A RETROSPECTIVE REVIEW OF CLINICAL-HISTOLOGICAL CHARACTERISTICS, TREATMENT MODALITIES AND SURVIVAL OF ADULT PATIENTS WITH ORAL CANCERS TREATED AT OCEAN ROAD CANCER INSTITUTE, TANZANIA.

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A Dissertation Submitted in Partial Fulfillment of the Requirements for the Degree of Masters of Medicine in Clinical Oncology of the Muhimbili University of Health and Allied Sciences

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Muhimbili University of Health and Allied Sciences

Department of Clinical Oncology

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CERTIFICATION

The undersigned certifies that she has read and hereby recommends for acceptance by the Muhimbili University of Health and Allied Sciences this research project entitled ***A Retrospective review of clinical-histological characteristics, treatment modalities and survival of adult Oral Cancer at Ocean Road Cancer Institute Tanzania,*** in Partial fulfillment of the requirements for the degree of Masters of Medicine in Clinical Oncology of the Muhimbili University of Health and Allied Sciences.

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Dr. Tausi Maftah

(Supervisor)

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Date

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Dr. Nazima Dharsee

(Co-supervisor)

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Date

DECLARATION AND COPYRIGHT

I, **Rehema Abdul-Rahman Mwabaya**, hereby declare that this research project 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. All references and other support have been acknowledged appropriately.

Signature: …….. Date: ……..

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DEDICATION

I humbly dedicate this work to my lovely late Husband Dr. Awadh Kitta Makoko and beloved late Son.

ALLAHUMMAGHFIRLAHU WARHAMHU WA'AFIHII WA'FU'ANHU.

They are the real reason for my strength, forever grateful for being part of me.

ABSTRACT

Background:

Oral cancer is the malignant neoplasm which arises from the oral cavity. The oral cavity includes; the upper and lower lips, gingivobuccal sulcus, buccal mucosa, upper and lower gingiva (including alveolar ridge), retromolar trigone, hard palate, floor of mouth, and anterior two-thirds of the tongue ("oral tongue"). The worldwide annual incidence of oral cancer is 354,864 with a mortality of 177,384. An increase in incidence of oral cancer has been seen worldwide, previously it was the disease of elderly over 60 years but currently seen in middle aged in 40's. Trends over time in incidence vary by country and for different subgroups of the population.

The treatment of oral cancer involves a multimodality approach which includes surgery, chemotherapy, and radiation resulting in increased disease control for locally advanced oral cancer. In Tanzania currently there is no information on the magnitude and trend of oral cancer so this study is going to fill up the gap by describing the disease in terms of social demographic data, risks factors, clinical presentation, histological types, stage, treatment modalities and overall survival for patients treated at Ocean Road Cancer Institute (ORCI).

Objectives

This study aimed to describe the epidemiology of oral cancer with regard to age, sex, histology and the clinical pathological profiles in adults presenting for treatment in Tanzania. Additionally, the study described the type of treatment applied and survival outcomes for adult patients seen at Ocean Road Cancer Institute (ORCI).

Materials and Methods

A descriptive retrospective study was carried out in adult oral cancer patients with a confirmed histological diagnosis who presented for treatment at Ocean Road Cancer Institute (ORCI) between January 2013 and December 2016. A proportionate quota sampling was applied to get the number of participants from each year followed by convenience sampling to collect 43 patients from each year. A sample size of 173 patients was gathered using a data extraction

forms. The data was analyzed using the statistical package for the social sciences (SPSS) version 23 for windows. Continuous variables were summarized using frequency and percentages were used to summarize the categorical data. Table and figures were used to present summarized data. Kaplan Meir time to event analyses was used for survival status and log-rank tests to identify predictive factors. The potential predictors of survival were assessed using cox regression and p value of < 0.05 was considered significant.

Results

A total of 173 cases were reviewed, where 61.8% were males and 38.2% were females. The mean age at time of diagnosis was 59.95 ± 12.92 years (21 to 90 years) and half of participants were more than 60 years (51.1%).

Tobacco use together with alcohol drinking was mostly commonly identified risk factor (39.2%) followed by tobacco use (37.6%). Smoking was the major route of tobacco use (68.4%).

Pain was the leading clinical presentation (28.9%), followed by pain with an oral lump (20.8%), lump alone (11.6%) and others in minority. Tongue was the commonest site affected for adult oral cancer followed by buccal mucosa, gingiva, lip, mouth floor and palate by 47.4%, 15.1%, 12.7%, 11%, 9.2%, and 4.6% respectively.

Histologically more than three quarter were squamous cell carcinoma type (95.3%) followed by minor salivary gland 2.3%, hematological 1.2% and others 1.2 % .Grade I was the leading tumor grade (65.3%) followed by grade II (22.5%) and grade III (7.5%).

Majority of participants (86.2%) presented with a late stage disease at the time of diagnosis while minority of the cases (13.8%) were in their early stage disease.

Concurrent chemoradiotherapy was mostly used as treatment modality to 61.8% of the participants while 37.6% were treated palliatively with either chemotherapy alone or radiotherapy alone for symptoms relief.

The study found that overall survivals of study participants in 2 year and 3 year were 26.3% and 18.8% respectively. Factors found to be significantly associated with a better survival include stage of disease and treatment modality.

Conclusion.

This study showed that the clinico-histological characteristics and overall survival of adult oral cancer patients attended at ORCI present with similar findings of those in other regions of the world.

Males are more affected than females and tobacco use and alcohol consumption being the commonest risk factors. The commonest site for adult oral cancer from the study is the tongue which is initially painless and later painful which brought the patients to seek medical attention with late stage disease. Disease stage is strongly related to treatment outcome with later stages of the disease having an overall poor outcome. 2 and 3 years overall survival is poor because of advanced stage of the disease at the time of diagnosis. Stage and treatment modalities are the most important outcome determinants of survival in adult oral cancer patients.

This study provides the basis for future prospective studies and will potentially contributes to improve some of our daily practices.

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LIST OF ABBREVIATIONS

ADH	Alcohol Dehydrogenase
AJCC	American Joint Committee on Cancer
ALDH	Aldehyde Dehydrogenase
CCRT	Concurrent chemo radiotherapy
EBRT	External Beam Radiation Therapy
ECE	Extra capsular Extension
IMRT	Intensity Modulated Radiation Therapy
MoHCDEC	Ministry *of Health*, Community Development, Gender, Elderly and Children
MUHAS	Muhmbili University of Health and Allied Sciences
ORCI	Ocean Road Cancer Institute
OC	Oral Cancer
OSCC	Oral Squamous Cell Carcinoma
RTOG	Radiation Therapy Oncology Group
SPSS	Statistical Package For The Social Sciences
TNM	Tumor, Node, Metastasis

DEFINITION OF TERMS

3D 3 Dimension Radiotherapy

3D-CRT 3 Dimension Conformal Radiotherapy

Brachytherapy- is the cancer treatment consisting precise placement of radioactive sources directly into or next to the tumor [1]

IMRT - is an advanced approach to 3 D treatment planning which enables precise conformation of the radiation dose to the target volume [2].

Partial response - at least 30% decrease in the sum of the largest diameter (LD) of target lesions [3].

Progressive disease – is at least 20% increase in the sum of the longest diameter of the target lesion taking as reference the smallest sum longest diameter since the treatment started or the appearance of one or more new lesion [4].

Radiotherapy- is a cancer treatment modality that uses high doses of ionizing radiation to kill cancer cells and shrink tumors. It can be delivered as the external beam or brachytherapy [5].

3D conformal radiation therapy - is a design and delivery of radiation therapy based on 3D image data where treatment fields are shaped to match the shape of the tumor and treat only the target tissue [6].

CHAPTER ONE

1.0 BACKGROUND AND LITERATURE REVIEW

1.1 Introduction

Oral cancer (OC) is the malignant neoplasm which arises from the oral cavity and imposes a significant burden on health in many parts of the world. The morbidity of the disease and its treatment results in disfigurement, pain, impaired speech, swallowing and overall decreased quality of life [**7**].

Worldwide oral cancer ranks as the eleventh leading cancer in the world with the incidence of 354,864 (2% of all malignancies) and mortality of 177,384 (1.9% of all malignancies).It represent about one-third of head and neck malignant tumors**.** In Tanzania oral cancer is the 10th commonest malignancy with incidence of 1098 (2.6%) [8].

Most publications from Africa dealing with major cancers record head and neck cancer on average 10% of all cancers but the incidence of cancers of the lip, oral cavity and tongue, pharynx and larynx is often aggregated and do not get the attention they deserve [9].

Risk factors for the developing oral cancer is mostly implicated to the use of tobacco, alcohol consumption and the least by chronic mucosa trauma, nutrition deficiency and Ultra Violet light exposure which is known to cause lip cancers mostly common in fair skin people by causing actinic cheilitis which may transform to oral squamous cell carcinoma [10]. Immunosuppression following viral infection with HIV has shown no increase in the risk of oral cancer.

The symptom in oral cancer patients depends on the site, for tongue cancers the main complain of the patients is pain, which represent 30–40% [11]. Regardless of pain being the main symptom, it is usually arises only when the lesions have increased to a remarkable size, and is at this time when the patient is bothered to seek a medical attention.

Early carcinomas in other sites are asymptomatic and often they are unnoticed [12]. The advanced cases are associated with neck metastases, seen as cervical lymph node enlargement.

It has been observed that early diagnosis is the most effective way of reducing the individual burden of the disease but unfortunately most patients are diagnosed with advanced stage disease and only one third of patients are diagnosed with early disease [13].

Imaging is essential to determine the stage of the tumor and presence of metastasis after definitive diagnosis is confirmed. Computerized Tomography (CT) with administration of intravenous contrast for initial assessment of soft tissue, bone and mucosal involvement. If there is concern regarding the invasion of the deep soft tissue, muscle or nerve, a magnetic resonance imaging (MRI) study may prove more accurate [14].

Technetium (Tc) 99^{m} bone scintigraphy in the form of planar views provide high diagnostic accuracy for mandibular invasion by OSCC of the alveolus. Ultrasound (US) can be employed for the assessment of the lymph nodes in the neck and if is combined with fine-needle aspiration biopsy its specificity reaches up to 100% [15].

CT and MRI are useful to detect the occult cervical nodal metastases which can be missed by physical examination although their capability to detect small nodal metastasis is limited hence the use of [^{18}F] Fluorodeoxyglucose positron emission tomography ([^{18}F]FDG PET) which has shown to be more sensitive on detecting metastatic neck nodes in oral cancer patients compared to CT/MRI [16].Assessment of cervical neck nodes in oral cancer is important in treatment planning and prognosis prediction and although[^{18}F]FDG PET is sensitive but it does not replace the pathological lymph node staging based on neck dissection [17].

