alpha/2})^2 P (1 - P)}{d^2 (N - 1) + (Z_{\alpha/2})^2 P (1 - P)} \quad \text{where,}$$

$$d^2 (N - 1) + (Z_{\alpha/2})^2 P (1 - P)$$

Nf is minimum sample size, which was calculated to be 919 samples, where P is taken from recent report of Addis Ababa Cancer Registry about cancer patterns in which the most common cancer, which is breast cancer and the proportion was 33% and the least common cancer was esophageal cancer and the proportion was 2% [21]. d is margin of error which is estimated to be 3% since P is less than 0.5. $Z_{\alpha/2}$ is the standard normal variable at 1 α % confidence level and α is mostly 5% at 95% CI level. N is population size which is total number of patients having biopsy

during the year January 1st, 2010 to December 15th, 2014 is 35,400.

5. Operational definitions

Time to presentation is the time from start of chief complaint up to the first time that the patient seeks medical care.

Type of cancer by site is the diagnosis of cancer after biopsy and is expressed by site of occurrence and the values include breast cancer, cervical cancer, prostate cancer, ovarian cancer, colorectal cancer, hematologic malignancies including leukemia and lymphoma, lung cancer, gastric cancer, esophageal cancer, liver cancer (hepatoma), skin, bone and soft tissue cancer, retinoblastoma, thyroid cancer, endometrial/genital cancers, bladder cancer, brain cancer, ear, nose and throat cancer, renal cancer, and neuroblastoma.

Stage of cancer at diagnosis is a measure of disease progression, detailing the degree to which the cancer has advanced. Surveillance Epidemiology and End Results (SEER) program has standardized and simplified staging to ensure consistent definitions over time and is used in countries with advanced population based cancer registry programs.

In-situ cancer is an early cancer that is present only in the layers of cells in which it began.

Localized cancer is cancer which is limited to the organ in which it began, without evidence of spread.

Regional cancer is a cancer that has spread beyond the primary site to nearby organs, lymph nodes (LNs) and tissues.

Distant cancer is cancer that has spread from primary site to distant organs.

Unstaged cancer is cancer for which there is not enough information to indicate stage.

Advanced stage of cancer is regional and/or distant cancer.

Dependent variables are stage of cancer (advanced stage of cancer).

Independent variables are age, sex, time of presentation of patients, types of cancer.

6. Statistical analysis

Descriptive statistical analysis was performed across the different types of cancers after stratifying by sex. Pearson chi-square test was used for categorical variables. ANOVA and *t*-tests were computed for continuous variables.

Univariate and multivariate binary logistic regression analyses were performed to examine factors associated with advanced stage cancers. The regression models were built with advanced stage cancers as the outcome variable after adjusting for

covariates. Covariates were included in the final regression model based on priori and our conceptual framework. Adjusted OR with 95% CI were used to determine the magnitude of associations among advanced stage cancers and various potential risk factors. Two-tailed statistical significance was assessed at $\alpha < 0.05$. All the analyses were conducted in 2019 using statistical software SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

RESULTS

Table 1 shows basic characteristics of the study participants. Out of the 919 patients in the study, 254 (27.6%) were males and 665 (72.4%) were females. The overall mean age was 45.2 ± 19.1 years and 44.6 ± 15.1 years among males and females, respectively. The most common malignancies among males were bone and soft tissue (16.5%), colorectal (12.2%), and esophageal (9.1%). Among females, the most common cancers were cervical (39.7%), breast (18.3%), and ovarian (7.1%). Among both males and females, retinoblastoma and thyroid cancers had the longest time-intervals (in months) between the onset of symptoms and presentation $34.0-19.3$ ($P < 0.01$) and $23.3-23.9$ ($P < 0.01$), respectively.

