CURRENT EPIDEMIOLOGICAL AND HISTOLOGICAL CHARACTERISTICS OF CANCER OF THE OESOPHAGUS (CoO) AT THE UNIVERSITY TEACHING HOSPITAL (UTH)

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A dissertation submitted to the University of Zambia in partial fulfillment of the requirements for the award of the degree of Master of Medicine in Surgery.

The University of Zambia

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DECLARATION

I hereby declare that this dissertation represents my own work. In my knowledge, it has not previously been submitted for a degree, diploma or any other qualification at this or any other University.

Signed.....

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CERTIFICATE OF APPROVAL

This dissertation entitled **CURRENT EPIDEMIOLOGICAL AND HISTOLOGICAL CHARACTERISTICS OF CANCER OF THE OESOPHAGUS (CoO) AT THE UNIVERSITY TEACHING HOSPITAL (UTH)** by Dr Joseph Musowoya has been approved as fulfilling part of the requirements for the award of the degree of Master of Medicine in Surgery by the University of Zambia.

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To my wife Mutale Mercy Sampa, my daughter Mirriam Musowoya and my son Emmanuel Musowoya. Without their love and support this could not have been possible.

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LIST OF ABBREVIATIONS

1. UTH: University Teaching Hospital
2. Ca: Cancer
3. CoO: Cancer of Oesophagus
4. DNA: Deoxyribonucleic Acid
5. U/S: Ultrasound
6. CT(S): Computer Tomography (Scan)
7. UK: United Kingdom
8. HIV: Human Immunodeficiency Virus
9. CIDRZ: Center for Infectious Diseases Research in Zambia
10. ART: Anti-Retrovirus Therapy
11. cm: Centimeters
12. US: United States
13. SCC: Squamous Cell Carcinoma

TERMINOLOGIES

The Oesophagus is conveniently divided into three parts for descriptive purposes.

1. **Upper third (U)**: 1/3 of the 25 cm translates to the first 8.3cm. This corresponds with the part within 23.3cm when measured from the incisor teeth at endoscopy. The distance from incisor teeth to the beginning of Oesophagus being 15cm.

2. **Middle third (M)**: the middle 8.3cm translates to the part of oesophagus between 8.3cm and 16.6cm. This corresponds with the part between 23.3cm and 31.6cm when measured from the incisor teeth at endoscopy.

3. **Lower third (L)**: the lower 8.3cm translates to the part of oesophagus from 16.6cm to its termination at 25cm, This corresponds with the part from 31.6cm to the termination at 40cm when measured from the incisor teeth at endoscopy

INTRODUCTION

Cancer of oesophagus is a malignant tumor arising from the layers of the Oesophagus, a tube that provides passage of food from the mouth to the stomach. It is a very dangerous and fatal condition. Once overt symptoms occur, the average survival without treatment is 9 months. (1)

The incidence varies more than any other cancer. (2)

Patients with disease often ignore the earlier symptoms and present when the cancer mass starts to cause obstructive symptoms.

In the literature, the tremendous increase in the incidence of esophageal adenocarcinoma has led to a complete epidemiological shift such that in the United States and other industrialized countries, adenocarcinoma has replaced squamous cell carcinoma as the most common esophageal malignancy. (3)

At UTH, it has become a common cause of admissions to surgical wards based on anecdotal data. Nearly all the patients seen have advanced disease with obstructive symptoms and mainly die from starvation, and possibly aspiration pneumonia. Despite this and the various possible treatment modalities, mortality remains high as patients are treated palliatively. The literature at UTH is over two decades old (4), during which period the epidemiological shift has been seen in industrialized nations. This research therefore will try and determine the profiles of patients with cancer of oesophagus presenting to UTH, the current epidemiology and histological proportions.

HYPOTHESIS

H_1 : There is an increase in the incidence of Cancer of Oesophagus at UTH and an increase in the proportion of adenocarcinoma among histological types.

H_2 : Factors associated with the increase are related to HIV

OBJECTIVES

General Objective

- To study the current characteristics of Cancer of Oesophagus at the University Teaching Hospital.

Specific Objectives

1. To determine the number of patients with Cancer of Oesophagus at the University Teaching Hospital over one year

2. To describe demographic characteristics associated with Cancer of Oesophagus at the University Teaching Hospital

3. To establish the commonest histological types of Cancer of Oesophagus at the University Teaching Hospital currently

4. To determine the association of Cancer of Oesophagus with HIV, alcohol and smoking

2. LITERATURE REVIEW

2.1. Historical perspective

Cancer of oesophagus has been known from as early as the second century. (4)

The first report of an esophageal adenocarcinoma is credited to White in 1898. (3)

It is the ninth most common cancer in the world and generally a disease of mid to late adult-hood with a poor survival rate. (5)

2.1.1. Worldwide

Worldwide, an estimated 462,000 new cases occurred in 2002. The majority of cases (80-85%) are diagnosed in developing countries where it is the fourth most common cancer in men and most cases are squamous cell carcinoma (SCC). Five to ten percent of those diagnosed will survive for 5 years. (6)

The area with the highest reported incidence for oesophageal cancer is the so-called Asian 'oesophageal cancer belt', which stretches from eastern Turkey through north-eastern Iran, northern Afghanistan and southern Russia to northern China. In the high risk area of Gonbad in Iran, world age-standardised rates are more than 200 per 100,000 and the male/female ratio is reported as 0.8:1.0. (1)

2.1.2. In Africa

In most of Africa, the incidence of this disease has not been studied. (2)

Table 1. (4)

INCIDENCE OF CARCINOMA OF OESOPHAGUS

COUNTRY	M:F RATIO	PER 100000
Tanzania	5:1	0.26
Kenya	8:1	0.67
Uganda	3:1	_____
Zimbabwe	2:1	55.85
Mozambique	26:1	_____

A review of all malignancies diagnosed at Tenwek Hospital (Bomet District, Kenya) between 1989 and 1998 showed that oesophageal cancer was the most common malignancy; 274 cases accounted for 19% of 1459 malignancies diagnosed. A striking feature in the study was the presence of a subset of very young patients. Twenty-six (11%) patients were aged 30 years or less at diagnosis, and the youngest patient was 14 years old. This area of West Kenya seems to be a high-risk region for oesophageal cancer. (7)

In South Africa, data regarding the incidence of oesophageal and other cancers during the period 1985-1990 reported for all clinics and hospitals in four selected districts of Transkei, i.e. Kentani, Butterworth, Lusikisiki and Bisana, showed that the mean annual number of cases recorded for the period 1985-1990 was 292. Cancer of the oesophagus was the most frequently recorded malignancy (11.7/100,000 in Bisana) and accounted for the 46.5% of the cases with the male/female ratio of 2.4:1. (8).