1.1.2. Epidemiology

Oral cancer is the disease of middle aged and elderly with the worldwide annual incidence of 354,864 cases and 177,384 deaths each year [8]. The females are affected about a decade older than males [18].

Oral cancer is commonly seen in males than females and the ratio varies as per geographical distribution.

A multicenter study of OC biopsies done across 5 continents showed the male were more affected than female with ratio of 2.2:1 and the mean age at the 5^{th} and 8^{th} decade of life [19]. In Kenya the study done showed male to female ratio of 1.6:1 and is more seen at 6^{th} – 7^{th} decades of life with few patients about 13.4% at age 40 years and below [20],[21]. Also a study which was done in Zimbabwe shows the males preponderance over females with a ratio of 1.9:1 [22].

The site for occurrence of OC varies though tongue is the commonest site [18], [19], [20], [21], [22], [23]. A multicenter study of OC biopsies across 5 continents found that tongue was the commonest site affected followed by labial/ buccal mucosa, gingiva, palate and lastly the alveolar mucosa by 25.4%, 21.7%, 14.0%, 9.9%, 7.9% respectively [19]. A study done in Kenya showed that the commonest site to be affected was the tongue by 35%, the palate by 22% and floor of the mouth was the least common site by 10% [20].Similarly another study in Kenya show that the tongue was the commonest affected site though it was followed by the mandible, maxilla, floor of the mouth and the lower lip [21]. In study review from population based cancer registry of 5 continents, it was found that the most common affected area was the oral tongue followed by floor of mouth and unspecified parts of mouth by 41%, 21.1% and 20.5% respectively [22]. In a paper review from African countries it was found that the commonest affected site was the alveolar ridge, followed by tongue, palate, oral mucosa, floor of mouth, non-specified site, lip and oropharynx being the least affected site [23].

1.1.3. Tumor characteristics

Oral squamous cell carcinoma (OSCC) is the commonest histological subtype as the oral cavity is mainly lined by squamous epithelial cells.

The results from a multicenter study across 5 continents found the epithelial tumor been the commonest OC by 85.09% followed by salivary gland tumor with 6.68%, 4.47% hematologic, 1.32% bone tumor, mesenchymal tumor by 1.19%, others tumor by 0.93% and odonto-genic tumor by 0.33%. Among all the epithelial tumors, the commonest type was the squamous cell by 94.08% of all epithelial tumors and 80.05% of all OC.

Lymphoma was the second common OC and was the commonest among hematologic tumors where it accounted for 86.91% and 3.89% of all OC and the mucoepidermoid carcinoma was the third commonest OC by 45.26% of all salivary gland tumors and 3.02% of all OC [18].

1.1.4. Risk factors.

In Africa risk factors include alcohol abuse and/or tobacco in forms of smoking and smokeless (chewing/snuff) but also mixed with other leaf and bark products including Toombak, Miraa, Areca nut and Kola nut. Smoking and alcohol-considered major risk factors for the development of oral cancer and have a synergic effect [24]. Smokeless tobacco use is highly associated with the risk of developing OSCC [25], [26]. A systematic global review and meta-analysis shown the relationship of smokeless tobacco and OC, whereby in Southeast Asia region the risk was found to be 4.44,95% CI = 3.51 to 5.61 and the risk for the East Mediterranean region was 1.28, 95% CI =2.93 to 11.58 [27]. Tobacco and betel quid chewing increases the risk of acquiring OSCC and chewing of betel quid without tobacco have an independent positive association with oral cancer [22], [28]. In India smokeless tobacco is the most common forms of tobacco abuse and is the leading cause of cancer especially of the buccal mucosa and alveolus [11]. Smokeless tobacco can be in the form of betel quid or oral snuff increases the risk of oral precancerous lesions and OC by 2-fold and 15-fold [26]. Daily chewing betel-liquid and alcohol consumption are associated with oral potentially malignant disorder which ultimately can transform to OC.

A study done in Sri Lanka showed that the population attributable risks for oral potentially malignant disorder for daily betel-quid chewing and regular consumption of alcohol are 84% and 25% respectively [29].

Heavy alcohol drinking contributes about 7–19% OC cases. The risk among alcohol drinkers increases more when used together with tobacco chewing or tobacco smoking and or betel quid chewing and it also attribute to a significant proportion of deaths [30]**.** Alcohol is found to increase the permeability of oral mucosa and dissolve lipids components of the epithelium resulting to epithelial atrophy; impair DNA synthesis and interference with the ability to repair and also has genotoxicity and mutagenicity effect which causes decrease in salivary flow [25].

Human Papilloma Virus infection has a little contribution to OC. Some studies revealed small percentage of adult patient's and others in young patients but it is rather implicated to be of more importance in oropharyngeal carcinomas [31]. A study done in USA showed that the overall prevalence of HPV was 19.2% in 114 of OSCC cases**.** HPV16 was detected in 68.2% tumors from young patients and 31.8% from control tumors [32]. A cohort study done in Brazil found that that there is low frequency of high-risk HPV types in oral cavity and is less than 4% [31].

OC has been related to chronic trauma at the sites of potential dental and denture trauma, especially in non-smokers without other risk factors. Chronic mucosal trauma results in inflammation which leads to oxidative stress and induce genetic and epigenetic changes damaging DNA, inhibiting its repair, altering transcription factors, preventing apoptosis, and stimulating angiogenesis, thus resulting in carcinogenesis [33]. In Argentina the study done showed that there was association between chronic mucosa irritation and trauma with either drinking alcohol and or tobacco use or not drinking alcohol or not using tobacco [33]. A study done in Australia showed that OC occur predominantly at sites of potential dental and denture trauma, especially in nonsmokers without other risk factors. 61% of female who are non-smokers had OC and mostly occurred on the lateral tongue and older patient's lesions occurred in gingival and floor of mouth due to chronic denture rubbing. Some patients had dental abnormalities recorded in close proximity to where their tumor developed. [34].

Human immunodeficiency virus (HIV) infected patient's shows the markedly increased risk of the human herpes virus cancers, hence predisposed to develop KS and non-Hodgkin lymphoma [35].

HIV/AIDS has no impact on OC and this was confirmed by a study on oral cancer at Kenyatta National Hospital in Nairobi which reported neither an increase in the frequency nor a change in the pattern of OC in this population in the last decades of the 20th century, despite changes in life style and the emergence of AIDS in Kenya [21].

1.1.5. Clinical presentation

Pain with or without ulceration is the commonest presenting symptom. In cancer of the tongue is the earliest symptom while with other site it is a complaint in advanced stages [12].

A study in Kenya showed the ulceration to be the most common symptom followed with pain 97.6% and 93.9% respectively. A study done in Israel reported a series of patients with cancer of the tongue where pain was the main symptom by 66.5% and lump on the tongue by 29% [36]. In advanced cases patients may present with cervical lymphadenopathy due to neck metastases and about 5% may be detected in the absence of any obvious primary tumor [12].

1.1.6. Diagnosis and Staging

The diagnosis at advanced stages is associated with primary tumor site [19]. Early-stage diagnosis is seen mostly in tongue, buccal mucosa and lip, whereas the floor of the mouth and the retromolar trigone has been linked to diagnosis at advanced stages. [37]. A study in Kenya revealed that 53.7% of patients were found to have had stage IV disease at the time of diagnosis, 11% with III, stages II accounted for 26.8% and stage I disease was diagnosed in 8.5% of the patients [21].

The staging is according to America Joint Cancer Committee (AJCC) staging system. Which grades primary tumor size and invasion features (T), regional lymph node spread (N) and the presence of distant metastasis (M) and it stage the disease from I through IV which reflects the increase in severity of the disease and decreasing survival. AJCC eighth edition has includes tumor depth invasion and extra capsular extension of lymph node metastases.

The retrospective review study showed that there are improved disease-free survival differences between overall stages and tumor categories in the eighth edition while the seventh edition did not show any differences of stage and overall survival [38].

The table below summarizes the TNM staging as per AJCC 8th edition of 2018.

TABLE 1:

TABLE 1: ILLUSTRATE AJCC 8th EDITION TNM STAGING

Stage	**T**	**Nodes**	**Mets**
1	T1	N0	M0
2	T2	N0	M0
3	T3	N0	M0
	T1,T2,T3	N1	M0
IVA	T4a	N0,N1	M0
	T1,T2,T3,T4a	N2	M0
IVB	Any T	N3	M0
	T4b	Any N	M0
IVC	Any T	Any N	M1

Where;

T Defines Primary Tumor

T1……. Tumor ≤ 2 cm, ≤ 5 mm DOI

T2……. Tumor ≤ 2cm, DOI > 5 mm and ≤ 10 mm, *or* tumor >2 cm but ≤ 4cm, and< 10 mm DOI

T3……. Tumor > 4 cm *or* any tumor > 10 mm DOI

T4a…… Moderately advanced local disease

Lip – Tumor invades through the cortical bone or involves the inferior alveolar nerve, floor of mouth, or skin of the face (i.e., chin or nose)

Oral cavity – Tumor invades adjacent structures only (e.g., through the cortical bone of mandible or maxilla or involves the maxillary sinus or skin of the face)

T4b……. Tumor invades masticator space, pterygoid plates, or skull base and/or encases the internal carotid artery

N Defines Regional Lymph nodes

N0……. No regional lymph node metastasis

N1……. Metastasis in a single ipsilateral lymph node, 3 cm or smaller in the greatest dimension without ENE.

N2a……Metastasis in a single ipsilateral node > 3 cm < 6 cm in greatest dimension and without ENE.

N2b…….. .Metastasis in multiple ipsilateral nodes <6 cm in the greatest dimension and without ENE.

N2c…… Metastasis in bilateral or contralateral lymph nodes, < 6 cm in the greatest dimension and without ENE.

N3a…… Metastasis in a lymph node > 6 cm in the greatest dimension and without ENE.

N3b……Metastasis in any node(s) and clinically overt ENE (+).

M Defines Distant metastasis

M0……..No distant metastasis

M1……..Distant metastasis

1.1.7. Treatment recommendations

The management includes surgery, radiation therapy and chemotherapy with agents such as cisplatin, carboplatin, 5-fluorouracil, paclitaxel and docetaxel [10], [35].

Early stage lip disease the modality is surgical resection of primary. Positive margin patients or patients with extra capsular extension (ECE) benefit from post-op chemo-radiotherapy [39].

