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Magnitude of metastatic esophageal cancer and associated factors among adult patients at Adama Hospital Medical College, Oncology Center, Adama, Central Ethiopia

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Abstract

Background

Cancer accounts for one in six deaths globally, with approximately 20 million new cases and over 10 million deaths reported in 2020. This study aimed to assess the factors associated with esophageal cancer metastasis among adult patients at Adama Hospital Medical College.

Methods

A facility-based cross-sectional study was conducted from December 2019 to December 2023. A total of 372 patient charts were reviewed from the oncology center's cancer registry. Data were collected via a data abstraction chart and analyzed via Epi-info version 7.2.6.0 and SPSS version 27. Descriptive statistics were used to summarize the data, and binary logistic regression was applied to identify significant associations between independent variables and esophageal cancer metastasis. Multivariate logistic regression was employed to control for confounding factors. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated, and statistical significance was set at $p < 0.05$.

Results

This study revealed that 44.6% of patients had esophageal cancer metastasis (95% CI: 39.5–49.6). The liver (24.5%) and lungs (17.7%) were the most common sites of metastasis. Significant predictors of metastasis included urban residency (AOR = 0.04; 95% CI: 0.006–0.287), both mucosal invasion and submucosal invasion (AOR = 0.02; 95% CI: 0.01–0.05), normal weight (AOR = 0.03; 95% CI: 0.001–0.65), formal education (AOR = 0.15; 95% CI: 0.07–0.34), and occupational exposure to chemicals (AOR = 4.12; 95% CI: 2.12–8.02).

Conclusion

Esophageal cancer metastasis is prevalent among patients at Adama Hospital. Residency, depth of invasion, occupational exposure and low body mass index were identified as the variables significantly associated with esophageal cancer metastasis. Early detection and routine screening, particularly for high-risk groups, are recommended.

1. Background

Esophageal cancer, a malignant condition originating in the esophagus, often progresses to metastatic stages and spreads to vital organs such as the liver, lymph nodes, lungs, and bones. Globally, cancer incidence and mortality are increasing due to factors such as population aging, lifestyle changes, and

socioeconomic development. While the "westernization" of lifestyles is often blamed, geographic variations persist, highlighting the influence of local risk factors (1, 2).

Esophageal squamous cell carcinoma (ESCC) and esophageal adenocarcinoma (EAC) are the primary histological subtypes (3). ESCC is more prevalent globally, especially in developing countries (4), whereas EAC is more common in Western nations (5). In Africa, ESCC is linked to risk factors such as alcoholism, smoking, and aflatoxin exposure (3, 6).

The high incidence of ESCC in Africa poses a significant health challenge because of late diagnosis and limited treatment options. Screening programs and awareness initiatives are lacking in many African countries, contributing to the high mortality rate. Additionally, the high cost of cancer care and scarcity of cancer facilities further hinder effective treatment (7).

Esophageal cancer, particularly its metastatic form, has a dismal prognosis. Despite its high prevalence in Ethiopia, the magnitude of metastasis and associated risk factors remain understudied. This lack of knowledge hampers efforts to allocate resources effectively and improve patient outcomes(8).

Esophageal cancer in Ethiopia is often diagnosed at late stages, limiting treatment options and leading to poor survival rates. Factors such as socioeconomic status, lifestyle, dietary habits, and access to healthcare can influence the likelihood of metastasis and treatment outcomes (9, 10).

This study aims to address the critical need for information on the prevalence of metastatic esophageal cancer and its associated risk factors in Ethiopia. By understanding these factors, targeted prevention and treatment strategies can be developed.

2. Methods

2.1. Study design and setting

The research was carried out at Adama Hospital Medical College, which is situated 99 kilometers southeast of Addis Ababa in Adama city. There is one government hospital, one AHMC, and eight private general hospitals in the city. To date, Somali regional states, Amhara, Oromia, and a catchment population of over 6 million people are served by the hospital on average 1000 patients per day, according to records from the Health Management Information System (HMIS).

