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Time intervals experienced between first symptom recognition to pathological diagnosis and stage at time of diagnosis among oesophageal cancer patients in Ethiopia: A cross-sectional study

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Abstract

Objective

The aim of this study was to estimate the magnitude of patients and diagnostic delays, stage at diagnosis, and determinant factors among oesophageal cancer patients in Ethiopia.

Methods

Design A cross-sectional study design was employed

Settings and participants Oesophageal cancer patients aged ≥18 years were included from health facilities of Addis Ababa, Ethiopia (n=338) from February 2019 to August 2020. The participants were selected consecutively from six health facilities provided cancer care nearly for 90% of patients.

Main outcomes and measurements The Aarhus statement criterias was applied to classify patient interval (time from first symptom recognition to presentation), and diagnostic interval (time from first presentation to diagnosis). Patient and diagnostic intervals >60 and >30 days were considered delays, respectively. For tumor classification, the American Joint Committee on cancer was used. Data were analyzed using SPSS Version 24. Descriptive statistics were applied to describe patients' characteristics. Poisson regression with robust variance was used to compute prevalence ratios. In all statistical tests, significances were declared at p-value of <0.05.

Results

The mean (SD) age of the study participants was 54.30 ± 12.49 years. About 75% of the study participants had never heard of oesophageal cancer before diagnosis. Dysphagia was commonly mentioned symptom. About 76% of the cases were diagnosed at advanced stages. The median patient interval was 108.5 days and the median diagnostic interval was 77.5 days. After adjusting for confounders, marital status, awareness of oesophageal cancer, cost of transportation, level of

first medical consultation and patient delay > two months were found statistically significant predictors.

Conclusion Oesophageal cancer patients in Ethiopia had prolonged patient and diagnostic delays. Increasing awareness about the commonest symptoms of oesophageal cancer and shortening the time to diagnosis helps to improve the out-come of oesophageal cancer care in Ethiopia.

Keywords: Oesophageal cancer, delay, intervals, tumor stage

Strengths and Limitations

- In Ethiopia, in case of patient and diagnostic delays and determinant factors, it is the first multifacility study
- Poisson regression with robust variance was used to compute the prevalence ratios
- It is the only research based on primary data in Ethiopia that estimates the patient and diagnostic intervals on oesophageal cancer patients
- However, the onset of symptoms is a subjective measurement that patients may not recall the exact time

1. Introduction

Cancers is a group of diseases characterized by uncontrolled growth and spread of abnormal cells. Globally, cancer becomes a major public health concern[1]. Oesophageal cancer, an aggressive tumor of the esophagus that develops in the organ's tissue lining, is the fourth most prevalent cancer in developing countries[2]. Oesophageal cancer caused significant morbidity and mortality throughout the world with a unique hallmark of poor prognosis and survival rate.[3-5] It is the sixth most common cause of mortality among all cancers and the seventh most common cancer in terms of incidence[1].

Squamous cell carcinoma and adenocarcinoma are the two most common subtypes of oesophageal cancer. Squamous cell carcinoma starts in the flat cells that line the esophagus, while adenocarcinoma starts in the cells that produces and releases mucus and other fluids. Oesophageal cancer mortality and incidence rates are higher in Africa than elsewhere in the world, owing mostly to squamous cell carcinoma [6 7].

The five-year survival rate for non-metastatic oesophageal cancer is between 19 and 30%, whereas, the median overall survival time for metastatic oesophageal cancer is between four and six months. Nonetheless, it is not uncommon for oesophageal cancer patients to be diagnosed at advanced stages ,because, in most cases, the oesophageal cancer patients have identified symptoms by the time the disease has reached its advanced stages, then lead to poor patients prognosis and survival rate[5 8 9].

Studies evidenced that the survival rate of oesophageal cancer patients has depended on the patients' commitment in early consultation and shortening the times of pathological diagnosis[10 11]. In practice, however, oesophageal cancer patients frequently have arrived late in

presentation and commonly lately referred to the appropriate health facilities. In addition, literatures also showed that shortening the time to presentation is an important step in reducing late in diagnosis, and improving the prognosis and survival of oesophageal cancer patients[12 13].

Oesophageal cancer is the overwhelming disease and among the commonest cause of cancer deaths in the world. Though, few patients can be cured, the treatment for oesophageal cancer is prolonged, quality of life is significantly compromised and cases fatality rate is high [1].

Ethiopia is a country, geographically located within the highest risk region of oesophageal cancer known to be the oesophageal cancer belt. And, the disease has created a huge burden interms of morbidity and mortality in the country[14]. In addition, few hospital reports revealed that over the last decades, the incidence and burden of oesophageal cancer has been increasing.

In Eastern African countries like Ethiopia, an up-to-date oesophageal cancer data are unequivocally important to design appropriate and resilient strategies. Hence, able to reduce morbidities and mortalities from oesophageal cancer mainly due to delay in patients' consultation and pathological diagnosis [7 15]

In Ethiopia, however, oesophageal cancer is not yet a public health priority, left in dark and is under-researched; as a result, there is no clear evidence about patient and diagnostic intervals and the stage at time of diagnosis. The goal of this study was to determine time to care seeking and pathological diagnosis, and the stage at time of diagnosis of oesophageal cancer patients. Meanwhile, we were also strived to identify predictors of patients and pathological diagnostic delays of > 60 and > 30 days, respectively.

2. Materials and methods

2.1. Study design and sample size

A cross-sectional study design was employed. The study involved 338 oesophageal cancer patients aged ≥18 years from February 2019 to August 2020 in Addis Ababa, Ethiopia. Using the expected proportion (p=32.0%) of patient delay to presentation (>2 months) from a similar study and assuming a 95% level of confidence, a 5% precision and 5% non-response rate [16].

2.2. Settings and participants

The Ethiopian health care delivery system has three tiers: primary, secondary and tertiary level health care facilities that are linked with a referral system. The setup differs slightly between urban and rural settings. The main healthcare service in the metropolitan city, such as Addis Ababa, Ethiopia's capital, includes public health centers, private clinics, and primary hospitals. Secondary and tertiary healthcare levels are general hospitals and specialty hospitals, respectively. The primary healthcare services in rural areas are made up of a health post, a health center, and primary hospitals. Secondary and tertiary healthcare levels are general hospitals and specialty hospitals, respectively. Nurses and health officers are the primary staff of public health centers, with the goal of providing preventative and primary health care services.

In the case of cancers, such as oesophageal cancer, health workers at the primary level care facilities are only expected to refer patients to general hospitals and other high-level facilities for further diagnosis and treatments[17].

Sampling procedure

A consecutive sampling method was used to recruit study participants. Six health facilities in Addis Ababa (Tikur Anbesa Specialized Hospital, St. Paul Hospital Millennium Medical College, Betezata Hospital, Hallelujah General Hospital, Landmark Hospital, and United Vision Medical Services Centre) were selected, where nearly 90% of cancer patients being diagnosed and treated. At each health facility, one focal person was assigned to identify eligible oesophageal cancer patients and communicate with the principal investigator and supervisor. To avoid duplication, the medical chart of the recruited patient was coded in red on the top cover page. Prior to the interview, study participants were informed about the purpose of the study and their right to withdraw under any circumstances without compromisation of any services.

2.3. Variables and Measurements

We used the Aarhus statement criteria to classify patient, diagnostic and symptoms intervals. Thus, patient interval was defined as the interval between the date of first symptom recognition (the time point at which the patient first noticed bodily changes and/or symptoms) and the date of first clinical presentation (the date at which the patient first presented to a healthcare provider after first recognizing symptoms), and symptom interval was defined as the time interval between the date of first symptom recognition and the date of pathological diagnosis[18 19]. The date of symptom recognition was determined based on participants recall. Furthermore, the diagnostic interval was defined as the time elapsed between the date of first clinical presentation and the date of the final pathological diagnosis (the date at which the first histological or cytological confirmation of this malignancy was documented in the pathology report). The pathology report of the patient was used to determine the date of diagnosis [18 19]. Tumors were

classified using the Tumor-Node-Metastasis method from the 7th edition of the American Joint Committee on Cancer (AJCC)[20]. And cases were histologically and endoscopically confirmed. Stages I and II were classified as early stages of diagnosis, while stage III and IV were classified as late stages of diagnosis [21]. A pretest for cultural suitability and clarity was performed prior to administering the tool to the participants. When the eligible participants were arrived for treatment, trained nurses interviewed them individually in a semiprivate room in Amharic. If the participants couldn't recall the exact date of their first symptom recognition, they were asked to provide a month or year ('was it at the beginning, middle, or end of the year'). For those who only remembered the month, the date was estimated to be the 15th day of that month. If the participants only said at the beginning, middle or at the end of the year, the estimated date was 15th of February, June or October of the year, respectively; if they only said the year, the estimated date was June 30th of that year. We performed sensitivity analyses excluding patients who had only remembered the beginning, middle or end of the year or a year for the date of first symptom recognition or clinical presentation[22].

2.4. Data Analysis

Epi-info version 7 was used for the data entry and SPSS Version 24 was used to analyze the data. Descriptive statistics were calculated for each variable. Numbers and percentages were used to summarize categorical variables. We presented mean and standard deviation for numerical variables with normal distributions, whereas median and IQR were employed for variables with skewed distributions. Patient and diagnostic delays were defined as >60-days patient intervals and >30-days diagnostic intervals, respectively, in the literature [11]. For cross-sectional research, OR is the default measure of association, and logistic regression is often used to estimate. Nevertheless, evidences suggest that when the proportion of the outcome exceeds 10%,

an odds ratio overestimates the risk ratio, leading to incorrect interpretations. As a result, to avoid these limitations, the prevalence ratio is preferred measure of association[23 24]. Hence, Poisson regression with robust variance was used to compute the adjusted prevalence ratios of factors associated with the prevalence of patient and diagnostic delays, as well as factors associated with stage at time of diagnosis. Variables having a p value on bivariable analysis were chosen based on literatures that have an effect on patient and diagnostic delays and stage at time of diagnosis. A two-sided p value of 0.05 was declared as statistically significant.

Patient and public involvement "No patient involved"

3. Results:

Socio-demographic and socio- economic characteristics of the study participants

We approached 351 participants those histologically confirmed and clinically staged for oesophageal cancer and among 96.3% of them were provided their oral for participation. The participants in the study were 54.30 ± 12.49 years old on average (SD). Male participants accounted for 52.4% of the total participants. More than half of the participants (52%) were above the age of 55 years, only 7.0% of the participants were below the age of 35 years. Approximately, two-thirds of the study participants were from rural areas of Ethiopia and were unable to read and write. Muslims and farmers participants accounted 52% and 38% of the total participants respectively. At the time of data collection, 75% of the participants in the study were married. More than half of the participants in the study earned not more than one USD per day or about 29 Ethiopian Birr. Among the participants, 73% had to travel long distances to receive cancer-specific diagnosis and treatment services, and had to pay more than seven USD or 203 Ethiopian Birr for a single trip just to cover only for transportation costs. Furthermore, nearly three-quarters of the study participants had paid their medical expenses out of their pockets **(Table 1).**

Table 1: Socio-demographic and socio-economic characteristics of esophageal cancer patients Addis Ababa, Ethiopia, February 2019 to August 2020 (n=338)

Variables	Frequency	Percent
Age categories (years)		
<35	24	7
35-44	46	14
45-54	91	27
≥55	177	52
Gender		
Male	177	52.4
Female	161	47.6
Religion		
Christianity	159	47
Islam	175	51.8
Wakefata	4	1.2
Residency		
Urban	126	37.3
Rural	212	62.7
Educational status of participants		
Unable to read and write	209	61.8
1-8 grade	72	21.3
9-12 grade	37	10.9
Diploma and above	20	5.9
Occupation of participants		
Government workers	38	1.2
House wife	118	34.9
Merchant	20	5.9
Private worker	35	10.4
Farmer	127	37.6
Marital status of participants during the data collection time		
Married	246	72.8
Single	92	27.2
Monthly income (USD)		
<35	171	50.6
35-106	130	38.5
106.6-177	21	6.2
>177	16	4.7
One way cost of transport (USD*)		
<7 dollar	93	27.5
>=7 dollar	245	72.5
Sources of medical expenses		
Employing organization	1	0.3
Free medical care	72	21.3
Government insurance	19	5.6
Out of pocket	242	71.6
Private insurance	4	1.2

3.1. Pre-symptomatic and pre-diagnostic characteristics of oesophageal cancer patients

Among the total participants, 21.3 % had reported a history of at least one chronic disease, with diabetes mellitus being the most common one. More than three-fourth of the study participants (77.8%, 95% CI [73.4%, 82.2%]) had never heard of oesophageal cancer prior to diagnosis for oesophageal cancer. For those who heard of oesophageal cancer prior to diagnosis, the main sources (48%) of the information were friends/ family members or neighbors, followed by printed and electronic medias such as (TV, radio, internet) (28%). Only eight participants (2.4%) had reported first degree family history of oesophageal cancer**.**

Dysphagia was the cardinal symptom mentioned by 84.6% of the study participants, followed by odynophagia of 54.1%. Approximately three-fourth of the study participants had linked the first symptom/s to gastritis. All patients had recognized at least one symptom. Moreover, a significant number of patients reported as having more than one oesophageal cancer symptom. About half of the cases stated that they did not take an immediate action for the first symptom/s because they thought that the symptom/s was/ were simple and self-limited. Meanwhile, about a quarter of the cases sought treatment from various traditional healers as a quick fix for the symptom/s**.**

More than half (58.9%) of the study participants felt compelled by their family members to seek medical help for the symptom/s. About half of the cases first went to public health facilities for their first symptom/s (health centers and health posts), followed by public hospitals (16%). At their first visit to health facilities, approximately to two-third of the study participants first contacted health officers and nurses as health care providers. The mean (SD) of health facilities visited by the cases until the data collection time was 6.6 ± 3.2. Meanwhile, 11% of the

participants had visited more than 10 health facilities until data collection time. The mean (SD) number of visits to health facilities by participants until the data collection time was 7.45 ± 3.63. The prominent reason mentioned by the participants for consultation delays was a financial issue, (61.5%).

3.2. Diagnosis characteristics of oesophageal cancer patients

Out of the total oesophageal cancer patients, about 76% (95% CI [71.0 %, 80.7%]) of the study participants were diagnosed at late stages (III and IV), and only 24% of the participants were diagnosed at early stages (I and II). In terms of histologic subtypes, 85.8%, 13.3% and 0.89% were oesophageal squamous cell carcinoma, oesophageal adenocarcinoma and undifferentiated carcinomas, respectively. For those with available grade on biopsy report, 59.8%, 15.7% and 8.9%) were well differentiated, unspecified and poorly differentiated respectively. Endoscopic appearance was ulcerative in 49.4% followed by an obliterative of 34.9%. In case of tumor locations, middle oesophagus 41.1% and lower oesophagus 30.8%. The most noticeable single factor mentioned by majority (78%) the participants for the diagnostic delay was longer appointments primarily associated with the health care organizations **(Table 2).**

Table 2: Diagnostic history of oesophageal cancer patients from February 2019 to August 2020Addis Ababa, Ethiopia,

Variable	Frequency	Percent
Stage at first diagnosis		
Stage I	20	6.0
Stage II	58	17.2
Stage III	167	49.4
Stage IV	76	22.4
Unknown	17	5.0
Histological sub-type		
Oesophageal squamous carcinoma	290	85.8
Oesophageal adenocarcinoma	45	13.3
Unknown	3	0.9
Histopathological differentiations		
Well-differentiated	202	59.8
Moderate differentiated	47	13.8
Poor differentiated	30	8.9
Undifferentiated	6	1.8
Unspecified	53	15.7
Morphology of tumor during upper gastrointestinal endoscopy		
Ulcerative	167	49.4
Obliterative	118	34.9
Proliferative	45	13.3
Ulceroproliferative	8	2.4
Tumor location(Histology)		
Upper (cervical)	95	28.1
Middle oesophagus	139	41.1
Lower oesophagus	104	30.8

Patient and diagnostic intervals

The median (IQR) patient interval was 108.5 (60.5-215) days. The magnitude of patient delay was 75% (95% CI [69.8%, 79.3%]). About ten percent of the participants had visited health facilities after a year of first symptom recognition. Only about 8% of the participants consulted health facilities within one month. Great majority (71%) of the participants mentioned their reason for late patients' consultation was financial problems (59.5%) followed by not bothering about the disease. The median (IQR) of diagnostic interval was 77.5 (39-133) days. The magnitude of diagnostic delay was 81.9% (95% CI [77.9%, 86.2%]). Three percent of those who took part in the study received diagnostic confirmation after a year of waiting and 18% of the participants got diagnosis confirmation less than a month. The median (IQR) symptom interval was 215(130-353) days.