Most early-stage OC with no cervical nodal metastasis are generally curable with single modality therapy with no or minimal functional and physical morbidity either be local excision or treated with radiotherapy with equivalent excellent cure rates [40]. Neoadjuvant chemo radiation is considered in cases which are inoperable [14].

The treatment of patients with neck diseases is surgery by neck dissection followed by post-operative chemo-radiotherapy. A RTOG randomized control trials show that a post-op chemo RT of Cisplatin 100 mg/m^2 on day 1, 22 and 43 with RT 66Gy over 6.5 weeks is more efficacious than RT alone and overall survival by 47% versus 36% [41].

Radiation therapy can be administered by external beam radiotherapy (EBRT) or brachytherapy alone in early stages for oral tongue, floor of mouth or buccal mucosa. When EBRT is used alone, the dose is 66-70 Gy in conventional fractionation over 6-7 weeks. When the modalities are combined, 45-50 Gy is given initially with conventional fractionation to the primary site and nodal stations with EBRT followed by brachytherapy boost to the primary tumor site with margins [42]. EBRT can be delivered by 2D, 3D or IMRT technique. Intensity modulated radiotherapy (IMRT). A single institutional study done in Boston showed that IMRT is efficacious at reducing loco regional recurrence, with a loco regional failure rate of less than 10%, improving overall survival and reducing late toxicity effects [43].

Locally advanced tumors are managed with a combined modality including surgery, radiotherapy with or without chemotherapy. Primary radiotherapy, with or without chemotherapy, is a reasonable option for locally advanced tumors without bone involvement [42]. Generally tumors invading the mandible are managed with segmental resection and require postoperative radiotherapy for improvement of the local control [43].

1.1.8. Treatment Outcome, Survival and Prognosis

The prognosis of OC depends on the TNM stage group, patient-related factors, such as co-morbidity and tumor-related factors, such as perineural invasion, depth of invasion or extra capsular nodal spread [44].

Early stage diseases are has a good prognosis with cure rates of 80% and 65% for stage I and II respectively [45]. Survival depends on the stage of presentation at treatment and tumor location.

Early stage disease has better survival outcome and late disease has poor survival outcome. A study done in Argentina on 274 patients with primary OC show that 65% were diagnosed at stage III and IV and the survival rate was 80% at 12 months, 60% at 24 months, 46% at 36 months, 40% at 48 months, and 39% at 60 months and this shows that diagnosis at advanced stages has low survival rate as compared to early stages.

Also according to the site they found the floor of the mouth and the tongue that has the worst prognosis with survival rates of 19% and 27%, respectively [46].

In Tanzania current there is no data about OC so this study is going to fill up the gap by describing the disease in terms of social demographic data, risks factors, clinical presentation, histological types, stage, treatment modalities and overall survival for patients attending at ORCI.

Figure 1: Conceptual frame work

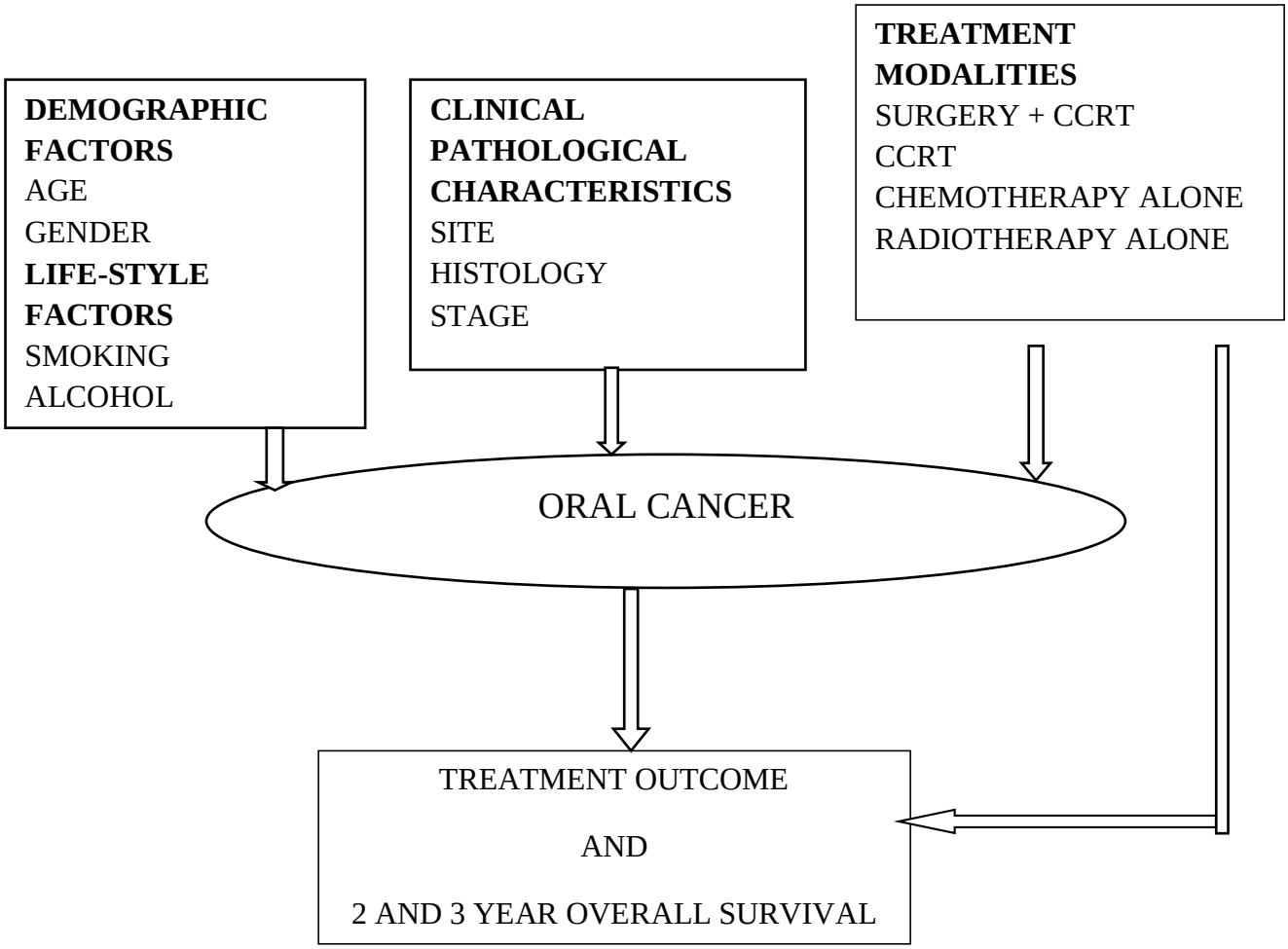


Figure 1: Conceptual framework of descriptive retrospective study of OC patients treated at ORCI.

The figure above demonstrates the interplay among several factors of interest in the study on OC patients at ORCI.

Tobacco and alcohol consumption are the commonly identified risk factors for the development of the disease. The site and stage are important in choosing the modality and intention (palliative or curative) of treatment (surgery, radiotherapy, chemotherapy or a combination). Finally, the overall survival assessed in terms of two and three years.

1.3 Problem statement

Oral cancer is currently increasing at an unprecedented rate with the disparity due to the difference in the distribution of risk factors in each geographical area. The proportional of occurrence varies from 1.38% to 24.8%. Management of these tumors of the oral cavity also ranges from surgery, chemotherapy and radiotherapy. Due to the location of the tumor surgery is the main treatment followed by chemo radiotherapy unless for advanced diseases. Most of the patients show up for medical consultation at late stage of the disease and together with the aggressive treatment the survival rate is reduced.

Majority of the patients in Tanzania are referred at ORCI for treatment. No study has been done to verify the profile for these patients of oral cancer and their status of treatment including modalities and outcome.

1.4 Rationale of the study

The prevalence of oral cancer is not high compared to other cancers but it poses a significant mortality and morbidity especially when discovered late stage of the disease. Majority of our patients with OC are seen at hospital with advanced stage. So, it is important to clearly understand the risk factors, symptoms, management and survival for this disease in our settings. Unfortunately there is paucity of studies regarding the OC in Tanzania; hence the study will give the clue on the magnitude of the disease and its impacts on survival.

Also, there is a gap in knowledge about this cancer in our population. This study will fill that gap of knowledge about risk factors, clinical profile, treatment modalities and its survival outcome for oral cancer patients treated at ORCI. Hence the results obtained from the study will be shared with Government through Ministry of Health and other health care stakeholders to increase the society's awareness, early diagnosis and treatment hence improving the survival. This study also provides the basis for future prospective studies and will potentially contributes to improve some of our practices.

1.5 Research question

1. What are the clinical characteristics and histological types of adult oral cancer patients seen at ORCI?
2. What are the treatments the patients received and 2 and 3 years overall survival?

1.6 Study objectives

1.6.1 Broad objective*:*

To determine the clinical characteristics, histopathological subtypes, treatment modalities used and the 2 and 3 years overall survival of oral cancer patients treated at ORCI from Jan 2013 to Dec 2016.

1.6.2 Specific objectives:

1. To determine the demography and clinical characteristics of adult patients with oral cancer attended at ORCI from Jan 2013 – Dec 2016.
2. To describe the various management modalities used for the treatment of adult patients of oral cancers treated at ORCI Jan 2013 – Dec 2016.
3. To describe 2 and 3 year overall survival for adult patients of oral cancers treated at ORCI Jan 2013 – Dec 2016.

CHAPTER TWO

2.0 METHODOLOGY

2.1. Study design

This was a descriptive retrospective study of adult patients with a histopathological confirmed OC diagnosis from Jan 2013 to Dec 2016.

2.2 Study Setting

The study was conducted at Ocean Road Cancer Institute (ORCI) in Ilala District, Dar es Salaam – Tanzania. ORCI was founded in 1895 by the German colonial government. It is a cancer treatment, research, and teaching center, affiliated with the Muhimbili University of Health and Allied Sciences with a capacity of 250 beds.

The hospital handles cancer patients from all over the country who pass through other hospital and are histologically confirmed with OC. The study area was chosen due to convenience, accessibility and the provision of specialized cancer treatment including chemotherapy, radiotherapy, palliative care and nuclear medicine**.**

The treatment of oral cancer at ORCI follows the National Cancer Treatment Guidelines of the United Republic of Tanzania. The mainstay of treatment is surgery with adjuvant therapy which can be either post-operative radiotherapy or post-operative chemoradiotherapy. Post-operative radiotherapy is indicated for patients with close margin or perineural invasion and post-operative chemoradiotherapy if pt has positive margins. Alternatively external beam radiotherapy +/- brachytherapy can be used followed by salvage surgery for residual disease. For unresectable disease concurrent chemoradiotherapy is preferred. The radiation dose is 66 – 70 Gray and 50 – 54 Gray to uninvolved neck.