The hospital can accommodate 1200 beds and sees 1000 patients a day on average at its six OPDs (medical case teams) and various specialized clinics. With 16 beds, the oncology unit can accommodate 16 patients per day and more than 3800 patients annually (data from the DHIS2 report). The hospital-based cross-sectional study design was conducted from April 15–May 15–2024.

All adult patients with esophageal cancer who visited the Adama Hospital Medical College Oncology Unit between December 2019 and December 30, 2023 and who fully met the eligibility criteria composed the study population.

2.2. Sample size determination

The sample size was calculated via a single population proportion formula considering important statistical assumptions, such as a proportion (P) of 50% and a level of significance (α) of 0.05; hence, the corresponding standardized values for 95% confidence (Z) were 1.96 and marginal (d) = 0.05.

The population proportion is 50% because, to the best of our knowledge, no study has been conducted on metastatic esophageal cancer and associated factors previously. Therefore, the sample size is calculated as shown below:

$$n = \frac{(\frac{z\alpha}{2})^2 \, \mathrm{p}(1-\mathrm{p})}{(d)^2} \qquad n = \frac{(1.96)^2 \, 0.5(1-0.5)}{(0.05)^2} = 384$$

Were,

n is the total sample size required

d, stands for margin of error

P, proportion of patients with esophageal cancer among patients

Z, statics for level of confidence.

The calculated sample size (n) was 384. Because of the small study population, N = 372, since there were no studies on metastatic esophageal cancer, the sample size calculation was greater than the total study population, so data from 372 patients were collected.

2.3. Subjects

All adult patients aged 18 years or older with histologically or clinically confirmed esophageal cancer whose medical records were kept at Adama Hospital Medical College, Oncology Unit, between January 1, 2019, and December 30, 2023 were included in the study, and patients whose medical charts were incomplete, i.e., when the necessary investigation was left to be performed, and patient medical charts with unknown metastasis (Mx) diagnoses were excluded.

2.4. Data collection

The data for this study were retrieved from patients' recorded data and from the cancer registry process. A structured data extraction checklist has been developed on the basis of available patient charts. This checklist served as a guide for the data extraction process. To obtain relevant information, the medical records of patients with esophageal cancer were systematically extracted.

A pretest was conducted at the Adama Hospital Medical College Oncology Center on 18 (5%) estimated sample sizes prior to data collection, and the results and observations gathered from the pretest were

utilized to adjust the checklist and the data collection procedure as necessary. Cronbach's alpha was calculated via SPSS version 27 to check internal consistency (reliability), and the result was 0.77. Every day, the gathered data were verified for correctness and completeness. Any gaps found were filled immediately before the data were processed and analyzed.

2.5. Data analysis

The collected data were cleaned, coded and entered into EPI Data version 3.1, after which they were exported for evaluation to SPSS model 27. The statistics were analyzed via binary and multivariate logistic regressions to determine the impact of different factors on the final result variable. The consequences inside the shape of tables, figures and textual content include the use of frequencies and precision statistics, which include fashionable deviations, means, and percentages, to explain the populace in terms of applicable variables. The degree of association between the dependent and independent variables was assessed via odds ratios with 95% confidence intervals, and a p value < 0.05 indicated statistical significance.

2.6. Ethical approval and consent to participate

The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and obtained ethical approval from the Institutional Review Board (IRB) of **Saint Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia by (Ref.no; - PM23/1146).** Because this study analyzed existing medical records, it wasn't possible to contact individual patients for consent. Therefore, the IRB granted a waiver, allowing us to proceed with the research using anonymized, routinely collected data. A letter of approval was obtained from Adama Hospital Medical College, Adama, Ethiopia and the Oncology department head was contacted. The approved letter were showed to the respective Oncology unit during data collection.

