



**MAGNITUDE OF METASTATIC ESOPHAGEAL CANCER AND
ASSOCIATED FACTORS AMONG ADULT PATIENTS AT ADAMA
HOSPITAL MEDICAL COLLEGE ONCOLOGY CENTER, ETHIOPIA.**

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**A THESIS TO BE SUBMITTED TO SPHMMC SCHOOL OF NURSING
DEPARTMENT OF MEDICAL SURGICAL NURSING PRESENTED IN
PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE
DEGREE OF MASTERS IN ONCOLOGY NURSING**

ADDIS ABABA, ETHIOPIA

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2024.**

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**A THESIS SUBMITTED TO THE DEPARTMENT OF MEDICAL
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ABSTRACT

Introduction: One out of six deaths worldwide is believed to be related to cancer, with around 20 million new cases and more than 10 million cancer deaths globally in 2020. In Ethiopia, there are limited data on factors associated with esophageal cancer metastasis. Current the study aimed to assess the factors having association with esophageal cancer metastasis among adult patients at Adama Hospital Medical College in Ethiopia.

Methods: A facility based cross sectional study design was employed to assess the magnitude of esophageal cancer metastasis among patients at Adama Hospital Medical College, cancer center from December 2019 to December 2023. Three hundred seventy two (372) patients' charts were retrieved from the Adama hospital medical college oncology center cancer registry. Data were collected using data abstraction chart. Data was entered into Epi-info version 7.2.6.0 and exported to SPSS version 27. Descriptive statistics such as mean, frequency and percentage were computed to describe and displayed in tables, graphs and charts. Binary logistics regression was applied to see the significant association of each independent variable with outcome variable. Multivariable logistics regression was employed to control the effect of cofounding in 95% CI level at p value < 0.05. Odds ratio (OR) with 95% confidence interval (CI) was calculated and P value <0.05 was accepted to be statistically significant.

Result: The magnitude of esophageal cancer metastasis was found to be 44.6% at 95% CI [39.5-49.6]. The leading site of distant organ metastasis were to liver 91(24.5%) and lung 66(17.7%) respectively. Being urban (AOR= 0.04, 95%CI: 0.006-0.287), both mucosal and Sub mucosal invasion (AOR= 0.02; 95%CI: 0.01-0.05), Normal weight (AOR=0.03.; 95%CI:0.001-0.65), having formal education (AOR= 0.15; 95%CI: 0.07-0.34), and occupational exposure to chemical (AOR= 4.12;95%CI:2.12-8.02) were among the statistically significantly associated predictors at the p-value of less than or equal to 0.05.

Conclusion and Recommendations: The magnitude of esophageal cancer metastases among patients with esophageal cancer is higher. Residency, depth of invasion (muscularis adventia & local structures), having occupational exposure, level of education (having no formal education) and body mass index (overweight) were identified as the variables with significant association with esophageal cancer metastasis. We recommend early detection strategies at all level to patients with cancer and routinely scheduled screening for vulnerable population groups.

Key words: Esophageal cancer, Metastasis, associated factors

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ACRONYMS AND ABBREVIATIONS

AHMC	Adama Hospital Medical College
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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
NCIUS	National Cancer Institute of United States
OR	Odds Ratio
SS	Socioeconomic Status
SPHMMC	St. Paul's Hospital Millennium Medical College
WHO	World Health Organization

1. INTRODUCTION

1.1. Background

Cancer is a complex group of diseases marked by the uncontrolled growth and spread of abnormal cells[1]. These cells can invade surrounding tissues and spread to other parts of the body[2]. The National Cancer Institute of the United States defined that cancer is a condition in which, at an advanced stage, some of the body's cells grow out of control and spread to other parts of the body [3].

One out of every six deaths worldwide is thought to be related to cancer, with 19.3 million new cases and nearly 10.0 million cancer deaths occurred globally in 2020[4]. According to projections, the number of cases will climb from 2020 to 28.4 million by 47% by 2040[5]. Esophageal Squamous cell carcinoma (ESCC) and Esophageal adenocarcinoma (EAC) are the two primary histological sub-types of esophageal cancer that are commonly identified[3]. Over 90% of instances of esophageal cancer globally are attributed to ESCC, the most prevalent subtype of the disease[6].

Esophageal cancer, which begins in the esophagus the tube that carries food from the mouth to the stomach, can develop into tumors that disrupt normal functions. Common symptoms include difficulty swallowing, chest pain, and weight loss, with a higher incidence observed in older adults, especially men.[7].

The term "metastatic esophageal carcinoma" describes the spread of esophageal cancer to other body organs, including the liver, lymph nodes, lungs, and bones[2, 6].

Globally, the incidence and death of cancer are rising quickly[8]. The causes are multifaceted and include population aging and expansion in addition to shifts in the distribution and prevalence of the primary cancer risk factors[9], many of which are linked to socioeconomic advancement[10].

The most noticeable cancer transitions occur in rising economies, where a shift in the common cancer kinds' profiles coincides with the disease's increasing severity[11]. One persistent finding is the continued displacement of malignancies associated with infections and poverty by diseases already prevalent in the wealthiest nations[12]. The so-called "westernization" of lifestyle is frequently blamed for these cancers[13], but the varying cancer profiles in different nations and between regions show that there is still a significant

geographic diversity, with local risk factors persisting in populations going through very different stages of social and economic transition[14].

On the other hand, EAC is more prevalent in Western nations, especially in the US and Europe [15, 16]. Although the exact causes of the histological sub-type disparities between African and Western nations are unknown, variations in risk factors, genetics, and environmental factors may be involved [17].

In Africa, a number of risk factors for ESCC have been found, such as alcoholism, smoking, and inadequate diet[7]. Aflatoxin exposure from contaminated food and environmental factors such high nitrosamine levels in conventional food preservation techniques have also been linked to the development of ESCC in Africa [18, 19]. According to traditional alcoholic beverages like mahewu in Zimbabwe and kachasu in Malawi and Mozambique have been linked[12] to ESCC in certain parts of Africa[20].

Because this histological sub-type is frequently detected at an advanced stage, which restricts treatment options and results in poor outcomes, the high frequency of ESCC in Africa is a serious cause for concern [21, 22].

In many African nations, screening programs and awareness are lacking, which results in a high number of esophageal cancer cases remaining undetected until it is too late for effective treatment[23]. Furthermore, there are sometimes few treatment options due to the high expense of cancer care and the scarcity of cancer care facilities in many African nations[24].