2.3. Study Population

Target population: All adult patients aged from 18 years and above with a diagnosis of oral cancer in Tanzania.

Accessible population: All patients referred to ORCI with a confirmed diagnosis of oral cancer.

Study population: All adult patients with oral cancer who met the eligibility criteria.

2.4. Inclusion Criteria

Study included all patients aged 18 years and above who were referred to ORCI with a confirmed histological diagnosis of oral cancer and who had follow up visit post treatment.

2.5 Exclusion Criteria

All patients whose records were incomplete (that is those who had missing histopathology results)

Patients with posterior one third of the tongue disease were not recruited.

Patients with no follow up visits after treatment.

2.6 Sample size

An estimation of sample size was derived using the Fischer's formula:

$$N = \frac{Z^2 P(1-P)}{\varepsilon^2}$$

Where:

Z score for 95% confidence interval = 1.96.

P= approximate proportion of the event in the population=1.3% obtained from the multicenter study on oral cancer done by Kittipong et al [20]

ε=margin error set at 5

N=1.96×1.96 x0.13 (1-0.13)/0.05x0.05 =173.79

Therefore 173 patients treated over a 4 years period (Jan 2013 to Dec 2016), were recruited in the study.

2.7. Sampling procedure

A convenient sampling procedure was used; whereby all adult aged between 18 years and above with histologically confirmed oral cancer treated at ORCI from Jan 2013 to Dec 2016 were involved in the study.

The patient files at ORCI records department were used to identify all cases of oral cancer.

2.8. Study Variables

1. Independent variables:

   Age, sex clinical presentations, site of disease, stage, histology and treatment modality.

2. Dependent variables.

   2 and 3 years overall survival

2.9 Data Collection

All adult patients who attended ORCI between the study periods with a diagnosis of oral cancer were identified from the hospital register. Hospital case notes were retrieved for each patient.

Research assistants under the supervision of the principal investigator used data extraction forms to retrieve data from patient's records stored in manual files and/or on the computer.

The data extraction form captured demographic characteristics, disease characteristics, treatment modalities and the survival.

Treatment charts were evaluated for information about treatment, and follow up notes and investigations if any were used to determine the outcome status for each case.

2.10. Data Management, Analysis and quality plan.

Data extraction forms were carefully reviewed for completeness and consistency while ensuring patient confidentiality in records and identity. In case we missed or inconsistent data we recalled the patient periodical records or medical registers and information traced back as necessary to minimize incomplete data while we ensured confidentiality of patient records and identity.

The data from the dully filled data extraction forms were given identification numbers and coded into a Microsoft Excel (Office 2016 database which was then exported to SPSS for data cleaning and statistical analysis. The data analysis was done using the SPSS version 24 for windows.

Continuous variables were summarized by means, medians, standard deviation and range. Whereas categorical data were summarized using frequencies, percentages and bar graphs for general description.

Then, summarized data were presented and described by using tables, graphs and texts.

Kaplan Meir curves times to event analyses were used to identify and compare survival outcome over the stipulated period and log-rank tests to identify predictive factors. The potential predictors of survival were assessed using cox regression and p value of <0.05 was considered significant.

The survival rates were estimated using the date of diagnosis and date of death or date of last visit. Cox proportional hazard model used to examine various factors with time to death hazard ratios (HRs) and 95% confidence interval will be presented. Two sided P-value < 0.05 considered as statistically significant.

2.11 Ethical consideration

Ethical clearance was obtained from the Muhimbili University of Health and allied sciences (MUHAS) Research Ethics and Publication Committee prior to implementation of this study.

To minimize the risk of disclosure of protected health information, efforts were made to ensure that the participants' confidentiality was protected by ensuring limited access to study records and password coded information on personal computer only accessible by Principle Investigator and Assistant Investigator.

2.12. Consent Process

This study was limited to a retrospective review of hospital registers/records. It involved no more than minimal risk and there was no need of informed consent from the individual participants.

2.13. Study limitations and mitigation

It is a retrospective cohort study which depends on data from patient's files and records. Some information ware missed and affected the availability of good quality data**.**

2.14. Publication and dissemination of study results

This study is a part of partial fulfillment of Master of Medicine in Clinical Oncology, so the results are presented to MUHAS, ORCI Authority and also published in local and international journals.

CHAPTER THREE

3.0 RESULTS

It is a hospital based retrospective study with a total number of 173 cases attended at ORCI for a period of 4 years between Jan 2013 to Dec 2016.

Of the 173 patients included in the analysis, males were 107 (61.8%) and 66 (38.2%) were females. Male to female ratio was 1.6:1.The mean age at diagnosis was 59.95 with a standard deviation of 12.92 years (range from 21 to 90 years) and half of participants were more than 60 years (51.1%).

Majority (35.3%) of oral cancer patients came from the Coastal zone of Tanzania while 30% came from the Northern zone, 9.2% from Southern zone. The Central and Lake Zone had 8.7% and 7.5% respectively. The least but not last Southern highlands 3.5% and lastly the Western zone and Zanzibar had the fewest number of cases 2.9% each (Figure 2).

Table 2: Summarizes the social demographic information of adult oral cancer patients treated at ORCI from Jan 2013 to Dec 2016.

		Frequency	Percentages
Age Range	<40	12	7
	41-60	72	41.9
	>61	89	51.1
Sex	Male	107	61.8
	Female	66	38.2
Marital Status	Married	122	70.5
	Single	8	4.6
	Divorced	12	6.9

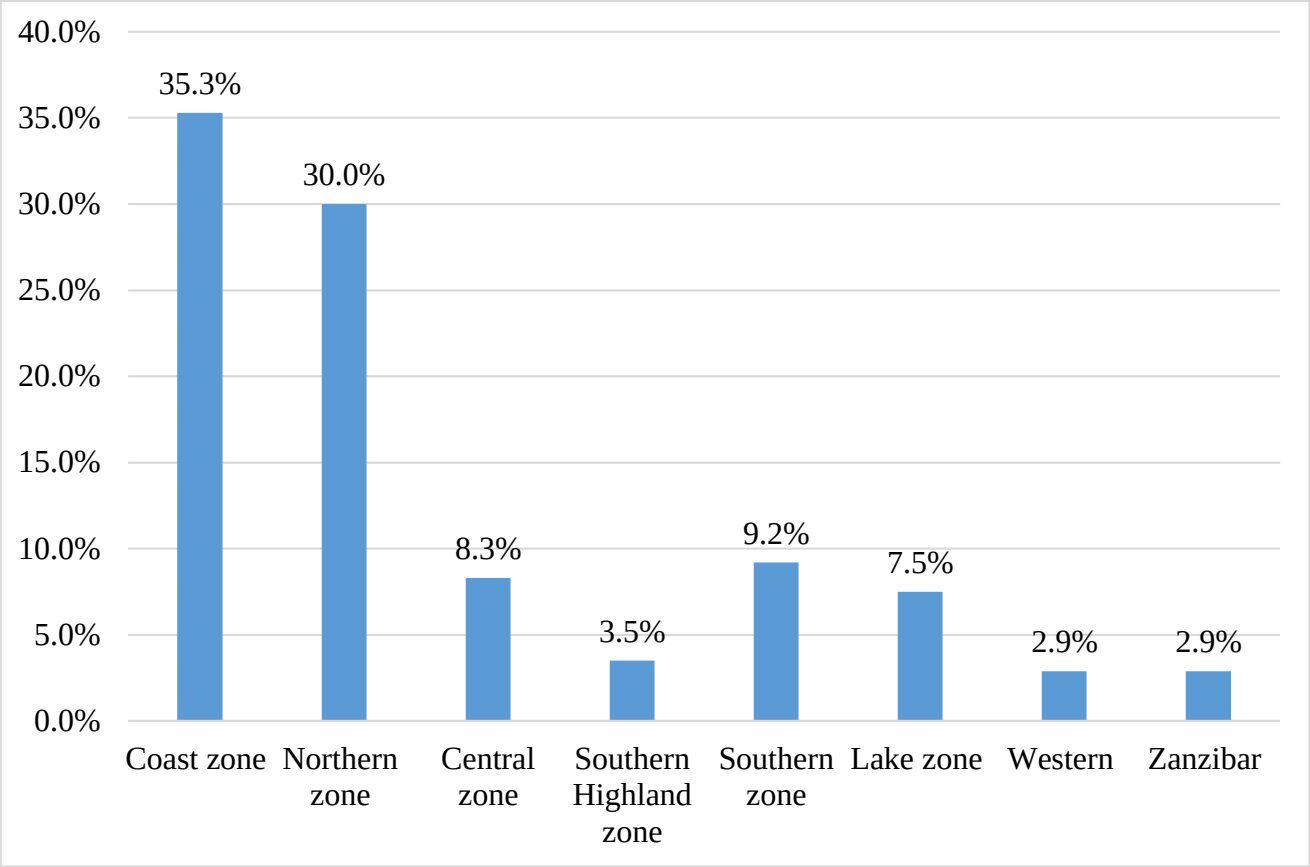
	Widowed	31	17.9
Educational Level	Primary	87	50.3
	Secondary	16	9.2
	Higher education	2	1.2
	Non formal	68	39.3
Occupation	Peasant	95	54.9
	Petty business	53	30.6
	Employed	9	5.2
	Others (dependent)	16	9.2
HIV status	Positive	12	6.9
	Negative	73	42.2
	Unknown	88	50.9

70.5% of patients were married and almost half of the participants 50.3% had primary school education as the highest level of education they attained although over quarter of them reported to have informal education.

50.9% of the participant HIV status was not reported whereas of those reported 42.2% were HIV negative and only 6.9% were positive.

Nearly half of the cases were peasants (54.9%), 30.6% of the participants were petty traders and the minorities were dependant (9.2%) and employed (5.2%).

Figure 2: below shows the geographical distribution of the adult oral cancer patients treated at ORCI from Jan 2013 to Dec 2016.



Key

Coast zone	Dar es Salaam, Coast and Morogoro.
Northern zone	Kilimanjaro, Arusha, Manyara and Tanga
Central zone	Dodoma and Singida.
Southern Highland zone	Mbeya, Rukwa, Iringa and Njombe.
Southern zone	Lindi, Mtwara and Ruvuma.
Lake zone	Mwanza, Simiyu, Shinyanga and Mara
Western	Katavi and Kigoma
Zanzibar	Pemba and Unguja.