3.3. Determinate factors associated with patient and diagnostic delays

In the bivariable analysis, participants unable to read and write (PR=1.2, 95% CI [1.05, 1.43]), being house wife (PR=1.14, 95%CI [1.01, 1.29]), single participants (PR=1.08, 95% CI [1.03, 1.14]) monthly income <35USD (PR=1.29,95%CI[1.09,1.55]) and 35-106 USD (PR=1.3,95%CI[1.17]CI[1.09,1.55]family monthly income<53USD(PR=1.17,95%CI[1.02,1.33]) and 53-141 USD (PR=1.17,95% CI [1.02,1.34]) and never heard of oesophageal cancer prior to diagnosis (PR=1.11,95%CI [1.03,1.97]) were significantly associated with higher prevalence of patient delay. However, after an adjustment, we only found marital status (Adjusted PR=1.09, 95% CI [1.03, 1.15]) and never heard of oesophageal cancer prior to diagnosis (Adjusted PR=1.08, 95% CI [1.03, 1.15]) were found statistically significant to increase the prevalence of patients delay among oesophageal cancer patients **(Table 3).**

Table 3 : Determinant factors associated with patient delay (>60 days) among oesophageal cancer patients from February 2019 to August 2020, Addis Ababa, Ethiopia (n=324)

Patient characteristics	Patient delay		Unadjusted		Adjusted	
	Yes (%)	No (%)	PR (95% CI)	P-value	PR (95% CI)	P-value
Age of participants (years)						
<35	14 (66.7)	7 (33.3)	Ref.		Ref.	
35-44	26 (59.1)	18 (40.9)	0.96 (0.82,1.11)	0.55	0.96 (0.86,1.07)	0.43
45-54	63 (72.4)	24 (27.6)	1.03 (0.91,1.18)	0.62	1.03 (0.94, 1.12)	0.56
≥55	140 (81.4)	32 (18.6)	1.10 (0.96,1.23)	0.18	0.99 (0.91,1.08)	0.81
Gender						
Male	127 (73.8)	45 (26.2)	0.99 (0.94,1.04)	0.61		
Female	116 (76.3)	36 (23.7)	Ref.		Not included	
Residency						
Urban	88 (71.0)	36 (29.0)	Ref.		Ref.	
Rural	155 (77.5)	45 (22.5)	1.04 (0.98,1.10)	0.19	1.04 (0.97,1.11)	0.29
Educational status of participants						
Unable to read and write	155 (77.1)	46 (22.9)	1.2 (1.05,1.43)	0.01	1.11 (0.94, 1.29)	0.22
Grade 1-8	56 (81.2)	13 (18.8)	1.25 (1.07,1.46)	0.006	1.15 (0.97, 1.35)	0.10
Grade 9-12	23 (67.6)	11 (32.4)	1.16 (0.97,1.38)	0.11	1.08 (0.91, 1.29)	0.38
Diploma and above	9 (45.0)	11 (55.0)	Ref.			
Occupation of participants						
Private worker	17 (56.7)	13 (43.3)	Ref.		Ref.	
Government workers	24 (68.6)	11 (31.4)	1.08 (0.93,1.24)	0.32	1.02 (0.94, 1.11)	0.57
House wife	82 (78.8)	22 (21.2)	1.14 (1.01,1.29)	0.03	0.94 (0.86, 1.02)	0.14
Merchant	24 (82.8)	5 (17.2)	1.17 (1.02,1.34)	0.03	1.03 (0.94,1.12)	0.54
Farmer	96 (76.2)	30 (23.8)	1.13(0.99,1.27)	0.06	0.93 (0.85, 1.02)	0.12
Marital status of participants during the data collection time						
Single	76 (85.4)	13 (14.6)	1.08 (1.03,1.14)	0.002	1.09 (1.03, 1.15)*	0.001
Married	167 (71.1)	68 (28.9)	Ref.			
Monthly income						
<35 US dollar	124 (78.5)	34 (21.5)	1.29 (1.09,1.55)	0.004	1.22(1.005,1.48)	0.045
35-106 US dollar	101 (78.9)	27 (21.1)	1.3 (1.09,1.55)	0.004	1.22(1.22,1.48)	0.042
106.6-177 US dollar	12 (54.5)	10 (45.5)	1.12 (0.90,1.39)	0.29	0.46(1.09)	0.46
>177 US dollar	6 (37.5)	10 (62.5)	Ref.			
One way cost of transport (USD)						
<7 dollar	71 (77.2)	21 (22.8)	1.02 (0.96,1.08)	0.56	Not included	
≥7 dollar	172 (74.1)	60 (25.9)	Ref			
Family monthly income(USD)						
<53	128 (77.1)	38 (22.9)	1.17 (1.02, 1.33)	0.025	1.12(0.98,1.27)	0.09
53-141	84 (77.8)	24 (22.2)	1.17 (1.02,1.34)	0.024	1.13(0.99,1.28)	0.08
141.4-230	18 (72.0)	7 (28.0)	1.13 (0.96,1.33)	0.14	1.1(0.94,1.29)	0.26
>230	13 (52.0)	12 (48.0)	Ref.			

Table 3 cont.….

Patient characteristics	Patient delay		Unadjusted		Adjusted	
	Yes (%)	No (%)	PR (95% CI)	P-value	PR (95% CI)	P-value
Prior information about esophageal cancer						
No	198 (79.0)	53 (21.0)	1.11 (1.03,1.97)	0.007	1.08(1.02,1.17)*	0.04
Yes	44 (61.1)	29 (38.9)	Ref.			
Family size in the house hold						
<3	9(64.3)	5 (35.7)	Ref.		Not included	
3-5	108 (74.0)	38 (26.0)	1.06 (0.90, 1.24)	0.48		
>5	126 (76.8)	38 (23.2)	1.08 (0.92, 1.26)	0.36		
Visiting traditional healers						
No	180(73.2)	66(26.8)	Ref.			
Yes	63(80.8)	15(19.8)	1.04(0.99,1.11)	0.15	1.04(0.98,1.10)	0.23

Meanwhile, in the bivariable analysis, single participants (PR=1.8,95%CI[1.74,1.85]),family monthly income 53-141 USD(PR=0.91,95%CI [0.85,0.99]),cost transport (one trip)>7USD(PR=1.07,95%CI[1.06,1.13]), first medical consultation at health center (PR=0.93,95%CI[0.88,0.99]) and number of health facilities visited < 3 health facilities (PR=0.93, 95%CI [0.87,0.99]) were significantly associated with higher prevalence of diagnostic delay. However, after an adjustment or in the multivariable analysis, we only found marital status (Adjusted PR=1.2, 95% CI [1.11,2.10]), sources of medical expenses (Adjusted PR=1.2,95% CI[1.13,2.40]), cost of transportation (Adjusted PR=1.2,95% CI [1.12,1.54]) and first medical consultation to health facilities (Adjusted PR= 1.4, 95% CI [1.20,2.30]) were statistically significant to increase the prevalence of diagnostic delay among oesophageal cancer patients **(Table 4).**

Table 4: Factors associated with diagnostic delay (>30 days) among oesophageal cancer diagnosed from February 2019 to August 2020, Addis Ababa Ethiopia (n=326)

Patient characteristics	Diagnosis delay		Unadjusted		Adjusted	
	Yes (%)	No (%)	PR (95% CI)	P-value	PR (95% CI)	P-value
Age of participants (years)						
<35	17 (77.2)	5 (22.8)	Ref.		Ref.	
35-44	33 (75.0)	11 (25.0)	0.94 (0.84, 1.04)	0.24	0.96(0.86,1.07)	0.45
45-54	75 (87.2)	11 (12.8)	1.01 (0.92, 1.09)	0.92	1.02(0.93,1.11)	0.69
≥55	140 (80.5)	34 (19.5)	0.97 (0.89, 1.05)	0.45	0.97(0.89,1.06)	0.53
Gender						
Male	144(83.2)	29(16.8)	1.02(0.97,1.06)	0.51		
Female	123(80.4)	30(19.6)	Ref.		Not included	
Residency						
Urban	102(82.9)	21(17.1)	Ref		Not included	
Rural	165(81.3)	38(18.7)	0.99(0.95,104)	0.71		
Marital status of participants during the data collection time						
Single	78(88.6)	10(11.4)	1.80(1.74,1.85)	0.0001	1.2 (1.1,2.10)**	0.04
Married	189(79.4)	49(20.6)	Ref.		Ref.	
Monthly income						
<35 US dollar	129(80.1)	32(19.9)	0.96(0.88,1.05)	0.39		
35-106 US dollar	103(81.1)	24(18.9)	0.97(0.88,1.06)	0.47		
106.6-177 US dollar	17(77.3)	5(22.7)	1.04(0.95,1.15)	0.40		
>177 US dollar	12(66.7)	6(27.3)	Ref.		Not included	
Family monthly income(USD)						
<53	139(82.7	29(17.3)	0.95(0.89,1.01)	0.11	0.98(0.88,1.09)	0.69
53-141	80(74.8)	27(25.2)	0.91(0.85,0.99)	0.008	0.91(0.82,1.002)	0.05
141.4-230	20(80.0)	5(20.0)	1.02(0.95,1.09)	0.57	1.01(0.93,1.09)	0.84
>230	19(73.1)	7(26.9)	Ref.		Ref.	
One way cost of transport (USD)						
<7 dollar	67(73.6)	24(26.4)	Ref.			
≥7 dollar	200(85.1)	35(14.9)	1.07(1.06,1.13)	0.03	1.2(1.12,1.54)**	0.04
First medical consultation						
Health post	35(87.5)	5(12.5)	0.99(0.94,1.07)	0.96	1.01(0.94,1.08)	0.83
Health center	123(77.4)	36(22.6)	0.93(0.88,0.99)	0.015	1.4 (1.2, 2.30)**	0.049
Private clinic	38(88.4)	5(11.6)	0.99(0.94,1.06)	0.78	1.01(0.94,1.08)	0.87
Private hospital	24(72.7)	9(27.3)	0.91(0.82,1.002)	0.054	0.92(0.83,1.02)	0.10
Public hospital	46(90.2)	5(9.8)	Ref.		Ref.	
Visiting traditional healers						
No	201(82.0)	44(18.0)	Ref.			
Yes	66(81.5)	15(18.5)	0.99 (0.95,1.05)	0.91	Not included	
Family size						
<3	9(64.3)	5(35.7)	Ref.		Not included	
3-5	122(83.6)	24(16.4)	0.99(0.89,1.09)	0.83		
>5	133(80.1)	33(19.9)	0.97(0.87,1.08)	0.57		

Table 4 cont.…

Patient characteristics	Diagnosis delay		Unadjusted		Adjusted	
	Yes (%)	No (%)	PR (95% CI)	P-value	PR (95% CI)	P-value
First consulted health care provider						
HEW	38(84.4)	7(15.6)	1.018(0.95,1.09)	0.62		
Nurse	61(68.5)	14(31.5)	1.001(0.94,1.07)	0.97		
Health officer	82(82.0)	18(18.0)	1.005(0.95,1.06)	0.87		
Medical doctor	86(81.1)	20(18.9)	Ref.		Not included	
Number of health facilities visited for diagnosis						
< 3 health facilities	13(72.2)	5(27.8)	Ref.		Ref.	
3-6 health facilities	153(80.5)	37(19.5)	0.93(0.87,0.99)	0.02	0.93(0.87,1.22)	0.054
7-10 health facilities	67(81.7)	15(18.3)	0.93(0.87,1.004)	0.06	0.94(0.87,1.01)	0.108
>10 health facilities	29(82.9)	6(17.1)	0.94(0.86,1.026)	0.17	0.94(0.86,1.03)	0.19
Source of medical expenses						
Free medical care	57(79.2)	15(20.8)	Ref.			
Governmental insurance	11(61.1)	7(38.9)	0.90(0.78.1.044)	0.16	1.22 (1.13, 2.40)*	0.048
Out of pocket	199(84.3)	37(15.7)	1.03(0.97,1.09)	0.34	1.03(0.98,1.09)	0.26
Prior information about oesophageal cancer						
No	205(81.0)	48(19.0)	0.98(0.93,1.03)	0.42		
Yes	62(85.0)	11(15.0)	Ref.		Not included	

3.4. Factors associated with advanced stages at diagnosis among oesophageal cancer patients

In the bivariable analysis, marital status, single (PR=1.16, 95% CI [1.02, 1.30]) and patients delay of > two months (PR=1.38, 95% CI [1.14, 1.68]) were significantly associated with late stage at first diagnosis. However, after an adjustment or multivariable analysis, marital status (Adjusted PR=1.16, 95% CI [1.03, 1.31]), female participants (Adjusted PR=1.15, 95% CI [1.015, 1.31]), patient delay > two months (Adjusted PR=1.41, 95% CI [1.15, 1.69])) and symptom intervals (Adjusted PR=1.26, 95% CI [1.12, 1.67]) were statistically significant to increase the prevalence of advanced stage at time of diagnosis **(Table 5).**

Table 5: Factors associated with advanced stages at diagnosis among oesophageal cancer patients from February 2019 to August 2020 Addis Ababa, Ethiopia (n=321).

Patient characteristics	Advanced-stage		Unadjusted		Adjusted	
	No (%)	Yes (%)	PR (95% CI)	P-value	aPR (95% CI)	P-value
Age						
<35	5(21.7)	18(78.3)	Ref.		Not included	
35-44	12(27.3)	32(72.7)	0.88(0.68,1.14)	0.34		
45-54	22(25.6)	64(74.4)	0.90(0.72,1.13)	0.36		
≥55	40(23.8)	128(76.2)	0.92(0.75,1.13)	0.44		
Gender						
Male	45(27.1)	121(72.9)	Ref.		Ref.	
Female	33(21.3)	122(78.7)	0.93(0.82,1.05)	0.22	1.15 (1.01,1.31)*	0.049
Residency						
Urban	33(27.5)	87(72.5)	Ref.			
Rural	45(22.4)	156(77.6)	1.07(0.94,1.22)	0.32	Not included	
Educational status of participants						
Unable to read and write	44(22.2)	154(77.8)	1.14(0.83,1.56)	0.42		
Grade 1-8	17(24.6)	52(75.4)	1.10(0.79,1.54)	0.57		
Grade 9-12	11(31.4)	24(68.6)	1.01(0.69,1.46)	0.99		
Diploma and above	6(31.6)	13(68.4)	Ref.		Not included	
Occupation of participants						
Private worker	5(17.2)	24(82.8)	Ref.			
Government workers	13(35.1)	24(64.9)	0.78(0.59,1.05)	0.10	0.77 (0.57, 1.02)	0.07
House wife	28(24.8)	85(75.2)	0.91(0.75,1.11)	0.34	0.89 (0.73,1.09)	0.25
Merchant	6(30.0)	14(70.0)	1.03(0.80,1.32)	0.83	0.99 (0.78,1.28)	0.98
Farmer	29(23.8)	93(76.2)	0.92(0.76,1.12)	0.41	0.89 (0.74,1.09)	0.29
Marital status of participants during the data collection time						
Single	14(16.1)	73(83.9)	1.16(1.02,1.30)	0.02	1.16 (1.03,1.31)*	0.015
Married	64(27.4)	170(72.6)	Ref.		Ref.	
Monthly income (USD)						
<35	37(22.8)	125(77.2)	0.95(0.74,1.20)	0.69		
35-106	31(25.6)	90(74.4)	0.92(0.71,1.18)	0.50		
106.6-177	7(31.8)	15(68.2)	0.84(0.58,1.22)	0.35		
>177	5 (31.3)	11(68.7)	Ref.		Not included	
Family monthly income(USD)						
<53	38(22.9)	128(77.1)	1.01(0.80,1.26)	0.98		
53-141	30(28.3)	76(71.7)	0.93(0.73,1.19)	0.57		
141.4-230	5(21.7)	18(78.3)	1.07(0.81,1.42)	0.62		
>230	6(23.1)	20(76.9)	Ref.		Not included	
Prior information about esophageal cancer						
No	59(23.5)	192(76.5)	1.05(0.89,1.23)	0.55	Not included	
Yes	19(27.1)	51(72.8)	Ref.			

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Patient characteristics	Advanced-stage		Unadjusted		Adjusted	
	No (%)	Yes (%)	PR (95% CI)	P-value	aPR (95% CI)	P-value
Family size in the house hold						
<3	6(37.5)	10 (62.5)	Ref.			
3-5	38(26.6)	105(73.4)	0.84(0.68,1.04)	0.10	0.82 (0.66, 1.03)	0.08
>5	38(23.5)	124(76.5)	0.88(0.71,1.07)	0.20	0.87 (0.69 ,1.07)	0.19
Visiting traditional healers						
No	61(25.2)	181(74.8)	Ref.			
Yes	17(21.5)	62(78.5)	1.05(0.92,1.20)	0.49	Not included	
One way cost of transport (USD)						
<7 dollar	28(31.1)	62(68.9)	Ref.			
≥7 dollar	50(21.6)	181(78.4)	1.14(0.98,1.33)	0.10	1.12 (0.96 , 1.30)	0.15
First medical consultation						
Health post	6(15.4)	33(84.6)	1.11(0.94,1.32)	0.22	1.11 (0.92, 1.33)	0.27
Health center	48(30.6)	109(69.4)	0.86(0.73,1.02)	0.08	0.87 (0.73 ,1.04)	0.12
Private clinic	6(14.3)	36(85.7)	1.06(0.88,1.27)	0.52	1.05 (0.88 , 1.30)	0.57
Private hospital	10(32.2)	21(67.8)	0.84(0.64,1.11)	0.21	0.83 (0.63 , 1.09)	0.18
Public hospital	10(19.2)	42(80.8)	Ref.			
Source of medical expenses						
Free medical care	19(26.8)	52(73.2)	Ref.		Not included	
Governmental insurance	7(38.9)	11(61.9)	1.06(0.91,1.24)	0.47		
Out of pocket	52(22.4)	180(77.6)	0.83(0.56,1.24)	0.37		
Patient delay (> 2 months)						
No	31(40.8)	45(59.2)	Ref		Ref.	
Yes	42(18.2)	189(81.8)	1.38(1.14,1.68)	0.001	1.41 (1.15, 1.69)*	0.001
Diagnosis delay(> 1 month)						
No	16(29.1)	39(70.9)	Ref.			
Yes	58(22.7)	197(77.3)	1.09(0.91,1.31)	0.36	Not included	
Number of health facilities visited						
<3	6(30.0)	14(70.0)	Ref.			
3-6	50(27.0)	135(73.0)	1.04(0.77,1.41)	0.79		
7-10	19(23.5)	62(76.5)	1.09(0.80,1.49)	0.57		
>10	5(14.3)	30(85.7)	1.31(0.96,1.77)	0.08		
Number of times visited health facilities prior to final diagnosis						
< 3 times	7(31.8)	15(68.2)	Ref.		Ref.	
3-6 times	40(26.8)	109(73.2)	1.07(0.79,1.45)	0.65	0.89 (0.69 , 1.16)	0.39
7-10 times	19(21.8)	68(78.2)	1.15(0.84,1.56)	0.38	0.93 (0.70 , 1.23)	0.61
>10 times	12(19.0)	51(81.0)	1.19(0.87,1.62)	0.24	1.12 (0.85 , 1.46)	0.43
Symptom interval						
< 3 months	12(36.4)	21(63.6)	Ref.		Ref.	
3-6 months	26(29.5)	62(70.3)	1.11(0.83,1.48)	0.49	1.09 (0.81 , 1.46)	0.51
> 6months	37(19.7)	151(80.3)	1.26(0.97,1.65)	0.08	1.26 (1.12 , 1.67)*	0.048

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Discussion

Longer consultation and diagnostic delays, as well as late stages at the time of diagnosis, were hypothesized before we started this study. We estimated prolonged presentation and diagnostic delays. In addition, most of the cases were diagnosed at advanced stages. The most common reason for patient delays was financial constraints. About 11% of the cases were forced to visit an average of 10 different health facilities looking for affordable care. The dominant histological subtype was oesophageal squamous carcinoma. In addition, risk factors for late consultation, diagnostic and late stage at the time of diagnosis were identified.

The median patient intervals were much lower in studies [11 21 25-27]. compared to the patient interval estimated from our study. This significant variation could be related to the socio-cultural, socio-economic differences in health-seeking behavior and a lack of awareness about oesophageal cancer symptoms across the groups/communities. Furthermore, the late presentation is heavily attributed to limited access to care as most of our participants were from rural areas and cancer care is provided by secondary and tertiary level care facilities located far from the most rural dwellers and mostly illiterates. Our study, however, is analogues to a study conducted in South Africa[28]. The comparable socio-economic, socio-cultural and literacy rates of the societies may explain for the parallel presentation delays.

The median diagnostic interval estimated from our study is higher than that of prior studies.[11 21 25 26]. The discrepancy may be the differences in diagnostic workups and the availability of experienced and trained health professionals in cancer related diagnostic and treatment services. On the other hand, our study is in line with the study[28]. The similarities could be attributed to the fact that diagnostic workups and health facilities status are comparable throughout African countries.

The proportion of advanced stages at first diagnosis is higher compared to study [21] this could be related to longer patient and diagnostic intervals and socio-economic difference among the communities. The cardinal symptom reported by majority of our participants was dysphagia this result is comparable with studies [21 26 27]. We discovered that oesophageal squamous carcinoma was the most prevalent, which is consistent with other studies. [21 29 30].

