


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

Berhe Dessalegn ¹, Sefonias Getachew,² Robel Yirgu,³ Fikre Enqueselassie,² Mathewos Assefa,⁴ Adamu Addissie⁵

To cite: Dessalegn B, Getachew S, Yirgu R, *et al*. Time intervals from first symptom recognition to pathological diagnosis among patients with oesophageal cancer in Ethiopia: a cross-sectional study. *BMJ Open* 2022;**12**:e060812. doi:10.1136/bmjopen-2022-060812

► Prepublication history for this paper is available online. To view these files, please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2022-060812>).

Received 06 January 2022
Accepted 21 July 2022



© Author(s) (or their employer(s)) 2022. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

¹Public Health, Adigrat University College of Health Sciences, Adigrat, Ethiopia

²Department of public health, Addis Ababa University, Addis Ababa, Ethiopia

³Department of Preventive Medicine, School of Public Health, College of Health Sciences, Addis Ababa University, Addis Ababa, Ethiopia

⁴Oncology, Addis Ababa University School of Medicine, Addis Ababa, Ethiopia

⁵Preventive Medicine, Addis Ababa University School of Public Health, Addis Ababa, Ethiopia

Correspondence to

Mr Berhe Dessalegn;
berhe_dessalegn@yahoo.com

ABSTRACT

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

Methods

Design A cross-sectional study design was employed.

Settings and participants Patients with oesophageal cancer 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 that provided cancer care nearly for 90% of patients.

Main outcomes and measurements The Aarhus statement criteria were 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 tumour classification, the American Joint Committee on Cancer was used. Data were analysed using SPSS V.24. Descriptive statistics were applied to describe patients' characteristics. Poisson regression with robust variance was used to compute prevalence ratios. In all statistical tests, significance was declared at a p value of <0.05 .

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

Approximately 78% of study participants had never heard of oesophageal cancer and thought they had gastritis. Dysphagia was the 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 of >2 months had association with late-stage diagnosis.

Conclusion Patients with oesophageal cancer in Ethiopia had prolonged patient and diagnostic intervals. Increasing awareness of symptoms of oesophageal cancer and shortening time to diagnosis will help to improve the outcome of oesophageal cancer care in Ethiopia.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ In Ethiopia, in case of patient and diagnostic interval and associated factors, this 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 patients with oesophageal cancer.
- ⇒ However, the onset of symptoms is a subjective measurement that patients may not recall the exact time.

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 tumour of the oesophagus 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 oesophagus. 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 5-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 4 and 6 months. Nonetheless, it is not uncommon for patients with oesophageal cancer to be diagnosed at advanced stages, because, in most cases, the patients with oesophageal cancer have identified symptoms by the time the disease has reached its advanced stages, then lead to poor patient prognosis and survival rate.^{5 8 9} The prognosis and time intervals of patients with oesophageal cancer have been solely dependent on the patients' awareness of symptoms and literacy rate that contribute to early consultation and shorter pathological diagnosis periods, according to studies.^{10 11} In practice, however, patients with oesophageal cancer frequently arrived late in presentation and commonly referred late to the appropriate health facilities. In addition, literature also showed that shortening the time to presentation is an important step in reducing late diagnosis, and improving the prognosis and survival of patients with oesophageal cancer.^{12 13}

Oesophageal cancer is an overwhelming disease and among the most common causes 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 case 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. Moreover, the disease has created a huge burden in terms 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 have 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 the dark and is under-researched; as a result, there is no clear evidence of 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 patients with oesophageal cancer. Meanwhile, we were also striven to identify predictors of patient and pathological diagnostic delays of >60 and >30 days, respectively.

MATERIALS AND METHODS

Study design and sample size

A cross-sectional study design was employed. The study involved 338 patients with oesophageal cancer 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 another similar study,¹⁶ we assumed a 95% level of confidence, a 5% precision and 5% non-response rate.

