A FIVE-YEAR TREND AND HISTOPATHOLOGICAL PATTERN OF CARCINOMA LOWER ESOPHAGUS MUHIMBILI NATIONAL HOSPITAL AND OCEAN ROAD CANCER INSTITUTE

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By

Frank Martin Sudai

A Dissertation Submitted in (Partial) Fulfillment of the Requirements for the Degree of Master of Medicine (Surgery) of

Muhimbili University of Health and Allied Sciences
October, 2019

CERTIFICATION

The under signed certifies that he has read and hereby recommend for acceptance by Muhimbili University of Health and Allied sciences a dissertation entitled: **"A five year trend and histopathological pattern of carcinoma lower esophagus Muhimbili National Hospital and Ocean Road Cancer Institute",** in (partial) fulfillment of the requirements for the degree of Master of Medicine (General Surgery) of Muhimbili University of Health and Allied Sciences.

_____

Dr. Larry O. Akoko

(Supervisor)

_____

Date

DECLARATION AND COPYRIGHT

I **Dr. Frank Martin Sudai**, declare that this **dissertation** is my own original work and that it has not been presented and will not be presented to any other University for a similar or any other degree award.

Signature…… **Date**……..

ACKNOWLEDGEMENT

First and foremost, I would like to unfold my inner appreciation to **Almighty God** for His protection and guidance during study period. I am heartily grateful to all who had their time to make this work complete.

I am utterly grateful to my supervisor **Dr. Larry O. Akoko** for his untiring assistance for giving me his constructive directives whenever the need arose, **Prof Mbembati** for his initial guidance whilst preparing this work, Dr. Jerry Hella, Dr. Danstan Ngenzi and Stanislaus Mwanisawa for their assistance to make this work complete.

I further extend my heartfelt gratitude to the Head of Department General Surgery, **Dr. Obadia Nyongole** and all other members in the department for their contributions and constructive ideas which made this work much better.

DEDICATION

I dedicate my dissertation work to the following:

My Parents, The late Mr. SUDAI M. SUDAI and Juliana P. Malula for their tireless guidance and support in my lifetime.

My beloved Wife, Jaqueline G. Bugenzi for her emotional support, prayers and courage during hard times.

My lovely son, Finley F. Sudai, who is the inspiration of my sleepless nights to accomplish more as a father.

ABSTRACT

Background: Esophageal cancer in the world is the eighth most common tumor, accounting for 481,000 new cases in 2008 (3.8% of all cancer cases) and sixth as a cause of tumor death with 406,000 deaths (5.4% of total). However, only few studies on trend are available in developing countries, especially from Asia and Africa. There is no information in Tanzania addressing trend in the occurrence of lower esophageal carcinoma (Esophageal Adenocarcinoma) as there is increased number of admissions, morbidity and mortality to surgical wards especially of lower esophagus.

Objective: To describe a five-year trend and histopathological pattern of carcinoma lower esophagus Muhimbili National Hospital and Ocean Road Cancer Institute.

Methodology: Hospital based retrospective cross-sectional study. The study was conducted at Muhimbili National Hospital (MNH) and ORCI from April 2013 to April 2017. Patients with histological confirmed of lower EC were taken into the study. A standard tool was used for extraction of data from patient files and database from electronic system such as socio-demographic data, documented risk factors, endoscopic findings, histological type at MNH and ORCI, data were managed and analyzed by using SPSS program version 23.

Results: A 341(34.1%) patients diagnosed to have lower esophagheal carcinoma histologically were enrolled during the study period. Mean age of the patients was 58.1+13.8(35 – 92) with no difference in mean age between male and female patients. Male predominant with a ratio of 2:1. Alcohol intake and cigarette smoking were the most reported risk factors by 227 (66.6%) and 200 (58.7%) respectively. History of GERD was reported in 132 (38.71%). A two-fold increment of lower EC was noted, especially between 2015 to 2017 with majority of patients having Squamous cell carcinoma 249 (73.1%)

Conclusion: A two-fold increase in lower EC has been noted with squamous cell carcinoma being the predominant histological sub type. Risk factors for this group were similar to that observed in upper and middle esophageal esophagus sub types with fewer patients reported to have GERD.

Key words: Trend, lower EC, MNH.

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LIST OF ABBRIVATIONS

AC	-	Adenocarcinoma
AJCC	-	America Joint Committee on Cancer
AEGJ	-	Adenocarcinoma Esophagogastric Junction
BE	-	Barret's esophagus
BMI	-	Body Mass Index
CM	-	Centimeter
EA		East Africa
EAC		Esophageal Adenocarcinoma
EC	-	Esophageal Cancer
ECSCC		Esophageal Cancer Squamous Cell Carcinoma
EGJ	-	Esophagogastric Junction
EUS	-	Endoscopic ultrasound
GERD	-	Gastro esophageal Reflux Disease
HIC		High Income Countries
HP	-	Histopathological
HPV	-	Human Papilloma Virus
LIC		Low Income Countries
MNH	-	Muhimbili National Hospital
MR number		Medical record number
MUHAS		Muhimbili University of Health and Allied Sciences
NACT		Neo Adjuvant Chemotherapy
OGD	-	Osephago-Gastroduodenoscopy

ORCI	-	Ocean Road Cancer Institute
PS	-	Performance status
SCC	-	Squamous Cell carcinoma
SPSS	-	Statistical Package for Social Sciences
Tsh	-	Tanzania shillings

DEFINITION OF TERMS

This study will take Lower EC as that occurring distal to 32 cm from the upper incisor teeth to just proximal to visible gastric folds, where the stomach begins. This will have to be documented from upper gastrointestinal endoscopy studies and nothing else. Gastro esophageal Junction (GEJ) tumors distal to this point will be excluded from this study.

Trend is the general movement over time of a statistically detectable change.

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background

The esophagus measures about 20cm to 25cm long and 2-3cm wide. The wall of the esophagus is composed of five histological layers namely: superficial mucosa layer, lamina propria, submucosa, muscularis propria and adventitia. The esophagus is inaccessible on clinical examination; hence the diagnosis of esophageal lesions is mainly based on symptoms and imaging studies. Esophageal carcinoma (EC) commences as a painless lesion to progressive dysphagia and ultimately leading to obstructive symptoms. Progressive dysphagia is the most common presentation of EC patients, manifest as lumen is 50-60% obstructed by the tumor and this is due to lack of serosa in the esophageal wall thus allowing the smooth muscle to stretch [1,2].

Data from the World Cancer Research Fund international in 2012, using age standardized rate per 100,000 (world), showed the highest rate of carcinoma of the oesophagus in Malawi, followed by Turkmenistan and Kenya, that is 24.2,19.7 and 17.6 respectively whilst in Tanzania it was found to be 9.2 in both sexes, even though, it was observed in majority of studies that oesophageal cancer is 3 to 4 times commonly in male than females [3].

In Tanzania, it is the third most common incident cancer as per ORCI data of 2013 and leading cause of admission for male patients in surgical ward at MNH (unpublished data).Epidemiological studies have revealed risks factors to lower EC to be cigarettes smoking, obesity, GERD, age, gender and Barret's esophagus [4–8].