Sizable amount of oesophageal cancer patients were diagnosed at advanced stages and this is comparable with studies. [29 31]. However, the proportion of those diagnosed with oesophageal cancer early is relatively higher in this study [30]. Increased patient delay (> two months) was found to be exacerbated by socio-economic level in our study. Our finding is equivalent to this study [32] , which evidenced those patients with lower socio-economic status sought medical help later. Furthermore, socioeconomic status has had an important influence in patients being diagnosed at advanced stages, which is similar to the findings of the study [32].

As an immediate measure for their symptom/s, a large percentage of oesophageal cancer patients contacted various traditional healers. This finding is consistent with the findings of a qualitative study conducted in Ethiopia's in Oromia Regional State [33]. The study's comparability is owing to the societies' similar socio-economic and socio-cultural characteristics. The prevalence of diagnostic delay was higher in single patients than the married participants. Thus, being married might have a better chance to seek medical care than unmarried participants. The reason could be, partners may influence each other on decision making to seek care as early as possible. In our findings, oesophageal cancer that paid their medical expense from their own pocket had longer patient interval than patients whose medical expenses covered by other organizations. The reason could be, they ignore the symptoms because patients with low socio-economic status had other unmet survival felt needs than investing money for medical cares [34].

4. Conclusion

Oesophageal cancer patients in Ethiopia had longer patients' presentation, diagnostic and symptom intervals. Moreover, majority of the oesophageal cancer patients had diagnosed at advanced stages (III and IV). Marital status and having never heard of oesophageal cancer prior to diagnosis were found to be predictors of increased patient intervals. The levels of first health facilities visited for medical consultation and the cost of transportation were identified as key factors in increasing diagnostic intervals. Furthermore, marital status, gender, patient delay of more than two months and symptom interval were revealed to be statistically significant factors in the occurrence of advanced stages at time of diagnosis. Patients' intervals could be shortened by increasing their awareness of oesophageal cancer symptoms.

Abbreviations

AJCC: American Joint Committee on Cancer

APR: Adjusted Prevalence Ratio

SD: Standard Deviation

IQR: Inter Quartile Range

P: Proportion

PR: Prevalence Ratio

USD: United States Dollar

Ethics approval and informed consent

The ethical clearance was obtained from the Institutional Review Board (IRB) of Addis Ababa University College of Health Sciences with a protocol number of 080/18/SPH. The study followed basic ethical principles of Helsinki declaration for medical research involving human

participants[35]. All of the study participants were informed about the purpose and procedure of the research and their right to withdrawal from the study at any time. Written informed consent was obtained from each of the study participants. Meanwhile, the study participants were agreed to the extent that the finding of this study will be subjected to publication. Participants were well informed not to disclose their information to a third person. The information was kept secured and put confidentially with the first author.

Data availability

Data will be available up on request

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Competing interests

There is no competing interest of this research

Authors' contributions

All authors contributed from the conception of idea up to data analysis and write up. They also participated in drafting or revising of the article and have agreed on to which journal the article shall be submitted and have given final approval of the version to be published, and agreed to be accountable for all aspects of the work. Specifically, BD was conceptualized the topic of interest, involved in data collection, coding, cleaning, analysis, interpretation of the result unto preparation of the manuscript. FE was involved in proposal development, planning the fieldwork

and result section. And RY, MA, SG and AA were involved in proposal development, data analysis and write up and in critical reviewing of manuscript.

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Time intervals from first symptom recognition to pathological diagnosis among oesophageal cancer patients in Ethiopia: A cross-sectional study

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Abstract

Objective

The aim of this study was to estimate the time intervals from first symptom recognition to pathological diagnosis among oesophageal cancer patients in Ethiopia.

Methods

Design A cross-sectional study design was employed

Settings and participants Oesophageal cancer patients aged ≥18 years were included from health facilities of Addis Ababa, Ethiopia (n=338) from February 2019 to August 2020. The participants were selected consecutively from six health facilities provided cancer care nearly for 90% of patients.

Main outcomes and measurements The Aarhus statement criterias was applied to classify patient interval (time from first symptom recognition to presentation), and diagnostic interval (time from first presentation to diagnosis). Patient and diagnostic intervals >60 and >30 days were considered as delays, respectively. For tumor classification, the American Joint Committee on cancer was used. Data were analyzed using SPSS Version 24. Descriptive statistics were applied to describe patients' characteristics. Poisson regression with robust variance was used to compute prevalence ratios. In all statistical tests, significances were declared at p-value of <0.05.

Results

The mean (SD) age of the participants was 54.30 ± 12.49 years.

Prior to diagnosis, 78% of the study participants had never heard of oesophageal cancer and believed suffering from gastritis. Dysphagia was commonly mentioned symptom. About 76% of the cases were diagnosed at advanced stages (III and IV). The median patient interval was 108.5 days and the median diagnostic interval was 77.5 days. After adjusting for confounders, marital

status, lack of awareness of oesophageal cancer, cost of transportation, first medical consultation and patient delay > two months were found statistically significant predictors.

Conclusion Oesophageal cancer patients in Ethiopia had prolonged patient and diagnostic intervals. Increasing awareness about the commonest symptoms of oesophageal cancer and shortening the time to diagnosis will help to improve the out-come of oesophageal cancer care in Ethiopia.

Keywords: Oesophageal cancer, delay, intervals, tumor stage

Strengths and Limitations

- In Ethiopia, in case of patient and diagnostic interval and associated factors, it is the first multifacility study
- Poisson regression with robust variance was used to compute the prevalence ratios
- It is the only research based on primary data in Ethiopia that estimates the patient and diagnostic intervals on oesophageal cancer patients
- However, the onset of symptoms is a subjective measurement that patients may not recall the exact time

1. Introduction

Cancer is a group of diseases in which abnormal cells grow and spread uncontrollably. Cancer has become a major public health concern on a global scale [1]. Oesophageal cancer is the fourth most common cancer in developing countries, and it is an aggressive tumor of the esophagus that develops in the organ's tissue lining [2]. Oesophageal cancer, which has a dismal prognosis and survival rate, has caused considerable morbidity and mortality around the world from the last three decades [3-5]. Globally, oesophageal cancer was the sixth most common cause of mortality among all cancers and the seventh most common cancer in terms of incidence[1].

The two most prevalent subtypes of oesophageal cancer are squamous cell carcinoma and adenocarcinoma. Adenocarcinoma begins in the cells that produce and release mucus and other fluids, whereas squamous cell carcinoma begins in the flat cells that line the esophagus. Oesophageal cancer mortality and incidence are higher in Africa than the rest of the world, with squamous cell carcinoma being the most common type [6 7].

The five-year survival rate of non-metastatic oesophageal cancer is between 19 and 30%, whereas, the median overall survival time for metastatic oesophageal cancer is between four and six months. Nonetheless, it is not uncommon for oesophageal cancer patients to be diagnosed at advanced stages ,because, in most cases, the oesophageal cancer patients have identified symptoms by the time the disease has reached its advanced stages, then lead to poor patients prognosis and survival rate[5 8 9]. The prognosis and time intervals of oesophageal cancer patients has been solely depended on the patients' awareness on symptoms and literates rate that contribute to early consultation and shorter pathological diagnosis periods, according to studies[10 11]. In practice, however, oesophageal cancer patients frequently have arrived late in presentation and commonly lately referred to the appropriate health facilities. In addition,

literatures also showed that shortening the time to presentation is an important step in reducing late in diagnosis, and improving the prognosis and survival of oesophageal cancer patients[12 13].

Oesophageal cancer is the overwhelming disease and among the commonest cause of cancer deaths in the world. Though, few patients can be cured, the treatment for oesophageal cancer is prolonged, quality of life is significantly compromised and cases fatality rate is high [1].

Ethiopia is a country, geographically located within the highest risk region of oesophageal cancer known to be the oesophageal cancer belt. And, the disease has created a huge burden interms of morbidity and mortality in the country[14]. In addition, few hospital reports revealed that over the last decades, the incidence and burden of oesophageal cancer has been increasing.

Diagnostic and consultation delays on cancers are common in underdeveloped countries, such as the Eastern part of Africa, and are closely linked to poor survival rates. As a result, obtaining updated information is crucial for establishing a resilient plan to reduce oesophageal cancer related morbidity and mortality [7 15].

In Ethiopia, however, oesophageal cancer is not yet a public health priority, left in dark and is under-researched; as a result, there is no clear evidence about patient and diagnostic intervals and the stage at time of diagnosis. The goal of this study was to determine time to care seeking and pathological diagnosis, and the stage at time of diagnosis of oesophageal cancer patients. Meanwhile, we were also strived to identify predictors of patients and pathological diagnostic delays of > 60 and > 30 days, respectively.

2. Materials and methods

2.1. Study design and sample size

A cross-sectional study design was employed. The study involved 338 oesophageal cancer patients aged ≥18 years from February 2019 to August 2020 in Addis Ababa, Ethiopia. Using the expected proportion (p=32.0%) of patients delay to presentation (>2 months) from another similar study [16] by assuming a 95% level of confidence, a 5% precision and 5% non-response rate

2.2. Settings and participants

The Ethiopian health care delivery system has three tiers: primary, secondary and tertiary level health care facilities that are linked with a referral system. The setup differs slightly between urban and rural settings. The main healthcare service in the metropolitan city, such as Addis Ababa, Ethiopia's capital, includes public health centers, private clinics, and primary hospitals. Secondary and tertiary healthcare levels are general hospitals and specialty hospitals, respectively. The primary healthcare services in rural areas are made up of a health post, a health center, and primary hospitals. Secondary and tertiary healthcare levels are general hospitals and specialty hospitals, respectively. Nurses and health officers are the primary staff of public health centers, with the goal of providing preventative and primary health care services. In the case of cancers, such as oesophageal cancer, health workers at the primary level care facilities are only expected to refer patients to general hospitals and other high-level facilities for further diagnosis and treatments[17].

Sampling procedure

A consecutive sampling method was used to recruit study participants. Oesophageal cancer patients histologically confirmed and clinically staged came to the selected health facilities were included in the study, whereas critically ill, diagnosed to other cancer types and non-Ethiopian patients were excluded from participation. Six health facilities in Addis Ababa (Tikur Anbesa Specialized Hospital, St. Paul Hospital Millennium Medical College, Betezata Hospital, Hallelujah General Hospital, Landmark Hospital, and United Vision Medical Services Centre) were selected, where nearly 90% of cancer patients being diagnosed and treated. At each health facility, one focal person was assigned to identify eligible oesophageal cancer patients and communicate with the principal investigator and supervisor. To avoid duplication, the medical chart of the recruited patient was coded in red on the top cover page. Prior to the interview, study participants were informed about the purpose of the study and their right to withdraw under any circumstances without compromisation of any services.

2.3. Variables and Measurements

We used the Aarhus statement criteria to classify patient, diagnostic and symptoms intervals. Thus, patient interval was defined as the interval between the date of first symptom recognition (the time point at which the patient first noticed bodily changes and/or symptoms) and the date of first clinical presentation (the date at which the patient first presented to a healthcare provider after first recognizing symptoms), and symptom interval was defined as the time interval between the date of first symptom recognition and the date of pathological diagnosis[18 19]. The date of symptom recognition was determined based on participants recall. Furthermore, the diagnostic interval was defined as the time elapsed between the date of first clinical presentation and the date of the final pathological diagnosis (the date at which the first histological or

cytological confirmation of the malignancy was documented in the pathology report). The pathology report of the patient was used to determine the date of diagnosis [18 19]. Tumors were classified using the Tumor-Node-Metastasis method from the 7th edition of the American Joint Committee on Cancer (AJCC)[20]. And cases were histologically and endoscopically confirmed. Stages I and II were classified as early stages of diagnosis, while stage III and IV were classified as late stages of diagnosis [21]. The interviews were conducted in Amharic, the country's working language. The study tool was initially prepared in English, then translated into Amharic by language translators, and finally back to English to ensure that the two versions were consistent. Experts in cancer research assessed the tool to ensure that the questions were clear and two days training was given data collectors and the supervisor about the objective of the study. A pretest for cultural suitability and clarity was performed prior to administering the tool to the participants. When the eligible participants were arrived for treatment, trained nurses interviewed them individually in a semiprivate room in Amharic. If the participants couldn't recall the exact date of their first symptom recognition, they were asked to provide a month or year ('was it at the beginning, middle, or end of the year'). For those who only remembered the month, the date was estimated to be the 15th day of that month. If the participants only said at the beginning, middle or at the end of the year, the estimated date was 15th of February, June or October of the year, respectively; if they only said the year, the estimated date was June 30th of that year. We performed sensitivity analyses excluding patients who had only remembered the beginning, middle or end of the year or a year for the date of first symptom recognition or clinical presentation[22].

2.4. Data Analysis

Epi-info version 7 was used for the data entry and SPSS Version 24 was used to analyze the data. Descriptive statistics were calculated for each variable. Numbers and percentages were used to summarize categorical variables. We presented mean and standard deviation for numerical variables with normal distributions, whereas median and IQR were employed for variables with skewed distributions. Patient and diagnostic delays were defined as >60-days patient intervals and >30-days diagnostic intervals, respectively, from previous similar study [11]. For cross-sectional research, OR is the common measure of association, and logistic regression is often used to estimate. Nevertheless, evidences suggest that when the proportion of the outcome exceeds 10%, an odds ratio overestimates the risk ratio, leading to incorrect interpretations. As a result, to avoid these limitations, the prevalence ratio is preferred measure of association [23 24]. Hence, Poisson regression with robust variance was used to compute the adjusted prevalence ratios of factors associated with the prevalence of patient and diagnostic delays, as well as factors associated with stage at time of diagnosis. Variables having a p value of <0.25 on bivariable analysis were chosen for the multivariable analysis based on literatures that have an effect on patient and diagnostic delays and stage at time of diagnosis. A two-sided p value of 0.05 was declared as statistically significant.

Patient and public involvement "No patient involved"

3. Results:

Socio-demographic and socio- economic characteristics of the study participants

We approached 351 participants those histologically confirmed and clinically staged for oesophageal cancer and among 96.3% (338) of them were provided their oral consent for participation. The participants in the study were 54.30 ± 12.49 years old on average (SD). Male participants accounted for 52.4% of the total participants. More than half of the participants (52%) were above the age of 55 years, only 7.0% of the participants were below the age of 35 years. Two-thirds of the study participants were from rural areas of Ethiopia and were unable to read and write. Muslims and farmers participants accounted 52% and 38% of the total participants respectively. At the time of data collection, 75% of the participants in the study were married. More than half of the participants in the study earned not more than one USD per day or about 29 Ethiopian Birr. Among the participants, 73% had to travel long distances to receive cancer-specific diagnosis and treatment services, and had to pay more than seven USD or 203 Ethiopian Birr for a single trip just to cover only for transportation costs. Furthermore, nearly three-quarters of the study participants had paid their medical expenses out of their pockets **(Table 1).**

Table 1: Socio-demographic and socio-economic characteristics of esophageal cancer patients Addis Ababa, Ethiopia, February 2019 to August 2020 (n=338)

Variables	Frequency	Percent
Age categories (years)		
<35	24	7
35-44	46	14
45-54	91	27
≥55	177	52
Gender		
Male	177	52.4
Female	161	47.6
Religion		
Christianity	159	47
Islam	175	51.8
Wakefata	4	1.2
Residency		
Urban	126	37.3
Rural	212	62.7
Educational status of participants		
Unable to read and write	209	61.8
1-8 grade	72	21.3
9-12 grade	37	10.9
Diploma and above	20	5.9
Occupation of participants		
Government workers	38	1.2
House wife	118	34.9
Merchant	20	5.9
Private worker	35	10.4
Farmer	127	37.6
Marital status of participants during the data collection time		
Married	246	72.8
Single	92	27.2
Monthly income (USD)		
<35	171	50.6
35-106	130	38.5
106.6-177	21	6.2
>177	16	4.7
One way cost of transport (USD*)		
<7 dollar	93	27.5
>=7 dollar	245	72.5
Sources of medical expenses		
Employing organization	1	0.3
Free medical care	72	21.3
Government insurance	19	5.6
Out of pocket	242	71.6
Private insurance	4	1.2

3.1. Symptoms and awareness of oesophageal cancer

Among the total participants, 21.3 % had reported a history of at least one chronic disease, with diabetes mellitus being the commonest one. More than three-fourth of the study participants (77.8%, 95% CI [73.4%, 82.2%]) had never heard of oesophageal cancer prior to diagnosis for oesophageal cancer. For those who heard of oesophageal cancer prior to diagnosis, the main sources (48%) of the information were friends/ family members or neighbors, followed by printed and electronic medias such as (TV, radio, internet) (28%). Only eight participants (2.4%) had reported first degree family history of oesophageal cancer**.**

Dysphagia was the cardinal symptom mentioned by 84.6% of the study participants, followed by odynophagia of 54.1%. Approximately three-fourth of the study participants had linked the first symptom/s to gastritis. All patients had recognized at least one symptom. Moreover, a significant number of patients reported as having more than one oesophageal cancer symptom. About half of the cases stated that they did not take an immediate action for the first symptom/s because they thought that the symptom/s was/ were simple and self-limited. Meanwhile, about a quarter of the cases sought treatment from various traditional healers as a quick fix for the symptom/s**.**

More than half (58.9%) of the study participants felt compelled by their family members to seek medical help for the symptom/s. About half of the cases first went to public health facilities for their first symptom/s (health centers and health posts), followed by public hospitals (16%). At their first visit to health facilities, approximately to two-third of the study participants first contacted health officers and nurses as health care providers. The mean (SD) of health facilities visited by the cases until the data collection time was 6.6 ± 3.2. Meanwhile, 11% of the participants had visited more than 10 health facilities until data collection time. The mean (SD)

number of visits to health facilities by participants until the data collection time was 7.45 ± 3.63. The prominent reason mentioned by the participants for consultation delays was a financial issue, (61.5%).