Settings and participants

The Ethiopian healthcare delivery system has three tiers: primary, secondary and tertiary-level healthcare facilities that are linked with a referral system. The set-up 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 centres, 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 centre 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 centres, with the goal of providing preventative and primary healthcare 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. Patients with oesophageal cancer who were histologically confirmed and clinically staged to the selected health facilities were included in the study; whereas those who were critically ill, diagnosed with 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 patients with cancer being diagnosed and treated. At each health facility, one focal person was assigned to identify eligible patients with oesophageal cancer 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 compromising any services.

Variables and measurements

We used the Aarhus statement criteria to classify patient, diagnostic and symptom 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 recognising 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} Tumours were classified using the tumour–node–metastasis method from the seventh edition of the American Joint Committee on Cancer.²⁰ Cases were histologically and endoscopically confirmed. Stages I and II were classified as early stages of diagnosis, while stages 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 2-day training was given to 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 arrived for the treatment, trained nurses interviewed them individually in Amharic in a semiprivate room. If the participants could not 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 15 February, June or October of the year, respectively; if they only said the year, the estimated date was 30 June 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

Data analysis

Epi-info V.7 was used for the data entry and SPSS V.24 was used to analyse the data. Descriptive statistics were calculated for each variable. Numbers and percentages were used to summarise categorical variables. We presented mean and SD 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 a previous similar study.¹¹ For cross-sectional research, OR is the common measure of association, and logistic regression is often used to estimate. Nevertheless, evidence suggests that when the proportion of the outcome exceeds 10%, an OR overestimates the risk ratio, leading to incorrect interpretation. As a result, to avoid these limitations, the prevalence ratio (PR) is the preferred measure of association.^{23 24} Hence, Poisson regression with robust variance was used to compute the adjusted PRs 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 literature that 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.

RESULTS

Sociodemographic and socioeconomic characteristics of the study participants

We approached 351 participants who were histologically confirmed and clinically staged for oesophageal cancer and 96.3% (338) of them 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 accounted for 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 US\$1 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 US\$7 or 203 Ethiopian birr for a single trip just to cover only the transportation costs. Furthermore, nearly three-quarters of the study participants had paid their medical expenses out of their pockets (table 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 most common one. More than three-fourths of the study participants (77.8%, 95% CI (73.4% to 82.2%)) had never heard of oesophageal cancer prior to diagnosis of oesophageal cancer. For those who heard of oesophageal cancer prior to diagnosis, the main sources (48%) of the information were friends/family members or neighbours, followed by printed and electronic media such as TV, radio and 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 mentioned by 54.1%. Approximately three-fourths of the study participants had linked the first symptom/s to gastritis. All patients had recognised 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

Table 1 Sociodemographic and socioeconomic characteristics of patients with oesophageal cancer in Addis Ababa, Ethiopia, February 2019–August 2020 (n=338)

Variables	Frequency	Per cent
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 worker	38	1.2
Housewife	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 (US\$)		
<35	171	50.6
35–106	130	38.5
106.6–177	21	6.2
>177	16	4.7
Cost of one-way transport (US\$)		
<7	93	27.5
≥7	245	72.5
Sources of medical expenses		
Employing organisation	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

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 centres and health posts), followed by public hospitals (16%). At their first visit to health facilities, approximately two-thirds of the study participants first contacted health officers and nurses as healthcare providers. The mean (SD) of health facilities visited by the patients 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%).

Diagnostic characteristics of patients with oesophageal cancer

Out of the total patients with oesophageal cancer, about 76% (95% CI (71.0% to 80.7%)) of the study participants were diagnosed at late stages (III and IV). In terms of histological 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 obliterative in 34.9%. In terms of tumour locations, middle oesophagus, lower oesophagus and upper (cervical) were reported by 41.1%, 30.8% and 28.1%, respectively (table 2).

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% to 79.3%)). About 10% of the participants had visited health facilities after 365 days of first symptom recognition. Only about 8% of the participants visited health facilities within 30 days. The majority (71%) of the participants mentioned their reason for late 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% to 86.2%)). Three per cent 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 30 days. The median (IQR) symptom interval was 215 (130–353) days. The most noticeable single factor mentioned by majority (78%) of the participants for the diagnostic delay was longer appointments primarily associated with the healthcare organisations.