Distribution patterns and stages of cancers at diagnosis are provided in Table 2. At the time of diagnosis, 3.9% and 12.0% of the malignancies were already distantly metastasized among males and females, respectively. While, regionally metastasized malignancies accounted for 20.9% in males and 25.6% in females. Half (50.0%) of the cancers among males and 45.0% of the cancers among females were unstageable. Males had less advanced (regional and distant metastasis) stage cancers at diagnosis than females (24.8% vs. 37.6%, $P < 0.01$). Among males, 46.7% of prostate, and 29.0% of colorectal cancers were at advanced stages at the time of diagnosis. Among females, 59.0% of breast, 41.7% of cervical, and 17.2% of colorectal cancers were at advanced stages at the time of diagnosis.

Table 3 shows the prevalence and risk factors associated with advanced stage cancers stratified by sex. Among females, the odds of having advanced stage malignancy was 221% (OR = 3.21; 95% CI = 1.69-6.10) higher in those who presented after 12 months, compared to those who presented within 6 months of the onset of symptoms. Among males, Prostate (OR = 5.22; 95% CI = 1.26-21.60) and breast (OR = 9.73; 95% CI = 2.31-40.92) cancers were more likely to be diagnosed at advanced stages, in comparison to bone and soft tissue cancers. Among females,

Table 1. Baseline characteristics and distribution of cancer at diagnosis at Tikur Anbessa Hospital in Ethiopia, 2010 to 2014

Site/type of cancer	Male			Female		
	Subject	Age (yr)	TOP ^a	Subject	Age (yr)	TOP ^a
All	254 (27.6)	45.2 ± 19.1	9.7 ± 8.1	665 (72.4)	44.6 ± 15.1	9.7 ± 7.1
Breast	14 (5.5)	52.6 ± 10.8	11.6 ± 8.9	122 (18.3)	40.6 ± 12.4	9.4 ± 6.9
Cervical	-	-	-	264 (39.7)	48.8 ± 11.6	8.6 ± 5.9
Prostate	15 (5.9)	62.3 ± 17.7	7.1 ± 5.4	-	-	-
Ovarian	-	-	-	47 (7.1)	43.1 ± 14.4	8.2 ± 4.7
Colorectal	31 (12.2)	44.9 ± 18.1	7.5 ± 4.5	29 (4.4)	50.1 ± 15.3	8.4 ± 3.5
Hematologic	2 (0.8)	58.0 ± 18.4	3.5 ± 0.7	3 (0.5)	39.3 ± 23.8	14.3 ± 8.7
Lung	5 (2.0)	46.8 ± 14.5	8.4 ± 3.0	3 (0.5)	49.2 ± 11.0	7.0 ± 6.6
Gastric	16 (6.3)	46.1 ± 9.9	7.5 ± 3.3	16 (2.4)	49.2 ± 15.7	7.8 ± 4.3
Esophageal	23 (9.1)	50.6 ± 15.2	8.3 ± 3.3	37 (5.6)	51.8 ± 11.1	9.4 ± 4.7
Liver	1 (0.4)	75.0	6.0	5 (0.8)	32.0 ± 21.8	4.8 ± 1.1
Skin	15 (5.9)	42.7 ± 19.9	8.4 ± 9.2	14 (2.1)	49.1 ± 15.1	5.9 ± 2.5
Bone and soft tissue	42 (16.5)	37.5 ± 19.6	10.2 ± 7.6	33 (5.0)	34.6 ± 17.9	9.0 ± 7.4
Retinoblastoma	6 (2.4)	3.8 ± 1.9	34.0 ± 11.8	9 (1.4)	9.0 ± 15.5	23.3 ± 12.9
Nephroblastoma	2 (0.8)	6.0	14.0 ± 14.1	2 (0.3)	5.0 ± 1.4	9.0 ± 4.2
Thyroid	12 (4.7)	42.1 ± 19.1	19.3 ± 15.1	31 (4.7)	38.3 ± 17.3	23.9 ± 17.8
Renal	8 (3.2)	45.4 ± 8.5	7.5 ± 3.6	9 (1.4)	29.2 ± 18.7	8.8 ± 4.5
ENT	18 (7.1)	48.2 ± 15.4	8.4 ± 6.4	1 (0.2)	18.0	3.0
Brain	10 (3.9)	24.6 ± 16.4	7.2 ± 2.9	4 (0.6)	35.0 ± 16.1	5.5 ± 2.6
Bladder	20 (7.9)	58.2 ± 11.7	6.9 ± 2.9	10 (1.5)	50.3 ± 12.9	8.2 ± 3.3
Endometrial and genital	6 (2.4)	50.0 ± 13.4	13.7 ± 6.7	22 (3.3)	48.2 ± 15.1	12.9 ± 6.8
Others	8 (3.2)	49.4 ± 18.1	8.8 ± 3.7	4 (0.6)	29.8 ± 10.3	8.3 ± 6.1