1.2.Statement of the problem

Esophageal cancer is the sixth deadliest cancer worldwide, with a very poor prognosis because to its extreme aggressiveness[6].The spread of cancer cells from the main tumor to other organs is known as metastasis, and it dramatically affects patient outcomes and lowers survival rates[5].

According to different literatures[7,11,26] esophageal cancer ranks eighth in the world in terms of incidence and sixth in terms of cancer-related deaths[26]. The prognosis of metastatic esophageal cancer is dismal, with a 5-year survival rate of fewer than 5%. Approximately 50% of patients with esophageal cancer present with metastasis at initial diagnosis[27]. In the African Esophageal cancer Belt, which stretches from Sudan to South Africa, esophageal cancer is the most common type of cancer [28].

In Ethiopia, Esophageal Cancer (EC) is one of the top ten cancer types [29], and its frequency is on the rise[1]. Arsi-Bale regions in the Oromia regional state of Ethiopia are particularly common places for Esophageal Cancer(EC) patients [30–32]. Ethiopia lacks an Esophageal Cancer screening program, even though the cancer leads to poor survival rate, delayed diagnosis and few treatment options are the double standard harms for this kind of cancer, which is also a common and customary similar health concern in most African nations [11].

Currently, esophageal cancer is challenging public health issue and is associated with poor prognosis and high morbidity and mortality[33]. According to study conducted at Mansoura University of Egypt the leading cause of cancer-related mortality is metastasis of esophageal cancer[1].

Besides the high prevalence of Esophageal Cancer, which approximately estimated as the sixth most common cancer type globally, it is one of the most highly devastating and hurting sickness with uncountable health damages, leading to poor quality of life and survival human burden [34].

some studies tell that around 30% of patients develop distant metastasis mostly within 6 months after radical treatment [35].

Even though treatment modality of Esophageal Cancer depends on the cancer stage and location of esophageal cancer, patients with esophageal cancer who visited health care institutions at late stages or after metastasis are believed to have poor treatment prognosis due to distant metastasis of the disease and swift progression capabilities of the disease[24].

Literatures dealing with factors associated with metastasis of esophageal cancer showed that factors like reduced socioeconomic status, way of life, culture and ethnicity, diet habit related to taking hot meals, educational status and health literacy has been linked to associate with esophageal cancer metastasis at diagnosis, a longer wait for medical care, and disparate results from treatment for esophageal cancer[20, 36].

Even though it is believed that, there is high prevalence of esophageal cancer in Ethiopia [3, 14, 20] the magnitude of metastasis and factors affecting esophageal cancer metastasis is less known, the investigators also believed that identification of factors affecting esophageal cancer metastasis are priority issues in resource allocation and management of patients with esophageal cancer.

There is currently little information available on the prevalence of esophageal cancer and its metastasis in Ethiopia[25]. On the other hand, the information at hand points to a worrying pattern. The crude incidence rate of esophageal cancer in the Ethiopian population aged ≥ 15 years per 100,000 people per year was estimated to be 2.4 with an age-specific rate of 3.4[3].

Therefore the main objective of this study is to assess the magnitude of esophageal cancer and identify factors associated with higher or lower magnitude of metastasis among patient visited Adama hospital medical college cancer center from 2019 to 2023.

1.3. Significance of the study

The purpose of this study is to determine the magnitude of metastatic cases of esophageal cancer and the risk factors for metastasis. In order to reduce the incidence and progression of the disease, prevention efforts and treatment plans are aided by the assessment of metastatic prevalence and related risk factors.

It provides guidance on how to allocate funds for esophageal cancer prevention and treatment. The findings of this study are anticipated to offer recommendations for pertinent stakeholders, governmental organizations operating at different levels, and non-governmental organizations involved in the field of esophageal cancer in order to design and promote the quality of life and long-term well-being of Patients with Esophageal cancer.

The study's results will serve as an input for the organization on optimal care for the patients with metastatic esophageal cancer, covering the disease's prevalence, solutions to its challenges, and areas needing improvement for better treatment.

The other important issue is transfer of knowledge and dissemination that used to improve understanding and management of esophageal cancer, researchers, hospitals, and healthcare professionals can collaborate to exchange study results.

2.LITERATURE REVIEW

2.1.Magnitude of Metastatic Esophageal carcinoma

The bulk of fatalities worldwide are currently attributed to Cancers with predicted to be the top cause of death and the main obstacle to raising life expectancy in every nation by the year 2000[37]. The study conducted in the south china revealed that the leading causes of cancer-related death globally are esophageal cancer[25]. One-third of all cancer-related disability-adjusted life-years (DALYs) is attributable to esophageal cancer and other gastrointestinal cancers[8].

In the United States, the financial burden of esophageal cancer is rising, highlighting the need for comprehensive data to support healthcare planning and resource allocation [38],underscoring the necessity to compile the worldwide cost of esophageal cancer in order to offer theoretical support for health care planning and resource distribution[14]. As per the World Health Organization's (WHO) 2015 estimations, cancer ranks first or second in 91 out of 172 nations as the primary cause of death before the age of 70, while it ranks third or fourth in another 22 countries[39].

Research on the overall magnitude of metastatic esophageal cancer reveals that distant metastasis is a common complication. A cohort study conducted in South China with 3,218 participants found that the most frequent sites of distant metastasis were the lymph nodes (16.9%), liver (21.8%), and lungs (9.47%[2]. Similarly, a study in Boston reported that lymph node metastases were prevalent, particularly at distant node stations in intramuscular tumors (50%)[5].

The study conducted in London revealed that the incidence of metastatic esophageal cancer varies significantly by region worldwide[7].The highest incidence rates are reported in Eastern and Southern Africa, namely in the "esophageal cancer belt" that includes areas of South Africa, Iran, and Central Asia[40] .

According to Estimates derived from multiple research, between 30 and 50 percent of patients diagnosed with esophageal cancer have distant metastases at the time of diagnosis[1, 2, 5]. This emphasizes the sizeable percentage of individuals with advanced illness stages and few therapeutic alternatives.

2.2. Factors associated with Magnitude of Metastatic Esophageal carcinoma

Determining the variables linked to the severity of metastatic esophageal cancer is essential for timely detection, risk assessment, and the creation of customized treatment plans[41]. This review examines a number of variables that may have an impact on how metastatic disease develops and spreads in individuals with esophageal cancer[11].