The most common types of EC are squamous cell carcinoma and adenocarcinoma. Predominantly, SCC involves the upper and middle esophagus where there are squamous epithelial cell that upon exposure to any insult leading to chronic inflammation, ultimately will undergo progressive dysplastic changes, thus resulting in squamous cell carcinoma in situ and eventually invasive cancer. Adenocarcinoma mainly affects the lower esophagus and/or the gastro-esophageal junction that result due to dysplastic changes of columnar

epithelium leading to premalignant condition of Barret's esophagus and ultimately adenocarcinoma [6,8].

For the past three decades, Esophageal Adenocarcinoma(EAC) has been the more predominant histological type in developed countries by 80% whilst SCC is still the predominant type in the developing countries[1,5,9]. SCC contribute majority of cases globally and it increases with age (with peak at seventh decade), and common among black (three times higher), men are 3-4 times more affected, and predominantly occur in the mid esophagus. In contrast to EAC it mostly occur at distal esophagus, mostly associated with obesity, Barret esophagus(BE) and GERD, both SSC and Stage at presentation presents, for local advanced has a 5 year survival rate of 4% to 12% in EAC to SCC respectively[10].Hence there is a need to be investigated and staged as it is similar in both cases.

There are other variants of malignancies that constitute to 1%-2% like sarcoma and small cell carcinoma of the esophagus, However, malignancies such as lymphoma, melanoma, leiomyosarcomas, carcinoids may also develop in esophagus, even though this study excluded them [8].

Cancers that occur at the junction between the esophagus and stomach that is Gastroesophageal Junction (GEJ) including 2 inches of the proximal stomach are called cardiac tumors. These tumors, clinically and histologically present as lower EC. Siewert and Stein recommended a classification to clarify the difference between the cardia tumors and lower EC which then help to decide the appropriate type of surgical intervention [8]. This study only looked at Lower EC and ignore the Siewert classes of GEJ cancers[11–13]. Lower EC if EAC carries poor prognosis and needs different approach to ESCC hence clinicians need to be aware of its incidence in the country among patients presenting with EC.

Diagnostic investigations for lower EC are Esophagogastroduodenoscopy (EGD), which can visualize the site of the tumor and measures its location as centimeters from the upper incisor teeth. (In terms of centimeter (cm) from the upper incisor) and take multiple biopsies from the tumor. Barium swallow (Gastrograffin swallow in patients with

tracheoesophageal fistula) can demonstrate irregular, persistent, intrinsic filling defects and shouldering[14].

Mode of spread and clinical staging is similar to the rest of the esophagus, that is, upper and middle.l[2,9,15].According to America Joint Committee on Cancer (AJCC8), clinical staging of esophageal cancer is assessed by the TNM system staging. This aspect of staging is essential in determining the stage-specific protocol for treatment[16].

Endoscopic ultrasonography is used to increase the accuracy of clinical staging by looking the depth of the wall penetration by the tumors and presence of nodal involvement that can be determined with 80% accuracy. Computer tomography scan is used to stage prior to surgery for locoregionalized lower EC. Other investigations for distant metastases are abdominal pelvic ultrasound, Liver function test, renal function test, complete blood count (CBC)[2,14].

Patient selection for curative versus a palliative operation for lower EC is based on the tumor location, age of the patient and general health condition determined by Performance Status (PS) score, extent of the disease, histological type and preoperative staging. Palliative esophagostomy is mostly being performed more due to late presentation at diagnosis and standard treatment of patients to the health care facilities [3,17];however, other options have been studied in recent years such as neo-adjuvant chemotherapy and radiotherapy [6,17].

1.2 Literature review

There is a steep increase in incidence of lower EC which has been more marked in High Income Countries (HICs) for over 25 years now. EAC has been the predominant histological type with male more affected than female. The overall EAC increase from 3.6per million in 1973 to 25.6 per million in 2006 [18,19]. A similar increase in Lower EC has been observed in Low and Middle Income Countries (LMICs)recently African and South America have both recorded an increase while the pattern has been stable in Asia [1,20]. There has been an increasing trend for all ECs regardless of histology, with LMICs not excluded showing male predominance[1,6,20–22].

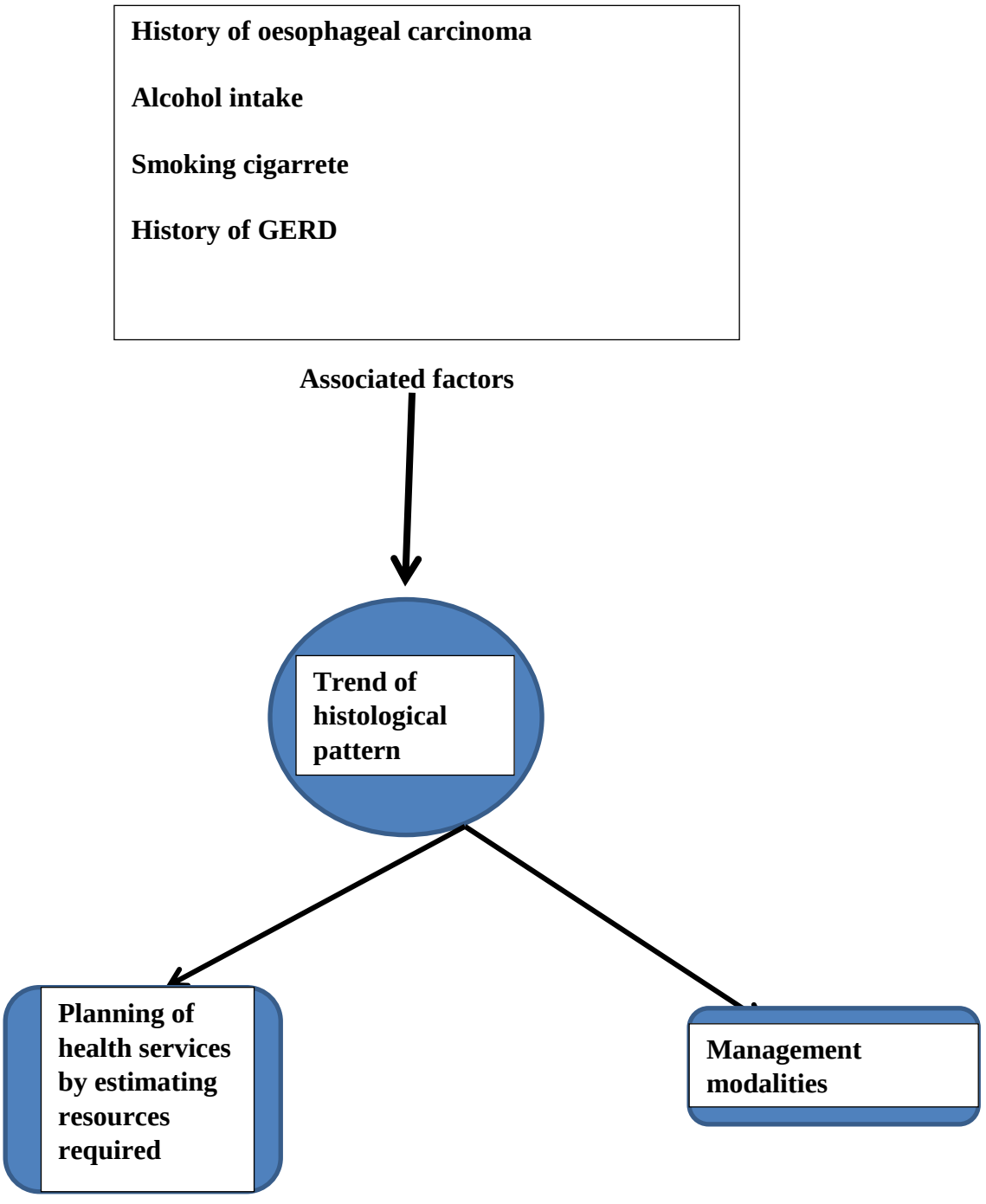
The middle third of the oesophagus is the most common site for the EC globally contributing to over half of all the cases followed by the lower and proximal parts respectively[6,20,21]. Histological pattern for upper and middle oesophagus is predominantly squamous cell in nature whilst the lower oesophagus is 52.3% adenocarcinoma and 47.7% squamous cell carcinoma[20]: with the former related to rising trend of Gastro Esophagheal Reflux disease(GERD), the main risk factor in HICs. Progressive dysphagia to solids is the main complaint that patients with EC presents with. There is a shift of trend from SCC to AC of the lower oesophagus in western literature [21]. In Africa, there is still high prevalence of SCC compared to AC as this epidemiological observation is important on grasping the aetiology and pathogenesis of EC in Africa[1].