Values are presented as number (%) or mean ± SD. ENT, ear, nose and throat; TOP, time of presentation from onset of symptoms in month. ^a $P < 0.01$ using ANOVA.

Table 2. Stages of cancer at diagnosis at Tikur Anbessa Hospital in Ethiopia, 2010 to 2014

Site/type of cancer	Sex	Unstaged (%)	Localized (%)	Regional (%)	Distant (%)	Advanced ^a (regional and distant) (%)
All	Male	50.0	25.2	20.9	3.9	24.8
	Female	45.0	17.4	25.6	12.0	37.6
Breast	Male	35.7	0.0	50.0	14.3	64.3
	Female	36.1	4.9	32.8	26.2	59.0
Cervical	Male	-	-	-	-	-
	Female	46.2	12.1	31.1	10.6	41.7
Prostate	Male	6.7	46.7	46.7	0.0	46.7
	Female	-	-	-	-	-
Ovarian	Male	-	-	-	-	-
	Female	38.3	19.2	23.4	19.2	42.6
Colorectal	Male	54.8	16.1	22.6	6.5	29.0
	Female	48.3	34.5	13.8	3.5	17.2
Hematologic	Male	100.0	0.0	0.0	0.0	0.0
	Female	100.0	0.0	0.0	0.0	0.0
Lung	Male	40.0	0.0	60.0	0.0	60.0
	Female	33.3	33.3	0.0	33.3	33.3
Gastric	Male	81.3	6.3	6.3	6.3	12.5
	Female	50.0	37.5	12.5	0.0	12.5
Esophageal	Male	56.5	17.4	17.4	8.7	26.1
	Female	59.5	18.9	21.6	0.0	21.6
Liver	Male	100.0	0.0	0.0	0.0	0.0
	Female	0.0	40.0	40.0	20.0	60.0
Skin	Male	40.0	53.3	6.7	0.0	6.7
	Female	14.3	42.9	21.4	21.4	42.9
Bone and soft tissue	Male	64.3	14.3	21.4	0.0	21.4
	Female	75.8	21.2	0.0	3.0	3.0
Retinoblastoma	Male	16.7	50.0	16.7	16.7	33.3
	Female	0.0	55.6	44.0	0.0	44.4
Nephroblastoma	Male	0.0	50.0	50.0	0.0	50.0
	Female	0.0	50.0	50.0	0.0	50.0
Thyroid	Male	41.7	41.7	16.7	0.0	16.7
	Female	25.8	45.2	25.8	3.2	29.0
Renal	Male	37.5	37.5	25.0	0.0	25.0
	Female	22.2	55.6	22.2	0.0	22.2
ENT	Male	66.7	11.1	16.7	5.6	22.2
	Female	0.0	0.0	100.0	0.0	100.0
Brain	Male	10.0	80.0	10.0	0.0	10.0
	Female	75.0	25.0	0.0	0.0	0.0
Bladder	Male	25.0	55.0	15.0	5.0	20.0
	Female	30.0	40.0	20.0	10.0	30.0
Endometrial and genital	Male	100.0	0.0	0.0	0.0	0.0
	Female	90.9	0.0	0.0	9.1	9.1
Others	Male	87.5	0.0	12.5	0.0	12.5
	Female	100.0	0.0	0.0	0.0	0.0

