PATTERNS OF PRIMARY ORAL AND MAXILLOFACIAL MALIGNANCY AT JIMMA MEDICAL CENTER: A CROSS-SECTIONAL STUDY FROM 2018 TO 2023

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ABSTRACT

Background: Cancers are the leading cause of death in economically developed countries and the second leading cause of death in developing countries including Ethiopia. Despite an increase in medical knowledge, the treatment need of head and neck cancers (HNCs) have not been improved in Ethiopia. In addition, there is no adequate published evidence on epidemiology of oral and maxillofacial malignancy in the country.

Objective: The present study aimed to determine the prevalence and patterns of primary orofacial cancer among patients seen at Jimma university medical center.

Methods: All patient records (201) of primary head and neck malignancy, from September 11, 2018 to September 10, 2023, were retrieved from the patient registry. Reports with doubtful diagnosis, skin cancers, and eye tumors were excluded. Finally, 194 eligible patients' data were collected and analyzed using the Statistical package for social science (SPSS) software version 23.0. Frequencies, percentages, cross tabulation of different variables were determined. A p-value ≤ 0.05 was used as the cut-off level for statistical significance.

Result and Discussion: The prevalence of primary oral and maxillofacial malignancy was 2.6% among total patients seen at maxillofacial unit of Jimma medical center. The mean age of all patients was 41.81 years (SD± 15.911, range: 10 to 73 years). The overall male to female ratio was 2.46:1. Squamous cell carcinoma (SCC) was the most common specific histological type followed by mucoepidermoid carcinoma (MEC) making up 59.5% and 16% of cases respectively. Oral tongue was the most frequently involved oral subsite (27.4%). Predisposing factors was identified in 92 (47.4%) patients. Majority of the patients (74.8%) were diagnosed at late stage (III & IV). Surgery was the main mode of treatment used in 148 (76.3%) cases.

Conclusion and Recommendation: Majority of primary malignant lesions of oral and maxillofacial region (OMFR) occurred in males and older adult age groups. Creating awareness and providing health education about orofacial cancers are helpful in prevention and early detection at curable stage of the disease.

Key Words: *Oral and Maxillofacial malignancy, prevalence, patterns, Risk factors, oral cavity*

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ACRONYMS AND ABBREVIATIONS

AIDS: Acquired Immuno-deficiency Syndrome

FMOH: Federal Minister of Health

HIV: Human Immuno-deficiency Virus

HNCs: Head and Neck Cancers

HPV: Human Papilloma Virus

ICD: International Classification of Diseases

JMC: Jimma Medical Center

JU: Jimma University

LRCs: Low-resource Countries

MEC: Mucoepidermoid Carcinoma

OC: Oral Cancer

OCC: Oral Cavity Cancer

OMFR: Oral and Maxillofacial Region

OMFS: Oral and Maxillofacial Surgery

SCC: Squamous Cell Carcinoma

WHO: World Health Organization

CHAPTER ONE

1. INTRODUCTION

1.1. Background

Oral and maxillofacial cancer is a malignant neoplasia arising from structure confined in the oral and maxillofacial regions (OMFR). Often it involves mucosa of oral cavity and lip, salivary gland, facial soft tissues, maxilla, mandible or other facial skeletons, and facial skin. They vary in their tissue of origin, anatomic sites and causative factors [1,2].

The molecular events leading to development of oral cancer (OC) is multistep process which typically follows an orderly histologic progression, although its timeline may be variable. These changes collectively initiate phenotypic transformation from normal epithelium to dysplastic and finally to invasive carcinoma [3].

Smoking and alcohol are two independent risk factors for OC and are present in 90% of cases. Although they show synergistic effect, their distribution vary among age, sex, and ethnicity [4]. Other less established risk factors includes ultra-violet radiation (UV), human papilloma virus (HPV 16 and 18), genetics, environmental agents, chronic irritation or infection, nutritional deficiency, premalignant lesions and condition, poor oral hygiene, and immune-suppression [5].