Research points to possible connections between genetic vulnerability, dietary practices (such as consuming a lot of pickled vegetables, hot beverages, and nitrosamines), and environmental factors[7, 9, 10, 20, 36].

2.2.1.Socio-demographic factors

While research looks into a variety of factors that affect metastatic spread, it is important to comprehend how these elements relate to socio-demographic traits.

Age: The research conducted in China indicates that age and the risk of metastatic disease may be related[4]. Another studies conducted in china show that there is strong correlation between metastatic diseases with increasing the age of the patients[1, 35].

Gender: While both sexes can be affected by esophageal cancer, certain research indicates that men are more likely to develop metastatic instances[25].

Socioeconomic Status: The risk of metastatic esophageal cancer might be indirectly influenced by socioeconomic factors, which include aspects such as income, education, and access to healthcare[14, 36]. People from lower socioeconomic backgrounds may have less access to early detection techniques, optimal treatment options, and preventive measures. This could result in delayed diagnosis and advanced stages at presentation, which are linked to an increased risk of metastasis[1]. In China having formal education was found to have the lower chance of esophageal cancer metastasis [36]. Additionally, being urban residence was also significantly protective [42].

Ethnicity: Geographic variations in esophageal cancer incidence are noteworthy, with the "esophageal cancer belt" in Eastern and Southern Africa exhibiting higher rates[41]. This raises the possibility of genetic and environmental variables unique to particular ethnic groups influencing the risk of metastatic disease[33].

2.2.2. Tumor Characteristics:

Tumor stage: The possibility for metastasis is significantly influenced by the stage of esophageal cancer upon diagnosis. Research has repeatedly shown that there is a substantial increase in the frequency of metastasis in advanced tumor stages (III and IV) when compared to early stages (I and II)[43]. This emphasizes how crucial early detection and treatment are in halting or delaying metastases.

Tumor Size and Location: Compared to lower esophageal cancers, larger tumors and those found in the upper or intermediate esophagus may be more likely to metastasize[35]. This might be brought on by enhanced lymphatic outflow and the possibility of cancer cells spreading earlier[44].

Histological Type: The likelihood of metastasis can also be influenced by the particular kind of esophageal cancer. The most prevalent kind of carcinoma, squamous cell carcinoma, typically has a higher risk for metastasis than adenocarcinoma. Knowledge of the distinct histological features can help with risk assessment and treatment selection[45].

2.2.3. Lifestyle and Environmental Factors:

Smoking and alcohol consumption: There is also a higher chance of metastasis linked to these known risk factors for esophageal cancer [7]. Drinking alcohol and smoking might cause harm to the esophageal mucosa, increase inflammation, and possibly hasten the emergence of a tumor phenotype that is more likely to spread[20, 46].

Diet: A number of dietary practices have been associated with an increased risk of esophageal cancer, including the consumption of hot beverages, pickled vegetables, and nitrosamines[47]. These food-related variables may cause damage to DNA and accelerate the growth of tumors.[48]

Obesity: Recent data points to a possible link between obesity and a higher chance of metastasis in a number of malignancies, including esophageal cancer[49]. Although the exact mechanisms are yet unknown, obesity may affect tumor cell activity and create an environment that is conducive to inflammation.

Genetic Predisposition: Certain genetic abnormalities may impact the likelihood of metastasis, and genetic factors contribute to the susceptibility to esophageal cancer. Though more investigation is required to completely comprehend the intricate interactions between genetics and metastasis in esophageal cancer, studies have found links between specific genes and a higher risk of metastasis[49].

3.CONCEPTUAL FRAMEWORK

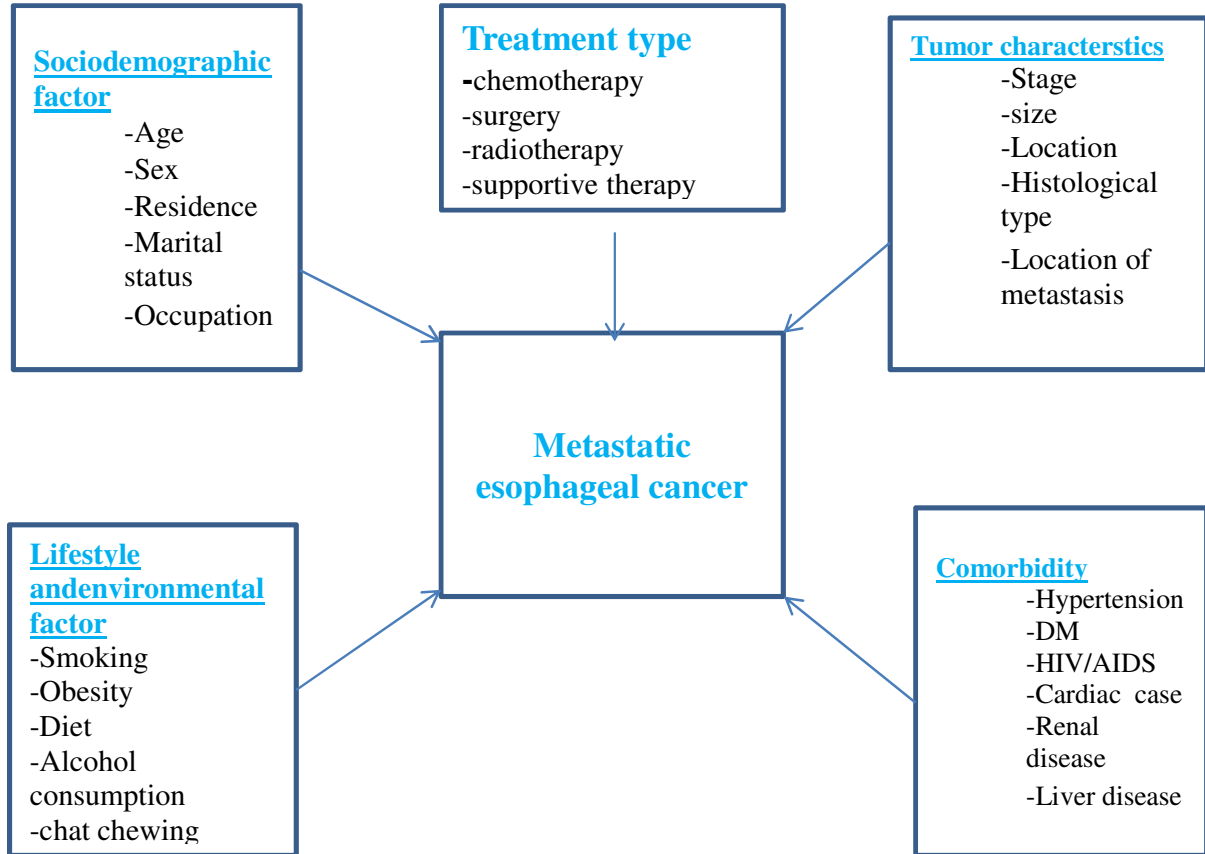


Figure -1: Conceptual frame work developed from literature review to show association between Metastatic esophageal carcinoma and different variables [20, 3, 8].