2.1.3. In Zambia

In Zambia the incidence was 1.84 per 100000 population in 1985, and represents 3.3% of the total cancers seen. (3) It was the seventh commonest cancer recorded country-wide. From cancer registry, in 2006, the numbers of new cases recorded were 26 in 2006, 18 in 2005 and 20 in 2004. It accounted for 1.5% of all the cancers seen from 1999 to 2004. Records show progressive increase in mortality from 2004 to 2006, 4, 5 and 7 respectively. But it is not known whether cancer of oesophagus was the direct cause. The majority of these patients are lost to follow up. (9)

At UTH, the average annual incidence was 38 patients between 1980 and 1984 with mean age at presentation of 56 years. Majority falling between the ages 55 and 64. The male: female ratio was 3.14:1. Alcohol and tobacco were found to play an insignificant role in the aetiology. The study showed that the cancer is predominantly squamous (95%) and affecting the middle third (39%). (4)

Squamous cell carcinoma was previously the most common form of esophageal malignancy worldwide especially in African American men. The incidence varies according to geographic location, with a global range from 2.5 to 5.0 for men and 1.5 to 2.5 for women for 100,000 populations. In the United States, African Americans have a four- to fivefold increased risk compared with whites. (10)

The incidence increases with each succeeding decade of life. The peak age of occurrence is between 50 and 70 years, with a median age of death of 66 years in the United States. (1)

Tobacco and alcohol constitute the largest risk factors in North America and Western Europe, each acting independently as risk factor. The relative risk was 2.0 for those who smoked fewer than 15 cigarettes per day and 6.2 for patients who smoked more than 25 cigarettes per day. (1)

Diet and nutrition; vitamin deficiencies, especially vitamins A and C, folic acid, vitamins E and B 12, and riboflavin, are crucial risk factors. (10)

Reports from industrialized nations indicate a rise in incidence of adenocarcinoma from previously 3% to more than half of all new carcinomas.(1)

Incidence rates between 1976 and 1987 were fairly stable for squamous-cell carcinoma, but increased more than 100 per cent for adenocarcinoma among men. (11)

2.2. Anatomy

For purposes of classification the esophagus may be divided into three anatomic areas, the upper, middle, and lower thirds. The upper third (cervical esophagus) extends from the cricopharyngeal sphincter to the thoracic inlet, the middle third from the thoracic inlet to 10 cm above the gastroesophageal junction, and the lower third from 10 cm above that junction to the cardia of the stomach.

2.3. Aetiology

Based on colonic paradigm, it is thought that the development of cancer of oesophagus results from the accumulation of alterations in oncogenes, tumor suppressor genes, and DNA mismatch repair genes, in co-operation with environmental factors. (12)

Celiac disease and Tylosis are associated with esophageal cancer while Plummer–Vinson (Patterson–Kelly) syndrome is associated with carcinoma of the upper third of the esophagus. (1)

Gastroesophageal reflux disease has a 30- to 40-fold increase in the incidence of adenocarcinoma of the esophagus compared to that in the general population. Other oesophageal disorders associated with an increased incidence of carcinoma include chronic lye strictures, achalasia, and perhaps diverticula. (1)

Over the past 50 years there has been a remarkable change in the epidemiology of esophageal cancer. Previously rare, adenocarcinoma of the esophagus and

gastroesophageal junction is now the most common esophageal cancer, and in the United States the incidence is increasing faster than that of any other malignancy. Once a rare tumor, adenocarcinoma of the esophagus is currently the cancer with the fastest increasing incidence in America, and recent data indicate that in the United States since 1975, the rate of increase of adenocarcinoma of the esophagus has outpaced the next closest cancer, melanoma, by nearly three times. (3).

The tremendous increase in the incidence of esophageal adenocarcinoma has led to a complete epidemiological shift such that in the United States and other industrialized countries, adenocarcinoma has replaced squamous cell carcinoma as the most common esophageal malignancy. (3).

The specific etiological factors responsible for the dramatic increase in the prevalence of esophageal adenocarcinomas are unknown. Many potential risk factors have been evaluated, but the one indisputable risk factor is increased exposure of the esophagus to refluxed gastric juice. (3).

People with long-standing severe reflux symptoms were 43 times more likely to develop adenocarcinoma of the esophagus. (3).

It has also been demonstrated that in people with reflux, it is Barrett's, that is the major risk factor for cancer. (3).

2.4. Pathology

SCC and adenocarcinoma are the commonest types. SCC usually affects the upper two-thirds, in 80% of patients. Adenocarcinoma affects the lower one-third. (1).
But there are frequent exceptions to this rule. Oat cell cancer occurs occasionally. (5).

Three gross patterns of growth are commonly seen. The tumor can be fungating, ulcerative or infiltrative. (1)
Patients who present with dysphagia have neoplasms that are usually transmural with regional lymph-node metastases which correlate with the depth of invasion. Lack of a serosal covering of the oesophagus may explain the early invasion of mediastinal structures. . Those commonly invaded include the trachea and left main bronchus, aorta, pericardium, pleura, lung, liver, bone, kidney, and brain. A malignant fistula between the airway and esophagus occurs more commonly than an aortoesophageal fistula. (13)

Lymph-node metastases are common and correlate with the depth of tumor invasion. (10)
For staging and general assessment, the most important aspect is a careful search for metastatic disease. U/S of the liver and CT scanning of the chest and abdomen are mandatory before resection to exclude metastatic disease from the lungs and liver. These methods are however, still inaccurate for staging the primary lesion and for staging lymph nodes. Endoluminal U/S, if available, is the best method for preoperative staging

of oesophageal cancer. Bronchoscopy should be done in lesions of the upper or middle thirds. Laparoscopy is useful for assessing adenocarcinoma of the distal oesophagus.(10)

The current staging system was developed by the American Joint Committee on Cancer in conjunction with the International Union Against Cancer. The staging system incorporates two critical variables. The depth of invasion and the presence of lymph-node metastases. Survival is stage dependent.

2.5. Diagnosis

Successful treatment relies on high index of suspicion and early prompt diagnosis. Dysphagia, odynophagia, chest pain, regurgitation, recent weight loss and voice changes should arouse the suspicion. Further tests to confirm the presence of the disease should be done. Histological diagnosis is the gold standard but there are other investigations possible, with variable accuracy.(4)

These include barium swallow, endoscopy, ultrasound, bronchoscopy and computer tomography (CT). These can be used in pre-operative staging of the cancer and thus as a guide to optimize the treatment.

In high risk individuals, screening with cytological smears has reported 90% accuracy rates for determining pre-malignant and early lesions in China. (14)

2.6. Treatment

The goal of treatment in carcinoma of the esophagus is twofold: palliation of dysphagia and cure of the cancer. Curative treatment involves radical surgery or radiotherapy. Early cancer is treatable by surgical resection. Resection quickly restores swallowing to normal and palliates dysphagia. As a single therapy, surgery offers the greatest chance for cure. (1).