According to 4th WHO classification, malignant oral and maxillofacial lesions are classified into tumours of the oral cavity, oropharynx, neck and lymph nodes, salivary glands and odontogenic and maxillofacial bone tumours. Odontogenic and maxillofacial bone tumours are sub-classified into odontogenic sarcomas, odontogenic carcino-sarcoma, odontogenic carcinomas (ameloblastic carcinoma, primary intraosseous carcinoma NOS, sclerosing odontogenic carcinoma, clear cell odontogenic carcinoma and ghost cell odontogenic carcinoma) and malignant maxillofacial bone and cartilage tumours (chondrosarcoma, mesenchymal chondrosarcoma and osteosarcoma) [6].

There is scarcity of published data on primary oral and maxillofacial malignancy in Ethiopia, despite one single-institution based research indicated a prevalence of 9.72% of head and neck malignancy [7]. This study covers the prevalence, risk factors, distribution by site, and stage at presentation of these malignancies.

1.2. Statement of the Problem

Worldwide, 405,000 new cases of oral cancer are anticipated each year, the countries with the highest rates being Sri Lanka, India, Pakistan, Bangladesh, Hungary, and France. In the European Union there are an estimated 66,650 new cases each year. The American Cancer Society estimates that there will be 45,780 new cancers of the oral cavity and pharynx in the United States in 2015, causing 8,650 deaths [1]. Wide variations are likely due to differences in risk factor exposure prevalence rates including tobacco, alcohol consumption, betel quid chewing, and HPV [8].

In sub-Saharan and Southern Africa, HNC was the fourth most common cancer, while it ranks third in Western Africa. Sudan has one of the highest burdens of HNCs in Africa, as HNCs are the second most common malignancy, while it ranks third, fourth, and fifth in Nigeria, Zambia, and South Africa, respectively [9,10].

The incidence of oral cancer increases with age and majority of cases occur among people in their fifth or older decade. However, reports have also shown an increased incidence of oral cancer cases among young people under the age of 40 years and HPV infection has been strongly implicated in these cases [11]. Therefore preventing premature deaths, which primarily affect working persons who support a family, would have social and economic benefits for low-resource countries (LRCs). The situation in LRCs is also further exacerbated by fewer, less accessible, less equipped and less affordable health and cancer care, coupled with a lack of education about cancer at all levels of society than in the rest of the world. Furthermore, patients and families in LRCs must pay out-of-pocket expenses, for health and cancer care, and treatment costs frequently result in catastrophic poverty, when spending is greater than 30% of personal annual income [12]. This is difficult to imagine in impoverished country like Ethiopia where around 80% of population live in rural areas, having only two functional radiation treatment centers and less than ideal specialists.

Regardless of advances in diagnosis and treatment, mortality from oral cancer has not changed significantly in the past 50 years. Approximately 50% of patients diagnosed with oral cancer will ultimately die of their disease and overall survival proportions vary by geographic region, topography and stage, with prognosis often poorer in transitioning countries [13]. Early detection

and appropriate treatment of cancers remain the most effective weapons against cancers of the oral cavity [3,14].

Late presentation (representing around 5 out of every 10 patients [12]) is an important issue in oral cancer, as advanced disease requires more radical treatment and is associated with poorer prognosis, additional treatment burden, patient and career distress and with worse health related quality of life outcomes. Furthermore, detecting oral cancer at an early stage (when lesions are small and localized) is believed to be the most effective means to reduce death, morbidity and disfigurement from this disease, along with reducing hospital cost, duration of treatment and professional fees [15,16]. Majority of the delay is in the time taken for the patient to present rather than professional delay and is frequently a result of the held myths and stigma about cancer and reliance on traditional medicine practices mostly given by untrained health workers, which often result in misdiagnosis and ineffective treatment [12,15]. Another factors contributing to delayed presentation and diagnosis are lack of adequate knowledge and awareness concerning oral cancer; hence, the need for public education about the risk factors and symptomatology of the OC cannot be over-emphasized [11,15].