3.2. Diagnosis characteristics of oesophageal cancer patients

Out of the total oesophageal cancer patients, about 76% (95% CI [71.0 %, 80.7%]) of the study participants were diagnosed at late stages (III and IV), and only 24% of the participants were diagnosed at early stages (I and II). In terms of histologic subtypes, 85.8%, 13.3% and 0.89% were oesophageal squamous cell carcinoma, oesophageal adenocarcinoma and unknown carcinomas, respectively. For those with available grade on biopsy report, 59.8%, 15.7% and 8.9%) were well differentiated, unspecified and poorly differentiated respectively. Endoscopic appearance was ulcerative in 49.4% followed by an obliterative of 34.9%. In case of tumor locations, middle oesophagus, lower oesophagus and upper (cervical) were 41.1%, 30.8% and 28.1% respectively **(Table 2).**

Table 2: Diagnostic history of oesophageal cancer patients from February 2019 to August 2020Addis Ababa, Ethiopia,

Variable	Frequency	Percent
Stage at first diagnosis		
Stage I	20	6.0
Stage II	58	17.2
Stage III	167	49.4
Stage IV	76	22.4
Unknown	17	5.0
Histological sub-type		
Oesophageal squamous carcinoma	290	85.8
Oesophageal adenocarcinoma	45	13.3
Unknown	3	0.9
Histopathological differentiations		
Well-differentiated	202	59.8
Moderate differentiated	47	13.8
Poor differentiated	30	8.9
Undifferentiated	6	1.8
Unspecified	53	15.7
Morphology of tumor during upper gastrointestinal endoscopy		
Ulcerative	167	49.4
Obliterative	118	34.9
Proliferative	45	13.3
Ulceroproliferative	8	2.4
Tumor location(Histology)		
Upper (cervical)	95	28.1
Middle oesophagus	139	41.1
Lower oesophagus	104	30.8

Patient and diagnostic intervals

The median (IQR) patient interval was 108.5 (60.5-215) days. The proportion of patient delay was 75% (95% CI [69.8%, 79.3%]). About ten percent of the participants had visited health facilities after 365 days of first symptom recognition. Only about 8% of the participants visited health facilities within thirty days. Great majority (71%) of the participants mentioned their reason for late patients' consultation was financial problems (59.5%) followed by not bothering about the disease. The median (IQR) of diagnostic interval was 77.5 (39-133) days. The proportion of diagnostic delay was 81.9% (95% CI [77.9%, 86.2%]). Three percent of those who took part in the study received diagnostic confirmation after 365 days of waiting and 18% of the participants got diagnosis confirmation less than thirty days. The median (IQR) symptom interval was 215(130-353) days. The most noticeable single factor mentioned by majority (78%) the participants for the diagnostic delay was longer appointments primarily associated with the health care organizations.

3.3. Factors associated with patient delay

In the bivariable analysis, participants unable to read and write (PR=1.2, 95% CI [1.05, 1.43]), being house wife (PR=1.14, 95%CI [1.01, 1.29]), single participants (PR=1.08, 95% CI [1.03, 1.14]) monthly income <35USD (PR=1.29,95%CI[1.09,1.55]) and 35-106 USD (PR=1.3,95%CI[1.17]CI[1.09,1.55]family monthly income<53USD(PR=1.17,95%CI[1.02,1.33]) and 53-141 USD (PR=1.17,95% CI [1.02,1.34]) and never heard of oesophageal cancer prior to diagnosis (PR=1.11,95%CI [1.03,1.97]) were significantly associated with higher prevalence of patient delay and adjusted for multivariable analysis. Therefore, after an adjustment, we only found marital status (Adjusted PR=1.09, 95% CI [1.03, 1.15]) and never heard of oesophageal

cancer prior to diagnosis (Adjusted PR=1.08, 95% CI [1.03, 1.15]) were found statistically significant to increase the prevalence of patients delay among oesophageal cancer patients **(Table 3).**

Table 3 : Determinant factors associated with patient delay (>60 days) among oesophageal cancer patients from February 2019 to August 2020, Addis Ababa, Ethiopia (n=324)

Patient characteristics	Patient delay		Unadjusted		Adjusted	
	Yes (%)	No (%)	PR (95% CI)	P-value	PR (95% CI)	P-value
Age of participants (years)						
<35	14 (66.7)	7 (33.3)	Ref.		Ref.	
35-44	26 (59.1)	18 (40.9)	0.96 (0.82,1.11)	0.55	0.96 (0.86,1.07)	0.43
45-54	63 (72.4)	24 (27.6)	1.03 (0.91,1.18)	0.62	1.03 (0.94, 1.12)	0.56
≥55	140 (81.4)	32 (18.6)	1.10 (0.96,1.23)	0.18	0.99 (0.91,1.08)	0.81
Residency						
Urban	88 (71.0)	36 (29.0)	Ref.		Ref.	
Rural	155 (77.5)	45 (22.5)	1.04 (0.98,1.10)	0.19	1.04 (0.97,1.11)	0.29
Educational status of participants						
Unable to read and write	155 (77.1)	46 (22.9)	1.2 (1.05,1.43)	0.01	1.11 (0.94, 1.29)	0.22
Grade 1-8	56 (81.2)	13 (18.8)	1.25 (1.07,1.46)	0.006	1.15 (0.97, 1.35)	0.10
Grade 9-12	23 (67.6)	11 (32.4)	1.16 (0.97,1.38)	0.11	1.08 (0.91, 1.29)	0.38
Diploma and above	9 (45.0)	11 (55.0)	Ref.			
Occupation of participants						
Private worker	17 (56.7)	13 (43.3)	Ref.		Ref.	
Government workers	24 (68.6)	11 (31.4)	1.08 (0.93,1.24)	0.32	1.02 (0.94, 1.11)	0.57
House wife	82 (78.8)	22 (21.2)	1.14 (1.01,1.29)	0.03	0.94 (0.86, 1.02)	0.14
Merchant	24 (82.8)	5 (17.2)	1.17 (1.02,1.34)	0.03	1.03 (0.94,1.12)	0.54
Farmer	96 (76.2)	30 (23.8)	1.13(0.99,1.27)	0.06	0.93 (0.85, 1.02)	0.12
Marital status of participants during the data collection time						
Single	76 (85.4)	13 (14.6)	1.08 (1.03,1.14)	0.002	1.09 (1.03, 1.15)*	0.001
Married	167 (71.1)	68 (28.9)	Ref.			
Monthly income						
<35 US dollar	124 (78.5)	34 (21.5)	1.29 (1.09,1.55)	0.004	1.22(1.005,1.48)	0.045
35-106 US dollar	101 (78.9)	27 (21.1)	1.3 (1.09,1.55)	0.004	1.22(1.22,1.48)	0.042
106.6-177 US dollar	12 (54.5)	10 (45.5)	1.12 (0.90,1.39)	0.29	0.46(1.09)	0.46
>177 US dollar	6 (37.5)	10 (62.5)	Ref.			
Family monthly income(USD)						
<53	128 (77.1)	38 (22.9)	1.17 (1.02, 1.33)	0.025	1.12(0.98,1.27)	0.09
53-141	84 (77.8)	24 (22.2)	1.17 (1.02,1.34)	0.024	1.13(0.99,1.28)	0.08
141.4-230	18 (72.0)	7 (28.0)	1.13 (0.96,1.33)	0.14	1.1(0.94,1.29)	0.26
>230	13 (52.0)	12 (48.0)	Ref.			

Table 3 cont.….

Patient characteristics	Patient delay		Unadjusted		Adjusted	
	Yes (%)	No (%)	PR (95% CI)	P-value	PR (95% CI)	P-value
Prior information about esophageal cancer						
No	198 (79.0)	53 (21.0)	1.11 (1.03,1.97)	0.007	1.08(1.02,1.17)*	0.04
Yes	44 (61.1)	29 (38.9)	Ref.			
Visiting traditional healers						
No	180(73.2)	66(26.8)	Ref.			
Yes	63(80.8)	15(19.8)	1.04(0.99,1.11)	0.15	1.04(0.98,1.10)	0.23

3.4. Factors associated with diagnostic delay

Meanwhile, in the bivariable analysis, single participants (PR=1.8,95%CI[1.74,1.85]),family monthly income 53-141 USD(PR=0.91,95%CI [0.85,0.99]),cost transport (one trip)>7USD(PR=1.07,95%CI[1.06,1.13]), first medical consultation at health center (PR=0.93,95%CI[0.88,0.99]) and number of health facilities visited < 3 health facilities (PR=0.93, 95%CI [0.87,0.99]) were significantly associated with higher prevalence of diagnostic delay. However, after an adjustment or in the multivariable analysis, we only found single participants (Adjusted PR=1.2, 95% CI [1.11,2.10]), sources of medical expenses (Adjusted PR=1.2,95% CI[1.13,2.40]), cost of transportation (Adjusted PR=1.2,95% CI [1.12,1.54]) and first medical consultation to health facilities (Adjusted PR= 1.4, 95% CI [1.20,2.30]) were statistically significant to increase the prevalence of diagnostic delay among oesophageal cancer patients **(Table 4).**

Table 4: Factors associated with diagnostic delay (>30 days) among oesophageal cancer patients from February 2019 to August 2020, Addis Ababa Ethiopia (n=326)

Patient characteristics	Diagnosis delay		Unadjusted		Adjusted	
	Yes (%)	No (%)	PR (95% CI)	P-value	PR (95% CI)	P-value
Age of participants (years)						
<35	17 (77.2)	5 (22.8)	Ref.		Ref.	
35-44	33 (75.0)	11 (25.0)	0.94 (0.84, 1.04)	0.24	0.96(0.86,1.07)	0.45
45-54	75 (87.2)	11 (12.8)	1.01 (0.92, 1.09)	0.92	1.02(0.93,1.11)	0.69
≥55	140 (80.5)	34 (19.5)	0.97 (0.89, 1.05)	0.45	0.97(0.89,1.06)	0.53
Marital status of participants during the data collection time						
Single	78(88.6)	10(11.4)	1.80(1.74,1.85)	0.0001	1.2 (1.1,2.10)**	0.04
Married	189(79.4)	49(20.6)	Ref.		Ref.	
Family monthly income(USD)						
<53	139(82.7	29(17.3)	0.95(0.89,1.01)	0.11	0.98(0.88,1.09)	0.69
53-141	80(74.8)	27(25.2)	0.91(0.85,0.99)	0.008	0.91(0.82,1.002)	0.05
141.4-230	20(80.0)	5(20.0)	1.02(0.95,1.09)	0.57	1.01(0.93,1.09)	0.84
>230	19(73.1)	7(26.9)	Ref.		Ref.	
One way cost of transport (USD)						
<7 dollar	67(73.6)	24(26.4)	Ref.			
≥7 dollar	200(85.1)	35(14.9)	1.07(1.06,1.13)	0.03	1.2(1.12,1.54)**	0.04
First medical consultation						
Health post	35(87.5)	5(12.5)	0.99(0.94,1.07)	0.96	1.01(0.94,1.08)	0.83
Health center	123(77.4)	36(22.6)	0.93(0.88,0.99)	0.015	1.4 (1.2, 2.30)**	0.049
Private clinic	38(88.4)	5(11.6)	0.99(0.94,1.06)	0.78	1.01(0.94,1.08)	0.87
Private hospital	24(72.7)	9(27.3)	0.91(0.82,1.002)	0.054	0.92(0.83,1.02)	0.10
Public hospital	46(90.2)	5(9.8)	Ref.		Ref.	
Number of health facilities visited for diagnosis						
< 3 health facilities	13(72.2)	5(27.8)	Ref.		Ref.	
3-6 health facilities	153(80.5)	37(19.5)	0.93(0.87,0.99)	0.02	0.93(0.87,1.22)	0.054
7-10 health facilities	67(81.7)	15(18.3)	0.93(0.87,1.004)	0.06	0.94(0.87,1.01)	0.108
>10 health facilities	29(82.9)	6(17.1)	0.94(0.86,1.026)	0.17	0.94(0.86,1.03)	0.19
Source of medical expenses						
Free medical care	57(79.2)	15(20.8)	Ref.			
Governmental insurance	11(61.1)	7(38.9)	0.90(0.78.1.044)	0.16	1.22 (1.13, 2.40)*	0.048
Out of pocket	199(84.3)	37(15.7)	1.03(0.97,1.09)	0.34	1.03(0.98,1.09)	0.26

3.5 Factors associated with advanced stages at diagnosis among oesophageal cancer patients

In the bivariable analysis, marital status, single (PR=1.16, 95% CI [1.02, 1.30]) and patients delay of > two months (PR=1.38, 95% CI [1.14, 1.68]) were significantly associated with late stage at first diagnosis. However, after an adjustment or multivariable analysis, marital status (Adjusted PR=1.16, 95% CI [1.03, 1.31]), female participants (Adjusted PR=1.15, 95% CI [1.015, 1.31]), patient delay > two months (Adjusted PR=1.41, 95% CI [1.15, 1.69])) and symptom intervals (Adjusted PR=1.26, 95% CI [1.12, 1.67]) were statistically significant to increase the prevalence of advanced stage at time of diagnosis **(Table 5).**

Table 5: Factors associated with advanced stages at diagnosis among oesophageal cancer patients from February 2019 to August 2020 Addis Ababa, Ethiopia (n=321).

Patient characteristics	Advanced-stage		Unadjusted		Adjusted	
	No (%)	Yes (%)	PR (95% CI)	P-value	aPR (95% CI)	P-value
Gender						
Male	45(27.1)	121(72.9)	Ref.		Ref.	
Female	33(21.3)	122(78.7)	0.93(0.82,1.05)	0.22	1.15 (1.01,1.31)*	0.049
Occupation of participants						
Private worker	5(17.2)	24(82.8)	Ref.			
Government workers	13(35.1)	24(64.9)	0.78(0.59,1.05)	0.10	0.77 (0.57, 1.02)	0.07
House wife	28(24.8)	85(75.2)	0.91(0.75,1.11)	0.34	0.89 (0.73,1.09)	0.25
Merchant	6(30.0)	14(70.0)	1.03(0.80,1.32)	0.83	0.99 (0.78,1.28)	0.98
Farmer	29(23.8)	93(76.2)	0.92(0.76,1.12)	0.41	0.89 (0.74,1.09)	0.29
Marital status of participants during the data collection time						
Single	14(16.1)	73(83.9)	1.16(1.02,1.30)	0.02	1.16 (1.03,1.31)*	0.015
Married	64(27.4)	170(72.6)	Ref.		Ref.	
Family size in the house hold						
<3	6(37.5)	10 (62.5)	Ref.			
3-5	38(26.6)	105(73.4)	0.84(0.68,1.04)	0.10	0.82 (0.66, 1.03)	0.08
>5	38(23.5)	124(76.5)	0.88(0.71,1.07)	0.20	0.87 (0.69 ,1.07)	0.19
One way cost of transport (USD)						
<7 dollar	28(31.1)	62(68.9)	Ref.			
≥7 dollar	50(21.6)	181(78.4)	1.14(0.98,1.33)	0.10	1.12 (0.96 , 1.30)	0.15
First medical consultation						
Health post	6(15.4)	33(84.6)	1.11(0.94,1.32)	0.22	1.11 (0.92, 1.33)	0.27
Health center	48(30.6)	109(69.4)	0.86(0.73,1.02)	0.08	0.87 (0.73 ,1.04)	0.12
Private clinic	6(14.3)	36(85.7)	1.06(0.88,1.27)	0.52	1.05 (0.88 , 1.30)	0.57
Private hospital	10(32.2)	21(67.8)	0.84(0.64,1.11)	0.21	0.83 (0.63 , 1.09)	0.18
Public hospital	10(19.2)	42(80.8)	Ref.			
Patient delay (> 2 months)						
No	31(40.8)	45(59.2)	Ref		Ref.	
Yes	42(18.2)	189(81.8)	1.38(1.14,1.68)	0.001	1.41 (1.15, 1.69)*	0.001
Number of times visited health facilities prior to final diagnosis						
< 3 times	7(31.8)	15(68.2)	Ref.		Ref.	
3-6 times	40(26.8)	109(73.2)	1.07(0.79,1.45)	0.65	0.89 (0.69 , 1.16)	0.39
7-10 times	19(21.8)	68(78.2)	1.15(0.84,1.56)	0.38	0.93 (0.70 , 1.23)	0.61
>10 times	12(19.0)	51(81.0)	1.19(0.87,1.62)	0.24	1.12 (0.85 , 1.46)	0.43
Symptom interval						
< 3 months	12(36.4)	21(63.6)	Ref.		Ref.	
3-6 months	26(29.5)	62(70.3)	1.11(0.83,1.48)	0.49	1.09 (0.81 , 1.46)	0.51
> 6months	37(19.7)	151(80.3)	1.26(0.97,1.65)	0.08	1.26 (1.12 , 1.67)*	0.048

Discussion

Longer consultation and diagnostic intervals, as well as late stages at the time of diagnosis, were hypothesized before we started this study. We estimated prolonged consultation and diagnostic intervals. In addition, most of the cases were diagnosed at advanced stages. The most common reason for patient delays was financial constraints. About 11% of the cases were forced to visit an average of 10 different health facilities in search of better and more effective care and treatment in areas where they believe they can afford it.

The dominant histological subtype was oesophageal squamous carcinoma. In addition, risk factors for late consultation, diagnostic and late stage at the time of diagnosis were identified.

The median patient intervals were much lower in studies conducted elsewhere [11 21 25-27] compared to the patient interval estimated from our study. This substantial gap could be attributed to socio-cultural and socio-economic disparities in health-seeking behavior, as well as a lack of understanding of oesophageal cancer symptoms among different groups/communities. Furthermore, because the majority of our participants were from rural areas, and cancer care is provided by secondary and tertiary care institutions that are located far from the majority of rural residents, the majority of them were illiterate, late presentation is strongly associated with poor access to care. Our research, on the other hand, is similar to the study conducted in South Africa [28]. The similarities in socioeconomic, sociocultural, and literacy rates could explain the same presentation delays The median diagnostic interval estimated from our study is higher than previous studies conducted in different part of the world [11 21 25 26]. The discrepancy may be the differences in diagnostic workups and the availability of experienced and trained health professionals in cancer related diagnostic and treatment services. On the other hand, our study is in line with the study conducted in South Africa [28]. The similarities could be explained by the

fact that the diagnostic procedures and health-care facilities are more or less similar among many of the African countries The proportion of advanced stages at time of first diagnosis is higher compared the study conducted Shandong University in Jinan (China) [21] this could be related to longer patient and diagnostic intervals and socio-economic difference among the communities. The cardinal symptom reported by majority of our participants was dysphagia this result is comparable with studies [21 26 27]. We discovered that oesophageal squamous carcinoma was the most prevalent, which is consistent with other studies conducted elsewhere in the world [21 29 30]. A significant number of patients with oesophageal cancer were diagnosed at advanced stages, which are consistent with previous studies [29 31]. However, the proportion of those diagnosed delay in oesophageal cancer was relatively higher in a nationwide cohort study conducted in Korean patients [30]. Increased patient delay (> two months) was found to be exacerbated by socio-economic characteristics in our study. Our finding is equivalent to this study [32] , which evidenced those patients with lower socio-economic status sought medical help later. Furthermore, socioeconomic status has had an important influence in patients being diagnosed at advanced stages, which is similar to the findings of the study conducted in China [32]. As an immediate measure for their symptom/s, a large percentage of oesophageal cancer patients contacted various traditional healers. This finding is consistent with the findings of a qualitative study conducted in Ethiopia's in Oromia Regional State [33]. The study's comparability is owing to the societies' similar socio-economic and socio-cultural characteristics. The prevalence of diagnostic delay was higher in single patients than the married participants. Thus, being married might have a better chance to seek medical care than unmarried participants. The reason could be partners may influence each other on decision making to seek care as early as possible. In our findings, oesophageal cancer patients that paid their medical expense from

their own pocket had longer patient interval than patients whose medical expenses covered by other organizations. The reason could be, they ignore the symptoms because patients with low socio-economic status had other unmet survival felt needs than investing money for medical care [34].