Several risks factors have been documented from different literatures basing on variations of geographical location in the incidence of lower EC to be associated with lower EC including gastroesophageal reflux disease, Barret's oesophagus, obesity and tobacco smoking. Other risks factors such as physical inactivity, use of medication and nutrition need further analysis with association with lower EC[4]. Other factors that area constant such as familial history, age, male sex as documented earlier are associated with lower EC[6,23].

Treatment approach is mainly based on the location, general health status, stage of the EC, Performance Status (PS).Treatment options were almost equal by 46% for curative and 46% for palliation, whilst 8% had undocumented treatment as was observed by *Elia J et al in* Tanzania. Mark T et al in Ghana reported a similar trend of treatment options. Treatment modality is mainly chemotherapy and radiotherapy along with surgery, being neoadjuvant

or adjuvant. Tumour stage determines the type of surgery the patient to undergo. Tis, T1 and some of T2 carcinoma of the oesophagus aim at definitive treatment. Most common surgical techniques are Trans hiatal Esophagectomy and Transthoracic esophagectomy. Other treatment aims at palliating dysphagia endoscopic and non-endoscopic by the use of self-expandable stent[1,9,21].

1.3 Conceptual framework



1.4 Problem statement

In the recent years, there is increase morbidity and mortality due to EC among patients attended at the surgical units of Muhimbili National Hospital and Ocean Road Cancer Institute in Tanzania. While traditionally believed to be a disease of the elderly and rural populations, emerging data indicates the most patients come from Dar es Salaam, the commercial capital of Tanzania. In spite of being the most common cause of admission, data on the trend and incidence of EC affecting the lower third of the esophagus has remained largely unknown. For this reason, all patients are treated as uniformly ignoring the possibility of an EAC that has different treatment protocol and 5-year survival for similar staged ESCC. Secondly, potential for differing risk factors exists with current efforts targeting ESCC hence EAC would be left out to continue in the rise.

1.5 Rationale

Knowing the histological pattern of lower EC in Tanzania will increase awareness of its existence and allow time trend in the cancer and individualized treatment to allow for improved care delivery and outcome. Similarly, this will allow comparison with other institutions as well as develop epidemiological studies specific to Lowe EC, especially EAC.

1.6 Research question

What is the burden of lower EC among subjects seen with EC at Muhimbili National Hospital? What is **trend of** their histological pattern?

1.7 Objectives

1.7.1 Broad Objectives

To describe a five-year trend and histopathological pattern of carcinoma lower esophagus Muhimbili National Hospital and Ocean Road Cancer Institute.

1.7.2 Specific Objectives

i. To determine the proportion of lower EC among all patients diagnosed with EC at MNH and ORCI.
ii. To determine the trend of histopathology of the lower esophagus at MNH and ORCI.
iii. To describe the histopathological pattern of the lower esophageal carcinoma at MNH and ORCI.
iv. To document the associated factors of patients with lower esophageal carcinoma at MNH and ORCI.

CHAPTER TWO

2.0 METHODOLOGY

2.1 Study design

Hospital based Cross-sectional retrospective study design, descriptive in nature.

2.2 Study area

Study was done at Muhimbili National Hospital and Ocean Road Cancer Institute located in Dar es Salaam city Tanzania, both hospitals act as teaching hospitals for MUHAS and other universities. Most patients with dysphagia are referred to MNH where investigations and treatment decisions are made during the once weekly multi-disciplinary tumor board meeting run jointly by ORCI. Hence using the two hospitals patients record would yield representative sample of patients with EC who seek medical attention. From its monthly morbidity and mortality report, MNH alone receives about 42 patients with EC every month. It also has full range of investigation capacity to manage patients with EC, being the only one in the country. However, some patients from private facilities can have straight access to ORCI without going through MNH.

2.3 Study duration

This study involved all patients who were attended at either MNH or ORCI with a diagnosis of EC between April 2013 and April 2017.

2.4 Study population

All patients who were histologically confirmed with EC.

2.4.1 Inclusion Criteria and Exclusion Criteria

Inclusion criteria

All patients with histologically confirmed lower EC; with age 18 years and above; endoscopically evaluated.

Exclusion criteria

Lower EC involving Siewert's classification 2 and 3; failure to get medical records or information on location of the EC.

2.5 Sample size

Using Leslie Kish formula for determining sample size, where prevalence of lower EC was taken to be 29% [5], 95% confidence interval set at 1.96, and the margin of acceptable error kept to with 5%, 316 patients with lower EC were required and we managed to recruit 341.

2.6 Recruitment procedure

The electronic patient management system at MNH was used to identify all patients with a diagnosis of EC. Medical records number was then obtained and a list sent to the medical records section to release case notes for confirmation of diagnosis. The same was done for ORCI patients. The patients' registration numbers and names were entered in an excel spread sheet during which duplicate entries were removed. Case notes with a diagnosis of lower EC were then kept a side for data extraction.

2.7 Data collection procedure

Using a predefined data collection tool, demography as well as clinical parameters of the patients was abstracted from the case notes by two independent abstractors. These included: age, sex, risk factors of EC, endoscopic (OGD) findings, histopathological results and date of diagnosis**.** Excel spread sheet was prepared for this purpose and later compared for similarity. Where there was disagreement, case note was reviewed by the investigator himself.

2.8 Variables

Independent variables

Age

Occupation

Time trend

GERD

Smoking cigarrete

History of esophageal carcinoma

Dependent variable

Lower esophagheal carcinoma

2.9 Data management and analysis

Data was cleansed, coded and transferred into SPSS version 23 where frequency tables were again run to check for completeness. Continuous variables were summarized as means with standard deviations and range while categorical variables were summarized as proportions.

2.10 Study limitation

The retrospective design of the study had significant limitation on the data on risk factor and obviously trend. Single hospital based, probably missing on the patients not reaching the referral centre had impact on ability to generalise these findings to the Tanzanian population.