A little is known about orofacial malignancy in Ethiopia. However like other sub-Saharan countries, the incidence of cancer is rising. The data from Black Lion radiotherapy center, where two third of patients seen comes from different regions of the country, shows that the commonest cancer in males are Head and Neck tumors, sarcomas and Gastro-intestinal malignancy [17]. Another study in same institution indicated the prevalence of HNCs to be 9.72% (n= 834, N= 8580) [7]. Awedew et al. in 2019 reported, in national burden and trend of cancer in Ethiopia, an increase in the incidence of lip and oral cavity cancer by 47% while death counts increased by 39% over ten years [18].

Given the complex dynamics of the underlying risk factors, description of patterns and trends in oral cancer are informative in providing insight into the shifting epidemiologic patterns and the potential prevention of these tumours or may provide tools for early diagnosis. We thus present a clue on the distribution and factors of primary orofacial cancer in study area.

1.3. Significance of the Study

According to the study in year 2019 the prevalence of lip and oral cavity cancer alone was 2.2% (n = 1170) and it accounts for around 2% (n = 780) of cancer death in Ethiopia. The national cancer mortality or incidence was estimated based on single-city population-based registry data (Addis Ababa City) which only covers 3–5 percent of the total population [18]. This estimation cannot exactly represent the regional variation in large and diverse country like Ethiopia, with more than 90 million populations and more than 70 ethnicities, with greatest diversity found in the south-west. The availability of data from JMC as the second cancer treatment center in the country is of paramount importance to depict regional variation.

Therefore, by conducting this study, the investigator aims to fill this data gap in Ethiopia, particularly in the study area. The study also contribute to existing knowledge about orofacial cancer and may use as a base for further study.

CHAPTER TWO

2. LITERATURE REVIEW

2.1. Socio-demographic Distribution of Primary Malignant Lesions

Study in Europe suggest that, incidence rates have shown a growing trend in recent decades, at 7 per 100,000 between 1975 and 1989 increasing to 10 per 100,000 in 2005, an increase of 41% since 1989. Female oral cancer rates have remained much lower than that of males. When oral cancer rates are analyzed by age group, the rates have halved for men older than age 80, remained stable for men age 60 to 70 years, but increased markedly in men between age 40 and 60 years. For men between age 40 and 49 years, incidence has more than doubled from 3.6 to 9.2 per 100,000 and from 11.5 to 25.3 for men age 50 to 59 years. As with incidence trends, the mortality figures reflect the age-specific incidence trends with halving of the figures for men age 70 to 80 years, but a steady increase in mortality for men in their 40s, 50s, and 60s [19].

According to the study in Pakistan from 1995-2002 the mean age of the patients was 53.0 years (95% CI 48.0; 58.0). About 30% of oral cancer cases, 28.6% of the nasopharyngeal, 6.3% of the oropharyngeal, and 2.6% of laryngeal cancers occurred in patients 40 years and younger. Twenty three percent of the oral cancer cases, 1% of nasopharyngeal, 43.5% of oropharyngeal, 35.9% of the hypo-pharyngeal and 22.3% of the laryngeal cases occurred in patients 65 years and older [20].

Joshi P et al. reported the mean age of HNCs patients to be fifth and early sixth decades compared with the seventh and eighth decades in the North American population [21].Study on prevalence of HNCs in the North East-India depicted that, the prevalence of head and neck malignancy was 54.48%. The commonest age group was 6th decade comprising of 31.13% and 22.8% cases were from the age group 40-49 years and 18% in 60 -69 years. In the gender distribution, male cases were far more common than female with 2.9:1 ratio [22].
According to studies in Arab countries, prevalence of orofacial malignancy ranges from 1.8 to 2.3 per 100,000 persons. OC patients were mostly in their fifth to sixth decade of life, and the incidence in younger age was reported in some Arab countries. Yemenis have an alarming high prevalence of OC among people younger than 45 years [23].

A study in Southeast of Iran on 1604 cases reported, the mean age of 53.03±17.18 years (range: 2 to 95 years). 18.4% of patients were < 41 years, 73.3% male, with overall male to female ratio of 2.74:1. Carcinoma cases were older than those with sarcoma and lymphoma ($p<0.01$) [24].