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

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

Factors associated with patient delay

Based on the cut-off point, age, residency, educational status, occupation, marital status, income, awareness about oesophageal cancer prior to diagnosis of oesophageal cancer, being a housewife and visiting traditional healers were potential candidates and included in the multivariable analysis. On the other hand, participants who were unable to read and write (PR=1.2, 95% CI (1.05 to 1.43)), being a housewife (PR=1.14, 95% CI (1.01 to 1.29)), single participants (PR=1.08, 95% CI (1.03 to 1.14)), monthly income <US\$35 (PR=1.29, 95% CI (1.09 to 1.55)) and US\$35–106 (PR=1.3, 95% CI (1.09 to 1.55)), monthly family income <US\$53 (PR=1.17, 95% CI (1.02 to 1.33)) and US\$53–141 (PR=1.17, 95% CI (1.02 to 1.34)), and having never heard of oesophageal cancer prior to diagnosis (PR=1.11, 95% CI (1.03 to 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 to 1.15)) and having never heard of oesophageal cancer prior to diagnosis (adjusted PR=1.08, 95% CI (1.03 to 1.15)) were found statistically significant to increase the prevalence of patient delay among patients with oesophageal cancer (table 3).

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; whereas single participants (PR=1.8, 95% CI (1.74 to 1.85)), monthly family income US\$53–141 (PR=0.91, 95% CI (0.85 to 0.99)), transport cost (one trip) >US\$7 (PR=1.07, 95% CI (1.06 to 1.13)), first medical consultation at a health centre (PR=0.93, 95% CI (0.88 to 0.99)) and <3 health facilities visited (PR=0.93, 95% CI (0.87 to 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 to 2.10)), sources of medical expenses (adjusted PR=1.2, 95% CI (1.13 to 2.40)), cost of transportation (adjusted PR=1.2, 95% CI (1.12 to 1.54)) and first medical consultation to health facilities (adjusted PR=1.4, 95% CI (1.20 to 2.30)) were statistically significant to increase the prevalence of diagnostic delay among patients with oesophageal cancer (table 4).

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

Based on the cut-off point, gender, occupation, family size, transport, first medical consultation, patient delay of >2 months and number of times visiting for diagnosis were included in the multivariable analysis; whereas marital status, being single (PR=1.16, 95% CI (1.02 to 1.30)) and patient delay of >2 months (PR=1.38, 95% CI (1.14 to 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 to 1.31)), female participants (adjusted PR=1.15, 95% CI (1.015 to 1.31)), patient delay of >2 months (adjusted PR=1.41, 95% CI (1.15 to 1.69)) and symptom intervals (adjusted PR=1.26, 95% CI (1.12 to 1.67)) were statistically significant to increase the prevalence of advanced stage at time of diagnosis (table 5).

DISCUSSION

Longer consultation and diagnostic intervals, as well as late stages at the time of diagnosis, were hypothesised before we started this study. This research has estimated prolonged patient 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 patients were forced to visit an average of 10 different health facilities in search of better and more