ENT, ear, nose and throat. ^a $P = 0.04$ among males; $P < 0.01$ among females, and all males verses females using chi-square test.

breast (OR = 1.93; 95% CI = 1.23-3.03) cancer was more likely to be diagnosed at advanced stages, while colorectal (OR = 0.30; 95% CI = 0.11-0.83), gastric (OR = 0.20; 95% CI = 0.04-0.90), esophageal (OR = 0.39; 95% CI = 0.17-0.90), bone and soft tissue (OR = 0.04; 95% CI = 0.01-0.29), thyroid (OR = 0.30; 95% CI = 0.12-0.78), and endometrial and genital (OR = 0.11; 95% CI =

0.02-0.48) cancers were less likely to be diagnosed at advanced stages, in comparison to cervical cancers.

The distribution of cancer at diagnosis by age group stratified by sex at Tikur Anbessa Hospital in Ethiopia, 2010 to 2014 is illustrated Table 4.

Selected cancers with high incidence rates and related factors

Table 3. Prevalence and risk factors associated with advanced stage cancers stratified by sex at diagnosis at Tikur Anbessa Hospital in Ethiopia, 2010 to 2014

Variable		Advanced stage ^a cancer			
		Male		Female	
		Prevalence (%)	OR (95% CI)	Prevalence (%)	OR (95% CI)
Age (yr)	< 30	28.6	1.00	33.7	1.00
	30-59	25.2	0.60 (0.24-1.48)	39.4	0.95 (0.52-1.75)
	≥ 60	21.1	0.37 (0.13-1.08)	34.1	0.89 (0.44-1.81)
TOP (mo)	< 6	22.4	1.00	36.7	1.00
	6-12	29.1	1.35 (0.69-2.68)	34.7	1.03 (0.71-1.49)
	> 12	16.7	0.40 (0.09-1.74)	52.6	3.21 (1.69-6.10)
Cancer type/site	Breast	64.3	9.73 (2.31-40.92)	59.0	1.93 (1.23-3.03)
	Cervical	N/A	N/A	41.7	1.00
	Prostate	46.7	5.22 (1.26-21.60)	N/A	N/A
	Ovarian	N/A	N/A	42.6	1.07 (0.56-2.03)
	Colorectal	29.0	1.78 (0.58-5.52)	17.2	0.30 (0.11-0.83)
	Hematologic	0.0	--	0.0	--
	Lung	60.0	5.67 (0.79-40.90)	33.3	0.51 (0.04-6.26)
	Gastric	12.5	0.62 (0.11-3.51)	12.5	0.20 (0.04-0.90)
	Esophageal	26.1	1.60 (0.45-5.65)	21.6	0.39 (0.17-0.90)
	Liver	0.0	--	60.0	2.26 (0.36-14.14)
	Skin	6.7	0.33 (0.04-3.02)	42.9	1.16 (0.39-3.47)
	Bone and soft tissue	21.4	1.00	3.0	0.04 (0.01-0.29)
	Retinoblastoma	33.3	3.56 (0.36-35.36)	44.4	0.52 (0.11-2.43)
	Nephroblastoma	50.0	4.53 (0.22-8.80)	50.0	1.44 (0.08-24.82)
	Thyroid	16.7	1.05 (0.18-6.09)	29.0	0.30 (0.12-0.78)
	Renal	25.0	1.40 (0.22-8.80)	22.2	0.36 (0.07-1.86)
	ENT	22.2	1.37 (0.34-5.57)	100.0	--
	Brain	10.0	0.32 (0.04-2.90)	0.0	--
	Bladder	20.0	1.39 (0.33-5.88)	30.0	0.66 (0.17-2.60)
	Endometrial and genital	0.0	--	9.1	0.11 (0.02-0.48)
Others	12.5	0.58 (0.06-5.63)	0.0	--	

TOP, time of presentation from onset of symptom in months; ENT, ear nose and throat; N/A, non-applicable; --, not enough sample size to compute OR. ^aRegional or distant metastasis.

are shown in Table 5.