3. Results

3.1. Sociodemographic traits of the respondents

All of the 372 reviewed patient charts were complete and included in the review, resulting in a response rate of 100%. The mean age of the participants was 54.3 ± 11.8 years, with 25 being the youngest and 95 years being the oldest. With respect to the age categories of the participants, more than one-third of the 117 (31.5%) were in the age group of 51–60 years, and as few as 7 (1.9%) were aged 30 years or younger. The participants aged 41–50 years held second place, with 107 (28.8%) following 51–60 years of age.

In terms of participant sex, more than half of the 222 participants (59.7%) were female; the male-to-female ratio was 1.5–1. With respect to participant residence, 324 (87.1%) of the study participants were from rural areas, whereas only 48 (12.9%) were from urban areas.

In terms of the patients' educational background, 313 (84.1%) did not participate in formal schooling. The majority of participants, 216 (58.1%), were farmers, followed by housewives, 126 (33.9%), and government-

appointed workers, 6 (0.8%). With respect to the distribution of religions in the research region, orthodox Christians (19.9%) and protestants (22.9%) followed second and third religions, respectively, with nearly three-quarters (73.7%) of the participants being Muslims. A total of 45 (12.1%) of the 311 (83.6%) married people were included (Table 1).

Table 1

Sociodemographic characteristics of adult patients with esophageal cancer at Adama Hospital Medical College, Ethiopia, 2024.

Variables	Categories	N	%
Age	<=30	7	1.9
	31–40	51	13.7
	41–50	107	28.8
	51–60	117	31.5
	61–70	64	17.2
	> 70	26	7
Sex	Male	150	40.3
	Female	222	59.7
Residence	Urban	48	12.9
	Rural	324	87.1
Education	not educated	313	84.1
	Educated	59	15.9
Occupation	Farmer	216	58.1
	gov't employee	6	1.6
	Merchant	3	.8
	daily laborer	17	4.6
	house wife	126	33.9
	Other*	4	1.1
Religion	Orthodox	74	19.9
	Muslim	274	73.7
	Protestant	22	5.9
	Other**	2	.5
Marital	Married	311	83.6
	Widowed	45	12.1
	Others2	16	4.3

*- NGO, broker, **- Wakefeta, **Others2-** unmarried, divorced

3.2. Lifestyle and comorbidity

In terms of lifestyle, 39 (10.5%) of the participants smoked cigarettes, whereas 25 (6.7%) smoked secondhand. Additionally, 67 (18%) chewed the chat, and 234 (62.9%) had occupational exposure. Only 51 (13.7%) patients drank alcohol, and 44 (11.85%) had a family history of cancer. More than three-fourths of the 314 (87.9%) were underweight (Table 2).

Table 2
Lifestyle and comorbidities of adult patients with esophageal cancer at Adama Hospital Medical College. Ethiopia, 2024.

Variables	Categories	N	%
Cigarette smoking	Yes	39	10.5
	No	333	89.5
Second hand smoker	Yes	25	6.7
	No	347	93.3
Chat	Yes	67	18
	No	303	81.5
Occupational exposure	Yes	234	62.9
	No	138	37.1
Alcohol	Yes	51	13.7
	No	321	86.3
Family hx of cancer	Yes	44	11.8
	No	327	87.9
BMI	Underweight	314	84.4
	Normal	55	14.8
	Over weight	3	.8
Comorbidity	Yes	24	6.5
	No	348	93.5

3.3. Tumor characteristics

Clinically, most of the participants (284; 76.3%) presented with dysphagia. The histological subtype was ESCC for 296 (79.6%) participants, and the tumor location was at the lower parts of the esophagus for 237 (63.7%) participants.

The tumor size of the patients during presentation was assessed. Accordingly, except for 4 (1.1%) who presented with T1 and 14 (3.8%) with T2, the majority of the participants presented with T3 (46 (12.6%)) and T4 (308 (82.8%) (Table 3).