Table 3 Factors associated with patient delay (>60 days) among patients with oesophageal cancer 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)	Reference		Reference	
35–44	26 (59.1)	18 (40.9)	0.96 (0.82 to 1.11)	0.55	0.96 (0.86 to 1.07)	0.43
45–54	63 (72.4)	24 (27.6)	1.03 (0.91 to 1.18)	0.62	1.03 (0.94 to 1.12)	0.56
≥55	140 (81.4)	32 (18.6)	1.10 (0.96 to 1.23)	0.18	0.99 (0.91 to 1.08)	0.81
Residency						
Urban	88 (71.0)	36 (29.0)	Reference		Reference	
Rural	155 (77.5)	45 (22.5)	1.04 (0.98 to 1.10)	0.19	1.04 (0.97 to 1.11)	0.29
Educational status of participants						
Unable to read and write	155 (77.1)	46 (22.9)	1.2 (1.05 to 1.43)	0.01	1.11 (0.94 to 1.29)	0.22
Grade 1–8	56 (81.2)	13 (18.8)	1.25 (1.07 to 1.46)	0.006	1.15 (0.97 to 1.35)	0.1
Grade 9–12	23 (67.6)	11 (32.4)	1.16 (0.97 to 1.38)	0.11	1.08 (0.91 to 1.29)	0.38
Diploma and above	9 (45.0)	11 (55.0)	Reference			
Occupation of participants						
Private worker	17 (56.7)	13 (43.3)	Reference		Reference	
Government worker	24 (68.6)	11 (31.4)	1.08 (0.93 to 1.24)	0.32	1.02 (0.94 to 1.11)	0.57
Housewife	82 (78.8)	22 (21.2)	1.14 (1.01 to 1.29)	0.03	0.94 (0.86 to 1.02)	0.14
Merchant	24 (82.8)	5 (17.2)	1.17 (1.02 to 1.34)	0.03	1.03 (0.94 to 1.12)	0.54
Farmer	96 (76.2)	30 (23.8)	1.13 (0.99 to 1.27)	0.06	0.93 (0.85 to 1.02)	0.12
Marital status of participants during the data collection time						
Single	76 (85.4)	13 (14.6)	1.08 (1.03 to 1.14)	0.002	1.09 (1.03 to 1.15)*	0.001
Married	167 (71.1)	68 (28.9)	Reference			
Monthly income (US\$)						
<35	124 (78.5)	34 (21.5)	1.29 (1.09 to 1.55)	0.004	1.22 (1.005 to 1.48)	0.045
35–106	101 (78.9)	27 (21.1)	1.3 (1.09 to 1.55)	0.004	1.22 (1.22 to 1.48)	0.042
106.6–177	12 (54.5)	10 (45.5)	1.12 (0.90 to 1.39)	0.29	0.46 (1.09)	0.46
>177	6 (37.5)	10 (62.5)	Reference			
Monthly family income (US\$)						
<53	128 (77.1)	38 (22.9)	1.17 (1.02 to 1.33)	0.025	1.12 (0.98 to 1.27)	0.09
53–141	84 (77.8)	24 (22.2)	1.17 (1.02 to 1.34)	0.024	1.13 (0.99 to 1.28)	0.08
141.4–230	18 (72.0)	7 (28.0)	1.13 (0.96 to 1.33)	0.14	1.1 (0.94 to 1.29)	0.26
>230	13 (52.0)	12 (48.0)	Reference			
Prior information about oesophageal cancer						
No	198 (79.0)	53 (21.0)	1.11 (1.03 to 1.97)	0.007	1.08 (1.02 to 1.17)*	0.04
Yes	44 (61.1)	29 (38.9)	Reference			
Visiting traditional healers						
No	180 (73.2)	66 (26.8)	Reference			
Yes	63 (80.8)	15 (19.8)	1.04 (0.99 to 1.11)	0.15	1.04 (0.98 to 1.10)	0.23

*level of confidence.
PR, prevalence ratio.