4. Conclusion

Oesophageal cancer patients in Ethiopia had longer patients' presentation, diagnostic and symptom intervals. Moreover, majority of the oesophageal cancer patients had diagnosed at advanced stages (III and IV). Being single and never heard of oesophageal cancer prior to diagnosis was found to be predictors of increased patient intervals. The levels of first health facilities visited for medical consultation and the cost of transportation were identified as key factors in increasing diagnostic intervals.

Furthermore, being single, being female, waiting more than two months for a diagnosis, and symptom interval were found to be statistically significant predictors in the incidence of advanced stages at diagnosis. Patients' intervals could be shortened by increasing their awareness of oesophageal cancer symptoms.

Abbreviations

AJCC: American Joint Committee on Cancer

APR: Adjusted Prevalence Ratio

SD: Standard Deviation

IQR: Inter Quartile Range

P: Proportion

PR: Prevalence Ratio

USD: United States Dollar

Ethics approval and informed consent

The ethical clearance was obtained from the Institutional Review Board (IRB) of Addis Ababa University College of Health Sciences with a protocol number of 080/18/SPH. The study followed basic ethical principles of Helsinki declaration for medical research involving human participants[35]. All of the study participants were informed about the purpose and procedure of the research and their right to withdrawal from the study at any time. Written informed consent was obtained from each of the study participants. Meanwhile, the study participants were agreed to the extent that the finding of this study will be subjected to publication. Participants were well informed not to disclose their information to a third person. The information was kept secured and put confidentially with the first author.

Data availability

Data will be available up on request

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There is no fund for this research project

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There is no competing interest of this research

Authors' contributions

All authors contributed from the conception of idea up to data analysis and write up. They also participated in drafting or revising of the article and have agreed on to which journal the article shall be submitted and have given final approval of the version to be published, and agreed to be accountable for all aspects of the work. Specifically, BD was conceptualized the topic of interest, involved in data collection, coding, cleaning, analysis, interpretation of the result unto preparation of the manuscript. FE was involved in proposal development, planning the fieldwork and result section. And RY, MA, SG and AA were involved in proposal development, data analysis and write up and in critical reviewing of manuscript.

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Time intervals from first symptom recognition to pathological diagnosis among oesophageal cancer patients in Ethiopia: A cross-sectional study

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Abstract

Objective

The aim of this study was to estimate the time intervals from first symptom recognition to pathological diagnosis among oesophageal cancer patients in Ethiopia.

Methods

Design Cross-sectional study design was employed

Settings and participants Oesophageal cancer patients aged ≥18 years were included from Addis Ababa, Ethiopia (n=338) from February 2019 to August 2020. The participants were selected consecutively from six health facilities provided cancer care nearly for 90% of patients.

Main outcomes and measurements The Aarhus statement criterias was applied to classify patient intervals (time from first symptom recognition to presentation), and diagnostic intervals (time from first presentation to diagnosis). Patient and diagnostic intervals >60 and >30 days were considered as delays, respectively. For tumor classification, the American Joint Committee on cancer was used. Data were analyzed using SPSS Version 24. Descriptive statistics were applied to describe patients' characteristics. Poisson regression with robust variance was used to compute prevalence ratios. In all statistical tests, significances were declared at p-value of <0.05.

Results

The mean (SD) age of the participants was 54.30 ± 12.49 years.

Approximately 78 percent of study participants had never heard of oesophageal cancer and thought they had gastritis. Dysphagia was commonly mentioned symptom. About 76% of the cases were diagnosed at advanced stages (III and IV). Median patient interval was 108.5 (60.5-215) days and median diagnostic interval was 77.5 (39-133) days. After adjusting confounders, being single and unawareness of oesophageal cancer had association with consultation delay,

cost of transportation and medical consultation had association with diagnostic delay and patient delay > two months had association with late stage at diagnosis.

Conclusion Oesophageal cancer patients in Ethiopia had prolonged patient and diagnostic intervals. Increasing awareness on symptoms of oesophageal cancer and shortening time to diagnosis will help to improve the out-come of oesophageal cancer care in Ethiopia.

Keywords: Oesophageal cancer, delay, intervals, tumor stage

Strengths and Limitations

- In Ethiopia, in case of patient and diagnostic interval and associated factors, it is the first multifacility study
- Poisson regression with robust variance was used to compute the prevalence ratios
- It is the only research based on primary data in Ethiopia that estimates the patient and diagnostic intervals on oesophageal cancer patients
- However, the onset of symptoms is a subjective measurement that patients may not recall the exact time

1. Introduction

Cancer is a group of diseases in which abnormal cells grow and spread uncontrollably. Cancer has become a major public health concern on a global scale [1]. Oesophageal cancer is the fourth most common cancer in developing countries, and it is an aggressive tumor of the esophagus that develops in the organ's tissue lining [2]. Oesophageal cancer, which has a dismal prognosis and survival rate, has caused considerable morbidity and mortality around the world from the last three decades [3-5]. Globally, oesophageal cancer was the sixth most common cause of mortality among all cancers and the seventh most common cancer in terms of incidence[1].

The two most prevalent subtypes of oesophageal cancer are squamous cell carcinoma and adenocarcinoma. Adenocarcinoma begins in the cells that produce and release mucus and other fluids, whereas squamous cell carcinoma begins in the flat cells that line the esophagus. Oesophageal cancer mortality and incidence are higher in Africa than the rest of the world, with squamous cell carcinoma being the most common type [6 7].

The five-year survival rate of non-metastatic oesophageal cancer is between 19 and 30%, whereas, the median overall survival time for metastatic oesophageal cancer is between four and six months. Nonetheless, it is not uncommon for oesophageal cancer patients to be diagnosed at advanced stages ,because, in most cases, the oesophageal cancer patients have identified symptoms by the time the disease has reached its advanced stages, then lead to poor patients prognosis and survival rate[5 8 9]. The prognosis and time intervals of oesophageal cancer patients has been solely depended on the patients' awareness on symptoms and literates rate that contribute to early consultation and shorter pathological diagnosis periods, according to studies[10 11]. In practice, however, oesophageal cancer patients frequently have arrived late in presentation and commonly lately referred to the appropriate health facilities. In addition,

literatures also showed that shortening the time to presentation is an important step in reducing late in diagnosis, and improving the prognosis and survival of oesophageal cancer patients[12 13].

Oesophageal cancer is the overwhelming disease and among the commonest cause of cancer deaths in the world. Though, few patients can be cured, the treatment for oesophageal cancer is prolonged, quality of life is significantly compromised and cases fatality rate is high [1].

Ethiopia is a country, geographically located within the highest risk region of oesophageal cancer known to be the oesophageal cancer belt. And, the disease has created a huge burden interms of morbidity and mortality in the country[14]. In addition, few hospital reports revealed that over the last decades, the incidence and burden of oesophageal cancer has been increasing.

Diagnostic and consultation delays on cancers are common in underdeveloped countries, such as the Eastern part of Africa, and are closely linked to poor survival rates. As a result, obtaining updated information is crucial for establishing a resilient plan to reduce oesophageal cancer related morbidity and mortality [7 15].

In Ethiopia, however, oesophageal cancer is not yet a public health priority, left in dark and is under-researched; as a result, there is no clear evidence about patient and diagnostic intervals and the stage at time of diagnosis. The goal of this study was to determine time to care seeking and pathological diagnosis, and the stage at time of diagnosis of oesophageal cancer patients. Meanwhile, we were also strived to identify predictors of patients and pathological diagnostic delays of > 60 and > 30 days, respectively.

2. Materials and methods

2.1. Study design and sample size

A cross-sectional study design was employed. The study involved 338 oesophageal cancer patients aged ≥18 years from February 2019 to August 2020 in Addis Ababa, Ethiopia. Using the expected proportion (p=32.0%) of patients delay to presentation (>2 months) from another similar study [16] by assuming a 95% level of confidence, a 5% precision and 5% non-response rate

2.2. Settings and participants

The Ethiopian health care delivery system has three tiers: primary, secondary and tertiary level health care facilities that are linked with a referral system. The setup differs slightly between urban and rural settings. The main healthcare service in the metropolitan city, such as Addis Ababa, Ethiopia's capital, includes public health centers, private clinics, and primary hospitals. Secondary and tertiary healthcare levels are general hospitals and specialty hospitals, respectively. The primary healthcare services in rural areas are made up of a health post, a health center, and primary hospitals. Secondary and tertiary healthcare levels are general hospitals and specialty hospitals, respectively. Nurses and health officers are the primary staff of public health centers, with the goal of providing preventative and primary health care services. In the case of cancers, such as oesophageal cancer, health workers at the primary level care facilities are only expected to refer patients to general hospitals and other high-level facilities for further diagnosis and treatments[17].

Sampling procedure

A consecutive sampling method was used to recruit study participants. Oesophageal cancer patients histologically confirmed and clinically staged came to the selected health facilities were included in the study, whereas critically ill, diagnosed to other cancer types and non-Ethiopian patients were excluded from participation. Six health facilities in Addis Ababa (Tikur Anbesa Specialized Hospital, St. Paul Hospital Millennium Medical College, Betezata Hospital, Hallelujah General Hospital, Landmark Hospital, and United Vision Medical Services Centre) were selected, where nearly 90% of cancer patients being diagnosed and treated. At each health facility, one focal person was assigned to identify eligible oesophageal cancer patients and communicate with the principal investigator and supervisor. To avoid duplication, the medical chart of the recruited patient was coded in red on the top cover page. Prior to the interview, study participants were informed about the purpose of the study and their right to withdraw under any circumstances without compromisation of any services.

2.3. Variables and Measurements

We used the Aarhus statement criteria to classify patient, diagnostic and symptoms intervals. Thus, patient interval was defined as the interval between the date of first symptom recognition (the time point at which the patient first noticed bodily changes and/or symptoms) and the date of first clinical presentation (the date at which the patient first presented to a healthcare provider after first recognizing symptoms), and symptom interval was defined as the time interval between the date of first symptom recognition and the date of pathological diagnosis[18 19]. The date of symptom recognition was determined based on participants recall. Furthermore, the diagnostic interval was defined as the time elapsed between the date of first clinical presentation and the date of the final pathological diagnosis (the date at which the first histological or

cytological confirmation of the malignancy was documented in the pathology report). The pathology report of the patient was used to determine the date of diagnosis [18 19]. Tumors were classified using the Tumor-Node-Metastasis method from the 7th edition of the American Joint Committee on Cancer (AJCC)[20]. And cases were histologically and endoscopically confirmed. Stages I and II were classified as early stages of diagnosis, while stage III and IV were classified as late stages of diagnosis [21]. The interviews were conducted in Amharic, the country's working language. The study tool was initially prepared in English, then translated into Amharic by language translators, and finally back to English to ensure that the two versions were consistent. Experts in cancer research assessed the tool to ensure that the questions were clear and two days training was given data collectors and the supervisor about the objective of the study. A pretest for cultural suitability and clarity was performed prior to administering the tool to the participants. When the eligible participants were arrived for treatment, trained nurses interviewed them individually in a semiprivate room in Amharic. If the participants couldn't recall the exact date of their first symptom recognition, they were asked to provide a month or year ('was it at the beginning, middle, or end of the year'). For those who only remembered the month, the date was estimated to be the 15th day of that month. If the participants only said at the beginning, middle or at the end of the year, the estimated date was 15th of February, June or October of the year, respectively; if they only said the year, the estimated date was June 30th of that year. We performed sensitivity analyses excluding patients who had only remembered the beginning, middle or end of the year or a year for the date of first symptom recognition or clinical presentation[22].

2.4. Data Analysis

Epi-info version 7 was used for the data entry and SPSS Version 24 was used to analyze the data. Descriptive statistics were calculated for each variable. Numbers and percentages were used to summarize categorical variables. We presented mean and standard deviation for numerical variables with normal distributions, whereas median and IQR were employed for variables with skewed distributions. Patient and diagnostic delays were defined as >60-days patient intervals and >30-days diagnostic intervals, respectively, from previous similar study [11]. For cross-sectional research, OR is the common measure of association, and logistic regression is often used to estimate. Nevertheless, evidences suggest that when the proportion of the outcome exceeds 10%, an odds ratio overestimates the risk ratio, leading to incorrect interpretations. As a result, to avoid these limitations, the prevalence ratio is preferred measure of association [23 24]. Hence, Poisson regression with robust variance was used to compute the adjusted prevalence ratios of factors associated with the prevalence of patient and diagnostic delays, as well as factors associated with stage at time of diagnosis. Variables having a p value of <0.25 on bivariable analysis were candidates for the multivariable analysis and other variables were also considered based on literatures had impacts on patient and diagnostic delays and stage at time of diagnosis. A two-sided p value of 0.05 was declared as statistically significant.

Patient and public involvement "No patient involved"

3. Results:

Socio-demographic and socio- economic characteristics of the study participants

We approached 351 participants those histologically confirmed and clinically staged for oesophageal cancer and among 96.3% (338) of them were provided their oral consent for participation. The participants in the study were 54.30 ± 12.49 years old on average (SD). Male participants accounted for 52.4% of the total participants. More than half of the participants (52%) were above the age of 55 years, only 7.0% of the participants were below the age of 35 years. Two-thirds of the study participants were from rural areas of Ethiopia and were unable to read and write. Muslims and farmers participants accounted 52% and 38% of the total participants respectively. At the time of data collection, 75% of the participants in the study were married. More than half of the participants in the study earned not more than one USD per day or about 29 Ethiopian Birr. Among the participants, 73% had to travel long distances to receive cancer-specific diagnosis and treatment services, and had to pay more than seven USD or 203 Ethiopian Birr for a single trip just to cover only for transportation costs. Furthermore, nearly three-quarters of the study participants had paid their medical expenses out of their pockets **(Table 1).**

Table 1: Socio-demographic and socio-economic characteristics of esophageal cancer patients Addis Ababa, Ethiopia, February 2019 to August 2020 (n=338)

Variables	Frequency	Percent
Age categories (years)		
<35	24	7
35-44	46	14
45-54	91	27
≥55	177	52
Gender		
Male	177	52.4
Female	161	47.6
Religion		
Christianity	159	47
Islam	175	51.8
Wakefata	4	1.2
Residency		
Urban	126	37.3
Rural	212	62.7
Educational status of participants		
Unable to read and write	209	61.8
1-8 grade	72	21.3
9-12 grade	37	10.9
Diploma and above	20	5.9
Occupation of participants		
Government workers	38	1.2
House wife	118	34.9
Merchant	20	5.9
Private worker	35	10.4
Farmer	127	37.6
Marital status of participants during the data collection time		
Married	246	72.8
Single	92	27.2
Monthly income (USD)		
<35	171	50.6
35-106	130	38.5
106.6-177	21	6.2
>177	16	4.7
One way cost of transport (USD*)		
<7 dollar	93	27.5
>=7 dollar	245	72.5
Sources of medical expenses		
Employing organization	1	0.3
Free medical care	72	21.3
Government insurance	19	5.6
Out of pocket	242	71.6
Private insurance	4	1.2

3.1. Symptoms and awareness of oesophageal cancer

Among the total participants, 21.3 % had reported a history of at least one chronic disease, with diabetes mellitus being the commonest one. More than three-fourth of the study participants (77.8%, 95% CI [73.4%, 82.2%]) had never heard of oesophageal cancer prior to diagnosis for oesophageal cancer. For those who heard of oesophageal cancer prior to diagnosis, the main sources (48%) of the information were friends/ family members or neighbors, followed by printed and electronic medias such as (TV, radio, internet) (28%). Only eight participants (2.4%) had reported first degree family history of oesophageal cancer**.**

Dysphagia was the cardinal symptom mentioned by 84.6% of the study participants, followed by odynophagia of 54.1%. Approximately three-fourth of the study participants had linked the first symptom/s to gastritis. All patients had recognized at least one symptom. Moreover, a significant number of patients reported as having more than one oesophageal cancer symptom. About half of the cases stated that they did not take an immediate action for the first symptom/s because they thought that the symptom/s was/ were simple and self-limited. Meanwhile, about a quarter of the cases sought treatment from various traditional healers as a quick fix for the symptom/s**.**

More than half (58.9%) of the study participants felt compelled by their family members to seek medical help for the symptom/s. About half of the cases first went to public health facilities for their first symptom/s (health centers and health posts), followed by public hospitals (16%). At their first visit to health facilities, approximately to two-third of the study participants first contacted health officers and nurses as health care providers. The mean (SD) of health facilities visited by the cases until the data collection time was 6.6 ± 3.2. Meanwhile, 11% of the participants had visited more than 10 health facilities until data collection time. The mean (SD)

number of visits to health facilities by participants until the data collection time was 7.45 ± 3.63. The prominent reason mentioned by the participants for consultation delays was a financial issue, (61.5%).

3.2. Diagnosis characteristics of oesophageal cancer patients

Out of the total oesophageal cancer patients, about 76% (95% CI [71.0 %, 80.7%]) of the study participants were diagnosed at late stages (III and IV)., In terms of histologic subtypes, 85.8%, 13.3% and 0.89% were oesophageal squamous cell carcinoma, oesophageal adenocarcinoma and unknown carcinomas, respectively. For those with available grade on biopsy report, 59.8%, 15.7% and 8.9%) were well differentiated, unspecified and poorly differentiated respectively. Endoscopic appearance was ulcerative in 49.4% followed by an obliterative of 34.9%. In case of tumor locations, middle oesophagus, lower oesophagus and upper (cervical) were 41.1%, 30.8% and 28.1% respectively **(Table 2).**

Table 2: Diagnostic history of oesophageal cancer patients from February 2019 to August 2020Addis Ababa, Ethiopia,

Variable	Frequency	Percent
Stage at first diagnosis		
Stage I	20	6.0
Stage II	58	17.2
Stage III	167	49.4
Stage IV	76	22.4
Unknown	17	5.0
Histological sub-type		
Oesophageal squamous carcinoma	290	85.8
Oesophageal adenocarcinoma	45	13.3
Unknown	3	0.9
Histopathological differentiations		
Well-differentiated	202	59.8
Moderate differentiated	47	13.8
Poor differentiated	30	8.9
Undifferentiated	6	1.8
Unspecified	53	15.7
Morphology of tumor during upper gastrointestinal endoscopy		
Ulcerative	167	49.4
Obliterative	118	34.9
Proliferative	45	13.3
Ulceroproliferative	8	2.4
Tumor location(Histology)		
Upper (cervical)	95	28.1
Middle oesophagus	139	41.1
Lower oesophagus	104	30.8

Patient and diagnostic intervals

The median (IQR) patient interval was 108.5 (60.5-215) days. The proportion of patient delay was 75% (95% CI [69.8%, 79.3%]). About ten percent of the participants had visited health facilities after 365 days of first symptom recognition. Only about 8% of the participants visited health facilities within thirty days. Great majority (71%) of the participants mentioned their reason for late patients' consultation was financial problems (59.5%) followed by not bothering about the disease. The median (IQR) of diagnostic interval was 77.5 (39-133) days. The proportion of diagnostic delay was 81.9% (95% CI [77.9%, 86.2%]). Three percent of those who took part in the study received diagnostic confirmation after 365 days of waiting and 18% of the participants got diagnosis confirmation less than thirty days. The median (IQR) symptom interval was 215(130-353) days. The most noticeable single factor mentioned by majority (78%) the participants for the diagnostic delay was longer appointments primarily associated with the health care organizations.