Table 3

Tumor characteristics of adult patients with esophageal cancer at Adama Hospital Medical College. Ethiopia, 2024.

Variables	Categories	N	%
Clinical presentation	Dysphagia	284	76.3
	odynophagia and chest pain	88	23.7
Histological subtype	ESCC	296	79.6
	EAC	76	20.4
Location	Lower	237	63.7
	Middle	118	31.7
	Upper	17	4.6
T stage	T1	4	1.1
	T2	14	3.8
	T3	46	12.4
	T4	308	82.8
M stage	MO	206	55.4
	M1	166	44.6
Lymph node metastasis	NX	1	0.3
	N0	7	1.9
	N1	94	25.3
	N2	57	15.3
	N3	213	57.3
Depth of invasions	Mucosa	117	31.5
	Sub mucosal	141	37.9
	muscularis adventia and local structures	114	30.6
Site of metastasis	No organ metastasis	206	55.4
	Liver	91	24.5
	Lung	66	17.7
	distant LN	9	2.4
Type of treatment	Chemotherapy	368	98.9
	Surgery	2	.5

Variables	Categories	N	%
	Other	2	.5
Tumor status	Metastasized	166	44.6
	Not metastasized	206	55.4

3.4. Magnitude of metastatic esophageal cancer among patients with esophageal cancer

In this study, the magnitude of esophageal metastasis among patients with esophageal cancer who visited Adama Hospital Medical College, Cancer Center, was 166 (44.6%) (Fig. 1). Among the 166 patients with metastatic esophageal carcinoma, 91 (54.82%) had esophageal metastasis to the liver, 66 (39.75%) had metastasis to the lung, and the remaining 9 (5.4%) had metastasized to distant lymph nodes.

3.5. Factors associated with metastatic esophageal carcinoma

In the bivariable logistic regression analysis, residence, level of education, depth of invasion, alcohol consumption, body mass index, occupational exposure history, clinical presentation and T stage were significantly associated with increased or decreased odds of metastasis among patients with esophageal cancer (Table 4).

However, in the multivariable logistic regression analysis, only residence, level of education, occupational exposure, depth of invasion, and BMI were significantly associated with the outcome variable at a p value ≤ 0.05.

Accordingly, as shown in Table 5 below, the odds of esophageal cancer metastasis among urban residents were approximately 96% lower than those among rural residents ({AOR = 0.04; 95% CI: (0.01–0.29) P = 0.00)}. On the other hand, participants who had higher odds of occupational exposure had 4 times greater odds of metastasis (AOR = 4.12; 95% CI: 2.12–8.022) (P = 0.00)} than those who had no occupational exposure.

The odds of esophageal cancer metastasis to distant organs for those with normal weight were 97% lower than those for those who were overweight ({AOR = 0.03. ; 95% CI: 0.001–0.65) p = 0.025)}. The level of education and magnitude of metastasis were also assessed to determine if the difference was statistically significant. Accordingly, participants who had formal education were 85% less likely to have distant organ metastasis than participants who had no formal education were [AOR = 0.15; 95% CI: 0.07–0.34; P = 0.00)].

Similarly, compared with esophageal cancers that invade or originate from the muscularis adventia and local structures, those that invade the submucosa and mucosa have 98% lower odds of metastasis ({AOR = 0.02; 95% CI: 0.01–0.05) P = 0.00)} and are summarized in Table 5.

Table 4
Binary logistic regression analysis of factors associated with mEC among adult patients at Adama Hospital Medical College, Ethiopia, 2024.