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 with the

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

Patient characteristics	Diagnostic delay		Unadjusted	P value	Adjusted	P value
	Yes (%)	No (%)	PR (95% CI)		PR (95% CI)	
Age of participants (years)						
<35	17 (77.2)	5 (22.8)	Reference		Reference	
35–44	33 (75.0)	11 (25.0)	0.94 (0.84 to 1.04)	0.24	0.96 (0.86 to 1.07)	0.45
45–54	75 (87.2)	11 (12.8)	1.01 (0.92 to 1.09)	0.92	1.02 (0.93 to 1.11)	0.69
≥55	140 (80.5)	34 (19.5)	0.97 (0.89 to 1.05)	0.45	0.97 (0.89 to 1.06)	0.53
Marital status of participants during the data collection time						
Single	78 (88.6)	10 (11.4)	1.80 (1.74 to 1.85)	0.0001	1.2 (1=1 to 2.10)**	0.04
Married	189 (79.4)	49 (20.6)	Reference		Reference	
Monthly family income (US\$)						
<53	139 (82.7)	29 (17.3)	0.95 (0.89 to 1.01)	0.11	0.98 (0.88 to 1.09)	0.69
53–141	80 (74.8)	27 (25.2)	0.91 (0.85 to 0.99)	0.008	0.91 (0.82 to 1.002)	0.05
141.4–230	20 (80.0)	5 (20.0)	1.02 (0.95 to 1.09)	0.57	1.01 (0.93 to 1.09)	0.84
>230	19 (73.1)	7 (26.9)	Reference		Reference	
Cost of one-way transport (US\$)						
<7	67 (73.6)	24 (26.4)	Reference		Reference	
≥7	200 (85.1)	35 (14.9)	1.07 (1.06 to 1.13)	0.03	1.2 (1.12 to 1.54)**	0.04
First medical consultation						
Health post	35 (87.5)	5 (12.5)	0.99 (0.94 to 1.07)	0.96	1.01 (0.94 to 1.08)	0.83
Health centre	123 (77.4)	36 (22.6)	0.93 (0.88 to 0.99)	0.015	1.4 (1.2 to 2.30)**	0.049
Private clinic	38 (88.4)	5 (11.6)	0.99 (0.94 to 1.06)	0.78	1.01 (0.94 to 1.08)	0.87
Private hospital	24 (72.7)	9 (27.3)	0.91 (0.82 to 1.002)	0.054	0.92 (0.83 to 1.02)	0.10
Public hospital	46 (90.2)	5 (9.8)	Reference		Reference	
Number of health facilities visited for diagnosis						
<3	13 (72.2)	5 (27.8)	Reference		Reference	
3–6	153 (80.5)	37 (19.5)	0.93 (0.87 to 0.99)	0.02	0.93 (0.87 to 1.22)	0.054
7–10	67 (81.7)	15 (18.3)	0.93 (0.87 to 1.004)	0.06	0.94 (0.87 to 1.01)	0.108
>10	29 (82.9)	6 (17.1)	0.94 (0.86 to 1.026)	0.17	0.94 (0.86 to 1.03)	0.19
Source of medical expenses						
Free medical care	57 (79.2)	15 (20.8)	Reference		Reference	
Government insurance	11 (61.1)	7 (38.9)	0.90 (0.78 to 1.044)	0.16	1.22 (1.13 to 2.40)*	0.048
Out of pocket	199 (84.3)	37 (15.7)	1.03 (0.97 to 1.09)	0.34	1.03 (0.98 to 1.09)	0.26

*level of confidence
PR, prevalence ratio.

patient interval estimated from our study. This substantial difference could be attributed to sociocultural and socio-economic disparities in health-seeking behaviour, 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 a study conducted in South Africa.²⁸ The similarities in socio-economic, 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 parts of the world.^{11 21 25 26} The discrepancy may be the differences in diagnostic workup 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

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

* level of confidence

aPR, adjusted PR; PR, prevalence ratio.

The similarities could be explained by the fact that the diagnostic procedures and healthcare 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, those who were 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, patients with oesophageal cancer who paid their medical expense from their own pocket had longer patient interval than patients whose medical

expenses were covered by other organisations. The reason could be that they ignore the symptoms because patients with low socioeconomic status had other unmet survival needs more than investing money for medical care.²⁹

The proportion of advanced stages at time of first diagnosis is higher compared with the study conducted in Shandong University in Jinan (China) by Wang *et al*²¹; this could be related to longer patient and diagnostic intervals and socioeconomic difference among the communities. The cardinal symptom reported by majority of our participants was dysphagia; this result is comparable with other 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 with oesophageal cancer late was relatively higher in a nationwide cohort study conducted in Korean patients.³¹ Increased patient delay (>2 months) was found to be exacerbated by socioeconomic characteristics in our study. Our finding is equivalent to this study,³³ which evidenced those patients with lower socioeconomic status sought medical help later. Furthermore, socioeconomic status has had an important influence on 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 patients with oesophageal cancer 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.