4.OBJECTIVE

4.1.General Objective

- ❖ To assess the magnitude and factors associated with Metastatic esophageal carcinoma among Adult patients with Esophageal cancer at Adama Hospital Medical College, Ethiopia,2024

4.2.Specific Objectives

- ❖ To determine the magnitude of Metastatic esophageal carcinoma among Adult patients with Esophageal cancer at Adama Hospital Medical College, Ethiopia,2024
- ❖ To identify factors that can affect Metastatic esophageal carcinoma among Adult patients with Esophageal cancer at Adama Hospital Medical College, Ethiopia,2024

5.MATERIALS AND METHODS

5.1.Study Setting

The research was carried out at the Adama Hospital Medical College, situated 99 kilometers southeast of Addis Ababa in Adama City. There are one government hospital, AHMC, and eight private general hospitals in the city. Afar, 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 DHIS2 report).

5.2.Study design and period

A Hospital based cross sectional study design was conducted from April 15- May 15/2024

5.3.Source population

All adult's patient with esophageal cancer who have visited Adama Hospital Medical College oncology center.

5.4. Study population

All Adult patients with esophageal cancer visited Adama Hospital Medical College oncology unit from December 2019 - December 30, 2023 and who full fill the eligibility criteria.

5.4.1.Inclusion Criteria

All Adults patients aged 18 years or older, histologically or clinically confirmed esophageal cancer.

5.4.2.Exclusion Criteria

- Incomplete patients' medical charts i.e. when the necessary investigation was left to perform.
- Patient medical charts with unknown metastasis (Mx) diagnosis

5.5. Data Extraction Procedure

To obtain relevant information, the medical records of patients with esophageal cancer were systematically extracted. A structured data extraction checklist has been developed based on available patient charts. This checklist served as a guide for the data extraction process.

5.6.Sample size determination

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

Population proportion is 50%, because of to the best of any knowledge no study was conducted on Metastatic esophageal cancer and associated factors previously. So, sample size is calculated as shown below:

$$n = \frac{\left(\frac{Z\alpha}{2}\right)^2 p(1-p)}{(d)^2} \quad n = \frac{(1.96)^2 0.5(1-0.5)}{(0.05)^2} = 384$$

Were,

n, is the total number of sample size required

d, stands for margin of error

P, proportion of esophageal cancer among patients

Z, statics for level of confidence.

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

5.7. Sampling procedures

All adult patients with esophageal cancer whose medical records were kept at Adama Hospital Medical College, oncology unit, between January 1, 2019, and December 30, 2023 was chosen.

5.8. Data collection procedure

The data for this study were retrieved from patients 'recorded data and the cancer registry located in the Oncology unit of Adama Hospital Medical College.

5.8.1. Data Collectors

Three trained BSC nurse, possessing the necessary skills for data extraction, were responsible for completing the data extraction checklist. Prior to data collection, these nurses were received specific training related to the purpose of the study and the methods of data collection. The training aimed to ensure uniformity and accuracy in the data extraction process.

5.8.2. Supervision

Data collection was conducted under the supervision of the principal investigator to maintain the quality and consistency of the collected data. The supervisor was available for consultation and clarification during the data extraction process.

5.9. Data quality control

A pretest was conducted at Adama Hospital Medical College oncology center on 18(5%) of estimated sample size prior to data collection, and the results and observations gathered from pretest was utilized to adjust the checklist and the data collection procedure as necessary. Cranach's alpha were calculated by using SPSS version 27 to check internal consistency(reliability) with result was 0.77. Every day, the gathered data were verified for correctness and completeness. Any gaps found were filled right away before the data was processed and analyzed.

5.10. Study variables

5.10.1. Dependent variable

- Magnitude of Metastasis on esophageal carcinoma (Metastasis or Not metastasis)

5.10.2. Independent variables

- **Sociodemographic variables:** Age, sex, residence, occupation, marital status
- **Tumor Characteristics:** - tumor stage, tumor size and location, histological type, organ of metastasis.
- **Lifestyle and Environmental Factors:** - Smoking and alcohol consumption, diet, Obesity
- **Type of treatments-** Chemotherapy, Surgery, Radiotherapy and supportive/palliative care.
- **Comorbidity:** - Hypertension, Diabetic Mellitus, HIV/AIDS, Renal, Diseases, Liver Disease and Cardiac Diseases.

5.11. Data Processing and Analysis

The data were entered and cleaned using Epi Info version 7.2.6.0 and then exported to SPSS version 27 for analysis. Descriptive analysis was used to summarize the data, and text, figures, and tables were used to analyze the study's final product. Multicollinearity is checked by using VIF which is 1.097. An analysis of binary logistic regression were performed to determine whether the independent and dependent variables are related. In multi-variable logistic regression, a significant correlations were determined based on $p < 0.05$ and an odds ratio (OR) with 95% confidence interval (CI) for all explanatory factors with $p < 0.25$ in binary logistic regression.

5.12. Operational definitions

Esophageal cancer (EC): is a malignant tumor that develops inside the esophagus as the result of alteration in epithelial linings. According to this study EC is marked as Esophageal Carcinoma in the patients' medical chart diagnosis[27].

Metastatic esophageal carcinoma: refers to the spread of esophageal cancer to other parts of the body, typically through the lymphatic system or bloodstream distant organs like liver, lung, bone, brain, distant lymph nodes and other distant organs[50]. It is a common complication of esophageal cancer and is associated with poor prognosis.