DISCUSSION

The majority of the biopsy-confirmed cancer diagnoses were made in females. We found bone and soft tissue (16.5%), colorectal (12.2%), and esophageal (9.1%) were the most common cancer diagnoses among males. Among females, the most common cancers were cervical (39.7%), breast (18.3%), and ovarian (7.1%). At the time of diagnosis, 3.9% and 12.0% of the malignancies were already distantly metastasized among males and females, respectively. Advanced stage cancers were more common among females than males at the time of diagnosis. Prostate and breast cancers among males, and breast cancer among females were more likely to be diagnosed at advanced stages. Significant proportions of cervical and colorectal cancers

were also diagnosed at advanced stages. Delayed presentation from onset of symptom was associated with more advanced stage cancer diagnoses among females.

Our study found the majority of patients with cancer were females (72.4%) with mean age of 44.6 ± 15.1 years. This finding concurs with a recent report of Addis Ababa cancer registry, where 67% of the registered cancer cases were women with highest incidence rate of 38.4% in the age group of 30 to 49 years [21]. Similarly, higher burden of cancer among females have been reported in other African countries [6,22]. A possible explanation could be the fact that females are more likely to be in contact with clinicians and utilize health services, largely due to pregnancy and childbirth [23]. Occurrence of different malignancies among females especially those related to reproductive organs could be the reason for this sex preference and the age group preference could be due to repeated exposure of these reproductive age

Table 4. Distribution of cancer at diagnosis by sex and age group at Tikur Anbessa Hospital in Ethiopia, 2010 to 2014

Site/type of cancer	Male ^a			Female ^a		
	Age (< 30 yr)	Age (30-59 yr)	Age (≥ 60 yr)	Age (< 30 yr)	Age (30-59 yr)	Age (≥60 yr)
All	22.1	50.0	27.9	13.8	66.8	19.4
Breast	0.0	71.4	28.6	14.8	75.4	9.8
Cervical	-	-	-	2.7	74.6	22.7
Prostate	13.3	13.3	73.3	-	-	-
Ovarian	-	-	-	19.2	65.9	14.9
Colorectal	19.4	54.8	25.8	3.5	68.9	14.9
Hematologic	0.0	50.0	50.0	33.3	33.3	33.3
Lung	20.0	60.0	20.0	0.0	66.7	33.3
Gastric	0.0	87.5	12.5	12.5	56.3	31.2
Esophageal	8.7	56.5	34.8	0.0	64.9	35.1
Liver	0.0	0.0	100.0	40.0	60.0	0.0
Skin	26.7	53.3	20.0	7.1	64.3	28.6
Bone and soft tissue	45.2	40.5	14.3	45.5	39.4	15.1
Retinoblastoma	100.0	0.0	0.0	88.9	11.1	0.0
Nephroblastoma	100.0	0.0	0.0	100.0	0.0	0.0
Thyroid	33.3	41.7	25.0	38.7	51.6	9.7
Renal	0.0	87.5	12.5	44.4	55.6	0.0
ENT	11.1	61.1	27.8	100.0	0.0	0.0
Brain	70.0	30.0	0.0	50.0	50.0	0.0
Bladder	0.0	40.0	60.0	10.0	60.0	30.0
Endometrial and genital	0.0	66.7	33.3	18.2	50.0	31.8
Others	12.5	50.0	37.5	50.0	50.0	0.0

Values are presented as percent only. ENT, ear nose and throat. ^a $P < 0.01$.

group population with different risk factors related to cancer [21]. Particular attention needs to be paid to this issue since predominantly the productive age groups, mainly females, are being affected, which in turn could have an impact on the economy of the country.