2.11 Ethical consideration

Ethical clearance was obtained from MUHAS research and publication committee and separate permissions from MNH and ORCI to conduct the study. The confidentiality of patient information contained in the research protocol is stored in the Surgery Department. Deidentification of the study participants was done by removing names and registration numbers after all data has been collected. This study carried no harm as care had already been provided long before the study onset and the study did not have any contact with the patients. The study has the potential to benefit future patients by raising the awareness of need to offer individualized care.

CHAPTER THREE

3.0 RESULTS

A total of 1632 and 1053 case notes with clinical suspicion for esophageal cancer were identified at MNH and ORCI respectively. The patients' registration numbers and names were entered in an excel spread sheet during which duplicate entries were removed. This left 1000 patients who had histological proof of EC of which 341(34.1%) had endoscopic diagnosis of lower EC. This paper therefore provides description of the 341 patients (over a five-year period) to note trend in numbers and histological types of this sub set of EC patients.

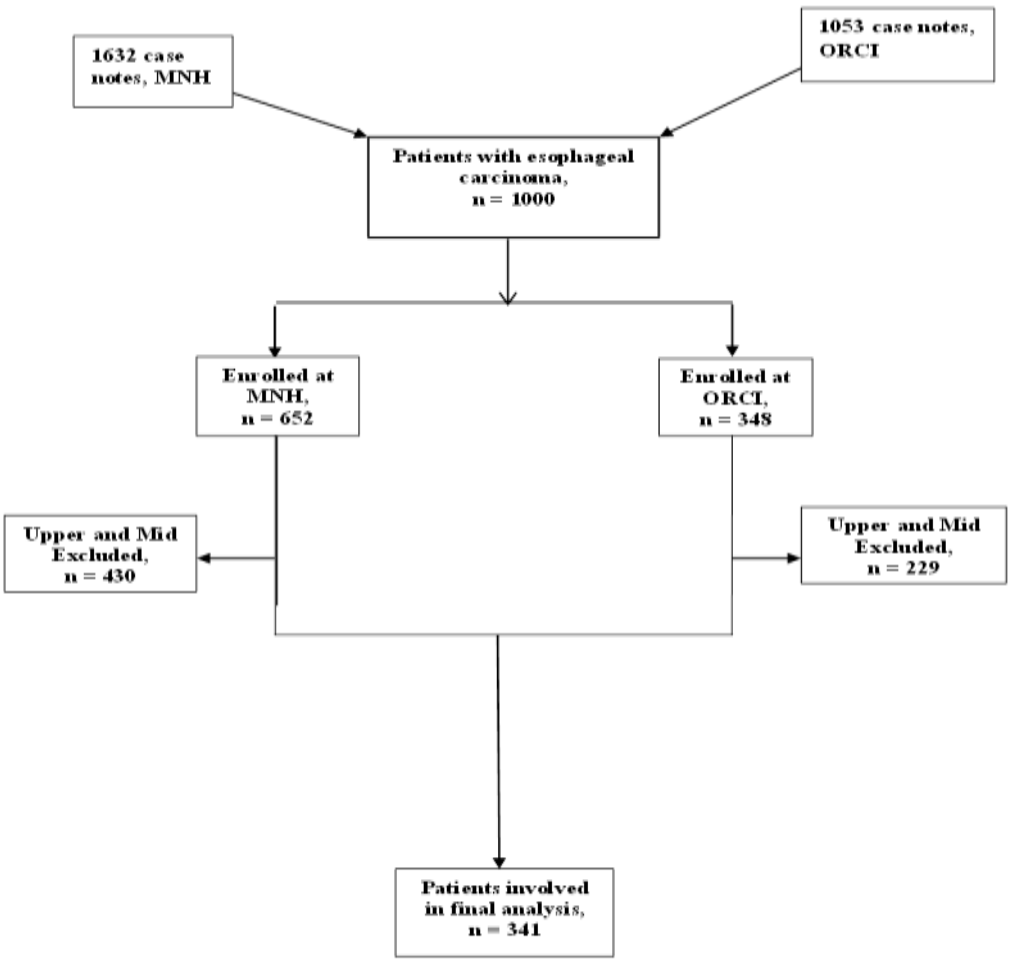


Figure 1: Flow chart showing how EC patients were recruited into the study

From Table 1, we can see that the mean age of the patients was 58.1+13.8(35 – 92) with no difference in mean age between male and female patients. Majority had primary level of education, 257(75.4%), and this was true for both sexes. Majority were peasants 189(55.4%) followed by the employed category by 117(34.3%): sex wise, proportionately more males were employed than did the females. A minority of patients, 115(33%), were referred to ORCI from other facilities without having to go through MNH referral system. Alcohol intake and cigarette smoking were the most reported risk factors by 227(66.6%) and 200(58.7%) respectively. History of GERD was only reported in 132 (38.71%).

Table 1: Demographic and clinical characteristics of adult patients with lower esophageal carcinomas, n = 341

Characteristic	Frequency (%)	Male, 228	Female 113	P values
Mean age in years (SD)	58.1 (13.8)	58.2 (14.2)	58 (13.2)	0.92
Education level				0.77
Primary	257 (75.37)	172 (75.4)	85 (75.2)	
Secondary	68 (19.94)	47 (20.6)	21 (18.5)	
College and above	13 (3.81)	7 (3)	6 (5.3)	
Unknown	3 (0.88)	2 (0.8)	1 (0.9)	
Occupation				0.04
Peasant	189 (55.43)	126 (55.3)	63 (55.7)	
Employed	117 (34.31)	82 (35.9)	35 (30.9)	
Unemployed	22 (6.45)	9 (4)	13 (11.5)	
Retired	11 (3.23)	10 (4.3)	1 (0.9)	
Unknown	2 (0.59)	1 (0.4)	1 (0.9)	
Hospital				0.15
MNH	226 (66.28)	157 (68.8)	69 (61.0)	
ORCI	115 (33.72)	71 (31.1)	44 (38.9)	
Risk factor				
History of GERD	132 (38.71)	92 (69.7)	40 (30.3)	0.80
Cigarette smoking	200 (58.65)	166 (83.0)	34 (17.0)	<0.001
Family history	20 (5.88)	16 (80.0)	4 (20.0)	0.12
Alcohol intake	227 (66.9)	176 (77.5)	51 (22.5)	<0.001
Appearance				0.51
Fungoid	288 (84.46)	188 (82.5)	100 (88.5)	
Ulcerative	38 (11.14)	28 (12.3)	10 (8.8)	
Stricture	9 (2.64)	6 (2.6)	3 (2.7)	
Infiltrative	4 (1.17)	4 (1.4)	-	
Unknown	2 (0.59)	2 (0.9)	-	

Figure 2 below shows the geographical residency of the patients with lower EC as was found in their documentation. Majority were documented as coming from Dar es Salaam region, 124 (36.47%), followed by Tanga 44 (12.94%), Morogoro 35 (10.29%), Dodoma 28 (8.24%) and Kilimanjaro 22 (6.47%). The disease was very lowly reported from the lake regions as was represented by Mwanza, Simiyu, Kagera, Tabora, and Mara. As is shown in Figure 2, this distribution did not change when we stratified residency by histological diagnosis of the malignancy.