According to study in western Iran, the prevalence of primary HNCs was 4.6 %, i.e., 181 cases from 3927 patients. The mean age of all patients was 63 years (range: 7–92 years). For all malignancy cases, 101 were male (56%) and 80 were female (44%); but for SCC cases, 60 (59%) were male and 41 (41%) were female. Mean age of males and females not differ significantly and was 63.7 (±14.3) and 62.3 (±16.2) years, respectively. The peak age was > 60(60.2%) [25].

A retrospective review from 1992–2003 in Lagos indicated that, malignant tumours constituted 18% of all the biopsies of orofacial lesions. The mean age of patients was 42.2 ± 21.5 years (range: 2.5 – 85 years), with overall male (n=171) to female (n=85) ratio of 2:1. Fifty-one (20%) of these patients were ≤20 years. Carcinoma was older than sarcoma and lymphoma ($P < 0.01$), and malignant lymphoma was significantly younger than sarcomas ($P < 0.01$). Almost 25% of carcinomas were below the age of 40 years. Concerning the epithelial lesions a ratio of male to female was 2:1. The peak malignant age of diagnosis was 5^{th}-8^{th}decade. Almost 25% of patients with carcinomas were below the age of 40 years [26].

A survey of histopathological charts in Ghana over two decade's shows male to female ratio of 1.84:1. This ratio was 2.63:1 for SCC. The average age was 45.55 for male, 44.21 for female and 45.08 years for both sexes [27].

A 10 years review of 1723 patients with histologically diagnosed primary malignant tumors of orofacial region at two hospitals in Harare Zimbabwe shows that, oral malignant neoplasms constituted 24.8% (n = 428). A male to female ratio was 1.9:1, with lesions being most common in the 41-60 years age group. SCC was most common in the 61-70 year age group [28].

According to study in East African countries done at two Tanzania and Uganda hospitals, males were more affected by malignant tumors of orofacial region than females with ratio 1.3:1. The peak age for oral cancer was 6th decades [29].

Despite inadequate published data regarding the primary malignant lesions of OMFR in Ethiopia, different studies show the prevalence of head and neck cancer in general. One unpublished retrospective study in Black Lion Hospital shows that, HNCs accounted for 9.72% of all malignancies. The male to female ratio of was 2:1 and mean age was 44.56 years with peak

occurrence between 41 and 60 years comprising 40.5%. Most of the carcinoma was old adults (41-60 years). The commonest age for lymphoma and sarcoma was youngsters (≤21 years). Males are predominantly affected than female [30].

Wondemagegnhu et al. in his study on patterns of cancer at Black Lion Hospital, shows that 72.8% are females and the rest 27.2 % are males. Most of the patients are found in productive age group between 40 to 50 years. 32% of the patient had stage III and IV, but only 10% came at early stage I and II. Surgery was performed in 32% of the cases. HNC is the leading malignancy in male 22% followed by sarcoma 15% and Gastrointestinal 12% [17].

2.2. Factors Associated with Oral Cancers

Saman Warnakulasuriya et al, on the study of Global epidemiology of oral and oropharyngeal cancer, revealed risk of OC due to both tobacco and alcohol is estimated to be > 80%. Heavy drinkers and smokers have 38 times the risk than non-users [31].

According to study in UK, the upward trend of oral cancer in younger birth cohorts of men has been attributed to increasing levels of alcohol consumption. The role of smokeless tobacco has remained unresolved and there is no evidence that HIV disease has contributed to the rising incidence in young males [19].

Fridriech et al in homburg German, reported as Smokers accounted about 66.7% a total of OC patients and 83.4% of them consumed 20 to 40 cigarettes per day; about 30% of cases were diagnosed with stage iv and 15% in stage iii [32].

Study done in India shows that, high prevalence in this region is indicative of several factors that predispose to orofacial cancer. The use of tobacco, lime, betel and smoking is a very common oral habit prevalent in this region which may be one of the prominent causes [22].

According to Mallath et al. an estimated 600,000–700,000 death in India was caused by cancer in 2012. Such figures are partly indicative of low rates of early-stage detection and poor treatment outcomes. Many cancer cases are associated with tobacco use, infections, and other avoidable causes. Measures such as fully committed effort to reduce, and, in the long term, eliminate, use of tobacco products would substantially decrease the incidence, and mortality [33].