Results of this study showed the most common cancers among females were cervical (39.7%), breast (18.4%), and ovarian (7.1%). These three top cancers were also reported by the Addis Ababa cancer registry report where the most common cancers in females were cancer of the breast 33%, followed by cancer of the cervix uteri 17% and ovary 6% [21]. These findings are also similar with studies done about pattern and trends of cancer in Odisha, India and in South Africa except that breast cancer in these countries is the most common cancer diagnosis [24,25]. In India carcinomas of breast (28.94%), cervix (23.66%), and ovary (16.11%) are leading causes among females and breast cancer was the leading cause of cancer followed by cervical cancer and colorectal cancer in South Africa [24,25]. This similarity could be explained by the similarity of the social and economic context of these countries, as well as due to lack of awareness of patients about the symptoms of cancer in these countries. The significant burden of cervical cancer has been attributed to the high prevalence of human papilloma virus (HPV) infection coupled with a lack of screening

services for prevention and early detection of the disease [26].

In the Global Cancer Incidence, Mortality and Prevalence (GLOBOCAN) 2012 report, the most commonly diagnosed cancers worldwide are those of the lung 13.0%, breast 11.9%, and colorectal 9.7% [5]. These differences from our study findings are mainly due to the disparity in standards of living between developed and developing countries, high prevalence of infections related to cancers especially cervical cancer in developing countries and increased lifestyle risk factors related to cancers, mainly smoking, in developed countries. This implies that in Ethiopia the risk could significantly increase in the near future since there is high prevalence of infection related cancers coupled with adoption of western lifestyle in the country [27]. In addition, these findings imply problem in the awareness among the general public regarding cancer or problem in availability and utilization of early screening modalities [26,28].

The study found the most common malignancies among males were bone and soft tissue (16.5%), colorectal (12.2%), and esophageal (9.1%) with some similarity with the report of the Addis Ababa cancer registry where colorectal cancer was the leading cancer among males at 19% [21]. However, the result is different from the study at Yirga Alem Hospital where the most common cancers by site in men were non-Hodgkin's lymphoma

Table 5. Selected high incident cancers, bone and soft tissue cancer and colorectal in males and cervical and breast cancer in females, and related factors at diagnosis at Tikur Anbessa Hospital in Ethiopia, 2010 to 2014

Variable		Value
Male		
Bone and soft tissue		
TOP (mo) ^a	< 6	33.30
	6-12	52.40
	> 12	14.30
Chief presenting complaints ^a	Difficulty walking	52.40
	Soft tissue swelling	11.90
	Difficulty swallowing	2.40
	Others	33.30
Colorectal cancer		
TOP (mo) ^a	< 6	54.80
	6-12	41.90
	> 12	3.20
Chief presenting complaints ^a	Constipation	45.20
	Abdominal pain	12.90
	Diarrhea	12.90
	Others	29.00
Female		
Cervical cancer		
TOP (mo) ^a	< 6	42.40
	6-12	49.60
	> 12	12.30
Chief presenting complaints*	Vaginal bleeding	54.90
	Post-coital bleeding	17.80
	Abdominal pain	5.30
	Others	22.00
Breast cancer		
TOP (mo) ^a	< 6	39.30
	6-12	48.40
	> 12	12.30
Chief presenting complaints ^a	Breast lump and swelling	45.10
	Ulcerative breast lesion	37.70
	Pain	6.60
	Others	10.60

Values are presented as percent only. TOP, time of presentation from onset of symptom in months. ^a $P < 0.01$.

(13.9%), soft-tissue sarcoma (12.7%), and non-melanoma skin cancer (12.2%) [29]. The reason for this disparity could be the difference in the study period since the study was done 20 years ago where non-Hodgkin's lymphoma was much more common due to high prevalence of HIV/AIDS at that time [29]. Some of these findings could also be due the relative ease of being able to obtain and confirm these types of cancers in resource limited settings, compared to other cancer types, which may require

more technical expertise and invasive procedures.

We found esophageal cancer is the third most common cancer among males in Ethiopia. Although other cancer studies in Ethiopia have not reported similar findings, esophageal cancer is common among several East African countries [30]. Studies have reported Malawi has the highest incidence rates in the world, while esophageal cancer is the leading cause of cancer mortality among men in Kenya [30]. The underlying risk factors vary greatly from tobacco smoking and heavy alcohol drinking in Western countries to drinking hot mate in South America. The cause for relatively high esophageal cancer rates in East Africa, including Ethiopia is unclear, given the relatively low rates of tobacco smoking and heavy alcohol drinking [30,31]. One possible explanation that needs to be further investigated is the high prevalence of Khat chewing among males in Ethiopia [31]. Khat is a stimulant containing Alkaloid Cathinone that has been linked to genetic tissue damage and esophageal cancer [32].