The Esophageal metastasis status is marked as either M0 or M1 in the medical chart of patients.

Patient charts with;

M1: indicates metastasis

M0: indicates no metastasis and

MX: indicates distant metastasis could not be assessed

NX: indicates regional lymph nodes could not be assessed

TX: indicates primary tumor could not be assessed

Underlying disease/comorbidity: presence of one or more additional disorders (diseases) co-occurring with a primary disease or disorder.

➤ **Stage of esophageal cancer**

Stage 0: The cancer is only in the epithelium (the top layer of cells lining the inside of the esophagus). It has not started growing into the deeper layers. This stage is also known as high-grade dysplasia. It has not spread to any lymph nodes or distant organs[50].

The cancer grade does not apply. The cancer can be located anywhere in the esophagus.

Stage IA: The cancer is growing into the lamina propria or muscularis mucosa (the tissue under the epithelium). It has not spread to any lymph nodes or distant organs. The cancer is grade 1 or an unknown grade and located anywhere in the esophagus.

Stage IB: The cancer is growing into the lamina propria, muscularis mucosa (the tissue under the epithelium), submucosa or the thick muscle layer (muscularis propria). It has not spread to nearby lymph nodes or to distant organs. The cancer can be any grade or an unknown grade and located anywhere in the esophagus.

Stage IIA: The cancer is growing into the thick muscle layer (muscularis propria). It has not spread to nearby lymph nodes or to distant organs. The cancer can be grade 2 or 3 or an unknown grade and located anywhere in the esophagus.

OR

The cancer is growing into the outer layer of the esophagus (the adventitia). It has not spread to nearby lymph nodes or to distant organs. The cancer can be any of the following:

Any grade and located in the lower esophagus OR

Grade 1 and located in the upper or middle esophagus.

Stage IIB: The cancer is growing into the outer layer of the esophagus (the adventitia). It has not spread to nearby lymph nodes or to distant organs. The cancer can be any of the following:

Grade 2 or 3 and located in the upper or middle of the esophagus OR An unknown grade and located anywhere in the esophagus OR

Any grade and have an unknown location in the esophagus.

OR

The cancer is growing into the lamina propria, muscularis mucosa (the tissue under the epithelium) or into the submucosa. It has spread to 1 or 2 nearby lymph nodes. The cancer can be any grade and located anywhere in the esophagus.

Stage IIIA: The cancer is growing into the lamina propria, muscularis mucosa (the tissue under the epithelium), sub mucosa or the thick muscle layer (muscularis propria). It has spread to no more than 6 nearby lymph nodes. It has not spread to distant organs. The cancer can be any grade and located anywhere in the esophagus.

Stage IIIB: The cancer is growing into:

The thick muscle layer (muscularis propria) and spread to no more than 6 nearby lymph nodes OR

The outer layer of the esophagus (the adventitia) and spread to no more than 6 nearby lymph nodes

OR

The pleura (the thin layer of tissue covering the lungs), the pericardium (the thin sac surrounding the heart), or the diaphragm (the muscle below the lungs that separates the chest from the abdomen) and spread to no more than 2 nearby lymph nodes.

It has not spread to distant organs. The cancer can be any grade and located anywhere in the esophagus.

Stage IVA: The cancer is growing into the pleura (the thin layer of tissue covering the lungs), the pericardium (the thin sac surrounding the heart), or the diaphragm (the muscle below the lungs that separates the chest from the abdomen) and spread to no more than 6 nearby lymph nodes OR

The trachea (windpipe), the aorta (the large blood vessel coming from the heart), the spine, or other crucial structures and no more than 6 nearby lymph nodes OR Any layers of the esophagus and spread to 7 or more nearby lymph nodes

It has not spread to distant organs. The cancer can be any grade and located anywhere in the esophagus.

Stage IVB: The cancer has spread to distant lymph nodes and/or other organs. such as the liver and lungs. The cancer can be any grade and located anywhere in the esophagus.[35].

➤ **BMI:** Underweight – less than 18.5

: Normal weight – 18.5-24.9

: Overweight – 25-30

: Obesity – greater than 30 [51].

➤ **Cigarette smoking:** is described as the habitual use of tobacco, whether locally produced or made in factories, by the participant/s on a daily, weekly, or monthly basis in any form or volume.

➤ **Secondhand smoke:** When a person smokes near somebody, then breathe secondhand smoke. Secondhand smoke is the combination of smoke from the burning end of the cigarette and the smoke breathed out by smokers. There is no safe amount of secondhand smoke and breathing even a little secondhand smoke can be dangerous[52].

➤ **Alcohol usage:** is defined as the use of any type of alcohol-based beverage, whether locally produced or manufactured in industries, by the participant/s in any volume regularly ranging from days to months. Occasional intakes for holidays, ceremonies, and intakes with a longer than monthly interval were ignored[20].

- **Chat-chewing:** is described as the participant/s' current use of the chat-plant in any form or volume on a daily, weekly, or monthly basis. chat is a plant whose leaves are chewed or dried, crushed, and sipped as tea in the East African region, as well as some parts of the Middle East, for stimulation or enlightenment[47].

5.13.Ethical clearance

The study was sought ethical approval from the Institutional Ethics Review Board of SPHMMC (IRB) by (Ref.no; - PM23/1146)and The ethical clearance was submitted to AHMC and the oncology department unit need to grant permission. Since the study used patients' medical records, individual informed permission and the patient's name would not collected.

5.14.Dissemination of results

The research findings will be shared with the appropriate district health offices, SPHMMC, the Oncology department, and AHMC. We will try to provide presentations at academic conferences and public health gatherings. If there are opportunities, they will be published ; if a prospect or condition materializes, they will also be disclosed.

6.RESULTS

6.1.Socio-demographic characteristics

Of the 372 reviewed patient charts, all were complete and included in the review, giving the response rate to be 100%. The mean age of the participants was 54.3 ± 11.8 years old, ranging from 25 being the youngest and 95 years old being the oldest participant. Regarding the age category of the participants more than one third 117(31.5%) were in the age group of 51-60 years and as few as 7 (1.9%) were aged 30 years old or below. Participants aged 41-50 hold the second place with 107(28.8%) following 51-60 years old.