According to study done in Nigeria, identified risks factors among HNC patients included: kola nuts, tobacco, farming, viral infections, alcohol and smoking. Kaposi sarcoma and salivary gland malignancy were the most common tumor in patients with HIV sero-positivity [34].

Osman, et al, in Sudan reported (73.6% n=192/ 261) of SCC cases of orofacial cancer and overlapping lesions of the mouth were more prevalent among subjects with Toombak dipping history, smoking and alcohol drinking account about 49.8% and SCC was found to be more common in subjects with history of Toombak dipping (88%) and 94.5% of patients were diagnosed with stage 4 and 41.9% of patient were treated surgically [35].

Girma in2016 reported that 31.88% of HNC had exposure to known predisposing factors. Males showed higher predisposition (90.87%) than females. Among exposed patients, 137 (56.8%) had more than one factors, 140 (18.5%) were cigarette smokers, 104 (13.8%) alcoholic, 165 (21.8%) Khat chewers, and 16 (2.1%) have HIV/AIDS. From a total 241 patients with exposure history 114 patients (47.3%) were affected with oral cavity and oropharyngeal malignancy [30]. The study on epidemiology of primary HNC in Black Lion Specialized Hospital Oncology Center, from 2010–2015, reported the same findings [7].

Another study at Black Lion Hospital from 2020 to 2022 showed that 32% of patient had known risk factor. From risk factors immunosuppression account for 13.7% (n = 24) followed by smoking 10.3% (n = 18), chat chewing 6.3% (n =11) and alcohol 1.7% (n =3) [36]. Tara Rick et al., also found 5% (n = 85) HIV case among cancer patients at this institution in 2019 [37].

Awedew in 2019, reported that behavioral risks, metabolic, occupational exposure, and air pollutions were attributed to approximately 20% (17–26%) of cancer in Ethiopia; however, changes in overall risk factors were less than 10% between 2010 and 2019 [18].

2.3. Prevalence of Oral Cancers

According to USA National Cancer Institute report, cancers of orofacial region account for 3-4%of all cancers with incidence of 10 per 100,000. Recent report shows an increasing oral cancer rate in some part of USA, especially in older white males. There was also a trend for African Americans to present with late disease stage compared with white Americans. Furthermore, African American male have a poorer 5-year relative survival rate compared with

other races. The racial differences were attributed to health care access, public education, and socioeconomic, cultural, or biologic issues [38].

According to the study in Pakistan from 1995-2002 HNCs accounted for approximately one-fifth (21%) of the cancers in males and about one-tenth (11%) in females in the study period [20]

The study on epidemiology of primary HNC in Black Lion Hospital Oncology Center, from 2010–2015, indicated that the prevalence of HNCs was 9.72% (n= 834, N= 8580) in the study area [7]. According to the study in year 2019 the prevalence of lip and oral cavity cancer alone was 2.2% (n = 1170) and it accounts for around 2% (n = 780) of cancer death in Ethiopia [37].

2.4. Sites of Oral Cancers

A study on prevalence of malignant orofacial lesions in Japan show that, the tongue (40.2%) was the most common site, followed by gingiva (32.7%), buccal mucosa (10.1%) and floor (9.0%). There were 6 cases of multiple intraoral cancers. SCC (88.7%) was the most common OC, followed by AdCC (2.1%) and MEC (1.7%). T2 were the most common (32.1%), followed by T1 (21.4%) andT4 (8.0%). Nonepithelial tumors, among which malignant melanoma was the most common accounted for 1.8% of the tumors [39].

Saman Warnakulasuriya et el , reported tongue as the most common site for intraoral cancer among European and the US populations, amounting to 40–50% of oral cancers. Buccal cancer is more common among Asian populations due to betel quid/tobacco chewing habits. In Sri Lanka, 40% of oral cavity cancers are found on buccal mucosa [31]. Azimi et al, reported lower lip as the common site affected by OC (22%), followed by tongue (15%) and parotid gland (13%) [25].