3.3. Factors associated with patient delay

Based on the cut of point, age, residency ,educational status, occupation, marital status, income, awareness about oesophageal cancer prior to diagnosis for oesophageal cancer, being house wife and visiting traditional healers were potential candidates and included in the multivariable analysis and among participants unable to read and write (PR=1.2, 95% CI [1.05, 1.43]), being house wife (PR=1.14, 95%CI [1.01, 1.29]), single participants (PR=1.08, 95% CI [1.03, 1.14]) monthly income <35USD (PR=1.29,95%CI[1.09,1.55]) and 35-106 USD (PR=1.3,95%CI[1.17]CI[1.09,1.55]family monthly income<53USD(PR=1.17,95%CI[1.02,1.33]) and 53-141 USD (PR=1.17,95% CI [1.02,1.34]) and never heard of oesophageal cancer prior to

diagnosis (PR=1.11,95%CI [1.03,1.97]) were significantly associated with higher prevalence of patient delay and adjusted for multivariable analysis. Therefore, after an adjustment, single participants (Adjusted PR=1.09, 95% CI [1.03, 1.15]) and never heard of oesophageal cancer prior to diagnosis (Adjusted PR=1.08, 95% CI [1.03, 1.15]) were found statistically significant to increase the prevalence of patients delay among oesophageal cancer patients **(Table 3).**

Table 3 : Factors associated with patient delay (>60 days) among oesophageal cancer patients from February 2019 to August 2020, Addis Ababa, Ethiopia (n=324)

Patient characteristics	Patient delay		Unadjusted		Adjusted	
	Yes (%)	No (%)	PR (95% CI)	P-value	PR (95% CI)	P-value
Age of participants (years)						
<35	14 (66.7)	7 (33.3)	Ref.		Ref.	
35-44	26 (59.1)	18 (40.9)	0.96 (0.82,1.11)	0.55	0.96 (0.86,1.07)	0.43
45-54	63 (72.4)	24 (27.6)	1.03 (0.91,1.18)	0.62	1.03 (0.94, 1.12)	0.56
≥55	140 (81.4)	32 (18.6)	1.10 (0.96,1.23)	0.18	0.99 (0.91,1.08)	0.81
Residency						
Urban	88 (71.0)	36 (29.0)	Ref.		Ref.	
Rural	155 (77.5)	45 (22.5)	1.04 (0.98,1.10)	0.19	1.04 (0.97,1.11)	0.29
Educational status of participants						
Unable to read and write	155 (77.1)	46 (22.9)	1.2 (1.05,1.43)	0.01	1.11 (0.94, 1.29)	0.22
Grade 1-8	56 (81.2)	13 (18.8)	1.25 (1.07,1.46)	0.006	1.15 (0.97, 1.35)	0.10
Grade 9-12	23 (67.6)	11 (32.4)	1.16 (0.97,1.38)	0.11	1.08 (0.91, 1.29)	0.38
Diploma and above	9 (45.0)	11 (55.0)	Ref.			
Occupation of participants						
Private worker	17 (56.7)	13 (43.3)	Ref.		Ref.	
Government workers	24 (68.6)	11 (31.4)	1.08 (0.93,1.24)	0.32	1.02 (0.94, 1.11)	0.57
House wife	82 (78.8)	22 (21.2)	1.14 (1.01,1.29)	0.03	0.94 (0.86, 1.02)	0.14
Merchant	24 (82.8)	5 (17.2)	1.17 (1.02,1.34)	0.03	1.03 (0.94,1.12)	0.54
Farmer	96 (76.2)	30 (23.8)	1.13(0.99,1.27)	0.06	0.93 (0.85, 1.02)	0.12
Marital status of participants during the data collection time						
Single	76 (85.4)	13 (14.6)	1.08 (1.03,1.14)	0.002	1.09 (1.03, 1.15)*	0.001
Married	167 (71.1)	68 (28.9)	Ref.			
Monthly income						
<35 US dollar	124 (78.5)	34 (21.5)	1.29 (1.09,1.55)	0.004	1.22(1.005,1.48)	0.045
35-106 US dollar	101 (78.9)	27 (21.1)	1.3 (1.09,1.55)	0.004	1.22(1.22,1.48)	0.042
106.6-177 US dollar	12 (54.5)	10 (45.5)	1.12 (0.90,1.39)	0.29	0.46(1.09)	0.46
>177 US dollar	6 (37.5)	10 (62.5)	Ref.			
Family monthly income(USD)						
<53	128 (77.1)	38 (22.9)	1.17 (1.02, 1.33)	0.025	1.12(0.98,1.27)	0.09
53-141	84 (77.8)	24 (22.2)	1.17 (1.02,1.34)	0.024	1.13(0.99,1.28)	0.08
141.4-230	18 (72.0)	7 (28.0)	1.13 (0.96,1.33)	0.14	1.1(0.94,1.29)	0.26
>230	13 (52.0)	12 (48.0)	Ref.			

Table 3 cont.....

Patient characteristics	Patient delay		Unadjusted		Adjusted	
	Yes (%)	No (%)	PR (95% CI)	P-value	PR (95% CI)	P-value
Prior information about esophageal cancer						
No	198 (79.0)	53 (21.0)	1.11 (1.03,1.97)	0.007	1.08(1.02,1.17)*	0.04

Yes	44 (61.1)	29 (38.9)	Ref.			
Visiting traditional healers						
No	180(73.2)	66(26.8)	Ref.			
Yes	63(80.8)	15(19.8)	1.04(0.99,1.11)	0.15	1.04(0.98,1.10)	0.23

3.4. Factors associated with diagnostic delay

Based on the cut off age, marital status, family size, transportation, first medical consultation, number of health facilities visited and sources of medical expenses were included in the multivariable analysis and among single participants (PR=1.8,95%CI[1.74,1.85]),family monthly income 53-141 USD(PR=0.91,95%CI [0.85,0.99]),cost transport (one trip)>7USD(PR=1.07,95%CI[1.06,1.13]), first medical consultation at health center (PR=0.93,95%CI[0.88,0.99]) and number of health facilities visited < 3 health facilities (PR=0.93, 95%CI [0.87,0.99]) were significantly associated with higher prevalence of diagnostic delay. However, after an adjustment or in the multivariable analysis, we found single participants (Adjusted PR=1.2, 95% CI [1.11,2.10]), sources of medical expenses (Adjusted PR=1.2,95% CI[1.13,2.40]), cost of transportation (Adjusted PR=1.2,95% CI [1.12,1.54]) and first medical consultation to health facilities (Adjusted PR= 1.4, 95% CI [1.20,2.30]) were statistically significant to increase the prevalence of diagnostic delay among oesophageal cancer patients **(Table 4).**

Table 4: Factors associated with diagnostic delay (>30 days) among oesophageal cancer patients from February 2019 to August 2020, Addis Ababa Ethiopia (n=326)

Patient characteristics	Diagnosis delay		Unadjusted		Adjusted	
	Yes (%)	No (%)	PR (95% CI)	P-value	PR (95% CI)	P-value
Age of participants (years)						
<35	17 (77.2)	5 (22.8)	Ref.		Ref.	
35-44	33 (75.0)	11 (25.0)	0.94 (0.84, 1.04)	0.24	0.96(0.86,1.07)	0.45
45-54	75 (87.2)	11 (12.8)	1.01 (0.92, 1.09)	0.92	1.02(0.93,1.11)	0.69
≥55	140 (80.5)	34 (19.5)	0.97 (0.89, 1.05)	0.45	0.97(0.89,1.06)	0.53
Marital status of participants during the data collection time						
Single	78(88.6)	10(11.4)	1.80(1.74,1.85)	0.0001	1.2 (1.1,2.10)**	0.04
Married	189(79.4)	49(20.6)	Ref.		Ref.	
Family monthly income(USD)						
<53	139(82.7	29(17.3)	0.95(0.89,1.01)	0.11	0.98(0.88,1.09)	0.69
53-141	80(74.8)	27(25.2)	0.91(0.85,0.99)	0.008	0.91(0.82,1.002)	0.05
141.4-230	20(80.0)	5(20.0)	1.02(0.95,1.09)	0.57	1.01(0.93,1.09)	0.84
>230	19(73.1)	7(26.9)	Ref.		Ref.	
One way cost of transport (USD)						
<7 dollar	67(73.6)	24(26.4)	Ref.			
≥7 dollar	200(85.1)	35(14.9)	1.07(1.06,1.13)	0.03	1.2(1.12,1.54)**	0.04
First medical consultation						
Health post	35(87.5)	5(12.5)	0.99(0.94,1.07)	0.96	1.01(0.94,1.08)	0.83
Health center	123(77.4)	36(22.6)	0.93(0.88,0.99)	0.015	1.4 (1.2, 2.30)**	0.049
Private clinic	38(88.4)	5(11.6)	0.99(0.94,1.06)	0.78	1.01(0.94,1.08)	0.87
Private hospital	24(72.7)	9(27.3)	0.91(0.82,1.002)	0.054	0.92(0.83,1.02)	0.10
Public hospital	46(90.2)	5(9.8)	Ref.		Ref.	
Number of health facilities visited for diagnosis						
< 3 health facilities	13(72.2)	5(27.8)	Ref.		Ref.	
3-6 health facilities	153(80.5)	37(19.5)	0.93(0.87,0.99)	0.02	0.93(0.87,1.22)	0.054
7-10 health facilities	67(81.7)	15(18.3)	0.93(0.87,1.004)	0.06	0.94(0.87,1.01)	0.108
>10 health facilities	29(82.9)	6(17.1)	0.94(0.86,1.026)	0.17	0.94(0.86,1.03)	0.19
Source of medical expenses						
Free medical care	57(79.2)	15(20.8)	Ref.			
Governmental insurance	11(61.1)	7(38.9)	0.90(0.78.1.044)	0.16	1.22 (1.13, 2.40)*	0.048
Out of pocket	199(84.3)	37(15.7)	1.03(0.97,1.09)	0.34	1.03(0.98,1.09)	0.26

3.5 Factors associated with advanced stages at diagnosis among oesophageal cancer patients

Based on the cutoff point, gender, occupation, family size, transport, first medical consultation, patients delay > two months and number of times visiting for diagnosis were included in the multivariable analysis and among, marital status, single (PR=1.16, 95% CI [1.02, 1.30]) and patients delay of > two months (PR=1.38, 95% CI [1.14, 1.68]) were significantly associated with late stage at first diagnosis. However, after an adjustment or multivariable analysis, marital status (Adjusted PR=1.16, 95% CI [1.03, 1.31]), female participants (Adjusted PR=1.15, 95% CI [1.015, 1.31]), patient delay > two months (Adjusted PR=1.41, 95% CI [1.15, 1.69])) and symptom intervals (Adjusted PR=1.26, 95% CI [1.12, 1.67]) were statistically significant to increase the prevalence of advanced stage at time of diagnosis **(Table 5).**

Table 5: Factors associated with advanced stages at diagnosis among oesophageal cancer patients from February 2019 to August 2020 Addis Ababa, Ethiopia (n=321).

Patient characteristics	Advanced-stage		Unadjusted		Adjusted	
	No (%)	Yes (%)	PR (95% CI)	P-value	aPR (95% CI)	P-value
Gender						
Male	45(27.1)	121(72.9)	Ref.		Ref.	
Female	33(21.3)	122(78.7)	0.93(0.82,1.05)	0.22	1.15 (1.01,1.31)*	0.049
Occupation of participants						
Private worker	5(17.2)	24(82.8)	Ref.			
Government workers	13(35.1)	24(64.9)	0.78(0.59,1.05)	0.10	0.77 (0.57, 1.02)	0.07
House wife	28(24.8)	85(75.2)	0.91(0.75,1.11)	0.34	0.89 (0.73,1.09)	0.25
Merchant	6(30.0)	14(70.0)	1.03(0.80,1.32)	0.83	0.99 (0.78,1.28)	0.98
Farmer	29(23.8)	93(76.2)	0.92(0.76,1.12)	0.41	0.89 (0.74,1.09)	0.29
Marital status of participants during the data collection time						
Single	14(16.1)	73(83.9)	1.16(1.02,1.30)	0.02	1.16 (1.03,1.31)*	0.015
Married	64(27.4)	170(72.6)	Ref.		Ref.	
Family size in the house hold						
<3	6(37.5)	10 (62.5)	Ref.			
3-5	38(26.6)	105(73.4)	0.84(0.68,1.04)	0.10	0.82 (0.66, 1.03)	0.08
>5	38(23.5)	124(76.5)	0.88(0.71,1.07)	0.20	0.87 (0.69 ,1.07)	0.19
One way cost of transport (USD)						
<7 dollar	28(31.1)	62(68.9)	Ref.			
≥7 dollar	50(21.6)	181(78.4)	1.14(0.98,1.33)	0.10	1.12 (0.96 , 1.30)	0.15
First medical consultation						
Health post	6(15.4)	33(84.6)	1.11(0.94,1.32)	0.22	1.11 (0.92, 1.33)	0.27
Health center	48(30.6)	109(69.4)	0.86(0.73,1.02)	0.08	0.87 (0.73 ,1.04)	0.12
Private clinic	6(14.3)	36(85.7)	1.06(0.88,1.27)	0.52	1.05 (0.88 , 1.30)	0.57
Private hospital	10(32.2)	21(67.8)	0.84(0.64,1.11)	0.21	0.83 (0.63 , 1.09)	0.18
Public hospital	10(19.2)	42(80.8)	Ref.			
Patient delay (> 2 months)						
No	31(40.8)	45(59.2)	Ref		Ref.	
Yes	42(18.2)	189(81.8)	1.38(1.14,1.68)	0.001	1.41 (1.15, 1.69)*	0.001
Number of times visited health facilities prior to final diagnosis						
< 3 times	7(31.8)	15(68.2)	Ref.		Ref.	
3-6 times	40(26.8)	109(73.2)	1.07(0.79,1.45)	0.65	0.89 (0.69 , 1.16)	0.39
7-10 times	19(21.8)	68(78.2)	1.15(0.84,1.56)	0.38	0.93 (0.70 , 1.23)	0.61
>10 times	12(19.0)	51(81.0)	1.19(0.87,1.62)	0.24	1.12 (0.85 , 1.46)	0.43
Symptom interval						
< 3 months	12(36.4)	21(63.6)	Ref.		Ref.	
3-6 months	26(29.5)	62(70.3)	1.11(0.83,1.48)	0.49	1.09 (0.81 , 1.46)	0.51
> 6months	37(19.7)	151(80.3)	1.26(0.97,1.65)	0.08	1.26 (1.12 , 1.67)*	0.048

Discussion

Longer consultation and diagnostic intervals, as well as late stages at the time of diagnosis, were hypothesized before we started this study. This research has estimated prolonged patients consultation and diagnostic intervals. In addition, most of the cases were diagnosed at advanced stages. The most common reason mentioned by the patients for their delays was financial constraints. About 11% of the cases were forced to visit an average of 10 different health facilities in search of better and more effective cancer care and treatments in areas where they believe they can afford it.

The dominant histological subtype was oesophageal squamous carcinoma. In addition, risk factors for late consultation, diagnostic and late stage at the time of diagnosis were identified.

The median patient intervals were much lower in studies conducted elsewhere [11 21 25-27] compared to the patient interval estimated from our study. This substantial difference could be attributed to socio-cultural and socio-economic disparities in health-seeking behavior, as well as a lack of understanding of oesophageal cancer symptoms among different groups/communities.

Furthermore, the bulk of our participants were from rural areas, and cancer care is given by secondary and tertiary care institutions located far from the majority of rural populations. Furthermore, the majority of the individuals were illiterate, implying that late presentation is closely linked to a lack of access to care.

.Our research, on the other hand, is similar to the study conducted in South Africa [28]. The similarities in socioeconomic, sociocultural, and literacy rates could explain the same presentation delays. The median diagnostic interval estimated from our study was higher than the previous studies conducted in different part of the world [11 21 25 26]. The discrepancy may be

the differences in diagnostic workups and the availability of experienced and trained health professionals in cancer related diagnostic and treatment services. On the other hand, our study is in line with the study conducted in South Africa [28]. The similarities could be explained by the fact that the diagnostic procedures and health-care facilities are more or less similar among many of the African countries. The prevalence of diagnostic delay was higher in single patients than the married participants. Thus, being married might have a better chance to seek medical care than unmarried participants. The reason could be partners may influence each other on decision making to seek care as early as possible.

In our findings, oesophageal cancer patients that paid their medical expense from their own pocket had longer patient interval than patients whose medical expenses covered by other organizations. The reason could be, they ignore the symptoms because patients with low socio-economic status had other unmet survival felt needs than investing money for medical care [29]

The proportion of advanced stages at time of first diagnosis is higher compared the study conducted Shandong University in Jinan (China) by Wang J, et al [21] this could be related to longer patient and diagnostic intervals and socio-economic difference among the communities. The cardinal symptom reported by majority of our participants was dysphagia this result is comparable with studies [21 26 27]. We discovered that oesophageal squamous carcinoma was the most prevalent, which is consistent with other studies conducted elsewhere in the world [21 30 31]. A significant number of patients with oesophageal cancer were diagnosed at advanced stages, which are consistent with previous studies [30 32]. However, the proportion of those diagnosed delay in oesophageal cancer was relatively higher in a nationwide cohort study conducted in Korean patients [31]. Increased patient delay (> two months) was found to be exacerbated by socio-economic characteristics in our study. Our finding is equivalent to this

study [33] , which evidenced those patients with lower socio-economic status sought medical help later. Furthermore, socioeconomic status has had an important influence in patients being diagnosed at advanced stages, which is similar to the findings of the study conducted in China [33]. In our study, the majority of oesophageal cancer patients sought rapid relief for their symptoms by contacting several traditional healers. This conclusion is in line with that of a qualitative study conducted in Ethiopia's Oromia Regional State.

4. Conclusion

Oesophageal cancer patients in the study area had longer patients' presentation, diagnostic and symptom intervals. Moreover, majority of the oesophageal cancer patients had diagnosed at advanced stages (III and IV). Being single and never heard of oesophageal cancer prior to diagnosis was found to be predictors of increased patient intervals. The levels of first health facilities visited for medical consultation and the cost of transportation were identified as key factors in increasing diagnostic intervals.

Furthermore, being single, being female, waiting more than two months for a diagnosis, and symptom interval were found to be statistically significant predictors in the incidence of advanced stages at diagnosis. Patients' intervals could be shortened by increasing their awareness of oesophageal cancer symptoms.

Abbreviations

AJCC: American Joint Committee on Cancer

APR: Adjusted Prevalence Ratio

SD: Standard Deviation

IQR: Inter Quartile Range

P: Proportion

PR: Prevalence Ratio

USD: United States Dollar

Ethics approval and informed consent

The ethical clearance was obtained from the Institutional Review Board (IRB) of Addis Ababa University College of Health Sciences with a protocol number of 080/18/SPH. The study followed basic ethical principles of Helsinki declaration for medical research involving human participants[34]. All of the study participants were informed about the purpose and procedure of the research and their right to withdrawal from the study at any time. Written informed consent was obtained from each of the study participants. Meanwhile, the study participants were agreed to the extent that the finding of this study will be subjected to publication. Participants were well informed not to disclose their information to a third person. The information was kept secured and put confidentially with the first author.