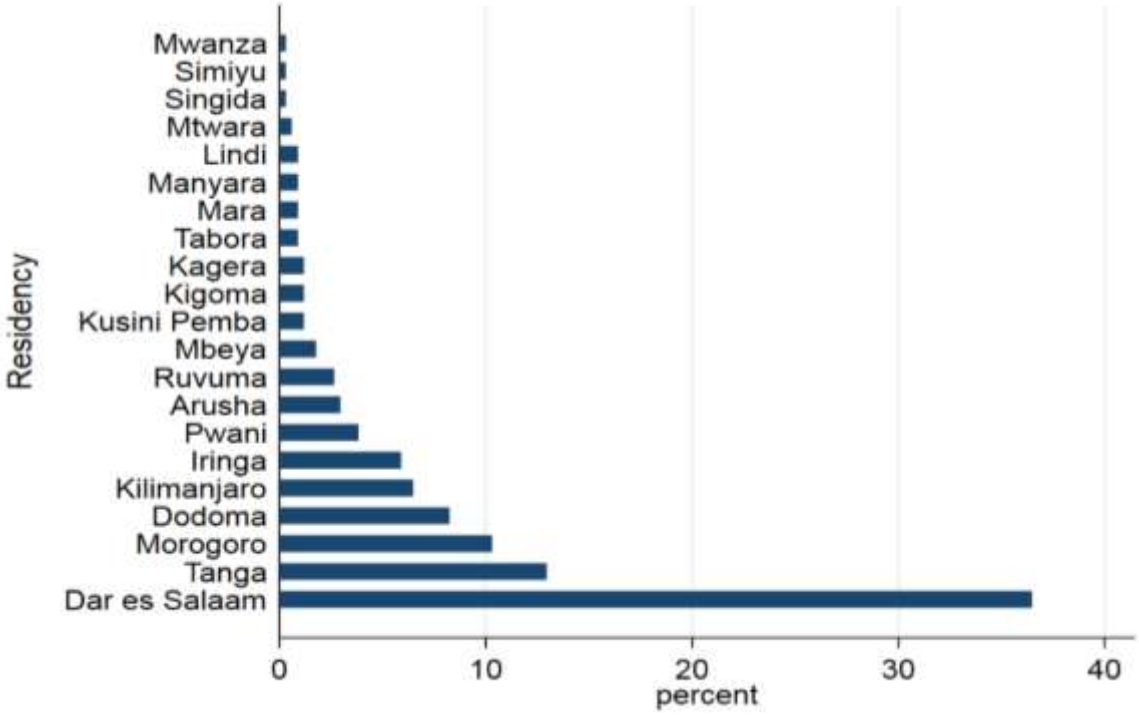


Figure 2: Distribution of study participants by region of residency Tanzania

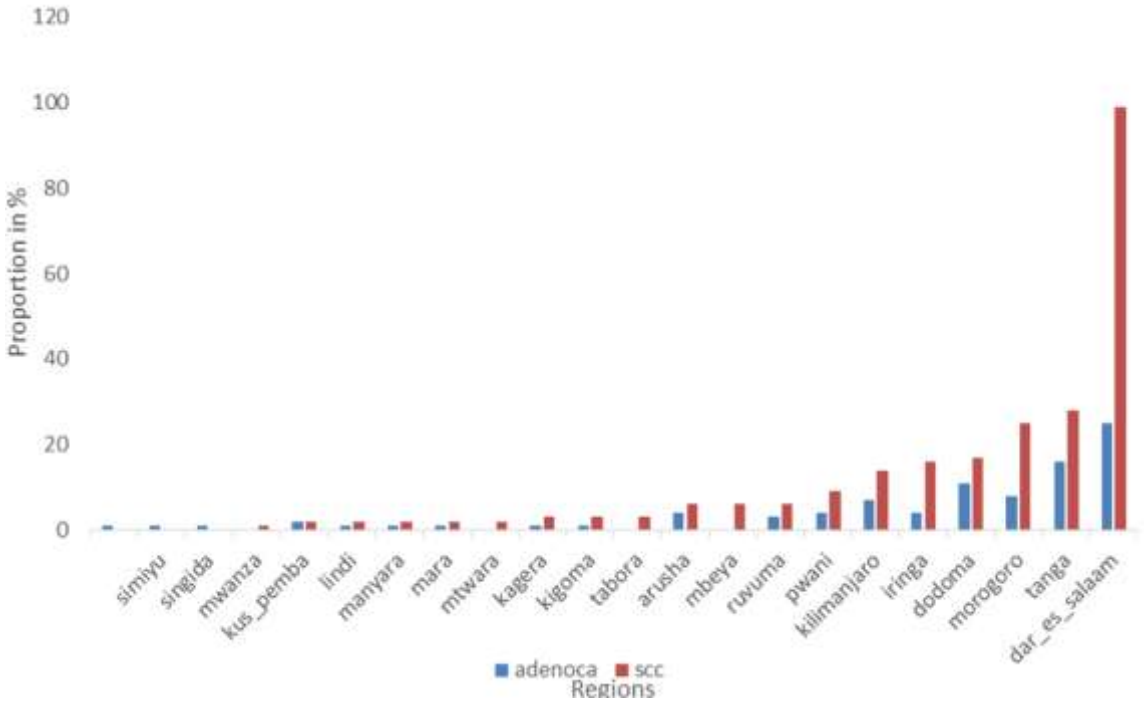


Figure 3: Distribution of study participants by region of residency stratified by histological diagnosis in Tanzania

When we assessed for tumor location and further analysed by histological types and by sex, we observed that, most tumors were at mean length, as was measured from the upper incisor teeth, of 35.73±2.8(32 – 40) cm with majority at 35cms as can be seen in **Figure 3.** However when we stratified by sex **Figure 4** more tumors were located more distal in males (40 cm) than among female patients (35 cm). Likewise, adenocarcinomas were more distally located in the last third of the eosophagus than were the squamous cell carcinoma **Figure 5.**