In a clinical report by EBFK Odimba, review of 84 patients, in developing countries, that underwent oesophageal surgery showed that the main indication for surgery was cancer, 54% (45/84). (15)

A cumulative review of all published reports in English for surgical resection of squamous-cell carcinoma of the esophagus by Muller demonstrates the magnitude of the problem and summarizes the experience with 76 900 patients. Only 56 per cent of patients had resectable disease at first presentation. Resection was associated with an operative mortality of 13 per cent. Survival was 27 per cent at 1 year, 12 per cent at 2 years, and only 10 per cent at 5 years. (16)

Recent reports from selected institutions have shown a decrease in operative mortality and an increase in 5-year survival. Many centers have reported mortality rates of under 5 per cent and 5-year survivals around 20 per cent with surgery alone for squamous-cell carcinoma of the esophagus.(1)

Radiotherapy may be a useful alternative to surgery, especially in unfit patients. Radical radiotherapy can produce long-term survival in oesophageal cancer. Although traditionally used for squamous cell cancer it may also be effective for adenocarcinomas. Survival following radio-therapy with a typical UK case mix is between 9 per cent and, exceptionally, 19 per cent. The average appears to be about 10 per cent. (5)

With the advent of regimens containing cis-platinum, chemo-therapy for oesophageal cancer has improved considerably. Chemotherapy never cures the disease, but can produce worthwhile shrinkage of disease in up to 60 per cent of cases. (5)

3. PATIENTS AND METHODS

3.1. Study site and duration:

This study was conducted at the University Teaching Hospital, Lusaka, Zambia, from December 2008 to November 2009.

3.2. Study design:

This study was a quantitative, descriptive cross-sectional study.

3.3. Case definition:

In this study, a case referred to a patient with positive histological diagnosis of the oesophageal lesion.

3.4. Inclusion criteria:

All patients with clinical suspicion of cancer of oesophagus were enrolled.

Patients had to undergo endoscopy at which biopsies samples were taken for histology.

Only those whose histologies came out with a diagnosis were considered for inclusion.

All patients had to consent for inclusion in the study.

3.5. Exclusion criteria:

Patients without clinical diagnosis or suspicion of cancer of Oesophagus were excluded from the study.

Those without histological diagnosis were also excluded. So were those whose histologies were inconclusive.

Patients whose histological diagnoses were already known were also excluded.

Refusal of consent was an exclusion criterion but all patients consented in this study.

3.6. Study sample size

All patients that presented to UTH during the study duration, met the inclusion criteria and consented for inclusion were captured and determined the sample size for the study.

The total number of endoscopies and biopsies that were done for suspected cancer of Oesophagus at UTH during the period of study were 115.

Fifty-one (51) of these had positive histologies for cancer of Oesophagus.

Fifty-six (56) had no evidence of cancer of Oesophagus.

Eight (8) had inconclusive histologies either because of inadequate tissue samples or the sample got lost.

3.7. Sampling technique:

The non-probability convenience sampling technique was used. All consented patients that presented to the University Teaching Hospital with suspected cancer of Oesophagus during the stated study period and fulfilling the inclusion criteria were enrolled.

3.8. Data Collection

Data was collected on pre- designed data collection sheets both at the time of patient enrollment into the study and prospectively to the time of laboratory results.

Data was collected from surgical admission wards, in-patient surgical wards and outpatient surgical clinics, from endoscopy clinic and from the histopathology laboratory.

3.9. End Point

The study involved a two point contact with the patient;

3.9.1. Questionnaire administration, HIV testing and endoscopy

3.9.2. Communication of results and referral of patient for appropriate management

The end point was therefore, at the time when histology results were communicated back to the patent.

3.10. Data Entry and Analysis

Data was entered into epidata software for checking and cleaning. It was then exported to STATA10 software for analysis.

Frequency tables and cross tabulation were used.

Chi square was used to compare categorical variables at 95% confidence interval (0.05).

After analysis, study conclusions were drawn based on statistical significance of the findings.

3.11. Study limitations

The sample size (51/107) used for the study on which the conclusions were drawn was small to be used for generalization.

The study only looked at three factors, HIV, alcohol and smoking, in trying to find the reason for the increasing incidence when the problem is multifactorial.

ETHICAL CONSIDERATIONS

This research project involving human beings was approved by the Research Ethics Committee of the University of Zambia (Assurance No. FWA00000338, IRB00001131 of IoRG0000774). All study participants gave an informed consent to freely be included in the study. Even after freely consenting to participation in the study, any one was free to withdraw anytime though this was not encouraged. The study subjects were treated with dignity and respect.

Study subject record confidentiality was maintained.

4. RESULTS

The examination of sample demographics forms a vital part of survey analysis. Sample demographics provide valuable insight into data quality thereby strengthening confidence in the quality of non-demographic aspects of data. These demographic characteristics include age and sex, etc and the relevant inter-relationships they form.

Results of this study were presented in two headings: Pooled results and cancer cases results.

The pooled results focused on the general demographics of all the cases studied. Cases with positive histology were isolated and analysed separately under the heading 'cancer cases results'.

4.1. Pooled results

4.1.1 Incidence

Total number of total cases studied for analysis was 107 after the inclusion and exclusion criteria were applied. 51 (47.7%) of these had positive histology for cancer of oesophagus while 56 (52.3%) had no cancer despite undergoing endoscopy and biopsy of the suspicious lesions.

See diagram number 1.

4.1.2. Sex distribution

Of all the cases studied, 71 male subjects and 36 female subjects (66% and 34% respectively) were studied.

See diagram 2.

4.1.3. Age distribution

The age range of participants was from 29 to 82 yrs of age. Demographic analysis revealed the mean age to be 54.14953 [95% CI 50.6649 - 57.63416] and a median age of 57 years. From these findings, the median was a better measure of central tendency because the age distribution is asymmetrical.

Interestingly, the commonest single age at presentation was 29 years representing 11.2% of the sample.

See diagram 3.

The diagram number 4 shows the combined results of sex and age. It compares the number of male and female subjects for categorical age groups.

4.2. Cancer results

This section sets out to investigate the incidence, sex and age distributions, commonest histological types and topographical distribution.

4.2.1. Age distribution

The majority of cases fell in 55-64 with the mean age 58.02 years at 95% C I. The median for the group was 57 years.

See diagram 5.

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4.2.2. Sex distribution

Among the subjects studied that had positive histological diagnosis for cancer of oesophagus, 35 were men and 16 were females. This translated into 68.63% and 31.37% respectively. Giving the male: Female ratio of 2.19:1.

See table 1.

4.2.3. Histological distribution

Squamous cell carcinoma accounted for 88.23% of all the cancers seen. Adenocarcinoma took up the remaining 11.77%. No other histological types of cancer or malignancy were seen.

See diagram 6

4.2.4. Topographical Site

The majority of the cancers were in the lower third of the oesophagus, 32 (62.75%) while the upper third had the minority 6 (11.76%). The middle third of the oesophagus had 13 (25.49%) of the cancers.

Adenocarcinoma was purely on the distal part of the oesophagus while squamous cell and non-malignant lesions showed a progressive increase towards the lower part.

See diagram 7.

4.2.5. Associations

Risk Association is a vital part of disease prevention and treatment. This subsection investigated whether HIV, alcohol and smoking were linked to cancer of oesophagus

HIV – In our study, there was no statistical association of HIV to development of CoO at the University Teaching Hospital. Among those with Ca, 12 also had HIV (50%). However statistical analysis using chi squares showed that this finding was not significant ($p = 0.795$).

See table 2.

Alcohol – Among those with Cancer, 32 also had positive history of alcohol ingestion (57.14%). Analysis using chi squares showed that this finding was statistically significant ($p = 0.040$). There was therefore, borderline association of alcohol to developing cancer of oesophagus.

See table 3.