Variables	Categories	Tumor status		COR with (95% CI)	P value
		Metastasis	Not metastasis		
Residence	Urban	2	46	0.042(0.01–0.178)	0.000
	Rural	164	160	Ref	
Level of Education	not educated	158	155	Ref	
	Educated	8	51	0.16(0.74 – 0.33)	0.000
Clinical presentation	Dysphagia	115	169	0.68(0.54–0.86)	0.004
	odynophagia and chest pain	51	37	Ref	
Depth of invasion	Mucosa	29	88	Ref	
	sub mucosal	29	112	1.27(0.709–2.29)	0.000
	muscularis adventia and local structures	108	6	0.018(0.007–0.046)	
Alcohol	Yes	16	35	Ref	
	No	150	171	0.521(0.277–0.97)	0.043
T-stage	3	1	3	Ref	
	4	1	13	0.34(4.33-90.847)	
	5	12	34	0.96(.944 – 9.97)	0.015
	6	152	156	0.35(0.342–3.325)	0.004
Body mass index category	Underweight	162	152	18.474(5.65–60.40)	
	Normal	3	52	2.13(0.19–23.75)	0.115
	Over weight	1	2	Ref	
Occupational exposure history	Yes	135	99	4.70(2.923–7.98)	0.000

	No	31	107	Ref

Table 5
Multivariable logistic regression analysis of factors associated with MBC at Adama Hospital Medical College, Ethiopia, 2024.

Variables	Categories	Tumor status		COR	AOR(95% CI)	P value
		Metastasis	No metastasis			
Residence	Urban	2	46	0.042(0.01–0.178)	0.04(0.01–0.29)	0.001**
	Rural	164	160	Ref	Ref	1
Level of Education	Not educated	158	155	Ref	Ref	1
	Educated	8	51	0.16(0.74 – 0.33)	0.15(0.07–0.34)	0.002**
Occupational exposure to chemical	Yes	135	99	4.70(2.923–7.98)	4.12(2.12–8.022)	0.00***
	No	31	107	Ref	Ref	1
Body mass index	Underweight	162	152	18.474(5.65–60.40)	0.82(0.97–3.974)	0.211
	Normal	3	52	2.13(0.19–23.75)	0.03(0.001–0.65)	0.025*
	Over weight	1	2	Ref	Ref	1
Depth of invasion	Mucosa	29	88	Ref	0.02(0.01–0.05)	0.000***
	sub mucosal	29	112	1.27(0.709–2.29)	0.02(0.01–0.05)	0.000***
	muscularis adventia and local structures	108	6	0.018(0.007–0.046)	Ref	1
NB: *=significant, *p < 0.05, **p < 0.01 and ***p < 0.001						

4. DISCUSSION

The current study assessed the magnitude of esophageal cancer metastasis among patients with esophageal cancer who visited the Adama Hospital Medical College Cancer Center from 2019–2023. Accordingly, the magnitude of esophageal metastasis among patients with esophageal cancer who visit Adama Hospital Medical College is 44.6% (CI: 39.5–50).

This finding is consistent with that of a study conducted in China, where the magnitude of metastasis among patients with esophageal cancer was 43.3% (11). However, this value is higher than that reported in another study conducted in southern China (21.4%) (12). On the other hand, this percentage was lower than that reported in a study conducted at Mansoura University, Egypt, where the magnitude of esophageal cancer metastasis was 50% (6).

On the other hand, the results of the present study revealed that 91 (54.82%) of the 166 metastatic esophageal carcinoma cases metastasized to the liver, 66 (39.75%) metastasized to the lung, and the remaining 9 (5.4%) metastasized to distant lymph nodes. The percentage of patients with metastatic esophageal cancer in the present study was consistent with studies conducted in Egypt on distant organ metastases, such as liver, lung, and distant lymph node metastases (45.5%, 30%, and 14.4%, respectively) (6). However, the magnitude of metastasis in the liver and lung was greater than that reported in studies in Egypt, with the exception of lymph node metastasis, compared with the current study. The most common site of distant metastasis was the distant lymph node (16.9%), liver (21.8%) and lung (9.47%). This discrepancy may be due to differences in medical literacy and cancer screening strategies (13).