Table 3: Summarizes the clinical characteristics among adult patients with oral cancer attended at ORCI from Jan 2013 to Dec 2016.

Characteristics		Frequency	Percentages
Presenting Symptoms	Pain	50	28.9
	Lump on oral cavity	20	11.6
	Neck swelling	2	1.2
	Bleeding	2	1.2
	Pain + lump	36	20.8
	Pain + lump +neck swelling	10	5.7
	Pain, lump, neck swelling, bleeding	3	1.7
	Pain, neck swelling	12	6.9
	Pain, lump, bleeding	13	7.5
	Pain, neck swelling, bleeding	8	4.6
	Pain + bleeding	10	5.8
	Pain +neck swelling	12	6.9
	Lump neck swelling	1	0.6
	Pain +ulceration	5	3.5
	Ulceration	1	0.6
Disease Site	Tongue	82	47.4
	Lip	19	11.0
	Gingiva	22	12.7
	Palate	8	4.6
	Buccal	26	15.1
	Mouth floor	16	9.2

Stage Of Disease At Diagnosis	I	3	1.7
	II	21	12.1
	III	25	14.5
	IV	124	71.7
Histology	SCC	165	95.3
	Salivary gland	4	2.3
	Hematological	2	1.2
	Others	2	1.2
Grade	I	113	65.3
	II	39	22.5
	III	13	7.5
	Not documented	8	4.6
Metastasis	Yes	18	10.4
	No	155	86.6
Metastatic Site N=18	Lungs	11	61.1
	Liver	6	33.3
	Both	1	5.6

Pain was the leading clinical presentation (28.9%), followed by pain with an oral lump was the second most (20.8%), lump alone (11.6%) and the minority presented with pain and neck swelling (0.6%) or ulceration (0.6%).

Tongue was the most reported site of disease (50.9%) followed by floor of the mouth (23.1%) whereby the gingiva, lip and palate by 13.9%, 7.5% and 4.6% respectively.

Histologically more than three quarter was squamous cell carcinoma type (95.3%) followed by minor salivary gland 2.3% with adenocystic 1.7% and mucoepidermoid 0.6%. Hematological tumors accounted for 1.2% with equal percentage of 0.6% of B-cell lymphoma and lymphoplasmatocysis lymphoma and others 1.2 % which include verrucous and fibro-

sarcoma. Grade I was the leading tumor grade (65.3%) followed by grade II (22.5%) and grade III (7.5 %).

More than half of the cases were grade 1 (65.3 %) while grade 2 and 3 were 16.8% and 7.5 % respectively moreover 4.6 % were not graded at all.

Majority of participants were on late stage (stage III and IV) accounting for 86.2 % and early stage (stage I and II) by 13.8 %. Of those diagnosed at late stage, 71.7 % were stage IV verging metastasis. Only 10.4% had metastasized to other site, commonly lung and relatively few on liver.

Table 4: Summarizes the risk factor associated with oral cancer among adult patients treated at ORCI from Jan 2013 to Dec 2016.

Characteristics		Frequency (n)	Percentage (%)
Risk			
	tobacco	65	37.6
	Alcohol	29	16.8
	tobacco+alcohol	68	39.2
	not identified	11	6.4
Mode of tobacco use			
	smoking	91	68.4
	smokeless	41	30.8
	Both	1	0.8

Tobacco combined with alcohol use was mostly commonly identified risk factor among the cases by 39.2% while tobacco only and alcohol only contributed 37.6% and 16.8% respectively. Smoking was the major route of tobacco use (68.4%) among all tobacco use either alone or with alcohol) and smokeless tobacco was the least (31.6%). Smoking is reported to be most frequent way of tobacco use.

Table 5: Summarizes the treatment modalities used to adult oral cancer among patient treated at ORCI from Jan 2013 to Dec 2016.

Characteristics		Frequency	Percentages
Treatment	Surgery + CCRT	1	0.6
	CCRT	107	61.8
	Chemotherapy alone	12	7.0
	Radiotherapy alone	53	30.6

Key:

CCRT = concurrent chemotherapy and radiotherapy.

Concurrent chemoradiotherapy used as treatment modality to 61.8% of the participants while 37.6% were treated palliatively with either chemotherapy alone or radiotherapy alone for symptoms relieve including bleeding and severe pain. Surgery (mucosectomy with right side lymph node neck dissection) in combination of post-operative chemotherapy radiotherapy was the least treatment offered to only 0.6%.

Table 6: Summarizes the univariate analysis of factors associated with survival among adult oral cancer patients treated at ORCI from Jan 2013 to Dec 2016.

		Survival					
		Dead		Total			
		n	%	n	%	X^2	P value
Gender	Male	90	(63.8)	90	(63.8)		
	Female	51	(36.2)	51	(36.2)	0.053	0.817
Age	<40	9	(6.4)	9	(6.4)		
	41-60	54	(38.3)	54	(38.3)		
	>60	77	(54.6)	77	(54.6)		
	5.00	1	(0.7)	1	(0.7)		
						3.214	0.360
Grade	0	6	(4.3)	6	(4.3)		
	1	88	(62.4)	88	(62.4)		
	2	34	(24.1)	34	(24.1)		
	3	13	(9.2)	13	(9.2)	2.797	0.592
Stage	I	1	(0.7)	1	(0.7)		
	II	18	(12.8)	18	(12.8)		
	III	11	(7.8)	11	(7.8)		
	IV	111	(78.7)	111	(78.7)	26.5	<0.0001
Disease site	Tongue	70	(49.6)	70	(49.6)		
	Lip	15	(10.6)	15	(10.6)		
	Gingiva	20	(14.2)	20	(14.2)		
	Palate	6	(4.3)	6	(4.3)		
	Buccal	17	(12.1)	17	(12.1)		
	Mouth	13	(9.2)	13	(9.2)		
	floor					5.932	0.313.
Treatment	CCRT	83		83			
	RT/Chem	57		57			
						33.461	<0.0001.

KEY:

Grade 0 = not documented

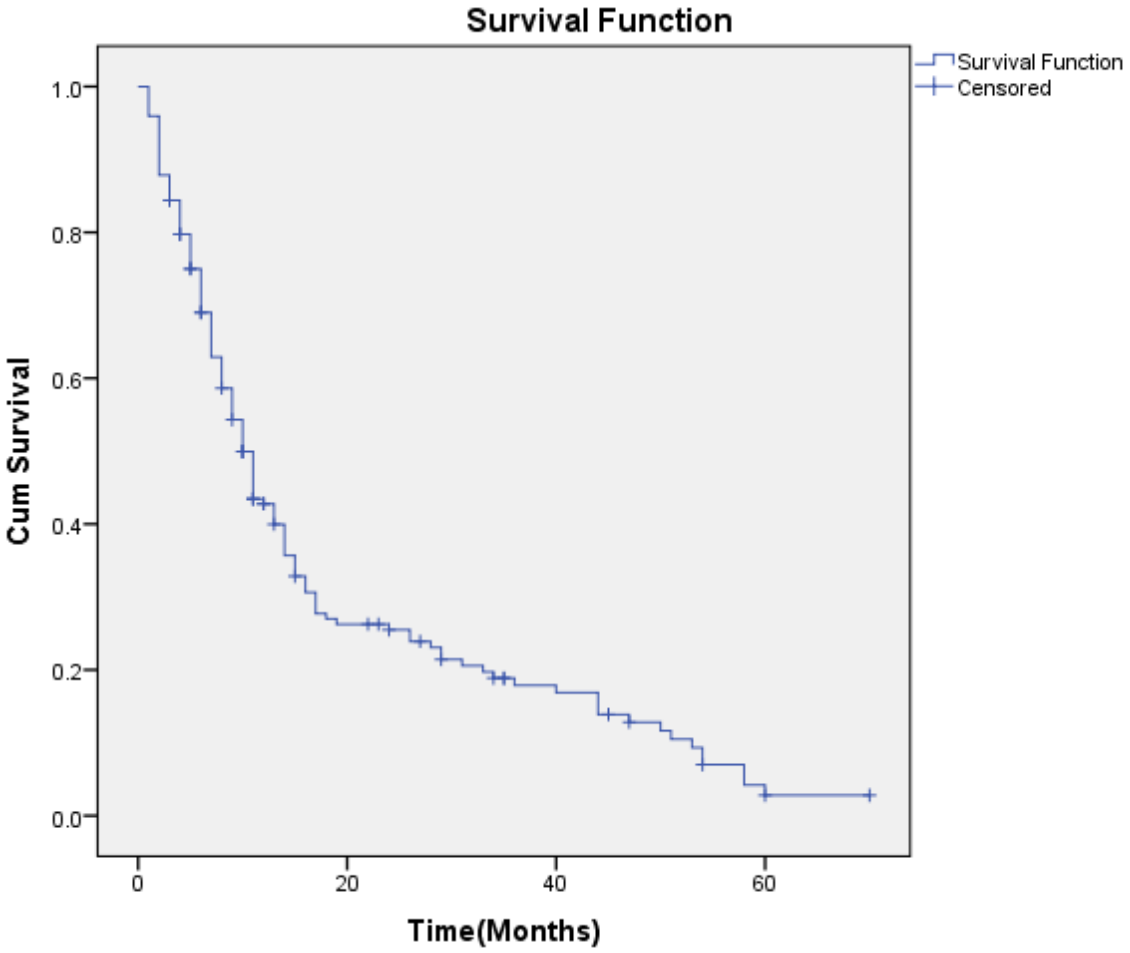
CCRT = concurrent chemoradiotherapy.