Smoking – Of the subjects with Ca, 14 also had history of smoking (63.64%). However analysis showed that this finding was not statistically significant but suggestive of the association ($p = 0.092$).

See table 4.

Diagram 1. Incidence of cancer of oesophagus at UTH (n=107).

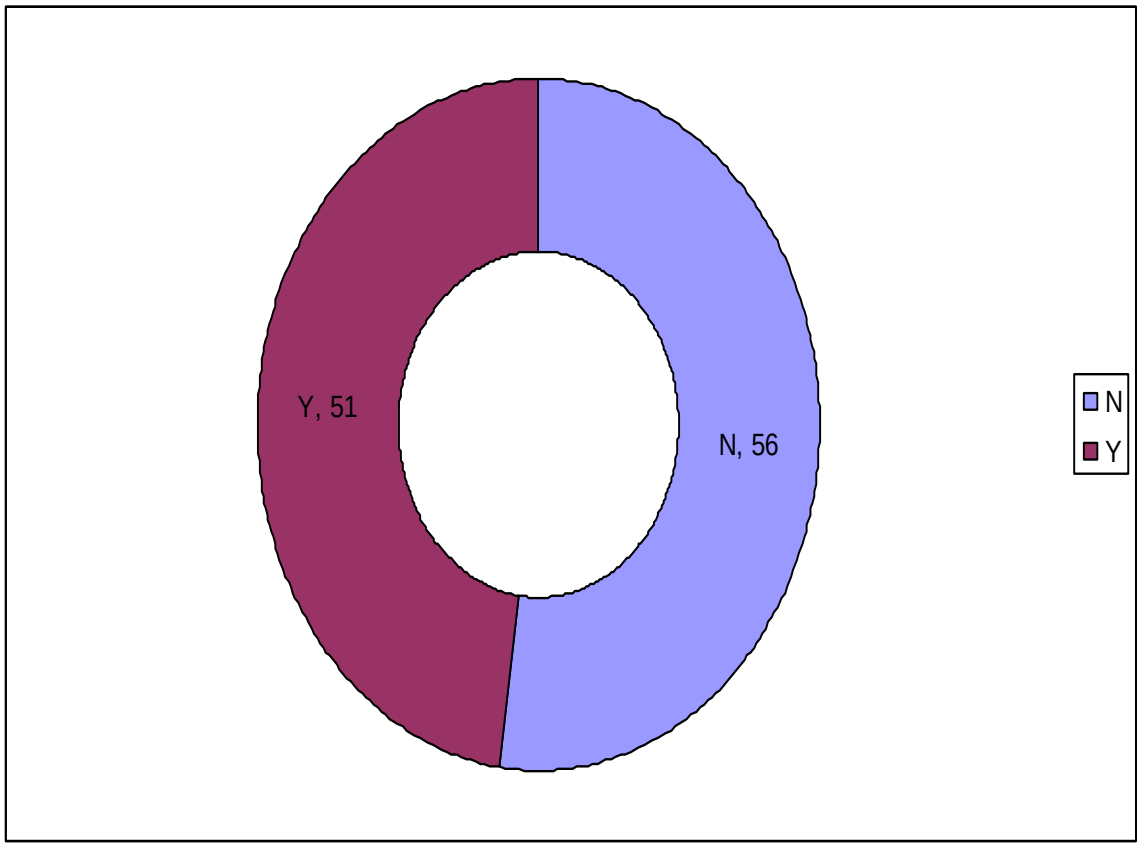
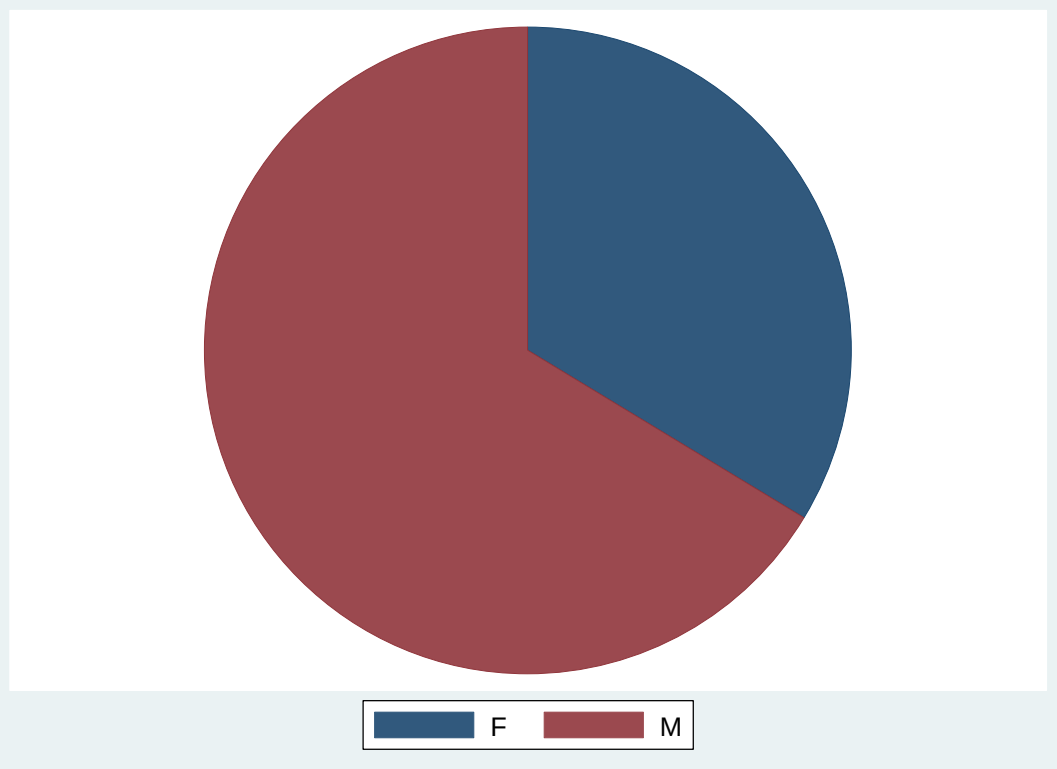


Diagram above shows that among participants, almost half (47.7% n= 51) had histological evidence of CoO. 52.3% had no cancer.

Diagram 2. Sex distribution of studied cases (n=107).



71 male subjects versus 36 female subjects (66% and 34% respectively).

Diagram 3. Age distribution for the studied cases.