Data availability

Data will be available up on request

Funding

There is no fund for this research project

Competing interests

There is no competing interest of this research

Authors' contributions

All authors contributed from the conception of idea up to data analysis and write up. They also participated in drafting or revising of the article and have agreed on to which journal the article shall be submitted and have given final approval of the version to be published, and agreed to be accountable for all aspects of the work. Specifically, BD was conceptualized the topic of interest, involved in data collection, coding, cleaning, analysis, interpretation of the result unto preparation of the manuscript. FE was involved in proposal development, planning the fieldwork and result section. And RY, MA, SG and AA were involved in proposal development, data analysis and write up and in critical reviewing of manuscript.

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Time intervals from first symptom recognition to pathological diagnosis among oesophageal cancer patients in Ethiopia: A cross-sectional study

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Abstract

Objective

The aim of this study was to estimate the time intervals from first symptom recognition to pathological diagnosis among oesophageal cancer patients in Ethiopia.

Methods

Design Cross-sectional study design was employed

Settings and participants Oesophageal cancer patients aged ≥18 years were included from Addis Ababa, Ethiopia (n=338) from February 2019 to August 2020. The participants were selected consecutively from six health facilities provided cancer care nearly for 90% of patients.

Main outcomes and measurements The Aarhus statement criterias was applied to classify patient intervals (time from first symptom recognition to presentation), and diagnostic intervals (time from first presentation to diagnosis). Patient and diagnostic intervals >60 and >30 days were considered as delays, respectively. For tumor classification, the American Joint Committee on cancer was used. Data were analyzed using SPSS Version 24. Descriptive statistics were applied to describe patients' characteristics. Poisson regression with robust variance was used to compute prevalence ratios. In all statistical tests, significances were declared at p-value of <0.05.

Results

The mean (SD) age of the participants was 54.30 ± 12.49 years.

Approximately 78 percent of study participants had never heard of oesophageal cancer and thought they had gastritis. Dysphagia was commonly mentioned symptom. About 76% of the cases were diagnosed at advanced stages (III and IV). Median patient interval was 108.5 (60.5-215) days and median diagnostic interval was 77.5 (39-133) days. After adjusting confounders, being single and unawareness of oesophageal cancer had association with consultation delay, cost of transportation

and medical consultation had association with diagnostic delay and patient delay > two months had association with late stage at diagnosis.

Conclusion Oesophageal cancer patients in Ethiopia had prolonged patient and diagnostic intervals. Increasing awareness on symptoms of oesophageal cancer and shortening time to diagnosis will help to improve the out-come of oesophageal cancer care in Ethiopia.

Keywords: Oesophageal cancer, delay, intervals, tumor stage

Strengths and Limitations

- In Ethiopia, in case of patient and diagnostic interval and associated factors, it is the first multifacility study
- Poisson regression with robust variance was used to compute the prevalence ratios
- It is the only research based on primary data in Ethiopia that estimates the patient and diagnostic intervals on oesophageal cancer patients
- However, the onset of symptoms is a subjective measurement that patients may not recall the exact time

1. Introduction

Cancer is a group of diseases in which abnormal cells grow and spread uncontrollably. Cancer has become a major public health concern on a global scale [1]. Oesophageal cancer is the fourth most common cancer in developing countries, and it is an aggressive tumor of the esophagus that develops in the organ's tissue lining [2]. Oesophageal cancer, which has a dismal prognosis and survival rate, has caused considerable morbidity and mortality around the world from the last three decades [3-5]. Globally, oesophageal cancer was the sixth most common cause of mortality among all cancers and the seventh most common cancer in terms of incidence[1].

The two most prevalent subtypes of oesophageal cancer are squamous cell carcinoma and adenocarcinoma. Adenocarcinoma begins in the cells that produce and release mucus and other fluids, whereas squamous cell carcinoma begins in the flat cells that line the esophagus. Oesophageal cancer mortality and incidence are higher in Africa than the rest of the world, with squamous cell carcinoma being the most common type [6 7].

The five-year survival rate of non-metastatic oesophageal cancer is between 19 and 30%, whereas, the median overall survival time for metastatic oesophageal cancer is between four and six months. Nonetheless, it is not uncommon for oesophageal cancer patients to be diagnosed at advanced stages ,because, in most cases, the oesophageal cancer patients have identified symptoms by the time the disease has reached its advanced stages, then lead to poor patients prognosis and survival rate[5 8 9]. The prognosis and time intervals of oesophageal cancer patients has been solely depended on the patients' awareness on symptoms and literates rate that contribute to early consultation and shorter pathological diagnosis periods, according to studies[10 11]. In practice, however, oesophageal cancer patients frequently have arrived late in presentation and commonly lately referred to the appropriate health facilities. In addition, literatures also showed that

shortening the time to presentation is an important step in reducing late in diagnosis, and improving the prognosis and survival of oesophageal cancer patients[12 13].

Oesophageal cancer is the overwhelming disease and among the commonest cause of cancer deaths in the world. Though, few patients can be cured, the treatment for oesophageal cancer is prolonged, quality of life is significantly compromised and cases fatality rate is high [1].

Ethiopia is a country, geographically located within the highest risk region of oesophageal cancer known to be the oesophageal cancer belt. And, the disease has created a huge burden interms of morbidity and mortality in the country[14]. In addition, few hospital reports revealed that over the last decades, the incidence and burden of oesophageal cancer has been increasing.

Diagnostic and consultation delays on cancers are common in underdeveloped countries, such as the Eastern part of Africa, and are closely linked to poor survival rates. As a result, obtaining updated information is crucial for establishing a resilient plan to reduce oesophageal cancer related morbidity and mortality [7 15].

In Ethiopia, however, oesophageal cancer is not yet a public health priority, left in dark and is under-researched; as a result, there is no clear evidence about patient and diagnostic intervals and the stage at time of diagnosis. The goal of this study was to determine time to care seeking and pathological diagnosis, and the stage at time of diagnosis of oesophageal cancer patients. Meanwhile, we were also strived to identify predictors of patients and pathological diagnostic delays of > 60 and > 30 days, respectively.

2. Materials and methods

2.1. Study design and sample size

A cross-sectional study design was employed. The study involved 338 oesophageal cancer patients aged ≥18 years from February 2019 to August 2020 in Addis Ababa, Ethiopia. Using the expected proportion (p=32.0%) of patients delay to presentation (>2 months) from another similar study [16] by assuming a 95% level of confidence, a 5% precision and 5% non-response rate

2.2. Settings and participants

The Ethiopian health care delivery system has three tiers: primary, secondary and tertiary level health care facilities that are linked with a referral system. The setup differs slightly between urban and rural settings. The main healthcare service in the metropolitan city, such as Addis Ababa, Ethiopia's capital, includes public health centers, private clinics, and primary hospitals. Secondary and tertiary healthcare levels are general hospitals and specialty hospitals, respectively. The primary healthcare services in rural areas are made up of a health post, a health center, and primary hospitals. Secondary and tertiary healthcare levels are general hospitals and specialty hospitals, respectively. Nurses and health officers are the primary staff of public health centers, with the goal of providing preventative and primary health care services. In the case of cancers, such as oesophageal cancer, health workers at the primary level care facilities are only expected to refer patients to general hospitals and other high-level facilities for further diagnosis and treatments[17].

Sampling procedure

A consecutive sampling method was used to recruit study participants. Oesophageal cancer patients histologically confirmed and clinically staged came to the selected health facilities were included in the study, whereas critically ill, diagnosed to other cancer types and non-Ethiopian patients were excluded from participation. Six health facilities in Addis Ababa (Tikur Anbesa Specialized Hospital, St. Paul Hospital Millennium Medical College, Betezata Hospital, Hallelujah General Hospital, Landmark Hospital, and United Vision Medical Services Centre) were selected, where nearly 90% of cancer patients being diagnosed and treated. At each health facility, one focal person was assigned to identify eligible oesophageal cancer patients and communicate with the principal investigator and supervisor. To avoid duplication, the medical chart of the recruited patient was coded in red on the top cover page. Prior to the interview, study participants were informed about the purpose of the study and their right to withdraw under any circumstances without compromisation of any services.

2.3. Variables and Measurements

We used the Aarhus statement criteria to classify patient, diagnostic and symptoms intervals. Thus, patient interval was defined as the interval between the date of first symptom recognition (the time point at which the patient first noticed bodily changes and/or symptoms) and the date of first clinical presentation (the date at which the patient first presented to a healthcare provider after first recognizing symptoms), and symptom interval was defined as the time interval between the date of first symptom recognition and the date of pathological diagnosis[18 19]. The date of symptom recognition was determined based on participants recall. Furthermore, the diagnostic interval was defined as the time elapsed between the date of first clinical presentation and the date of the final pathological diagnosis (the date at which the first histological or cytological confirmation of the malignancy was documented in the pathology report). The pathology report of the patient was used

to determine the date of diagnosis [18 19]. Tumors were classified using the Tumor-Node-Metastasis method from the 7th edition of the American Joint Committee on Cancer (AJCC)[20]. And cases were histologically and endoscopically confirmed. Stages I and II were classified as early stages of diagnosis, while stage III and IV were classified as late stages of diagnosis [21]. The interviews were conducted in Amharic, the country's working language. The study tool was initially prepared in English, then translated into Amharic by language translators, and finally back to English to ensure that the two versions were consistent. Experts in cancer research assessed the tool to ensure that the questions were clear and two days training was given data collectors and the supervisor about the objective of the study. A pretest for cultural suitability and clarity was performed prior to administering the tool to the participants. When the eligible participants were arrived for treatment, trained nurses interviewed them individually in a semiprivate room in Amharic. If the participants couldn't recall the exact date of their first symptom recognition, they were asked to provide a month or year ('was it at the beginning, middle, or end of the year'). For those who only remembered the month, the date was estimated to be the 15th day of that month. If the participants only said at the beginning, middle or at the end of the year, the estimated date was 15th of February, June or October of the year, respectively; if they only said the year, the estimated date was June 30th of that year. We performed sensitivity analyses excluding patients who had only remembered the beginning, middle or end of the year or a year for the date of first symptom recognition or clinical presentation[22].

2.4. Data Analysis

Epi-info version 7 was used for the data entry and SPSS Version 24 was used to analyze the data. Descriptive statistics were calculated for each variable. Numbers and percentages were used to summarize categorical variables. We presented mean and standard deviation for numerical variables with normal distributions, whereas median and IQR were employed for variables with skewed distributions. Patient and diagnostic delays were defined as >60-days patient intervals and >30-days diagnostic intervals, respectively, from previous similar study [11]. For cross-sectional research, OR is the common measure of association, and logistic regression is often used to estimate. Nevertheless, evidences suggest that when the proportion of the outcome exceeds 10%, an odds ratio overestimates the risk ratio, leading to incorrect interpretations. As a result, to avoid these limitations, the prevalence ratio is preferred measure of association [23 24]. Hence, Poisson regression with robust variance was used to compute the adjusted prevalence ratios of factors associated with the prevalence of patient and diagnostic delays, as well as factors associated with stage at time of diagnosis. Variables having a p value of <0.25 on bivariable analysis were candidates for the multivariable analysis and other variables were also considered based on literatures had impacts on patient and diagnostic delays and stage at time of diagnosis. A two-sided p value of 0.05 was declared as statistically significant.

Patient and public involvement "No patient involved"

3. Results:

Socio-demographic and socio- economic characteristics of the study participants

We approached 351 participants those histologically confirmed and clinically staged for oesophageal cancer and among 96.3% (338) of them were provided their oral consent for participation. The participants in the study were 54.30 ± 12.49 years old on average (SD). Male participants accounted for 52.4% of the total participants. More than half of the participants (52%) were above the age of 55 years, only 7.0% of the participants were below the age of 35 years. Two-thirds of the study participants were from rural areas of Ethiopia and were unable to read and write. Muslims and farmers participants accounted 52% and 38% of the total participants respectively. At the time of data collection, 75% of the participants in the study were married. More than half of the participants in the study earned not more than one USD per day or about 29 Ethiopian Birr. Among the participants, 73% had to travel long distances to receive cancer-specific diagnosis and treatment services, and had to pay more than seven USD or 203 Ethiopian Birr for a single trip just to cover only for transportation costs. Furthermore, nearly three-quarters of the study participants had paid their medical expenses out of their pockets **(Table 1).**

Table 1: Socio-demographic and socio-economic characteristics of esophageal cancer patients Addis Ababa, Ethiopia, February 2019 to August 2020 (n=338)

Variables	Frequency	Percent
Age categories (years)		
<35	24	7
35-44	46	14
45-54	91	27
≥55	177	52
Gender		
Male	177	52.4
Female	161	47.6
Religion		
Christianity	159	47
Islam	175	51.8
Wakefata	4	1.2
Residency		
Urban	126	37.3
Rural	212	62.7
Educational status of participants		
Unable to read and write	209	61.8
1-8 grade	72	21.3
9-12 grade	37	10.9
Diploma and above	20	5.9
Occupation of participants		
Government workers	38	1.2
House wife	118	34.9
Merchant	20	5.9
Private worker	35	10.4
Farmer	127	37.6
Marital status of participants during the data collection time		
Married	246	72.8
Single	92	27.2
Monthly income (USD)		
<35	171	50.6
35-106	130	38.5
106.6-177	21	6.2
>177	16	4.7
One way cost of transport (USD*)		
<7 dollar	93	27.5
>=7 dollar	245	72.5
Sources of medical expenses		
Employing organization	1	0.3
Free medical care	72	21.3
Government insurance	19	5.6
Out of pocket	242	71.6
Private insurance	4	1.2

3.1. Symptoms and awareness of oesophageal cancer

Among the total participants, 21.3 % had reported a history of at least one chronic disease, with diabetes mellitus being the commonest one. More than three-fourth of the study participants (77.8%, 95% CI [73.4%, 82.2%]) had never heard of oesophageal cancer prior to diagnosis for oesophageal cancer. For those who heard of oesophageal cancer prior to diagnosis, the main sources (48%) of the information were friends/ family members or neighbors, followed by printed and electronic medias such as (TV, radio, internet) (28%). Only eight participants (2.4%) had reported first degree family history of oesophageal cancer**.**

Dysphagia was the cardinal symptom mentioned by 84.6% of the study participants, followed by odynophagia of 54.1%. Approximately three-fourth of the study participants had linked the first symptom/s to gastritis. All patients had recognized at least one symptom. Moreover, a significant number of patients reported as having more than one oesophageal cancer symptom. About half of the cases stated that they did not take an immediate action for the first symptom/s because they thought that the symptom/s was/ were simple and self-limited. Meanwhile, about a quarter of the cases sought treatment from various traditional healers as a quick fix for the symptom/s**.**

More than half (58.9%) of the study participants felt compelled by their family members to seek medical help for the symptom/s. About half of the cases first went to public health facilities for their first symptom/s (health centers and health posts), followed by public hospitals (16%). At their first visit to health facilities, approximately to two-third of the study participants first contacted health officers and nurses as health care providers. The mean (SD) of health facilities visited by the cases until the data collection time was 6.6 ± 3.2. Meanwhile, 11% of the participants had visited more than 10 health facilities until data collection time. The mean (SD) number of visits to

health facilities by participants until the data collection time was 7.45 ± 3.63. The prominent reason mentioned by the participants for consultation delays was a financial issue, (61.5%).

3.2. Diagnosis characteristics of oesophageal cancer patients

Out of the total oesophageal cancer patients, about 76% (95% CI [71.0 %, 80.7%]) of the study participants were diagnosed at late stages (III and IV)., In terms of histologic subtypes, 85.8%, 13.3% and 0.89% were oesophageal squamous cell carcinoma, oesophageal adenocarcinoma and unknown carcinomas, respectively. For those with available grade on biopsy report, 59.8%, 15.7% and 8.9%) were well differentiated, unspecified and poorly differentiated respectively. Endoscopic appearance was ulcerative in 49.4% followed by an obliterative of 34.9%. In case of tumor locations, middle oesophagus, lower oesophagus and upper (cervical) were 41.1%, 30.8% and 28.1% respectively **(Table 2).**

Table 2: Diagnostic history of oesophageal cancer patients from February 2019 to August 2020Addis Ababa, Ethiopia,

Variable	Frequency	Percent
Stage at first diagnosis		
Stage I	20	6.0
Stage II	58	17.2
Stage III	167	49.4
Stage IV	76	22.4
Unknown	17	5.0
Histological sub-type		
Oesophageal squamous carcinoma	290	85.8
Oesophageal adenocarcinoma	45	13.3
Unknown	3	0.9
Histopathological differentiations		
Well-differentiated	202	59.8
Moderate differentiated	47	13.8
Poor differentiated	30	8.9
Undifferentiated	6	1.8
Unspecified	53	15.7
Morphology of tumor during upper gastrointestinal endoscopy		
Ulcerative	167	49.4
Obliterative	118	34.9
Proliferative	45	13.3
Ulceroproliferative	8	2.4
Tumor location(Histology)		
Upper (cervical)	95	28.1
Middle oesophagus	139	41.1
Lower oesophagus	104	30.8

Patient and diagnostic intervals

The median (IQR) patient interval was 108.5 (60.5-215) days. The proportion of patient delay was 75% (95% CI [69.8%, 79.3%]). About ten percent of the participants had visited health facilities after 365 days of first symptom recognition. Only about 8% of the participants visited health facilities within thirty days. Great majority (71%) of the participants mentioned their reason for late patients' consultation was financial problems (59.5%) followed by not bothering about the disease. The median (IQR) of diagnostic interval was 77.5 (39-133) days. The proportion of diagnostic delay was 81.9% (95% CI [77.9%, 86.2%]). Three percent of those who took part in the study received diagnostic confirmation after 365 days of waiting and 18% of the participants got diagnosis confirmation less than thirty days. The median (IQR) symptom interval was 215(130-353) days. The most noticeable single factor mentioned by majority (78%) the participants for the diagnostic delay was longer appointments primarily associated with the health care organizations.