In terms of participant gender, more than half 222(59.7%),were female; the male to female ratio was 1.5 to 1. As far as participant residence goes, out of the study subjects, 324 (87.1%) were from rural areas, while 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%). When it came to the distribution of religions in the research region, orthodox Christians (19.9%) and protestants (22.9%) followed second and third, respectively, with nearly three-quarters (73.7%) of the participants being Muslims. 45 (12.1%) of the 311 (83.6%) married people.(Table-2)

Table 1: socio-demographic 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 labourer	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

Others2- unmarried, divorced

6.2. Life style and comorbidity

In terms of the life style of the participants 39(10.5%) of them smoke cigarettes while 25(6.7%) were second hand smokers. Additionally 67(18%) chewed the chat and 234(62.9%) had the occupational exposure. Only 51(13.7%) drunk alcohol and 44(11.85%) had the family history of cancer. More than three fourth 314(87.9%) were underweight (**Table-3**).

Table 2: Life style and comorbidity 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

6.3. Tumor characteristics

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

In terms of the tumors size of the patients during presentation their tumor status was assessed. Accordingly except 4(1.1%) who presented with T1, and T2 14(3.8%) the great majority of the participants were presented with T3 46(12.6%) and T4 in 308(82.8%).

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
	Other	2	.5
Tumour status	Metastasized	166	44.6
	Not metastasized	206	55.4

6.4.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 is 166(44.6%), (fig 3). From the 166 metastasis esophageal carcinoma cases majority 91(54.82%) of the esophageal metastasis were to the liver, while 66(39.75%) were to the lung and the remaining 9(5.4%) were metastasized to distant lymph nodes.

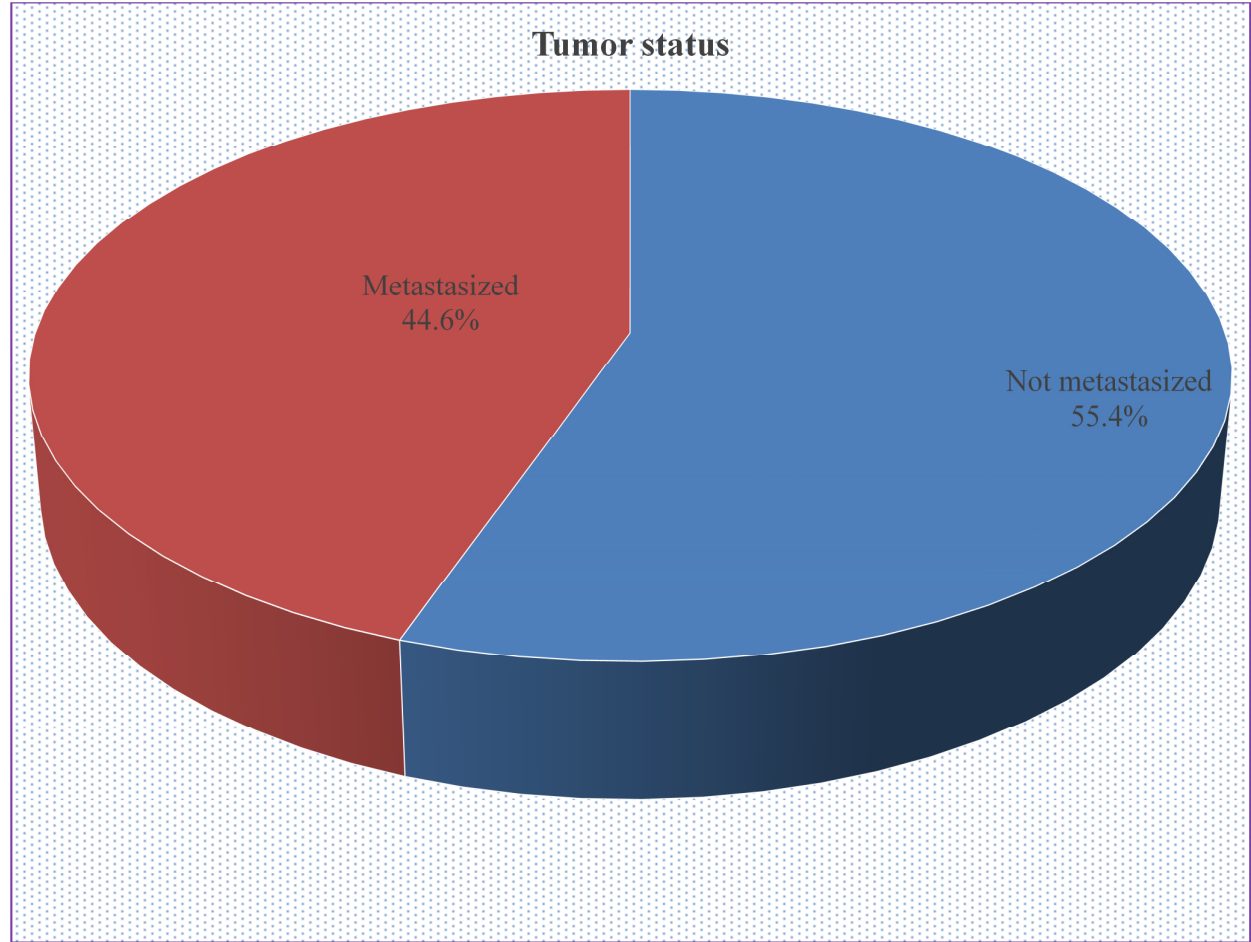


Figure- 2: Magnitude of Metastasized Esophageal Cancer to Distant Organs Among Patients at Adama Hospital Medical College Cancer Center, 2019-2023, May 2024.

6.5. Factors associated with metastatic esophageal carcinoma

In the bivariable logistic regression analysis, Residence, level of education, depth of invasion, Alcohol drinking, body mass index, occupational exposure history, Clinical presentation and T- Stage were found to be significantly associated with higher or lower odds of metastasis among patients with esophageal cancer.

In the multivariable logistic regression analysis however, only residence, level of education, occupational exposures, depth of invasion, and BMI were statistically significantly associated with the outcome variable at the p-value ≤ 0.05 .

Accordingly as shown in the table 5 below the odds of esophageal cancer metastasis among the urban residents were about 96% less likely to have metastasis compared to 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 higher odds of metastasis (AOR=4.12;95% CI: 2.12-8.022) P = 0.00)} compared to those who had no occupational exposure.