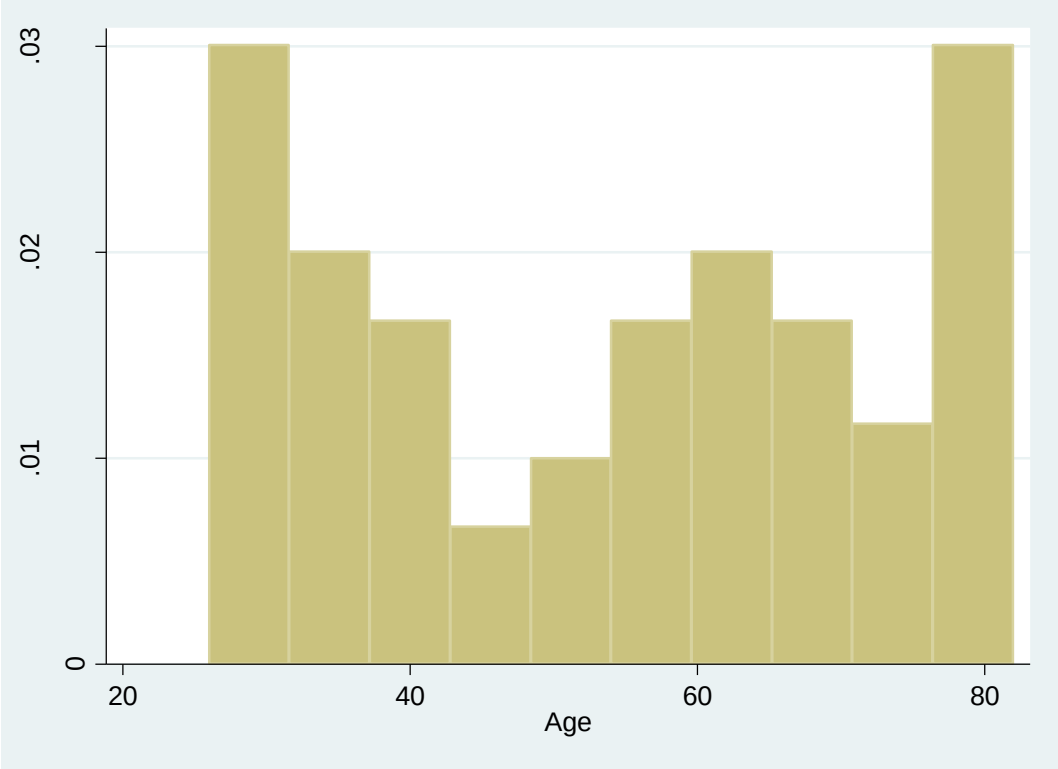
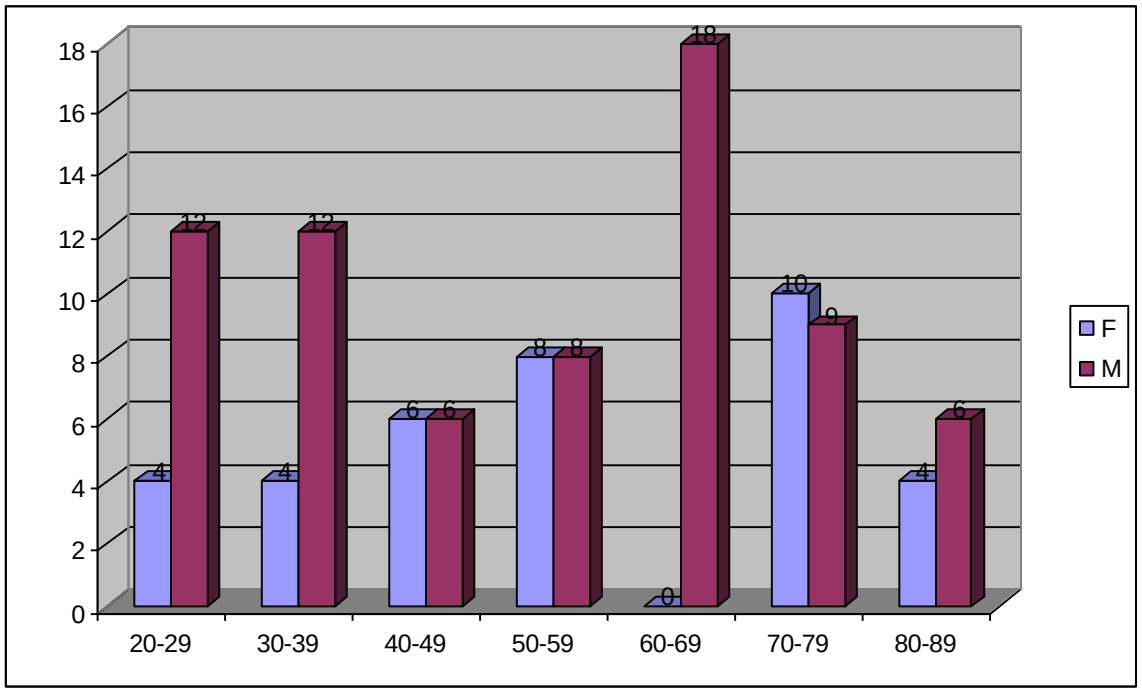


Diagram 3 shows that the age range of participants was from 29 to 82 yrs of age. The Mean age was 54.14953 [95% CI 50.6649 - 57.63416] and a median age of 57 years. The commonest age at presentation was 29 years representing 11.2% of the sample.

Mean age was 54.14953 (50.6649 - 57.63416) at 95% Confidence Interval.

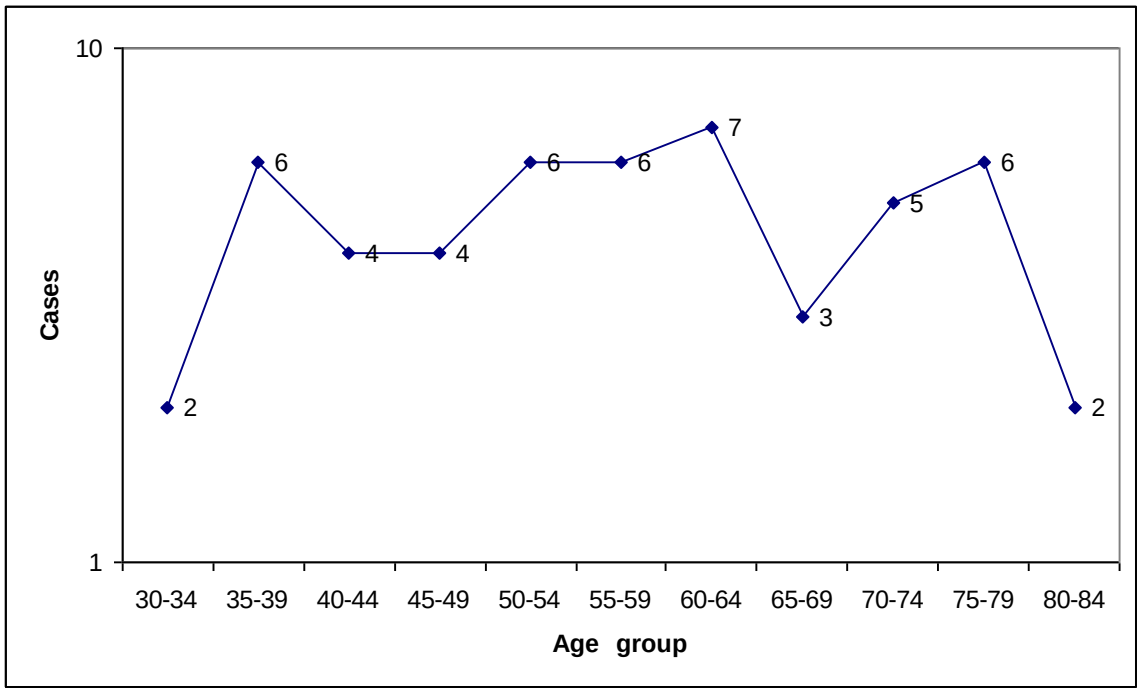
Median age for the sample was 57.