3.3. Factors associated with patient delay

Based on the cut of point, age, residency ,educational status, occupation, marital status, income, awareness about oesophageal cancer prior to diagnosis for oesophageal cancer, being house wife and visiting traditional healers were potential candidates and included in the multivariable analysis and among participants unable to read and write (PR=1.2, 95% CI [1.05, 1.43]), being house wife (PR=1.14, 95%CI [1.01, 1.29]), single participants (PR=1.08, 95% CI [1.03, 1.14]) monthly income <35USD (PR=1.29,95%CI[1.09,1.55]) and 35-106 USD (PR=1.3,95%CI[1.17]CI[1.09,1.55]family monthly income<53USD(PR=1.17,95%CI[1.02,1.33]) and 53-141 USD (PR=1.17,95% CI [1.02,1.34]) and never heard of oesophageal cancer prior to

diagnosis (PR=1.11,95%CI [1.03,1.97]) were significantly associated with higher prevalence of patient delay and adjusted for multivariable analysis. Therefore, after an adjustment, single participants (Adjusted PR=1.09, 95% CI [1.03, 1.15]) and never heard of oesophageal cancer prior to diagnosis (Adjusted PR=1.08, 95% CI [1.03, 1.15]) were found statistically significant to increase the prevalence of patients delay among oesophageal cancer patients **(Table 3).**

Table 3 : Factors associated with patient delay (>60 days) among oesophageal cancer patients from February 2019 to August 2020, Addis Ababa, Ethiopia (n=324)

Patient characteristics	Patient delay		Unadjusted		Adjusted	
	Yes (%)	No (%)	PR (95% CI)	P-value	PR (95% CI)	P-value
Age of participants (years)						
<35	14 (66.7)	7 (33.3)	Ref.		Ref.	
35-44	26 (59.1)	18 (40.9)	0.96 (0.82,1.11)	0.55	0.96 (0.86,1.07)	0.43
45-54	63 (72.4)	24 (27.6)	1.03 (0.91,1.18)	0.62	1.03 (0.94, 1.12)	0.56
≥55	140 (81.4)	32 (18.6)	1.10 (0.96,1.23)	0.18	0.99 (0.91,1.08)	0.81
Residency						
Urban	88 (71.0)	36 (29.0)	Ref.		Ref.	
Rural	155 (77.5)	45 (22.5)	1.04 (0.98,1.10)	0.19	1.04 (0.97,1.11)	0.29
Educational status of participants						
Unable to read and write	155 (77.1)	46 (22.9)	1.2 (1.05,1.43)	0.01	1.11 (0.94, 1.29)	0.22
Grade 1-8	56 (81.2)	13 (18.8)	1.25 (1.07,1.46)	0.006	1.15 (0.97, 1.35)	0.10
Grade 9-12	23 (67.6)	11 (32.4)	1.16 (0.97,1.38)	0.11	1.08 (0.91, 1.29)	0.38
Diploma and above	9 (45.0)	11 (55.0)	Ref.			
Occupation of participants						
Private worker	17 (56.7)	13 (43.3)	Ref.		Ref.	
Government workers	24 (68.6)	11 (31.4)	1.08 (0.93,1.24)	0.32	1.02 (0.94, 1.11)	0.57
House wife	82 (78.8)	22 (21.2)	1.14 (1.01,1.29)	0.03	0.94 (0.86, 1.02)	0.14
Merchant	24 (82.8)	5 (17.2)	1.17 (1.02,1.34)	0.03	1.03 (0.94,1.12)	0.54
Farmer	96 (76.2)	30 (23.8)	1.13(0.99,1.27)	0.06	0.93 (0.85, 1.02)	0.12
Marital status of participants during the data collection time						
Single	76 (85.4)	13 (14.6)	1.08 (1.03,1.14)	0.002	1.09 (1.03, 1.15)*	0.001
Married	167 (71.1)	68 (28.9)	Ref.			
Monthly income						
<35 US dollar	124 (78.5)	34 (21.5)	1.29 (1.09,1.55)	0.004	1.22(1.005,1.48)	0.045
35-106 US dollar	101 (78.9)	27 (21.1)	1.3 (1.09,1.55)	0.004	1.22(1.22,1.48)	0.042
106.6-177 US dollar	12 (54.5)	10 (45.5)	1.12 (0.90,1.39)	0.29	0.46(1.09)	0.46
>177 US dollar	6 (37.5)	10 (62.5)	Ref.			
Family monthly income(USD)						
<53	128 (77.1)	38 (22.9)	1.17 (1.02, 1.33)	0.025	1.12(0.98,1.27)	0.09
53-141	84 (77.8)	24 (22.2)	1.17 (1.02,1.34)	0.024	1.13(0.99,1.28)	0.08
141.4-230	18 (72.0)	7 (28.0)	1.13 (0.96,1.33)	0.14	1.1(0.94,1.29)	0.26
>230	13 (52.0)	12 (48.0)	Ref.			

Table 3 cont.....

Patient characteristics	Patient delay		Unadjusted		Adjusted	
	Yes (%)	No (%)	PR (95% CI)	P-value	PR (95% CI)	P-value
Prior information about esophageal cancer						

No	198 (79.0)	53 (21.0)	1.11 (1.03,1.97)	0.007	1.08(1.02,1.17)*	0.04
Yes	44 (61.1)	29 (38.9)	Ref.			
Visiting traditional healers						
No	180(73.2)	66(26.8)	Ref.			
Yes	63(80.8)	15(19.8)	1.04(0.99,1.11)	0.15	1.04(0.98,1.10)	0.23

3.4. Factors associated with diagnostic delay

Based on the cut off age, marital status, family size, transportation, first medical consultation, number of health facilities visited and sources of medical expenses were included in the multivariable analysis and among single participants (PR=1.8,95%CI[1.74,1.85]),family monthly income 53-141 USD(PR=0.91,95%CI [0.85,0.99]),cost transport (one trip)>7USD(PR=1.07,95%CI[1.06,1.13]), first medical consultation at health center (PR=0.93,95%CI[0.88,0.99]) and number of health facilities visited < 3 health facilities (PR=0.93, 95%CI [0.87,0.99]) were significantly associated with higher prevalence of diagnostic delay. However, after an adjustment or in the multivariable analysis, we found single participants (Adjusted PR=1.2, 95% CI [1.11,2.10]), sources of medical expenses (Adjusted PR=1.2,95% CI[1.13,2.40]), cost of transportation (Adjusted PR=1.2,95% CI [1.12,1.54]) and first medical consultation to health facilities (Adjusted PR= 1.4, 95% CI [1.20,2.30]) were statistically significant to increase the prevalence of diagnostic delay among oesophageal cancer patients **(Table 4).**

Table 4: Factors associated with diagnostic delay (>30 days) among oesophageal cancer patients from February 2019 to August 2020, Addis Ababa Ethiopia (n=326)

Patient characteristics	Diagnosis delay		Unadjusted		Adjusted	
	Yes (%)	No (%)	PR (95% CI)	P-value	PR (95% CI)	P-value
Age of participants (years)						
<35	17 (77.2)	5 (22.8)	Ref.		Ref.	
35-44	33 (75.0)	11 (25.0)	0.94 (0.84, 1.04)	0.24	0.96(0.86,1.07)	0.45
45-54	75 (87.2)	11 (12.8)	1.01 (0.92, 1.09)	0.92	1.02(0.93,1.11)	0.69
≥55	140 (80.5)	34 (19.5)	0.97 (0.89, 1.05)	0.45	0.97(0.89,1.06)	0.53
Marital status of participants during the data collection time						
Single	78(88.6)	10(11.4)	1.80(1.74,1.85)	0.0001	1.2 (1.1,2.10)**	0.04
Married	189(79.4)	49(20.6)	Ref.		Ref.	
Family monthly income(USD)						
<53	139(82.7	29(17.3)	0.95(0.89,1.01)	0.11	0.98(0.88,1.09)	0.69
53-141	80(74.8)	27(25.2)	0.91(0.85,0.99)	0.008	0.91(0.82,1.002)	0.05
141.4-230	20(80.0)	5(20.0)	1.02(0.95,1.09)	0.57	1.01(0.93,1.09)	0.84
>230	19(73.1)	7(26.9)	Ref.		Ref.	
One way cost of transport (USD)						
<7 dollar	67(73.6)	24(26.4)	Ref.			
≥7 dollar	200(85.1)	35(14.9)	1.07(1.06,1.13)	0.03	1.2(1.12,1.54)**	0.04
First medical consultation						
Health post	35(87.5)	5(12.5)	0.99(0.94,1.07)	0.96	1.01(0.94,1.08)	0.83
Health center	123(77.4)	36(22.6)	0.93(0.88,0.99)	0.015	1.4 (1.2, 2.30)**	0.049
Private clinic	38(88.4)	5(11.6)	0.99(0.94,1.06)	0.78	1.01(0.94,1.08)	0.87
Private hospital	24(72.7)	9(27.3)	0.91(0.82,1.002)	0.054	0.92(0.83,1.02)	0.10
Public hospital	46(90.2)	5(9.8)	Ref.		Ref.	
Number of health facilities visited for diagnosis						
< 3 health facilities	13(72.2)	5(27.8)	Ref.		Ref.	
3-6 health facilities	153(80.5)	37(19.5)	0.93(0.87,0.99)	0.02	0.93(0.87,1.22)	0.054
7-10 health facilities	67(81.7)	15(18.3)	0.93(0.87,1.004)	0.06	0.94(0.87,1.01)	0.108
>10 health facilities	29(82.9)	6(17.1)	0.94(0.86,1.026)	0.17	0.94(0.86,1.03)	0.19
Source of medical expenses						
Free medical care	57(79.2)	15(20.8)	Ref.			
Governmental insurance	11(61.1)	7(38.9)	0.90(0.78.1.044)	0.16	1.22 (1.13, 2.40)*	0.048
Out of pocket	199(84.3)	37(15.7)	1.03(0.97,1.09)	0.34	1.03(0.98,1.09)	0.26

3.5 Factors associated with advanced stages at diagnosis among oesophageal cancer patients

Based on the cutoff point, gender, occupation, family size, transport, first medical consultation, patients delay > two months and number of times visiting for diagnosis were included in the multivariable analysis and among, marital status, single (PR=1.16, 95% CI [1.02, 1.30]) and patients delay of > two months (PR=1.38, 95% CI [1.14, 1.68]) were significantly associated with late stage at first diagnosis. However, after an adjustment or multivariable analysis, marital status (Adjusted PR=1.16, 95% CI [1.03, 1.31]), female participants (Adjusted PR=1.15, 95% CI [1.015, 1.31]), patient delay > two months (Adjusted PR=1.41, 95% CI [1.15, 1.69])) and symptom intervals (Adjusted PR=1.26, 95% CI [1.12, 1.67]) were statistically significant to increase the prevalence of advanced stage at time of diagnosis **(Table 5).**

Table 5: Factors associated with advanced stages at diagnosis among oesophageal cancer patients from February 2019 to August 2020 Addis Ababa, Ethiopia (n=321).

Patient characteristics	Advanced-stage		Unadjusted		Adjusted	
	No (%)	Yes (%)	PR (95% CI)	P-value	aPR (95% CI)	P-value
Gender						
Male	45(27.1)	121(72.9)	Ref.		Ref.	
Female	33(21.3)	122(78.7)	0.93(0.82,1.05)	0.22	1.15 (1.01,1.31)*	0.049
Occupation of participants						
Private worker	5(17.2)	24(82.8)	Ref.			
Government workers	13(35.1)	24(64.9)	0.78(0.59,1.05)	0.10	0.77 (0.57, 1.02)	0.07
House wife	28(24.8)	85(75.2)	0.91(0.75,1.11)	0.34	0.89 (0.73,1.09)	0.25
Merchant	6(30.0)	14(70.0)	1.03(0.80,1.32)	0.83	0.99 (0.78,1.28)	0.98
Farmer	29(23.8)	93(76.2)	0.92(0.76,1.12)	0.41	0.89 (0.74,1.09)	0.29
Marital status of participants during the data collection time						
Single	14(16.1)	73(83.9)	1.16(1.02,1.30)	0.02	1.16 (1.03,1.31)*	0.015
Married	64(27.4)	170(72.6)	Ref.		Ref.	
Family size in the house hold						
<3	6(37.5)	10 (62.5)	Ref.			
3-5	38(26.6)	105(73.4)	0.84(0.68,1.04)	0.10	0.82 (0.66, 1.03)	0.08
>5	38(23.5)	124(76.5)	0.88(0.71,1.07)	0.20	0.87 (0.69 ,1.07)	0.19

One way cost of transport (USD)						
<7 dollar	28(31.1)	62(68.9)	Ref.			
≥7 dollar	50(21.6)	181(78.4)	1.14(0.98,1.33)	0.10	1.12 (0.96 , 1.30)	0.15
First medical consultation						
Health post	6(15.4)	33(84.6)	1.11(0.94,1.32)	0.22	1.11 (0.92, 1.33)	0.27
Health center	48(30.6)	109(69.4)	0.86(0.73,1.02)	0.08	0.87 (0.73 ,1.04)	0.12
Private clinic	6(14.3)	36(85.7)	1.06(0.88,1.27)	0.52	1.05 (0.88 , 1.30)	0.57
Private hospital	10(32.2)	21(67.8)	0.84(0.64,1.11)	0.21	0.83 (0.63 , 1.09)	0.18
Public hospital	10(19.2)	42(80.8)	Ref.			
Patient delay (> 2 months)						
No	31(40.8)	45(59.2)	Ref		Ref.	
Yes	42(18.2)	189(81.8)	1.38(1.14,1.68)	0.001	1.41 (1.15, 1.69)*	0.001
Number of times visited health facilities prior to final diagnosis						
< 3 times	7(31.8)	15(68.2)	Ref.		Ref.	
3-6 times	40(26.8)	109(73.2)	1.07(0.79,1.45)	0.65	0.89 (0.69 , 1.16)	0.39
7-10 times	19(21.8)	68(78.2)	1.15(0.84,1.56)	0.38	0.93 (0.70 , 1.23)	0.61
>10 times	12(19.0)	51(81.0)	1.19(0.87,1.62)	0.24	1.12 (0.85 , 1.46)	0.43
Symptom interval						
< 3 months	12(36.4)	21(63.6)	Ref.		Ref.	
3-6 months	26(29.5)	62(70.3)	1.11(0.83,1.48)	0.49	1.09 (0.81 , 1.46)	0.51
> 6months	37(19.7)	151(80.3)	1.26(0.97,1.65)	0.08	1.26 (1.12 , 1.67)*	0.048

Discussion

Longer consultation and diagnostic intervals, as well as late stages at the time of diagnosis, were hypothesized before we started this study. This research has estimated prolonged patients consultation and diagnostic intervals. In addition, most of the cases were diagnosed at advanced stages. The most common reason mentioned by the patients for their delays was financial constraints. About 11% of the cases were forced to visit an average of 10 different health facilities in search of better and more effective cancer care and treatments in areas where they believe they can afford it.

The dominant histological subtype was oesophageal squamous carcinoma. In addition, risk factors for late consultation, diagnostic and late stage at the time of diagnosis were identified.

The median patient intervals were much lower in studies conducted elsewhere [11 21 25-27] compared to the patient interval estimated from our study. This substantial difference could be attributed to socio-cultural and socio-economic disparities in health-seeking behavior, as well as a lack of understanding of oesophageal cancer symptoms among different groups/communities.

Furthermore, the bulk of our participants were from rural areas, and cancer care is given by secondary and tertiary care institutions located far from the majority of rural populations. Furthermore, the majority of the individuals were illiterate, implying that late presentation is closely linked to a lack of access to care.

Our research, on the other hand, is similar to the study conducted in South Africa [28]. The similarities in socioeconomic, sociocultural, and literacy rates could explain the same presentation delays. The median diagnostic interval estimated from our study was higher than the previous studies conducted in different part of the world [11 21 25 26]. The discrepancy may be the differences in diagnostic workups and the availability of experienced and trained health professionals in cancer related diagnostic and treatment services. On the other hand, our study is in line with the study conducted in South Africa [28]. The similarities could be explained by the fact that the diagnostic procedures and health-care facilities are more or less similar among many of the African countries. The prevalence of diagnostic delay was higher in single patients than the married participants. Thus, being married might have a better chance to seek medical care than unmarried participants. The reason could be partners may influence each other on decision making to seek care as early as possible.

In our findings, oesophageal cancer patients that paid their medical expense from their own pocket had longer patient interval than patients whose medical expenses covered by other organizations.

The reason could be, they ignore the symptoms because patients with low socio-economic status had other unmet survival felt needs than investing money for medical care [29]

The proportion of advanced stages at time of first diagnosis is higher compared the study conducted in Shandong University in Jinan (China) by Wang J, et al [21] this could be related to longer patient and diagnostic intervals and socio-economic difference among the communities. The cardinal symptom reported by majority of our participants was dysphagia this result is comparable with studies [21 26 27]. We discovered that oesophageal squamous carcinoma was the most prevalent, which is consistent with other studies conducted elsewhere in the world [21 30 31]. A significant number of patients with oesophageal cancer were diagnosed at advanced stages, which are consistent with previous studies [30 32]. However, the proportion of those diagnosed delay in oesophageal cancer was relatively higher in a nationwide cohort study conducted in Korean patients [31]. Increased patient delay (> two months) was found to be exacerbated by socio-economic characteristics in our study. Our finding is equivalent to this study [33] , which evidenced those patients with lower socio-economic status sought medical help later. Furthermore, socioeconomic status has had an important influence in patients being diagnosed at advanced stages, which is similar to the findings of the study conducted in China [33]. In our study, the majority of oesophageal cancer patients sought rapid relief for their symptoms by contacting several traditional healers. This conclusion is in line with that of a qualitative study conducted in Ethiopia's Oromia Regional State.

4. Conclusion

Oesophageal cancer patients in the study area had longer patients' presentation, diagnostic and symptom intervals. Moreover, majority of the oesophageal cancer patients had diagnosed at advanced stages (III and IV). Being single and never heard of oesophageal cancer prior to diagnosis was found to be predictors of increased patient intervals. The levels of first health facilities visited for medical consultation and the cost of transportation were identified as key factors in increasing diagnostic intervals.

Furthermore, being single, being female, waiting more than two months for a diagnosis, and symptom interval were found to be statistically significant predictors in the incidence of advanced stages at diagnosis. Patients' intervals could be shortened by increasing their awareness of oesophageal cancer symptoms.

Ethics approval and informed consent

The ethical clearance was obtained from the Institutional Review Board (IRB) of Addis Ababa University College of Health Sciences with a protocol number of 080/18/SPH. The study followed basic ethical principles of Helsinki declaration for medical research involving human participants[34]. All of the study participants were informed about the purpose and procedure of the research and their right to withdrawal from the study at any time. Written informed consent was obtained from each of the study participants. Meanwhile, the study participants were agreed to the extent that the finding of this study will be subjected to publication. Participants were well informed not to disclose their information to a third person. The information was kept secured and put confidentially with the first author.

Abbreviations

AJCC: American Joint Committee on Cancer

APR: Adjusted Prevalence Ratio

SD: Standard Deviation

IQR: Inter Quartile Range

P: Proportion

PR: Prevalence Ratio

USD: United States Dollar

Data availability

Data will be available up on request

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Authors' contributions

All authors contributed from the conception of idea up to data analysis and write up. They also participated in drafting or revising of the article and have agreed on to which journal the article shall be submitted and have given final approval of the version to be published, and agreed to be accountable for all aspects of the work. Specifically, BD was conceptualized the topic of interest, involved in data collection, coding, cleaning, analysis, interpretation of the result unto preparation

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Ethics approval statement

We have obtained verbal consent from the study participants and the ethical clearance was obtained from the Institutional Review Board (IRB) of Addis Ababa University College of Health Sciences with a protocol number of 080/18/SPH.

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