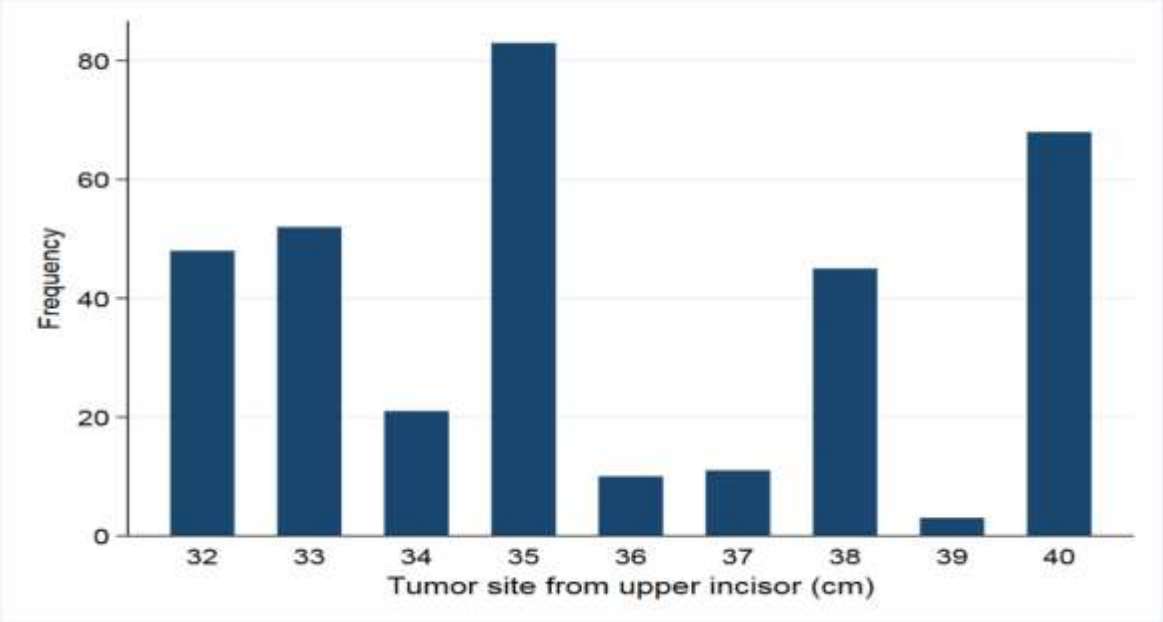


Figure 4: Overall distance of tumors from the upper incisor teeth

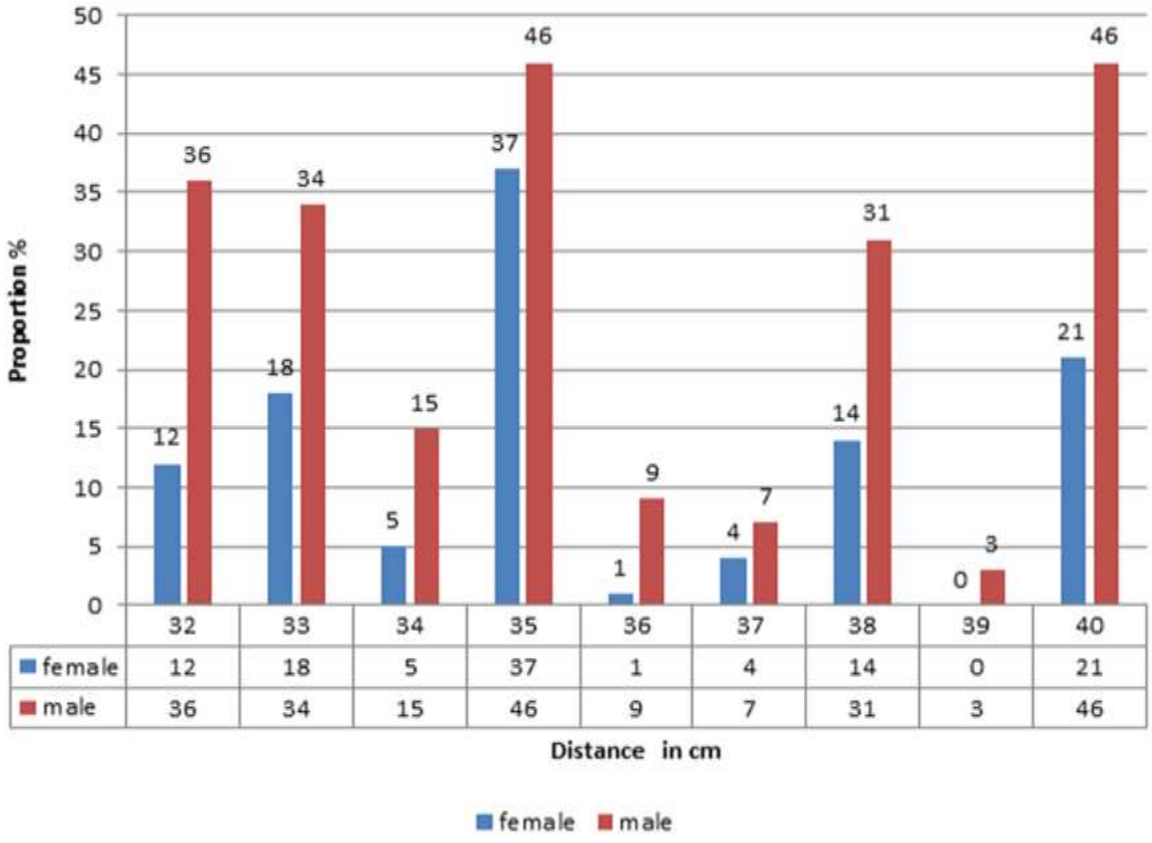


Figure 5: Distance of tumors from the upper incisor teeth by sex

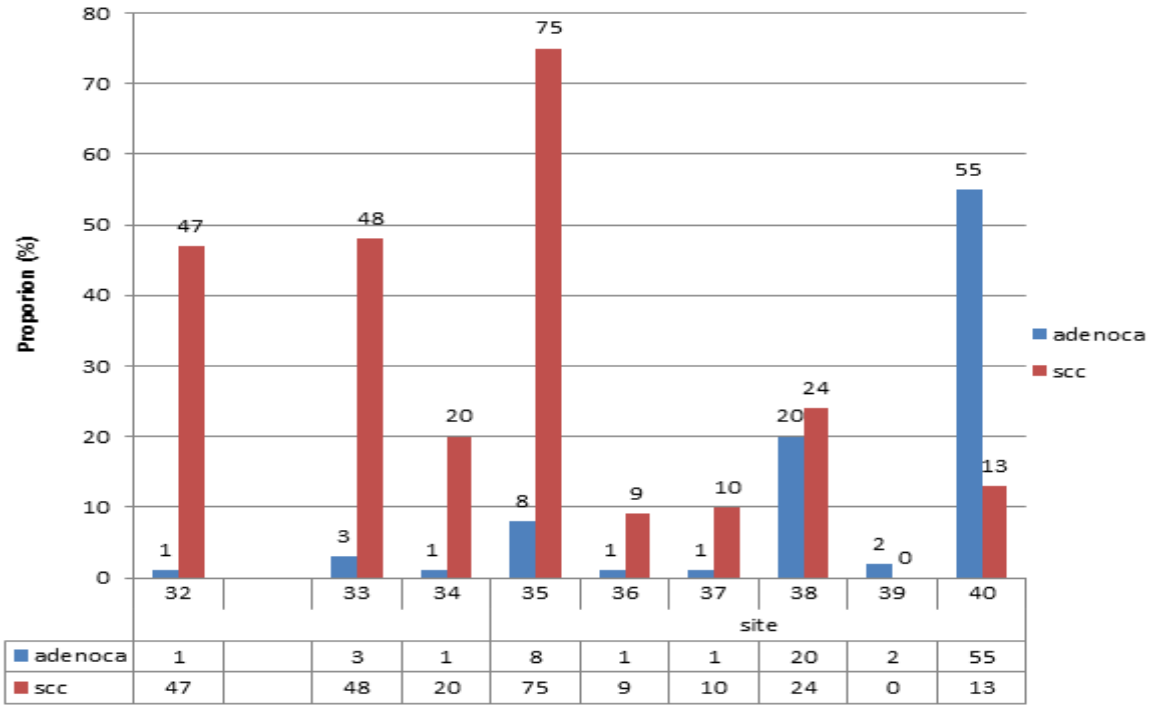


Figure 6: Distances from upper incisors stratified by histologic diagnosis.