The odds of esophageal cancer metastasis to the distant organs for those with normal weight were 97% less likely compared to those who were overweight ({AOR=0.03.;95% CI:0.001-0.65) p = 0.025}). Level of education and magnitude of metastasis were also attempted to assess if there is significant statistical significance. Accordingly participants who had formal education had shown to be 85% less likely to have distant organ metastasis compared to participants who had no formal education{(AOR= 0.15; 95% CI: 0.07-0.34) P = 0.00}).

Likewise, based on tissue type esophageal cancer which invades the submucosa and mucosa had 98% lower odds of metastasis compared to esophageal cancers that invade or originate in muscularis adventitia and local structures ({AOR=0.02;95% CI: 0.01-0.05) P=0.00})and summarized by (**Table-6**).

Table 4: Binary Logistic Regression Analysis of Factors Associated with Metastatic Esophageal Carcinoma among Adult Patients, Adama Hospital Medical College, Ethiopia, 2024.

Variables	Categories	Tumour 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	0.000**
	Educated	8	51	0.16(0.74-0.33)	
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	0.000**
	sub mucosal	29	112	1.27(0.709-2.29)	
	muscularis adventia and local structures	108	6	0.018(0.007-0.046)	
Alcohol	Yes	16	35	Ref	0.043
	No	150	171	0.521(0.277-0.97)	
T-stage	3	1	3	Ref	0.015
	4	1	13	0.34(4.33-90.847)	
	5	12	34	0.96(.944-9.97)	
	6	152	156	0.35(0.342-3.325)	
Body mass index category	Underweight	162	152	18.474(5.65-60.40)	0.004
	Normal	3	52	2.13(0.19-23.75)	
	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 Metastatic Esophageal Carcinoma at Adama Hospital Medical College, Ethiopia, 2024.

Variables	Categories	Tumour 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*
Depth of invasion	Over weight	1	2	Ref	Ref	1
	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

***: p value ≤ 0.05 , **: p value ≤ 0.001**

7. DISCUSSION

The current study assess the magnitude of esophageal cancer metastasis among patients with esophageal cancer who visited Adama Hospital medical college cancer center from 2019-2023. Accordingly the magnitude of esophageal metastasis among patients with esophageal cancer who visited Adama hospital medical college is 44.6%(CI:39.5-50).Factors significantly associated with metastasis were rural residence, occupational exposure to chemical, increased depth of invasion and illiterate. Our finding implies the significance of these factors during esophageal diagnosis and prioritizes patients care in resource limiting setting.

This is consistent compared to a study conducted in china whereby the magnitude of metastasis among patients with esophageal cancer was[41] 43.3%. However it is higher than another study conducted in south china (21.4%) [1]. On the other hand it was lower than the study conducted in Mansoura University ,Egypt, where the magnitude of esophageal cancer metastasis was found to be 50%[43].

On the other hand the current study revealed that from the 166 metastasis esophageal carcinoma cases majority 91(54.82%) of the esophageal metastasis were metastasized to the liver, while 66(39.75%) were to the lung and the remaining 9(5.4%) were metastasized to distant lymph nodes. The percentage of metastatic esophageal cancer in current study's result was consistent, with study conducted in Egypt on distant organ metastasis like liver, lung, distant lymph nodes (45.5%, 30%, 14.4%)[53] respectively. But the magnitude of metastasis in liver and lung was higher than study in Egypt except lymph nodes metastasis compared with current study.

The most common site of distant metastasis was to the distant lymph node 16.9%, liver(21.8%) and lung 9.47%, This discrepancy may due to difference in level of medical literacy and cancer screening strategies[5].

The current study found that in the multivariable logistic regression analysis ;residence, level of education, occupational exposures, depth of invasion, and BMI were statistically

significantly associated with magnitude of metastasis among patients with esophageal cancer in Adama hospital medical college oncology center, at $p \text{ value} \leq 0.05$.

Studies conducted in Sweden[54] and Turkey [36] have consistent finding with the finding of the current study, revealing level of education and residence have shown to significantly affect magnitude of esophageal cancer metastasis. This may be due to the fact that “the risk of metastatic esophageal cancer might be indirectly influenced by factors like having no formal education and lack of access to healthcare.

Patients those who have no formal education, being rural residents and hard to reach area may have less access to early detection, optimal treatment options, and preventive measures[36].

The current study showed that, the odds of esophageal cancer metastasis among the urban residents were about 96% less likely to have metastasis compared to rural residents. This is consistent compared to a study conducted in Southern Africa [55] revealing “geographic variations in esophageal cancer incidence are noteworthy, with the "esophageal cancer exhibiting higher rates.

The current study disproved that tumor stage has no association with magnitude of metastasis. However study conducted in South Korea [56] revealed that “the possibility for metastasis is significantly influenced by the stage of esophageal cancer upon diagnosis. The research also showed there is a substantial increase in the frequency of metastasis in advanced tumor stages (III and IV) when compared to early stages (I and II)[1, 3, 57]. This may be due to very few number of participants were found with metastasized and late stage presentations in the current study, this can be evidenced by 354 of the participants were presented with Tumor stage 4 or 3.

The current study showed that participants who had higher odds of occupational exposure had 4 times higher odds of metastasis compared to those who had no occupational exposure. Although we have found no study to discuss with occupational exposure to chemical that directly related to metastatic esophageal cancer, the systematic review and meta-analysis study on “occupational exposure to chemical and esophageal cancer” conducted in France revealed that the odds of metastasis in esophageal cancer have associated with increasing the risks of esophageal cancer metastasis [9].

In this study smoking and alcohol consumption had no significant association with metastasis of esophageal carcinoma however, this is not congruent compared to study conducted in south Korean [56], which revealed that “there is a higher chance of metastasis linked to smoking and alcohol intake or consumption as these are known risk factors for esophageal cancer. This discrepancy may be due to difference in the life style, cultural and religious factors, as the current study is influenced with major Muslim participants 274(73.7%), where alcohol intake and smoking is considered as a taboo practice. In addition the current study has very low or only 51(13.7%) consuming alcohol and 39(10.5%) smoking cigarettes.

The current study showed that, having normal body weight or BMI was 97% less chance of esophageal cancer metastasis compared to those who were overweight. This is consistent compared to another study conducted in South Korea [49], which revealed “possible link between obesity and a higher 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 the depth of invasion, mucosal invasion and sub mucosal invasion were 98% less likely to be metastasized to the distant organs compared to muscularis adventia and local structure which is slightly in line with study conducted in southern California university of USA with 80% in muscularis adventia and local structures invasion [34]. The study done in oxford university of England[38] and USA[58] reported consistent remark.