RT = radiotherapy

Chem = chemotherapy

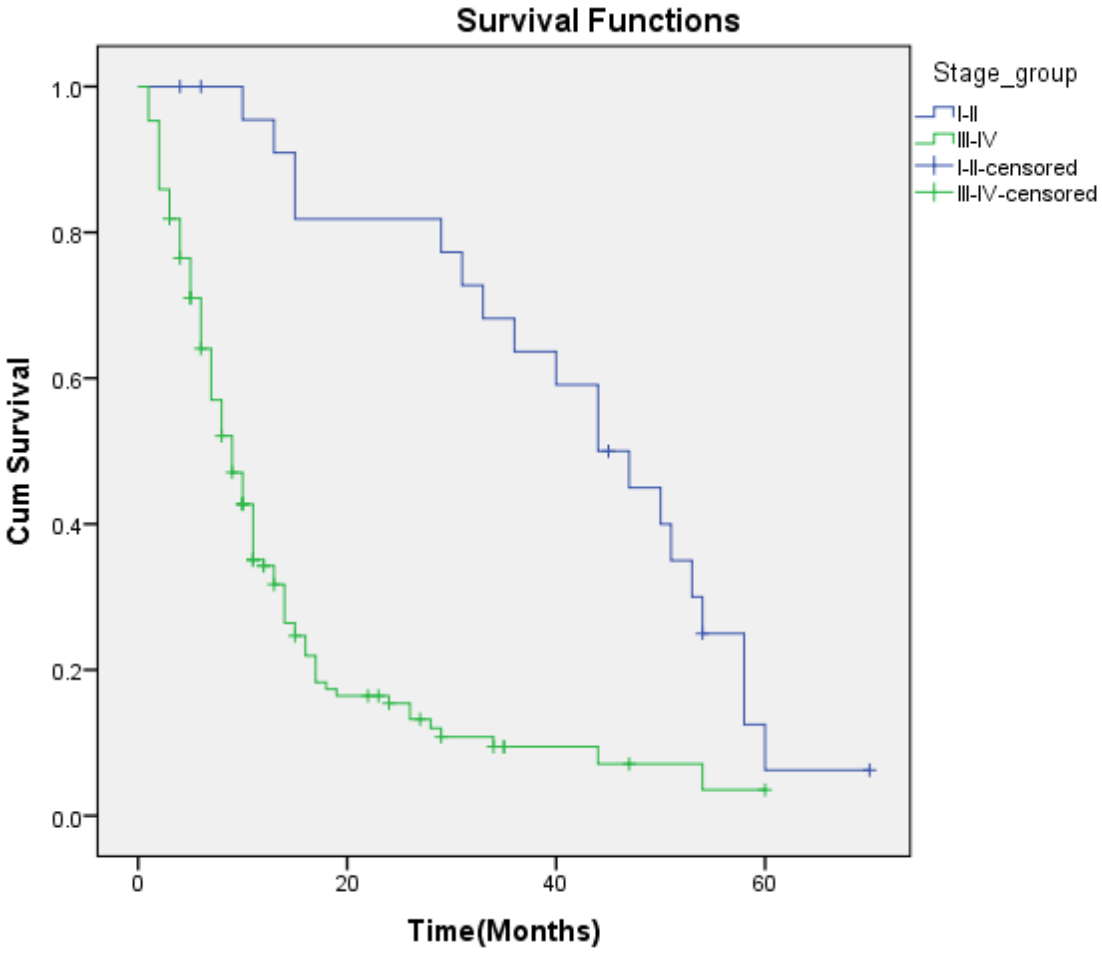
Stage and treatment modality found to have statistical significance with survival.

Figure 2: Overall survival function curve of adult oral cancer patients treated at ORCI from Jan 2013 to Dec 2016.



The figure above shows that the overall survival for 2and 3years were 26.3% and 18.8% respectively.

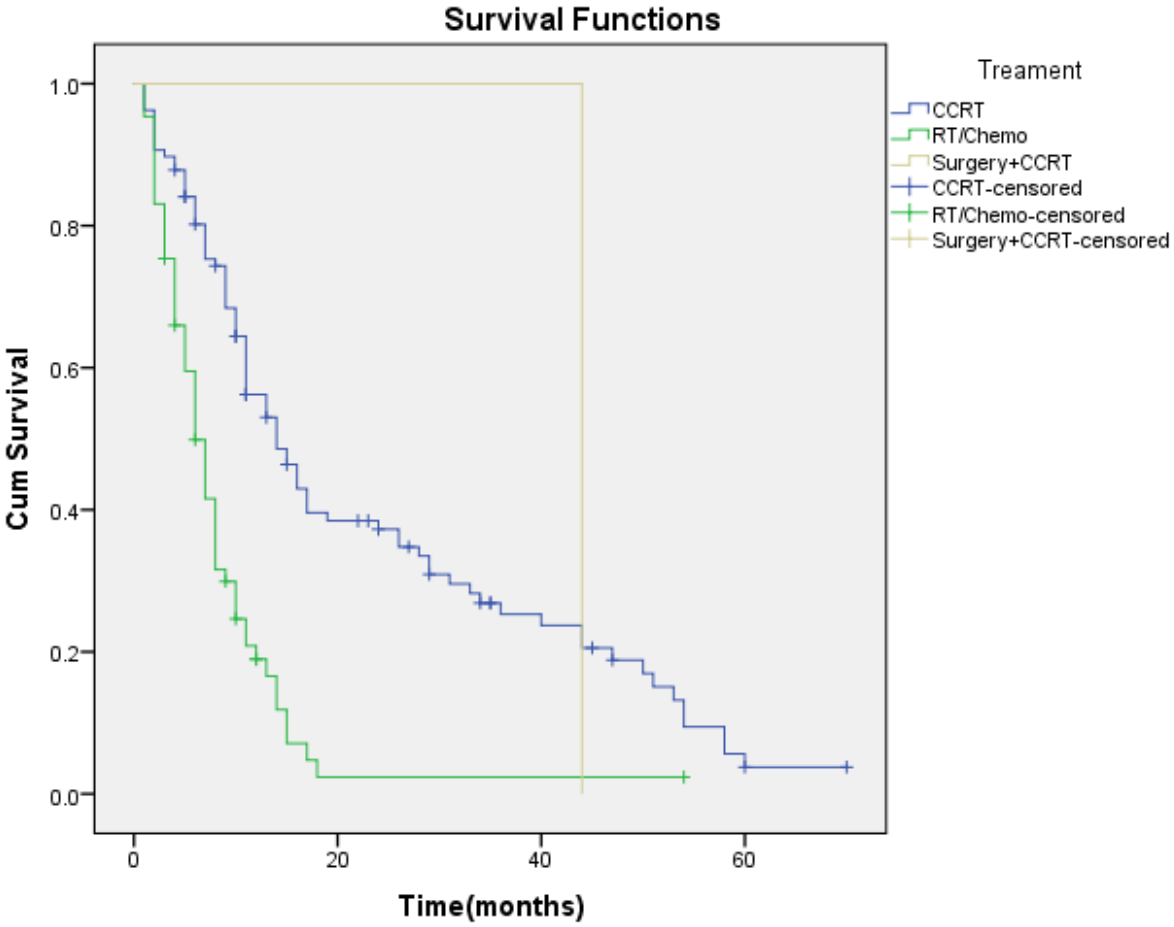
Figure 3: Survival estimates in relation to the disease stage of adult oral cancer patients treated at ORCI from Jan 2013 to Dec 2016.



A log rank test was run to determine if there were differences in the survival distribution for the different stage of disease at the time of diagnosis. The survival distributions between early stages and advanced stages were statistically significantly different, χ^2 (1) = 26.5, p < 0.0001.

Early stages (stage I and II) had better overall survival rates than the late stages (stage III and IV).

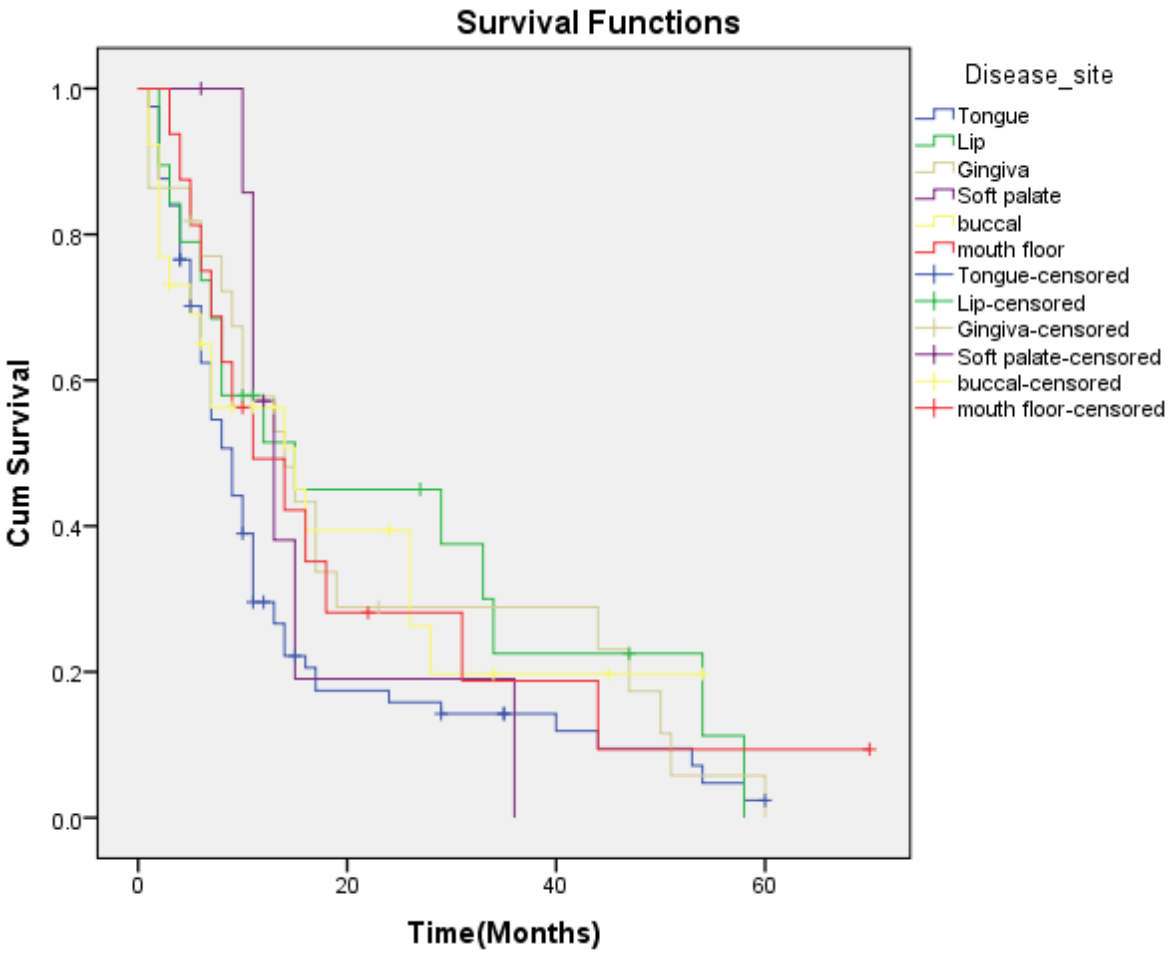
Figure 4: Association between survival and treatment modality of adult oral cancer patients treated at ORCI from Jan 2013 to Dec 2016



A log rank test was run to determine if there were differences in the survival distribution for the different treatment. The survival distributions were statistically significantly different, $\chi 2$ (1) = 33.461, p <0.0001.