Diagram 4. Clustered sex versus age group distribution (n=107).



From graph above, 71/107 were males and 36/107 females with more men compared to women presenting with suspicious lesions.

Diagram 5. Age group distribution in Cancer cases.



Majority of cases fell in 55-64 followed by 60-69 (19 and 18 patients respectively).

However, it doesn't show a significant rise with age.

Mean age 54.15 years at 95% Confidence Interval.

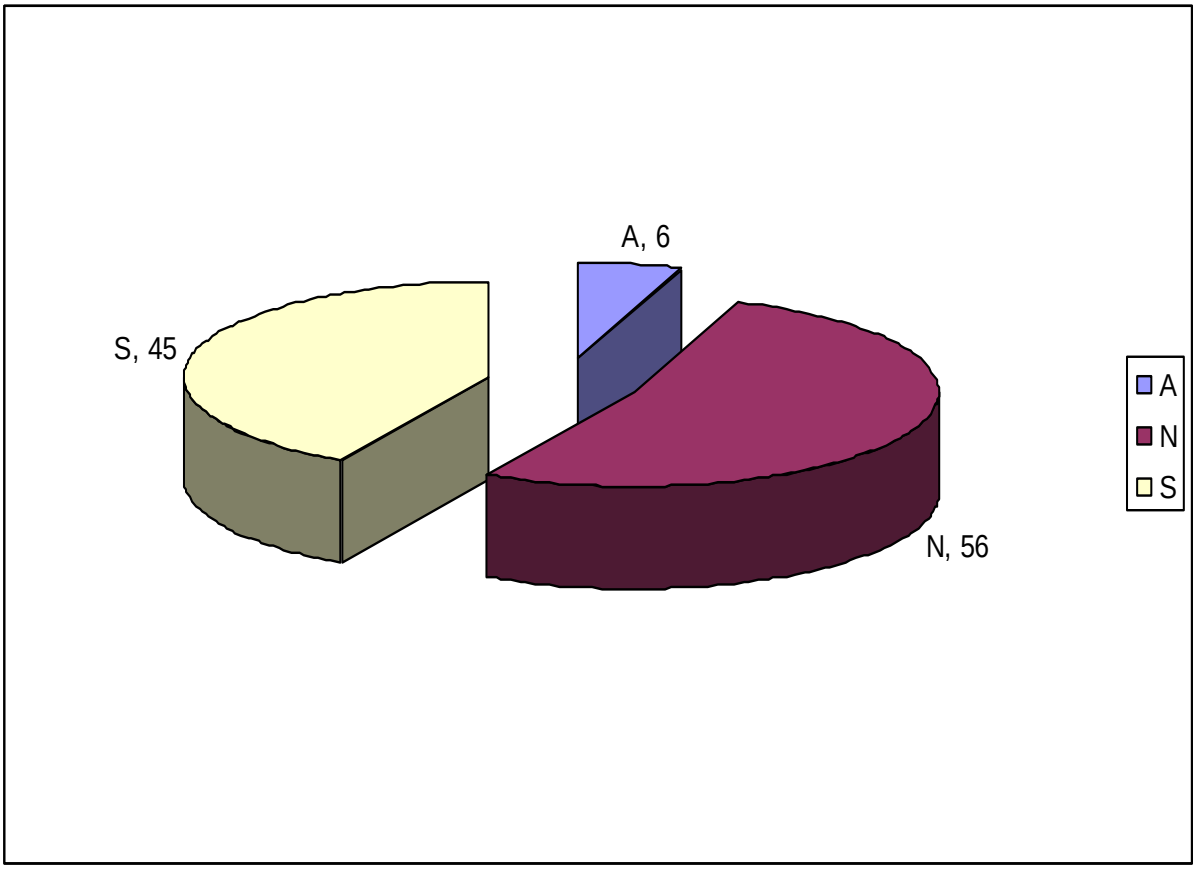
Median was age was 57.

Table 1. Sex distribution ratio among the cancer cases.

Sex	Frequency	%
Female	16	31.37
Male	35	68.63
Total	51	**100**

The above table shows that among the affected population studied, there were 2.19 times more males than females. Male: Female ratio = **2.19:1.**

Diagram 6. Pie chat showing the histological diagnoses.

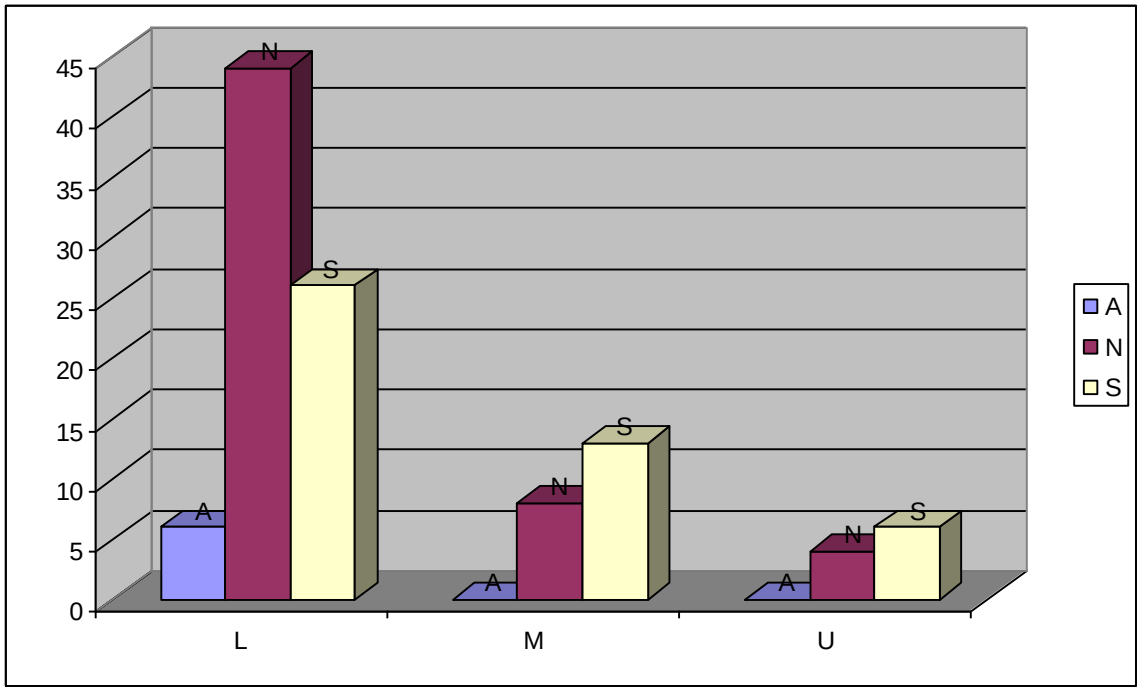


N = No cancer = 52.3% of all the subjects.

S = Squamous cell carcinoma = 42.06% (88.23% of the cancers).

A = Adenocarcinoma = 5.61% (11.77% of the cancers).

Diagram 7. Topographical distribution of the oesophageal lesions.