The results of the multivariable logistic regression analysis revealed that residence, level of education, occupational exposure, depth of invasion, and BMI were significantly associated with the magnitude of metastasis among patients with esophageal cancer in the Adama Hospital Medical College Oncology Center (p value ≤ 0.05).

Studies conducted in Sweden (14) and Turkey (9) are consistent with the findings of the present study, revealing that the level of education and residence significantly affect the magnitude of esophageal cancer metastasis. This may be because “the risk of metastatic esophageal cancer might be indirectly influenced by factors such as having no formal education and lack of access to healthcare. Patients who have no formal education, are rural residents and have difficulty reaching an area may have less access to early detection, optimal treatment options, and preventive measures (9).

The current study revealed that the odds of esophageal cancer metastasis among urban residents were approximately 96% lower than those among rural residents. This finding is consistent with that of a study conducted in southern Africa (15), which revealed that “geographic variations in esophageal cancer incidence are noteworthy, with "esophageal cancer exhibiting higher rates.

The current study revealed that participants who had higher odds of occupational exposure had 4 times greater odds of metastasis than did those who had no occupational exposure. Although we have found no studies discussing occupational exposure to chemicals that are directly related to metastatic esophageal cancer, a systematic review and meta-analysis on “occupational exposure to chemical and esophageal cancer” conducted in France revealed that the odds of metastasis in esophageal cancer patients are associated with increased risk of esophageal cancer metastasis (11).

The current study revealed that individuals with a normal body weight or BMI were 97% less likely to have esophageal cancer metastasis than were those who were overweight. This finding is consistent with that of another study conducted in South Korea (16), which revealed **a** “possible link between obesity and a

greater chance of metastasis in a number of malignancies, including esophageal cancer." Even though the exact mechanisms are yet known, obesity may affect tumor cell activity and create an environment that is conducive to inflammation.

In terms of depth of invasion, mucosal and submucosal invasion were 98% less likely to metastasize to distant organs than invasion into the muscularis adventitia and local structures. This finding is slightly consistent with a study conducted at Southern California University in the USA, which reported an 80% metastasis rate for invasion into the muscularis adventitia and local structures (17). A study performed at Oxford University in England (18) and the USA (19) reported consistent results.

5. Conclusions

The magnitude of metastatic esophageal cancer is a significant issue in the current study. Factors such as residence, education, occupational exposure to chemicals, BMI and depth of invasion are associated with metastasis. The implementation of early detection and education programs is crucial for improving patient outcomes and reducing the burden of esophageal cancer in Ethiopia.

Abbreviations

AHMC
Adama Hospital Medical College
AIDS
Acquired Immune Deficiency Syndrome
CI
Confidence Interval
DNA
Deoxyribo-Nucleic Acid
DM
Diabetes Mellitus
DALYs
Disability-Adjusted Life-Years
EA
Esophageal adenocarcinoma
EC
Esophageal Cancer
ESCC
Esophageal Squamous Cell Carcinoma
HIV
Human Immunodeficiency Virus
IRBs
Institutional Ethical Review Board's
LN

Lymph Node
MEC
Metastatic Esophageal Cancer
NCIOUS
National Cancer Institute of United States
OR
Odds Ratio
SS
Socioeconomic Status
SPHMMC
St. Paul's Hospital Millennium Medical College
WHO
World Health Organization

Declarations

Consent for publishing

'Not Applicable'

Competing interests

There are no competing interests among the authors.

Availability of data and materials

Data "available on request".

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Authors' contributions

Design and conception of the study: WF, GF, and AD; Performed the study: WF, AD, TG, MA, BD, TA, and HS; Data analysis and interpretation: AD, TT, WF, and GF; Writing of the manuscript: AD, WF, and YC; All the authors have read and approved the final manuscript.