Patients treated with surgery + CCRT and those who treated with concurrent CCRT had better overall survival than those who were treated palliatively with chemotherapy alone or radiotherapy alone.

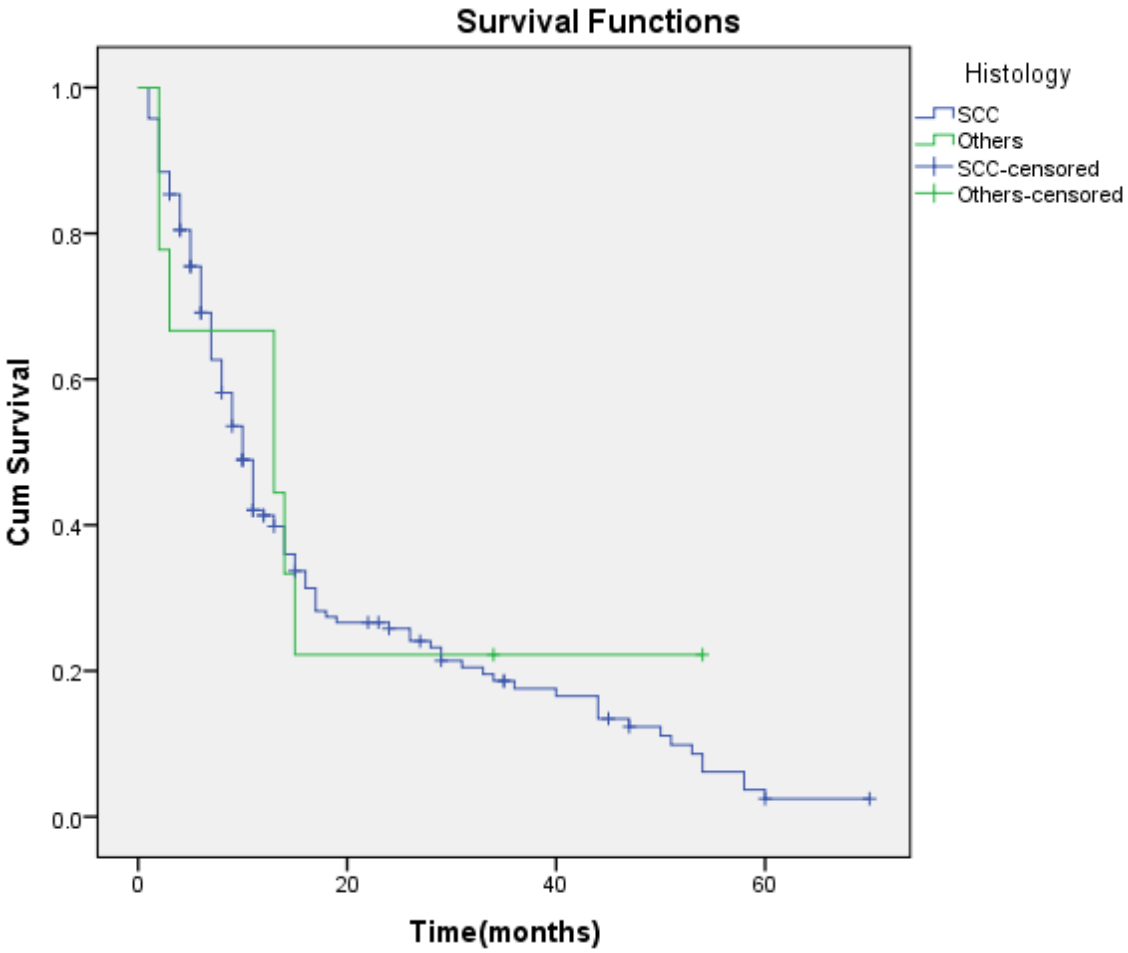
Figure 5: Association between survival and site of disease foradult oral cancer patients treated at ORCI from Jan 2013 to Dec 2016.



A log rank test was run to determine if there were differences in the survival distribution for the different disease site at the time of diagnosis. The survival distributions were not statistically significantly different, $\chi 2$ (5) = 5.932 p=0.313.

The study shows no relation between disease site and survival.

Figure 6: Survival curve for histological types of oral cancer patientstreated at ORCI from Jan 2013 to Dec 2016.



KEY:

Others include mucoepidermoid, lymphoma and fibrosarcoma.

A log rank test was run to determine if there were differences in the survival distribution for the different disease histological types time of diagnosis. The survival distributions were not statistically significantly different, $\chi 2$ (2) = 0.251 p=0.616.

The study shows no relation between disease histology and survival.

Table 7: Multivariate analysis of factors associated with oral cancer patients.

Variable	P value	HR	95.0% CI for HR	
			Lower	Upper
Stage	0.0001	3.792	2.197	6.544
Treatment	0.0001	2.831	1.955	4.099

HR=hazard ratio

Stage and initial treatment offered were independent predictive factors for death for OC patients. Advanced staged patients were 3.792 times more likely to die than early stage at any point, Hazard ration=3.792, 95% CI 2.197-6.544, p value <0.001whereas the those who were prescribed either only RT or Chemo were 2.831 times likely to die than those prescribed concurrent chemorad HR=2.831, 95% CI 1.955 - 4.099 and p value <0.001.

CHAPTER FOUR

4.0 DISCUSSION

4.1 Brief Overview

To the author's knowledge, this is the first study to document the epidemiology and treatment outcome of adult oral cancer at Ocean Road Cancer Institute in Tanzania. The results from this study demonstrate similarities to other countries but patients seek medical attention with advanced stage disease in this setting than in the developed countries.

4.2 Socio-Demographic and Clinical-Pathological Characteristics

In our study, we found male preponderance of 61.8% and 38.2% for female with a male to female ratio of 1.6:1. Participants aged more than 61 years (7^{th} decade) were the majority by 88% followed by those aged 41-60 who were 41.8% and below 40 years were minority accounting for 6.9%. The study corresponds with other studies within the world showing male been more affected than female [19, 20, 21, and 22]. In East Africa a study done in Kenya by Muange et al, showed similar results whereby male were more affected than female (61% and 39% respectively) with a M:F= 1.6:1 and majority were in their 6^{th} and 7^{th} decade [21]. In contrary the study does not collates with Kittipong et al, where the male-to-female ratio was 2.22:1 and majority were in their $5^{th} – 8^{th}$ decade (20). Also our results differ with the study done in Zimbabwe by Chidzonga et al, where male were more prominent by 2.2:1 [22]. Men are more prevalent because they are more exposed to risk factors than females.

In our present study tobacco combined with alcohol use was mostly commonly identified risk factor among the cases followed by tobacco only and alcohol only respectively. Alcohol and tobacco are the major risk factors for development of oral cancer and combining together has a synergistic effect**.** Alcohol is first oxidized to acetaldehyde which is carcinogen and also and generates free radicals which have the deleterious effects on DNA leading to inability to repair hence mutations which on the long run will develop cancer [25].

Cigarette smoke contains carcinogens including tobacco-specific N-nitrosamines which results in DNA adducts that may induce mutations in oncogenes and tumor suppressor genes which could be considered as tumor initiation.

Smoking was the commonest route of tobacco use followed by smokeless tobacco and in few cases utilized both forms of tobacco use.A systematic global review and meta-analysis Smitha Asthana et al, which show the relationship of smokeless tobacco and OC, whereby in Southeast Asia region the risk was found to be 4.44; 95% CI = 3.51 to 5.61 and the risk for the East Mediterranean region was 1.28; 95% CI =2.93 to 11.58 [27].

The commonest clinical presentation of OC patients in this study was a pain (30.2%) followed by pain with a lump on oral cavity 28.5%; lump 13.4%; pain, lump, neck swelling and bleeding 11.6%; pain, lump and neck swelling 7%; pain and ulceration 3.4%; bleeding 2.3% meanwhile the minority presented with pain with neck swelling and ulceration only in 1.7%. Our findings are the same with study done in Israel by Gorsky et al, where a series of patients with cancer of the tongue has pain as their main symptom by 66.5% and lump on the tongue by 29% [36]. Another study from Sao Paul, Brazil by Scully C et al showed that the initial presentation was pain (19.2%). In advanced cases patients may present with cervical lymphadenopathy due to neck metastases and about 5% may be detected in the absence of any obvious primary tumor [12].

Regarding the anatomical distribution of oral cancer in our study, the 6 most common sites for oral cancer in descending order of frequency were tongue (47.4%), labial/buccal mucosa (15.1%), gingiva (12.7%), lip (11.0%), mouth floor (9.2%) and palate (4.6%) respectively. The reasons why the tongue is the site for oral cancer is because it is covered by thin and non-keratinized mucosa hence provide less protection against the carcinogen. Buccal and gingiva mucosa are constantly in contact with the carcinogens for a long period of time especially smoking and smokeless tobacco. This correlates with most studies of which the tongue was found to be the commonest site affected though the series of the proceeding sites differ in different anatomical regions [18], [19], [20], [21], [22], [23].

Our data findings are similar with a study in Thailand by Kittipong et al, which found that tongue was the commonest site affected followed by labial/ buccal mucosa, gingiva, palate and lastly the alveolar mucosa by 25.4%, 21.7%, 14.0%, 9.9% and 7.9% respectively [20]. The study differ from a study review from population based cancer registry of 5 continents by Camargo et al, which found that the most common affected area was the oral tongue followed by floor of mouth and unspecified parts of mouth by 41%, 21.1% and 20.5% respectively [22]. In contrary study done in Zimbabwe by Chidzonga et al, which reported that gingiva was the most common site for oral cancer followed by the tongue [19]. Also the results of our study differ with Faggons et al, which found the alveolar ridge as commonest affected site, followed by tongue, palate, oral mucosa, floor of mouth, non-specified site, lip and oropharynx being the least [23].

The most common type of histology is squamous cell carcinoma (SCC), this was also observed in this study, and it constituted about 95.4% of all cases followed by salivary gland 2.3%, hematological and others 1.2 % each. Oral cavity is lined by stratified squamous epithelium which protects the cavity thus is the commonest histology. The results from a study correlates with a multicenter study across 5 continents which found that among all the epithelial tumors, the commonest type was the squamous cell by 94.08% of all epithelial tumors and 80.05% of all OC. Lymphoma was the second common OC and was the commonest among hematologic tumors where it accounted for 86.91% and 3.89% of all OC and the mucoepidermoid carcinoma was the third commonest OC by 45.26% of all salivary gland tumors and 3.02% of all OC [18]. However low figures of squamous cell histology (73.1%) has been reported by Chidzonga et al from Zimbabwe [19].