CONCLUSION

Patients with oesophageal cancer in this study area had longer patient presentation, diagnostic and symptom intervals. Moreover, majority of the patients with oesophageal cancer were diagnosed at advanced stages (III and IV). Being single 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, being single, being female, waiting more than 2 months for a diagnosis and symptom interval were found to be statistically significant predictors in the incidence of advanced stages at diagnosis. Patient intervals could be shortened by increasing their awareness of oesophageal cancer symptoms.

Acknowledgements We would like to forward our gratitude to our data collectors, supervisors and study participants for their time and genuine responses. Last but not least, we would like to appreciate the health facilities for their cooperation.

Contributors All authors contributed to 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 conceptualised the topic of interest and was involved in data collection, coding, cleaning, analysis, interpretation of the result and preparation of the manuscript. FE was involved in proposal development, planning the fieldwork and result section. RY, MA, SG and AA were involved in proposal development, data analysis, write-up and in critical reviewing of the manuscript. May 2022. The gaurantor and the responsible author for any request for this specific article is BD.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Ethics approval 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. All of the study participants were informed about the purpose and procedure of the research and their right to withdraw from the study at any time. Written informed consent was obtained from each of the study participants. Meanwhile, the study participants 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 by the first author.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

ORCID iD

Berhe Dessalegn <http://orcid.org/0000-0001-6735-3562>

REFERENCES

- 1 Bray F, Ferlay J, Soerjomataram I, *et al*. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2018;68:394–424.
- 2 Sinha R, Anderson DE, McDonald SS, *et al*. Cancer risk and diet in India. *J Postgrad Med* 2003;49:222–8.
- 3 Ferlay J, Colombet M, Soerjomataram I, *et al*. Cancer incidence and mortality patterns in Europe: estimates for 40 countries and 25 major cancers in 2018. *Eur J Cancer* 2018;103:356–87.
- 4 Polite BN, Adams-Campbell LL, Brawley OW, *et al*. Charting the future of cancer health disparities research: a position statement from the American association for cancer research, the American cancer Society, the American Society of clinical oncology, and the National cancer Institute. *Cancer Res* 2017;77:4548–55.
- 5 International Agency for Research on Cancer (IARC) WHO. GLOBOCAN; 2012, Section of Cancer Surveillance.
- 6 PDFJ H-C, MSFT JO. Cancer in Africa, epidemiology and prevention. In: *IARC scientific publications No. 153*. 417. Lyon: IARC, 2003.
- 7 Kachala R. Systematic review: epidemiology of oesophageal cancer in sub-Saharan Africa. *Malawi Med J* 2010;22:65–70.
- 8 Dassen AE, Dikken JL, Bosscha K, *et al*. Gastric cancer: decreasing incidence but stable survival in the Netherlands. *Acta Oncol* 2014;53:138–42.
- 9 Bernards N, Haj Mohammad N, Creemers GJ, *et al*. Improvement in survival for patients with synchronous metastatic esophageal cancer in the South of the Netherlands from 1994 to 2013. *Acta Oncol* 2016;55:1161–7.
- 10 Wang G-Q, Jiao G-G, Chang F-B, *et al*. Long-term results of operation for 420 patients with early squamous cell esophageal carcinoma discovered by screening. *Ann Thorac Surg* 2004;77:1740–4.
- 11 Grotenhuis BA, van Hagen P, Wijnhoven BPL, *et al*. Delay in diagnostic workup and treatment of esophageal cancer. *J Gastrointest Surg* 2010;14:476–83.
- 12 Lee A, Khulusi S, Watson R. Which interval is most crucial to presentation and survival in gastroesophageal cancer: a systematic review. *J Adv Nurs* 2017;73:2270–82.