Figure 3 Represents annual proportion of all patients diagnosed with Lower EC. It can be seen that the overall, disease was stable in the first two years, and then sharply declined by nearly 9% before doubling the next year.

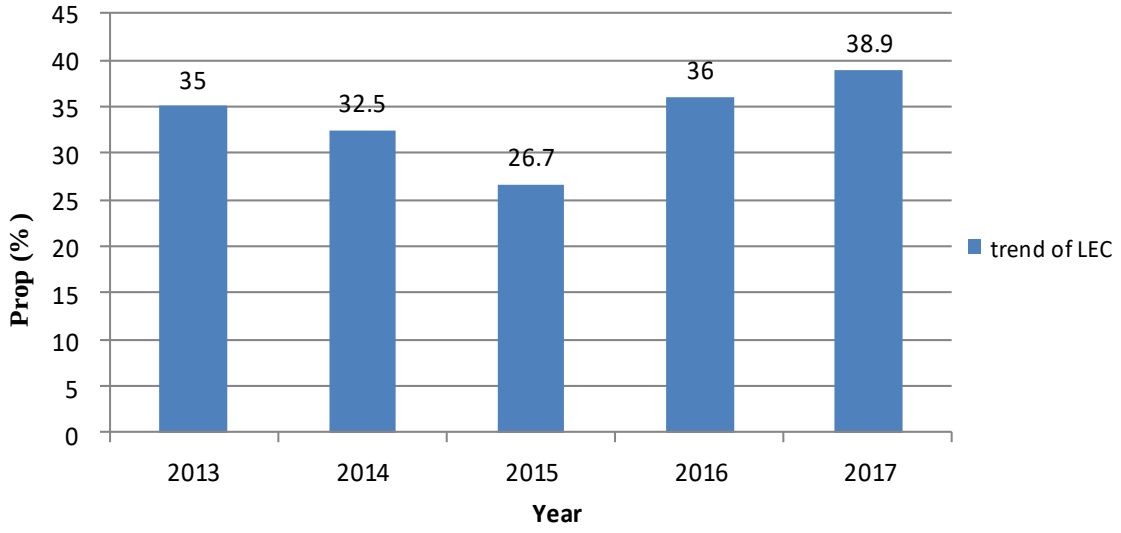


Figure 7: Trend of lower esophageal carcinomas over all esophageal carcinomas between "2013 – 2017"

From **Figure 8** below, we see the five-year trend of lower EC comparing the proportions among those with ADC versus SCC histological types. We can see that there was a slight increase of proportion with ADC in 2016 accompanied with a decline in SCC when compared to other years. Otherwise, the trend shows a stable pattern of the lower EC among patients seen at MNH and ORCI in Dar-es-Salaam, Tanzania with the predominance of SCC.

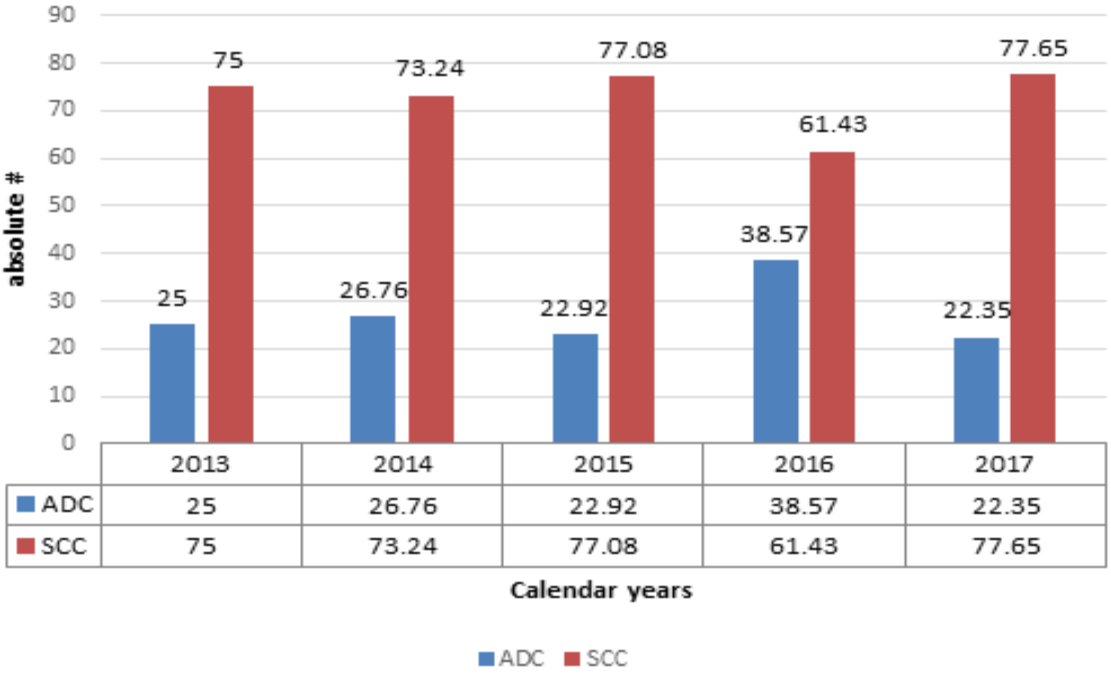


Figure 8 : 5-year trend of lower EC compared by histological type from 2013 to 2017.

Two major histological subtypes were encountered among these patients with lower EC as shown in **Table 2** below. Squamous Cell Carcinoma (SCC) was the most predominant type with 246(72.8%) of all patients. Majority of the patients presented with local disease, 286(84.62%). Metastatic disease was most prevalent among the patients with Adenocarcinoma (ADC) compared to those with SCC, a finding which was significant (p value <0.019).

Table 2: Histologic type and stage of EC among the 341 patients with lower EC comparison

Stage	Local disease	Metastatic disease	Total	P-value
ADC	73 (79.3)	19 (20.7)	92 (26.9)	
SCC	222 (89.2)	27 (10.84)	249(73.1)	**<0.0019**
Total	286 (86.5)	46 (13.4)	341	

CHAPTER FOUR

4.0 DISCUSSION

We believe this was one of the few studies trying to look at lower EC in a developing country context. We conducted a retrospective search of hospital records to identify patients who had a diagnosis of EC. We therefore report absolute numbers of cases with lower EC as retrospective nature and the difficulty in collecting and analyzing all case notes made it difficult to determine this trend as a proportion of all EC regardless of site. In spite of this limitation, this is useful as a guide in clinical practice as ADC of the lower esophagus is on the rise globally and needs a different algorithm both in the treatment and screening. This being a hospital-based study, the main limitation other than being retrospective is also due to the fact that only cases reaching the hospital were studied. The entire population of patients with EC were not available for the study hence findings may not be generalizable.

This study recruited patients from MNH and ORCI simultaneously: traditionally, patients were referred to ORCI from MNH hence the cumbersome need to recruit from the two sites was not necessary. But from this study, an increase in EC patients directly referred to ORCI without the need to go through MNH has been noted. One in three of the studied patients were referred from private facilities compared to about one in five previously reported some years back [21]. Private and public health facilities have significant socio-economic divides hence capturing patients from a single facility carries certain biases in making conclusions. In the absence of national cancer registry, capturing all patients is therefore a worthwhile pain. Furthermore, this increase in patients directly referred from private centers signifies improvement in cancer diagnostics (endoscopic and pathologic) but needs to be streamlined to any existing national treatment guidelines and protocols.