From the study, nearly three quarter of participants (86.2%) had presented with the late stage disease at the time of diagnosis (stage III and IV) while nearly quarter of them (13.8%) were in the early stages of the disease (stage I and II). This late presentation is due to the nature of the disease especially tongue area which are initially painless and become painful at advanced stage. The results concur with a study in Brazil by Anna Carolina et al, which found the advanced stage disease patients were majority by 85.1% and early stage by 14.9% [47].

Another study in Kenya by Muange et al, revealed that nearly half of the cases of patients were found to have had stage IV and III disease (64.7%) at the time of diagnosis while early stages (II and I) accounted for 35.3% [21].

4.3 Treatment, Treatment Outcome and Survival

A significant percentage of participants in this study had late stage disease at presentation (86.2%) and were treated with CCRT and others were palliated upfront with either chemotherapy or radiotherapy alone due to presence of metastasis or inability to tolerate extensive management. The remaining percentage of cases who presented with early stage disease (13.8%) was treated with either surgery in combination of post-operative chemotherapy radiotherapy or concurrent chemo radiotherapy. A study done in Argentina by Brandizzi et al, showed the majority of participants are diagnosed at late stage where that 65% were diagnosed at stage III and IV and the remainder (35%) were diagnosed in stage I and II [46].The data doesn't concur exactly with ours due to a smaller sample size we had.

With regard to treatment modalities used in the present study, those treated with surgery followed by adjuvant CCRT and those treated with CCRT had better survival than those who were treated palliatively with chemotherapy alone or radiotherapy alone. Similarly, the randomized controlled trial done in US by Iyer et al, showed a significant advantage for primary surgery in oral cancer patients than those who underwent CCRT hence primary surgery of treatment for better overall survival 45% versus 35%, p=0.262 [48].

The study showed poor overall survivals of study participants at 2 year and 3 year by 26.3% and 18.8% respectively. Furthermore early stage disease (stage I and II) had better overall survival rates than the late stage disease (stage III and IV). Our survival rates are very low compared to other studies [46], [50]. This is because most of participants came for medical attention on late stage of disease. In Sub- Saharan Africa a study by Asio et al in Uganda showed overall survival at 2 years of 43.6%.The discrepancy between our results and Uganda may be due to our smaller sample size but they found that majority of the cases were in late stage (61%) early stage (20.8%) and not staged 18.2% [49]. The study done in Argentina by Brandizzi et al shows the survival

rate at 2 and 3 years were 60% and 46% respectively [46]. In contrary a study done in Italy by Rossi et al showed a better survival with early stage disease (stage I and II) of 84% at 2 years [50]. Hence early diagnosis plays a major role in the survival of OC patients.

In our current study we found there was no any association between disease site and survival. Similarly the study done by Anna Carolina et al, in Brazil showed the same results [47].

CHAPTER FIVE

5.0 STUDY LIMITATIONS, CONCLUSIONS AND RECOMMENDATIONS

We acknowledge limitations in this study. The nature of the study being retrospective resulted in a substantial amount of missing information which led to most of the patients to be excluded from the study otherwise we could have more than the estimated sample.

The study does not represent the real situation of oral cancer burden in Tanzania because is the single institution study. A multicenter study would simulate the burden of disease within the country.

5.1 Conclusions

This study showed that adult oral cancer patients in Tanzania present with similar epidemiological and clinical features as in other countries.

Males are more affected than females and tobacco use and alcohol consumption being the commonest risk factors.

The commonest site for adult oral cancer from the study is the tongue which is initially painless and later painful which brought the patients to seek medical attention with late stage disease.

Disease stage is strongly related to treatment outcome with later stages of the disease having an overall poor outcome.

2 and 3 years overall survival is poor because of advanced stage of the disease at the time of diagnosis.

Stage and treatment modalities are the most important outcome determinants of survival in adult oral cancer patients.

This study provides the basis for future prospective studies and will potentially contributes to improve some of our daily practices.

5.2 Recommendations

1. Create community awareness on oral cancer risk factors via posters, radio, television and social media.
2. Primary health care workers to have ongoing educational sessions so as to diagnose disease early.
3. Proper documentation by clinicians of all necessary information especially during the follow up visits.
4. Patients` treatment should be based on standard management following established guidelines i.e. The Tanzania National cancer treatment guidelines).
5. Records department reinforced for proper records keeping of patients' data.
6. Surgeons encouraged in performing surgery as being the mainstay of treatment.
7. There is a need of implementing a national cancer registry, which can help on contact tracing.

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APPENDICES

Appendix i

DATA EXTRACTION FORM FOR ADULT ORALCANCER PATIENTS TREATED AT ORCI

Identification:

1. File Registration number ……

2. Study serial number…….

3. Age (Years)……

   a. < 40yrs……..…b. 41 – 60 yrs…….c. > 60 yrs……

4. Residence

   a. Northern zone b. Central zone c. Coastal zone

   d. Lake zone e. Southern zone f. Western zone g. Zanzibar

5. Gender

   a. Male……..b. Female……

6. Marital status

   a. Married…….b. Single……c. Divorced /Separated……. d.Widowed……

7. HIV status

   a. Negative……. b. Positive……c. Unknown

8. Education level

   a. Primary level ……b. Secondary level …….

c. Higher education level …… d. None formal…….

9. Occupation

a. Peasant……b. Petty trader/ Business…….c. Employed…….d. Others (specify)…..

Disease Profile:

10. Presenting symptom

a. Pain…….b. Lump on oral cavity…….c. Neck swelling……..

d.Bleeding……

e. Pain + lump…….. f. Pain + lump + neck swelling……

g. Pain + lump + neck swelling +bleeding …… h. Pain + lump + bleeding……

i. Pain + neck swelling + bleeding…… j. Pain + neck swelling……

k. Pain + bleeding…… l. Lump + neck swelling……..

m. Pain + ulceration…… n. Ulceration…….

11. Disease Site

a. Tongue…….b. Lip……c. Gingiva……..

d. Palate……. e. Other (specify)…… f. Buccal/ mouth floor ……..

12. Histology

a. SCC……b. Salivary gland tumor……

c. Hematological…….d. Others (specify)…….

13. Grade

a.1 …… b. 2……

c. 3..…… d. Not mentioned/ no grade……. (Specify)

14. Risk identified

a. Tobacco use ……b. Alcohol ……. c. Alcohol + tobacco use…….

d. Ultraviolet rays……. e. No risk identified……

15. Mode of tobacco use

a. Smoking……..b. Chewing……c. Both……

16. Stage of the disease

a. 1……b. 2……c. 3……d. 4……....

17. Metastases:

a. YES …….. b. NO ……

18. Metastatic site:

a. Lungs……b. Liver……..c. Others (specify)…….

Treatment modality:

19. Surgery:

a. YES …… b. NO …….

20. Type of surgery ……. (Specify)

21. Surgical margins:

a. Clear……. b. Positive……. c. Microscopic margins……

d. Gross disease…….....e. Not mentioned……

22. Treatment modality

a. Surgery + CCRT……..

b. CCRT……..

c. Chemo alone……..

d. RT alone…….

23. Survival:

a. Alive: ……Date of last follow up: ……

b. Dead: ……Date of death: ……

c. Unknown…….

Date of diagnosis……..

Duration of survival……..

Appendix ii: Kiswahili Version

FOMU YA KUKOKOTOA TAARIFA KUHUSU SARATANI YA KINYWA KWA WATU WAZIMA WALIOTIBIWA KATIKA HOSPITALI YA RUFAA YA TAIFA YA KANSA YA OCEAN ROAD.

SIFA BINAFSI ZA KIJAMII ZA WAGONJWA

1. Namba ya jalada ya usaili ……

2. Miaka (tarehe ya kuzaliwa) ……

3. Makazi……

4. Jinsia

a.Mume……b.Mke……

5. Hali ya ndoa

a. Nimeoa/nimeolewa……..b.Sijaoa/sijaolewa……c.Mtalaka/Tumetengana……..

d. Mjane……

6. Hali ya maambukizi ya VVU.

a. Hasi …….b.Chanya……..…… c. Haijulikani……..

7. Kiwango cha elimu

A.Elimu ya msingi b.Elimu ya sekondari……c.Elimu ya juu……. d.Sikwenda shuleni……..

8. Shughuli

a. Mkulima mdogo……b.Mfanya biashara ndogondogo…….c.Mwajiriwa…….

d. Tegemezi……

Sifa za ugonjwa

9. Sababu ya kumuona daktari

a. Maumivu…… b. Uvimbe kinywani ……..c. Uvimbe shingoni……..

d. Kutoka damu……. e. a+b……. f.a+b+c…….g. a+b+c+d…….

h. a+b+d…… i. a+c+d…… j. a+d…….. k .a+c……..

l. b+c…… m. a+ kidonda kilichochanika ……. n. Kidonda kilichochanika…….

10. Sehemu ya kinywa ugonjwa ulipo……

11. Aina ya kiini cha ugonjwa……

12. Daraja la kiini

a. Daraja la 1…….b. Daraja la 2……c. Daraja la 3…….d. Nyenginezo(taja)…..

13. Kiashiria hatari cha ugonjwa kilichoonekana

a. Tumbaku…….b. Pombe...……..c.Nyenginezo (orodhesha)……d.haijulikani……

14. Mfumo wa utumiaji wa Tumbaku

a. Kuvuta……..b. kuweka mdomoni…….c. a+b……..d. Haikuorodheshwa…….

15. Hatua ya ugonjwa

a. Hatua ya 1…… b.hatua ya 2……..c.hatua ya 3……d.hatua ya 4….

16. Ugonjwa umesambaa sehemu nyengine ya mwili:

a.Ndio…….. b. Hapana ……

17. Sehemu ya mwili ugonjwa uliposambaa:

a. Mapafu…….. b. ini……..c.nyenginezo…….(taja)

Tiba aliyopata mgonjwa:

18. Upasuaji

a. Ndio…… b. Hapana……..

19. Aina ya Upasuaji

……

20. Mipaka ya upasuaji:

a-Hakuna ugonjwa…….b. –uwepo wa ugonjwa kidogo…….c. –ugonjwa mkubwa……...

d. Haikuorodheshwa……..

21. Aina ya matibabu aliyopata mgonjwa

a. Upasuaji + mionzi + dawa kemia……. b.. Mionzi + dawa kemia…….

c. Dawa kemia pekee ……. d. mionzi pekee……..

22. Hali ya kuishi:

Tarehe ugonjwa ulipogunduliwa: …….

1. Yupo hai: …… Tarehe ya mwisho kuhudhuria kliniki: …….
2. Amekufa: …… Tarehe ya kifo: …….