- 13 Wijnhoven BPL, Tran KTC, Esterman A, *et al.* An evaluation of prognostic factors and tumor staging of resected carcinoma of the esophagus. *Ann Surg* 2007;245:717–25.
- 14 Melhado RE, Alderson D, Tucker O. The changing face of esophageal cancer. *Cancers* 2010;2:1379–404.
- 15 Edgren G, Adami H-O, Weiderpass E, *et al.* A global assessment of the oesophageal adenocarcinoma epidemic. *Gut* 2013;62:1406–14.
- 16 Cavallin F, Scarpa M, Cagol M, *et al.* Time to diagnosis in esophageal cancer: a cohort study. *Acta Oncol* 2018;57:1179–84.
- 17 FEDERAL DEMOCRATIC REPUBLIC OF ETHIOPIA MINISTRY OF HEALTH. *Guideline for implementation of a patient referral system medical services Directorate*, 2010.
- 18 Weller D, Vedsted P, Rubin G, *et al.* The Aarhus statement: improving design and reporting of studies on early cancer diagnosis. *Br J Cancer* 2012;106:1262–7.
- 19 Olesen F, Hansen RP, Vedsted P. Delay in diagnosis: the experience in Denmark. *Br J Cancer* 2009;101 Suppl 2:S5–8.
- 20 Edge SB, Compton CC. The American joint Committee on cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. *Ann Surg Oncol* 2010;17:1471–4.
- 21 Wang J, Liu F, Gao H, *et al.* The symptom-to-treatment delay and stage at the time of treatment in cancer of esophagus. *Jpn J Clin Oncol* 2008;38:87–91.
- 22 Kamau E, Marial C, Joshi M. Time to presentation and diagnosis of esophageal cancer in patients seen at the Kenyatta national Hospital. *East Afr Med J* 2019;95.
- 23 Martinez BAF, Leotti VB, Silva GdeSE, *et al.* Odds ratio or prevalence ratio? An overview of reported statistical methods and appropriateness of interpretations in cross-sectional studies with dichotomous outcomes in veterinary medicine. *Front Vet Sci* 2017;4:193.
- 24 Tamhane AR, Westfall AO, Burkholder GA, *et al.* Prevalence odds ratio versus prevalence ratio: choice comes with consequences. *Stat Med* 2016;35:5730–5.
- 25 van Erp NF, Helsper CW, Slottje P, *et al.* Time to diagnosis of symptomatic gastric and oesophageal cancer in the Netherlands: where is the room for improvement? *United European Gastroenterol J* 2020;8:607–20.
- 26 Martin IG, Young S, Sue-Ling H, *et al.* Delays in the diagnosis of oesophagogastric cancer: a consecutive case series. *BMJ* 1997;314:467–70.
- 27 Subasinghe D, Samarasekera DN. Delay in the diagnosis of esophageal carcinoma: experience of a single unit from a developing country. *Indian J Cancer* 2010;47:151–5.
- 28 Govender M, Ferndale L, Clark DL. Oesophageal cancer in South Africa: the long timeline from onset of symptoms to definitive management. *S. Afr. j. oncol.* 2017;1:3.
- 29 Thein H-H, Anyiwe K, Jembere N, *et al.* Effects of socioeconomic status on esophageal adenocarcinoma stage at diagnosis, receipt of treatment, and survival: a population-based cohort study. *PLoS One* 2017;12:e0186350.
- 30 Abdullah M, Karim AA, Goh K-L. Late presentation of esophageal cancer: observations in a multiracial South-East Asian population. *J Dig Dis* 2010;11:28–33.
- 31 Jung H-K, Tae CH, Lee H-A, *et al.* Treatment pattern and overall survival in esophageal cancer during a 13-year period: a nationwide cohort study of 6,354 Korean patients. *PLoS One* 2020;15:e0231456.
- 32 Rubenstein JH, Shaheen NJ, Epidemiology SNJ. Epidemiology, diagnosis, and management of esophageal adenocarcinoma. *Gastroenterology* 2015;149:302–17.
- 33 Wang N, Cao F, Liu F, *et al.* The effect of socioeconomic status on health-care delay and treatment of esophageal cancer. *J Transl Med* 2015;13:241.