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Figures

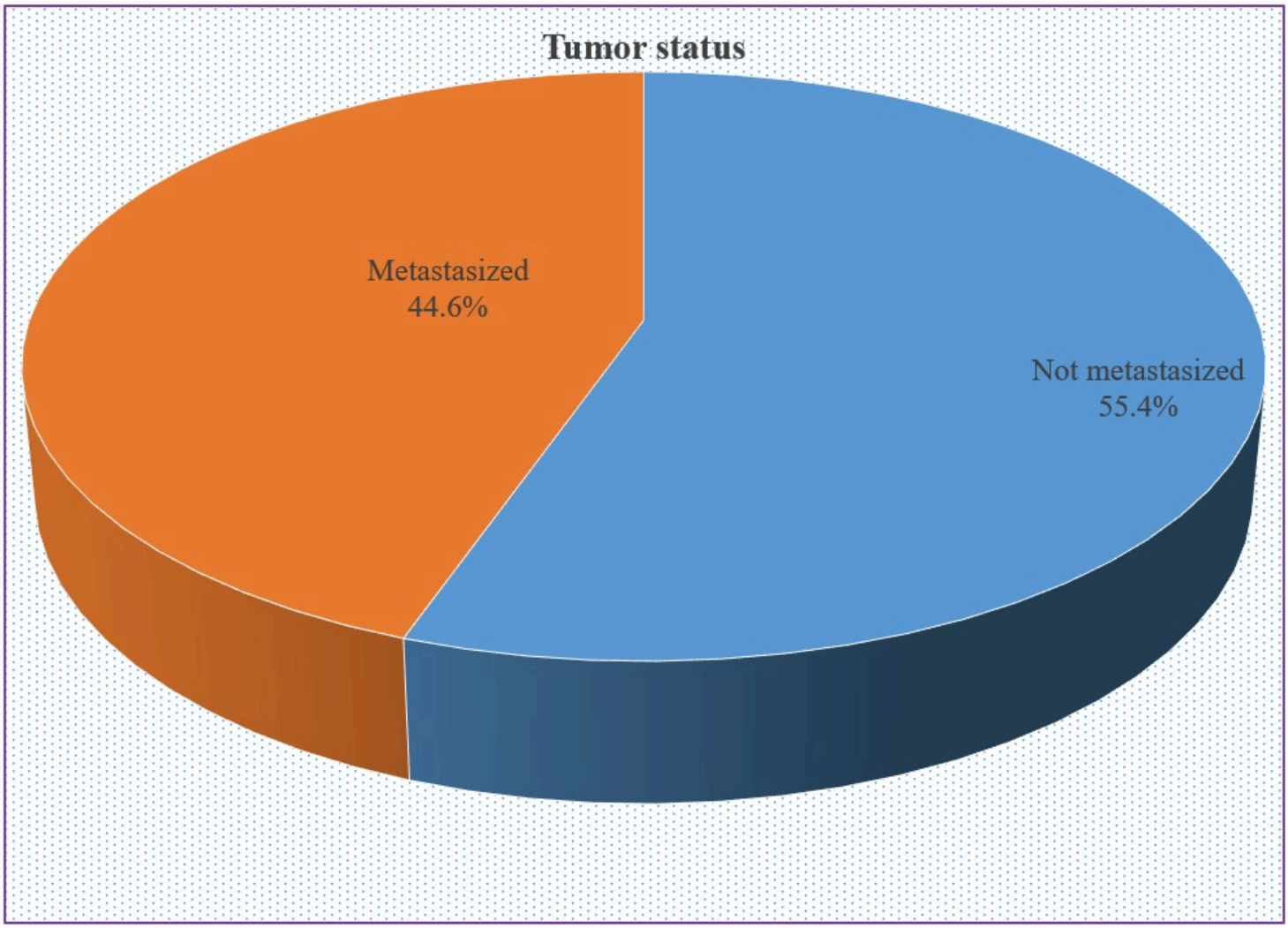


Figure 1

Magnitude of Metastasized Esophageal Cancer to Distant Organs among Patients at Adama Hospital Medical College Cancer Center, 2019--2023, May 2024.