8.STRENGTH AND LIMITATION

8.1.STRENGTH

It is the first study in kind that assess the magnitude of esophageal cancer metastasis and its associated factors in Ethiopia. The strengths of studying metastatic esophageal cancer and its associated factors lie in the comprehensive epidemiological data, understanding of metastatic patterns, and identification of key socio-demographic, tumor-specific, lifestyle, and genetic factors and observation of all adult patient charts with confirmed esophageal cancer is advantageous compared to utilizing the sample of population.

8.2.LIMITATION

The study employed a cross-sectional design, which inherently limits the ability to establish causality due to its snapshot approach to data collection. This type of study captures a single moment in time, making it challenging to determine the direction of causation between variables. Furthermore, the reliance on chart reviews introduces the potential for difficult to get relevant variables. Incomplete or inaccurate charts can result in gaps in data, which may skew findings and affect the reliability of the conclusions drawn. These limitations highlight the need for caution when interpreting the results and suggest that additional research with longitudinal designs could provide a more comprehensive understanding of causative relationships.

9.CONCLUSSION AND RECOMMENDATIONS

9.1.CONCLUSION

The study concludes that the magnitude of metastatic esophageal cancer is a significant issue in the current study. Factors like residence, education, occupational exposures to chemical, BMI and depth of invasion are associated with metastasis. Implementing early detection and education programs is crucial for improving patient outcomes and reducing the burden of esophageal cancer in Ethiopia.

9.2.RECOMMENDATION

- **Strengthen Early Detection and Screening Programs:** Given the significant impact of residence, level of education, and BMI on esophageal cancer metastasis, it is crucial to enhance early detection and screening efforts, particularly in rural areas. Targeted awareness programs should be implemented to educate populations with lower literacy levels and improve access to cancer screening.
- **Promote Preventive Health Measures:** The association between occupational exposure and metastasis underscores the need for stricter occupational health regulations and preventive measures. Employers and health authorities should work together to minimize exposure to harmful chemicals, especially in high-risk industries.
- **Address Obesity as a Risk Factor:** Public health initiatives should focus on obesity prevention as a means to reduce the risk of esophageal cancer metastasis. Encouraging healthy lifestyles and providing resources for weight management could significantly lower the chances of metastasis in at-risk populations.

- **Enhance Clinical Monitoring of Tumor Invasion:** The study highlights the importance of monitoring the depth of tumor invasion. Healthcare providers should be vigilant in assessing the invasion depth to determine the likelihood of metastasis and adjust treatment plans accordingly.

- **Further Research:** Additional studies should be conducted to explore the underlying mechanisms linking occupational exposure, obesity, and esophageal cancer metastasis. This could provide deeper insights and inform more effective prevention and treatment strategies.

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11.DATA EXTRACTION CHECK LIST

	Variables	
A	Contact Information	
1	Code of Study of Participant: _____	
2	Registered Patient ID card: _____	
3	Phone number: +251 _____ or +251 _____	
B	Socio-demographics Information	
1	Sex:	1.Mal ☐ 2. Femal ☐
2	Age in years	_____
3	Residence	1.Urban ☐ 2.Rural ☐ Adama Surrounding Arsi Others _____
4	Level of education	1.Not educated ☐ 2.below high school ☐ 3.high school ☐ 4.college and above ☐
5	Occupation	1.Farme ☐ 2.Government employ ☐ 3. Merch ☐ 4. Daily ☐ orer 5.House Wife ☐ 6. Other _____
6	Religion	1.Orthodox ☐ 2. Muslim ☐ 3. Protes ☐ t 4. Others _____
7	Marital status	1.marrie ☐ 2. unmarrie ☐ 3.Divo ☐ d 4.wid ☐ ed 5. number of children _____
C	Patients Clinical characteristics at presentation	
1	Clinical presentation	1.Dysphagi ☐ 2. Odynophagia and chest pai ☐ 3.Other _____
2	Body Mass Index (BMI)	_____
D	Esophageal cancer	
1	Histological Sub-types	1.ESCC ☐ 2. EAC ☐ 3. Other _____
2	Location	1.Lower ☐ 2. Middle ☐ 3. Upper ☐
3	T stage	1.TX ☐ 2. ☐ 3. ☐ 1 4. ☐ T2 5. ☐ T3 6. ☐ T4
4	M Stage	1. M0 ☐ 2. M1 ☐ ☐
5	Tumor status	1.Disseminated ☐ 2. Not disseminate.d ☐
6	Lymph node metastasis (Na stage)	1.N ☐ 2. ☐ 3. ☐ 4. ☐ N3
7	Depth of invasion	1.Mucosa ☐ 2. Sub mucosa ☐ 3.Muscularis Adventitia and local ☐

		structures
8	Site of metastasis	1.No organ mets 2. Liver ☐ 3. Lung ☐ 4 bone ☐ 5. brain ☐ 6.distant LN ☐
D	Treatment status	
1. 1	Type of treatment started	1. Chemotherapy ☐ 2. Surgery ☐ 3. Radiation ☐ 4. Other ☐
E	Exposure history and current status	
1	Cigarette smoking history	1. yes ☐ 2. No ☐ If yes pack per yrs _____
2	Second Hand Smoke (SHS)	1.Yes ☐ 2. No ☐
3	Chat chewing history	1.Yes ☐ 2. No ☐
4	Occupational exposure to chemicals	1.Yes ☐ 2. No ☐ If yes, specify _____
5	Alcohol drinking history	1.Yes ☐ 2. No ☐ If yes, specify _____
7	Family history of cancer	1.Yes ☐ 2. No ☐ If yes, who _____ what type _____
8	Under lying disease	1.Yes ☐ 2.No ☐ If yes, specify _____

12. DECLARATION

I declare that this Research result entitled " **Magnitude of metastatic esophageal cancer and associated factors among adult patients at Adama Hospital Medical college,Ethiopia,2024** " is my first work that have not been addressed in the study area as far as my knowledge touched and all the sources I used has been indicated and acknowledged as complete reference.

Name of investigator

Signature

Date

1.Warati Fekede

Name of advisor

1. _____

2. _____

Name of invigilator

1. _____

2. _____