Overall, males had less advanced stage cancers at diagnosis than females (24.8% vs. 37.6%, $P < 0.01$). Among females 59.0% of the breast cancers were at advanced stages at the time of diagnosis. This finding is in contrast to lower advanced stage breast cancer rates at diagnosis in developing countries, such as the recently reported 46.0% in the Netherlands [33]. This is likely to be multifactorial, including lack of awareness about cancer among females or ignoring what they think is minor symptoms because of their low economic status or social stigma. This result is similar with a study published in Lancet in 2013, where patients often present with aggressive features; concluding Ethiopian women with breast cancer often ignore lumps, and usually seek treatment only when symptoms such as pain and itching occur [15].

Among females, the odds of having advanced stage malignancy was 3.21 times higher in those who presented more than a year after having the first symptom compared to those with shorter presentation within 6 months and Breast cancer was more likely to be diagnosed at advanced stage. This is also comparable with a study done on the influence on survival of delay in the presentation and treatment of symptomatic breast cancer, where 32% of patients had symptoms for 12 or more weeks before their first hospital visit and 32% of patients with delays of 12 or more weeks had locally advanced or metastatic disease, compared with only 10% of those with delays of less than 12 weeks ($P < 0.0001$) [34].

Significant proportion (41.7%) of cervical cancers were also diagnosed at advanced stages, which previous studies have attributed to several factors, including lack of awareness and

access to appropriate health services, and the use of traditional remedies for early stages of the disease [32]. The cancer stage at presentation will have impact not only on the treatment outcome and survival of patients, but also on costs related to treatment and follow ups. Substantial progress could be made through effective public health education, along with HPV vaccine and HPV-based cervical cancer screening programs [35].

In both males and females, retinoblastoma and thyroid cancers had the longest time-intervals between the onset of symptoms and presentation. This is in contrast to a study conducted in England on risk factors for delay in symptomatic presentation of cancer, prostate (44%) and rectal cancers (37%) were most likely to delay and patients with breast cancer least likely to delay (8%) [36]. In our study, we did find prostate cancer was most likely to be diagnosed at more advanced stage. On the contrary, diagnosis of advanced stage prostate cancer has been declining in developed countries, such as the United Kingdom [37]. This is likely due to the difference in the cancer patterns and having the awareness and access to appropriate medical care to diagnose symptomatic cancers, such as prostate, thyroid and breast cancers in developed countries.

The study has several strengths. First, cancer diagnoses were confirmed with biopsy, as opposed to diagnoses made solely clinically or from patient surveys. Second, the study was conducted at Tikur Anbessa Hospital, the country's sole cancer referral center. Finally, a large representative sample size was used over a 5-year time-period. One of the study limitations is the fact that it was based on patients who were able to have a biopsy done. Many factors could influence this, including whether or not a patient was able to present to appropriate medical facility and obtained a timely referral to Tikur Anbessa Hospital. It also depends on whether or not the patient was able to undergo a biopsy and on the availability of equipment and technical expertise in a low resource country. Finally, nearly half of the cancers were unstageable. These limitations could underestimate certain types of cancers and should be considered when interpreting the study findings and future studies should be designed to identify factors associated with common cancer occurrences in Ethiopia.

In conclusion, we found cancers with effective screening tests, such as cervical, breast and colorectal cancers are common in Ethiopia and significant proportions of these were diagnosed at advanced stages, typically several months after onset of symptoms. Timely access to preventive care along with effective educational and screening strategies is needed in Ethiopia to detect and treat cancer early.

CONFLICTS OF INTEREST

No potential conflicts of interest were disclosed.

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