The diagram above shows that adenocarcinoma was purely on the distal part of the oesophagus while squamous cell and non-malignant lesions showed a progressive increase towards the distal part.

The majority of lesions were non cancerous but among those with cancer, squamous was more common (45/51%) and predominantly in the lower esophagus.

A = Adenocarcinoma

N = No cancer

S = Squamous cell carcinoma

Table 2. Association of HIV to CoO.

		CoO		
		N	**Y**	**Total**
HIV	**N**	44 (53.01%)	39 (46.99%)	83 (100%)
	Y	12 (50%)	12 (50%)	24 (100%)
	Total	56 (52.34%)	51 (47.66%)	107 (100%)

Table shows that among those with Cancer, 12 also had HIV. However statistical analysis using chi squares showed that this finding was not statistically significant ($p = 0.795$).

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Table 3. Association of alcohol to CoO.

		CoO		
		N	**Y**	**Total**
Alcohol	**N**	32 (62.75%)	19 (37.25%)	51 (100%)
	Y	24 (42.86%)	32 (57.14%)	56 (100%)
	Total	56 (52.34%)	51 (47.66%)	107 (100%)

Table shows that among those with Cancer, 32 also had positive history of alcohol ingestion. Statistical analysis using chi squares showed that this finding was statistically significant (p = 0. 040).

Table 4. Association of smoking to CoO.

		CoO		
		N	**Y**	**Total**
Smoking	**N**	48	37	85
		(56.47%)	(43.53%)	(100%)
	Y	8	14	22
		(36.36%)	(63.64%)	(100%)
		56	51	107
	Total	(52.34%)	(47.66%)	(100%)

Table shows that among those with Ca, 14 also had history of smoking. However statistical analysis using chi squares showed that this finding was not statistically significant but suggestive ($p = 0.092$).

5. DISCUSSIONS

A total of 115 cases were studied; out of which 51 (47.7%) had positive histological diagnosis of cancer of oesophagus. 56 had no histological evidence of the cancer, and 8 were excluded from the study for one reason or another. Our study sample was purely of black Africans and mostly of low socioeconomic status.

Incidence

The study shows an increase in the annual hospital incidence of 34%. Previously, the average incidence between 1980 and 1984 was 38 (4). In our study, it rose to 51. This is in agreement with anecdotal observations at the University Teaching Hospital. The reasons for the increase remain unknown. It could relate directly to the increase in the disease incidence, or the proficiency of the clinicians that raises the index of suspicion and hence the number of referrals; especially that the new Cancer Diseases Hospital is near the hospital under study.

Age

The age range for the studied sample was from 29 to 82 years. While the range for the cases that had positive histological diagnosis for cancer of oesophagus was 31 to 81. Majority of the subjects fell between the ages of 55 and 64. This is the same age

range that was mostly affected in the previous study (4). Therefore, there is no change in the peak age range in Zambia.

In the US, the peak range, 50 to 70 years (1), subsets the age range in Zambia. A generalization can thus be drawn that the cancer mostly affects those in the fifth to seventh decades.

The median age in our studied subjects was 57 (mean age of 54.15). It has remained fairly stable since 1984 – 56 (1). It is not known what it is in other Southern African countries, but is higher in the US, 66 years (1). Factors responsible for this discrepancy are not clear. It could be related to racial differences in the study subjects, or even differences in diet.

A study done in Kenya between 1980 and 1998 showed that 11% of the subjects were 30 years old or less, youngest being 14 (7). In our study, none of the subjects were 30 years or less. The youngest subject was 31. It is in keeping with the literature which says that the risk of developing the disease increases with age (1, 3).

Sex

In our study, the male to female ratio was found to be 2.19:1. Previously in 1984, it was 3.14:1 (4). There was an increase in the female population being affected in Zambia. Ratios from other countries in the sub-Sahara region did not lead to any meaningful conclusions as they are very variable: 26:1 for Mozambique, 2:1 for

Zimbabwe and 2.4:1 for South Africa. (4). In Iran however, the cancer affects more women than it affect men. The male: female ratio being 0.8:1.0 (1).

Histological types

Squamous cell carcinoma accounted for the majority of the cancer, 88.23%. Adenocarcinoma contributed 11.77%. Bhura reported SCC to be at 95% two decades ago (4). The histological predominance was still favoring SCC despite the slight reduction in the percentage constituency. It was difficult to determine whether the finding was incidental or had a causal influence.

In US, there was an overall increase in the disease rates between 1976 and 1987. Rates for SCC remained fairly stable but an increase of more than 100% was seen for Adenocarcinoma. Adenocarcinoma now accounts for over 50% of all cases (1). No explanation was given in the study to account for such an epidemiological shift.

SCC showed a progressive increase down the oesophagus. Lower third being mostly affected, 26 (57.8%). Thirteen (13, (28.9%)) and 6 (13.3%) were in the middle and upper oesophagus respectively. Previously, SCC was predominant in the middle third, 39% (4).

Adenocarcinoma in our study remained restricted to the lower third of the oesophagus. No other histological types of cancer were found in the studied sample.

Associations

The HIV pandemic has seen a rise in the occurrence of most cancers. It has changed the practice of medicine especially in the developing world. The study did not however, show any statistical association to the development of cancer of oesophagus ($p = 0.795$ at 95% CI). To my knowledge, there are no studies around the region to compare with, nor have there been any such studies in the developed world.

Alcohol despite having been found to play an insignificant role in the previous study, it had borderline association with the cancer ($p = 0.040$). This is in accordance with the literature elsewhere (2, 10, and 17).

Smoking was not associated with the disease in the study sample ($p = 0.092$). There is no change from the previous study despite the strong association in the literature from western countries (17). The reason for this could be that there are fewer smokers in developing countries compared to the developed countries.

6. CONCLUSIONS

6.1.0 The total number of patients with cancer of oesophagus seen at the University Teaching Hospital has increased from 38 between 1980 and 1984, to 51 in 2009. This translates to an increment of 34% and is suggestive of an increase in the annual incidence of the disease.

6.2.0 The most affected age range (55-64) by the cancer has remained unchanged over the years. It is fairly comparable to the age range mostly affected in the United States (50-70).

6.2.1 The median age for the disease has not significantly increased. I.e. from 56 years two decades ago, to 57 years in this study. When compared to the United States, 66, the disease is commoner in a much younger age group in Zambia.

6.2.2 Like most other places, cancer of oesophagus has predilection for males. The male: female ratio 2.19:1 speaks for itself. However, more women are being affected now than before in Zambia. The ration previously being 3.14:1.

6.3.0 Squamous cell carcinoma is still the predominant histological type in Zambia, 88.23%, followed by adenocarcinoma at 11.77%. Other histological types are rare.

6.3.1 There is no marked epidemiological shift in the histological proportions in Zambia as seen in the western countries and in the Eastern Europe.

6.3.2 Adenocarcinoma remains the disease of the lower third oesophagus.

6.3.3 The disease is commonest in the lower oesophagus and still significantly common in the middle oesophagus, 63% and 26% respectively. This is notably in contrast with the literature and also with the earlier study two decades ago.

6.4.0 HIV and smoking did not show any role in the aetiology of cancer of oesophagus. Alcohol, like other literature says, showed to have a significant association to the cancer. The association is however, borderline.