In this study we have established the rate of lower EC as seen at the National referral hospital to be 34.1%: 1 in 3 of the patients with EC will have lower third location of their tumor. This finding was similar to that reported form India of 34.8% [20]. With globally reported increasing trend of EC, lower EC will also increase in absolute numbers as a fraction of the total EC patients. This reflect a new finding in East Africa which will need more (further) longitudinal studies to be done, while this finding is contrary to developed

countries (Olmsted County, Minnesota) and China, which shows the proportion is 74% of adenocarcinoma lower esophageal which can be associated with sedentary lifestyles [24,25].

Patients with lower EC were found to have similar age and sex distribution to the general population of patients with EC: with a mean age of 58 years, and a two-fold male predominance [8,20,26]. Furthermore, the study did not reveal sex different when compared by age just like in other studies [6,26]. The significant of these similarities in age and sex means that same preventive measures and screening practices can be adopted for the early detection and diagnosis of EC. Patients were largely from the lower socio-economic class as was represented by being peasants with lower levels of education as was also demonstrated in previous studies[6,20,21]. The consistent association of EC with lower SEC needs to be further looked at and compared to the higher SECs in LMICs. Factors that reduce the incidence of EC among the Higher SECs need to be understood and applied to the lower classes.

This study added the already growing evidence of rising trend of EC in the commercial city, Dar es Salaam where more than two thirds of the patients were registered. Traditionally majority of the patients came from the highlands of the country (Kilimanjaro and the southern regions). These highlands had high local brewed alcohol consumption which was long thought to be the main risk factor for EC following the Kenya and South African publication[27–29]. This emerging regional variation is the new center of research especially on how the residency data was collected as MNH is a referral hospital. It is important since factors responsible for EC in the traditional highlands might differ from those reported in the low lands. Several new factors have recently come under scrutiny from hot drinks [30–33], selenium content in food, there is a need to develop and drinks[6,21,30,33–35]and more recently role of tooth loss, fluoride and dental fluorosis [27,35]. This is similar to developed countries as reflected from China which show similar increase on trend of adenocarcinoma, this is attributed with life style [25].

Globally, there has been a steady rise in the incidence of lower EC, as has been shown also by our current study: this was similar to a study done in India [20]. In the absence of population studies, whether this is a true increment or a temporal one due to improvement in health services is not clear. There are more ongoing studies over the last five years

concentrating in Dar es Salaam and Kilimanjaro regions hence could result in the said increase. Nearly all the patients were sent to ORCI for definitive and palliative chemo-radiation therapy.

We observed that, most tumors were found to be located 35cms from the upper incisor. However when we stratified by sex , more tumors were located more distal in males (40 cm) than among female patients (35 cm). Likewise, adenocarcinomas were more distally located in the last third of the eosophagus than were the squamous cell carcinoma. Again it was observed that, one third of patients diagnosed with adenocarcinoma presents with metastatic disease compared with squamous cell carcinoma which is similar to other study done in India[20].

Two third were SCC, that was a prevalent form of carcinoma of the lower esophagheal region. These observations were contrary to study done in India which reflects there was no change for pattern and frequency of squamous carcinoma[20] .

Two third of patients with lower EC were observed to have history of alcohol intake. This is not surprising observation as alcohol intake is a known risk factor for EC as has been shown in other studies[15,23]. Half of the patients had history of smoking cigarette with similar study in developed and developing countries [22,23,36]. One third of patient had history of GERD; there was no patient that was found with early stage, which can be explained due to the lack of screening services for cancer of lower esophagus in high risk populations according to geographical distribution such as Dar es Salaam, Morogoro, Kilimanjaro, Tanga and Dodoma.

In one third of all patients, no risk factor was documented making retrospective study on risk factors more difficult. This lack of data was also observed in previous studies conducted locally among similar patients [21]. This highlights the absence of standard data capture tool for clerking EC patients in Tanzania. There is a need for data capture tool that is regionally standardized to ease data collection and comparison over time to monitor time trend changes and pick newer risk factors.

While many patients were sent for palliative services, as was the case in previous studies [6,21,37], this might have been an under treatment to a significant number of patients. Fungating lesions tend to present early with dysphagia and do not necessarily mean an advanced disease. Similarly, stricturing and ulcerative lesions tend to present early. In these patients, nutritional support as a step to surgery would be of much survival advantage when they become surgical candidates. The place of NACT in patients with lower EC, especially Adenocarcinoma, needs to be evaluated among our patients as they carry a different prognosis when compared to ESCC. This study treated them the same which was not to any protocol.

CHAPTER FIVE

5.0 CONCLUSION AND RECOMMENDATION

5.1Conclusion

We notice there is an absolute increase of lower esophageal cancer over the last five years. SCC remained the most predominant histological subtype while EAC contributed to about one third of all cases of lower EC. Lower socioeconomic status was predominant among the patient population. Cigarette smoking and history of GERD were documented associated risk factors with lower EC who attended MNH and ORCI.

5.2 Recommendations

i. A prospective study looking at all EC is needed to further understand Lower EC in the setting of current definitions.
ii. MNH and ORCI should jointly establish EC registry which will make future time trend analysis much easier and regular.

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APPENDICES

Appendix I: Data collection tool

Questionnaire number: ……

Participants' contact: …….

MR number:……

HP number…….

Specific objective 1: To determine the pattern of cancer of the lower esophagus among patients with cancer of the lower esophagus at MNH and ORCI.

Demographic characteristics of the study population

1. **Date of diagnosis:**
2. Age …… (in years)
3. Sex
    a. Male
    b. female
4. Residency…….……..(REGION)
5. Level of education;
    a. Primary education and below
    b. Secondary education
    c. Secondary education and above
6. Occupation
    1. Peasant
    2. Employed
    3. Unemployed
    4. Retired

7. Body weight…….(Kg)
   Height in……(Cm)

ANATOMICAL SITESE, GROSS APPEARANCE, HISTOPATHOLOGICAL TYPE/GRADE AND METASTASES AT TIME OF DIAGNOSIS

8. Anatomic site ……cm from upper incisor
9. Gross appearance
    a. Fungoid
    b. Ulcerative
    c. Infiltrative
    d. Stricture
    e. Not documented
10. What is the histological diagnosis?
    a. Squamous cell carcinoma
    b. Adenocarcinoma
11. What is the grade of differentiation of the tumor?
    a. Grade I
    b. Grade II
    c. Grade III
    d. Grade IV
    e. Not documented
12. What is the stage of cancer of the esophagus?
    a. Early cancer- Stage I, II
    b. Locally advanced cancer- Stage II, III
    c. Distant metastases
    d. Not specified

Specific objective 2: To determine the associated risk factors of patients with lower esophageal carcicoma at MNH and ORCI.

13. History of GERD…….. 1)Yes 2)No 3)Not documented
14. History of Cigarette smoking…… 1)Yes 2)No 3)Not documented

15. Family history of esophageal carcinoma……..... 1)Yes 2)No 3)Not documented

16. Alcohol intake…….. 1)Yes 2)No 3)Not documented

17. Others……