7. RECOMMENDATIONS

Considering that there is an increase in incidence of cancer of oesophagus at UTH without any reasons for the increase being found, more studies are needed in Zambia to look at other factors that have been shown to contribute to the aetiology of cancer of oesophagus in other studies elsewhere. Such factors may include diets, vitamin deficiencies, and chronic oesophagitis among other things.

The cancer registry is poorly updated at UTH such that about half of the cases go unreported annually. We therefore recommend that the cancer registry be managed by the laboratory that directly deals with the histology results; or at least to allocate personnel to be stationed within the laboratory.

Treatment options are very limited at UTH. The hospital should come up with management protocols for the disease and continuously provide for the necessary supplies.

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9. APPENDIX A

DATA COLLECTION SHEET Form Number: _____

File number:_____

Attending Surgical Firm: (Blue/Green/Yellow/White/Red)

QUESTIONAIR

1. Demographic data

Sex……..

Age……..

Tribe……

Date first seen…..…….

Date of endoscopy……

Contact details of patient or next of kin _____

_____

_____

2. Symptoms presenting

I. Symptoms patient has had before seeking medical attention (Tick were applicable)

[ ] Chest pain at rest

[ ] Pain on swallowing

[ ] Difficult swallowing

[ ] Regurgitation

[ ] Vomiting blood

[ ] Wasting

[ ] Voice changes

[ ] Other:_____

II. Duration of symptoms before medical attention in months

[ ] Less than 1 month

[ ] 1 - 3

[ ] 4 - 6

[ ] 7 - 12

[ ] More than one year

3. Risk factors under study

I. History of alcohol intake

[ ] Yes

[ ] No

II. History of smoking cigarettes

[ ] Yes

[ ] No

III. Does the patient have HIV?

[ ] Yes

[ ] No.

Kindly request to collect blood sample for HIV testing.

Clinical Diagnosis at UTH

How the diagnosis was made at UTH

[ ] Before first attendance at UTH (referral letter)

[ ] On attendance at UTH ; Date

[ ] History ……/……/……

[ ] Barium swallow ……/……/……

FOLLOW UP DATA

5**.** HIV test result…

[ ] Reactive

[ ] Non-reactive

6. Endoscopy findings

Date done ……/……/……

Level of involvement

[ ] Upper 1/3

[ ] Middle 1/3

[ ] Lower 1/3

7. Biopsy result

Histology report No.:_____/_____

Date: ____ / ____/ _____

[ ] Squamous Cell Carcinoma

[ ] Adenocarcinoma

[ ] Others (specify):_____

APPENDIX B

PATIENT INFORMATION SHEET

A. TITLE

CURRENT EPIDEMIOLOGICAL AND HISTOLOGICAL CHARACTERISTICS OF CANCER OF THE OESOPHAGUS (CoO) AT THE UNIVERSITY TEACHING HOSPITAL (UTH)

B. PURPOSE

- To Collect Information About The Possible Causes Of Your Disease.
- To collect information about the specific type of disease that you have.

CoO is a disease of the food pipe; a tube through which food passes from the mouth to the stomach. It is characterized by uncontrolled growth and spread of abnormal cells. If not controlled, it can lead to death. Most of the patients present to hospital when the uncontrolled growth of cells starts blocking passage of food down the food-pipe.

The exact cause of this cancer is not known but there are a number of factors that are linked to its development in other regions; notably alcohol and smoking. This is not established in our country. More so, the HIV pandemic that has seen a number of other cancers on the increase has not been studied in linking with CoO. It is for this reason that we have decided to establish the association.

The food pipe has mainly two types of cells on its upper and lower parts. Previously, cells of the upper part were noted to be involved in cancer disease in over 80% of the patients. Worldwide, it has been shown that cells of the lower part have overtaken the predominance. It has also been shown that the disease has become commoner overall. There is no recent information in Zambia to show any such changes neither in the proportions nor in the numbers of patients seen. Hence the reason to establish whether

there is any change in the proportions of the types of the disease or not, and if there is an actual increase in the number of patients seen currently compared to the past. This information is necessary for planning and will help us manage cancer of oesophagus patients better.

Your participation in this study will be by answering a questionnaire of simple questions read to you by medical personnel (doctor or nurse) on duty.

Further participation will be by samples collected at endoscopy (refer to C) at The University Teaching Hospital. This material will be examined in the laboratory to determine the disease you have. If it is a cancer, the types of cells are involved. You will then be asked to return for follow up once the results from the laboratory are out for definitive management of your condition. You will not by any way deviated from the standard way of management of you condition at UTH.

C. PROCEDURES:

Endoscopy is a diagnostic medical procedure that is used to assess the interior surfaces of an organ by inserting a tube into the body. The instrument not only provides an image for visual inspection and photography, but also enables taking biopsies and retrieval of foreign objects.

For the procedure you will swallow a thin, flexible, lighted tube called an endoscope (EN-doh-skope). Right before the procedure the physician will spray your throat with a numbing agent that may help prevent gagging. You may also receive pain medicine and a sedative to help you relax during the exam.

D. RISKS AND DISCOMFORTS:

The procedure is considered to be relatively painless and, at worst, associated with mild discomfort. Most patients tolerate the procedure with only topical anaesthesia of the oropharynx using lignocaine spray.

Complications are not common (only 5% of all operations), but can include perforation of the organ under inspection with the endoscope or biopsy instrument.

E. CARE, BENEFITS AND ALTERNATIVES:

Your participation in the study will expose you to beneficial information, which will help you deal the disease and you will be in a position to advise others with similar problems. You are free to withdraw from the study at any time for any reason; the action will not in any way disadvantage you from seeking medical attention at this institution.

If you have any questions not properly answered by the nurse attending to you and you need clarification please call me Dr Joseph Musowoya on 0977 746075 or ask the Nurse to get in touch with me on your behalf

I …….
Have read/been read to the context of the study and fully understand the risks and advantages of participating in the study described above.

Signed this day.....

Witness this day.....

If you have any questions not properly answered by the nurse attending to you and you need clarification please call me Dr Joseph Musowoya on 0977 746075 or ask the Nurse to get in touch with me on your behalf.

APPENDIX C

CONSENT TO PARTICIPATE IN THE CANCER OF OESOPHAGUS STUDY

I have been asked to participate in the above research. The information about the study has been explained and given to me by way of the patient information sheet.

I understand that:

If I do not volunteer, or decide to withdraw from the study, my decision will be accepted and this will not influence the continuing management of my condition.

I have read (or) and understood the information that has been given to me in my vernacular language and have had all my questions answered to my satisfaction.

I am further aware that the information I divulge will be treated in a confidential manner and I will not be personally identified.

I have given my consent freely and willingly by signing this form.

_____	_____
Signature or thumb print of patient	Signature of Investigator
_____	_____
Date	Place

N.B.: In case of any questions, please contact Dr. Joseph Musowoya Department of Surgery, University Teaching Hospital (UTH), Lusaka. Tel 0977 746075, Email: musowoya@yahoo.com

Or

UNZA Biomedical Research Ethics Committee Tel; +260-1-256067, Fax +260 1-250753 or E-mail: unzarec@zamtel.zm.