According to the study in Pakistan from the most common affected sites by orofacial cancer were oral cavity, larynx and pharynx. Mucosa cheek was the most common sub-site for oral cancer (55.9%), followed by the tongue (28.4%), palate (6.8%), gum (4.4%), lip (3.1%) and floor of mouth (1.4%). The predominant morphology was SCC in 96.5% of the cases [20].

According to Solange N´uñez-Gonz´ alez, tongue represented 34% of deaths (n = 349), parotid gland tumors 14.8% (n = 152), and neoplasms of other and unspecified major salivary glands 8.7% (n = 89). Ibikunle et al, study shows, in Nigeria, buccal mucosa and gingivae were the most

common sites affected by intraoral epithelial malignancies [40]. Reports of Gbotolorun et al [41] and Daramola et al [42] found the tongue as the most common subsite affected.

A study in Southeast of Iran on a total of 1604 cases reported that larynx was the most commonly affected site (46.76%) followed by oral cavity (15.9%) and neck (13.72%). SCC was the most common histologic diagnoses (77.5%), followed by lymphoma (9.4%). In oral cavity the most affected site was tongue (35%) followed by lip (31%) and gingiva (17%) [24].

A study in Lagos indicated that, SCC (44%) was the most common orofacial tumour. There were 69% epithelial, 18% sarcomas and 13% lymphomas. Osteosarcoma (32%) and Burkitt's lymphoma (56%) was the predominant sarcoma and lymphoma, respectively. SCC was the most common carcinoma (63%), followed by adenocarcinoma (15%) and AdCC (9%). Melanoma of mandibular gingiva was seen in a 42-year-old woman. Common sites of carcinoma were maxillary antrum (33%), mandible gingival/alveolus (22%), palate (15%) and tongue (7%) [26].
A 17 years review on the primary malignant tumors of orofacial region at Benghazi, Libya showed that carcinoma case was 82%, followed by tumors of immune system (11%) and tumors of mesenchymal origin (7%). Malignant non-odontogenic tumors were seen in 194 patients (99%) and malignant odontogenic tumors were seen in 2 patients (1%). Among the epithelial tumors, squamous cell carcinoma (50.6%) was the most common neoplasm, followed by mucoepidermoid carcinoma (15%) and adenoid cystic carcinoma (8.7%) [43].
Study done in Harare Zimbabwe shows that, squamous cell carcinoma (73.1%) was the predominant oral malignancy with 21.1% occurring on the mandibular gingivae, followed by the tongue (20.5%) and floor of the mouth (18.5%). Lip was the least affected (3.3%). The remaining oral malignancies included Burkitt's lymphoma 4.7%; Kaposi's sarcoma 3.7%; osteosarcoma 2.6% and malignant melanoma (1.9%). Well-differentiated was the most common oral malignant neoplasm [28].

A retrospective study done in Ethiopia on primary HNC at Black Lion Hospital shows that, oral cavity was the most commonly involved site. SCC (72%) was the most common lesion followed by adenocarcinoma (5.6%) [44].

The study on epidemiology of primary head and neck cancer in Black Lion Specialized Hospital Oncology Center, from 2010–2015 (n= 834, N= 8580), oral cavity and oropharynx (30%), and

nasopharyngeal (27%) were the commonly affected sites by the primary HNCs. SCC was most commonly presented in the oral cavity and oropharynx, nasopharynx and larynx, while lymphoma was highly prevalent in the nasopharynx. Ninety-nine patients revealed a malignancy of the salivary glands, 544 cases were SCC and 35 lymphomas [7].

According to the study at Black Lion Hospital by Chala Ararsa et al. from 2020 to 2022 on 175 patient oral cavity were the most commonly affected anatomic site by orofacial cancer with 52.6% (n= 92) followed by parotid 14.3% and maxillary sinus 13.7%. Tongue was the commonly affected oral cavity sub-site with 20% (n=35) followed by lip and palate, 9.1 % (n=16) and 8.6% (n=15) respectively [36].

2.5. Stage at Presentation of Oral Cancers

According to Joshi P et al., 75% to 80% of patients were cancers presented with late-stage incurable disease and hence increased mortality. Reasons for delayed diagnosis are lack of access to health care, poor socioeconomic status, cost of care and high rate of illiteracy [21].
The study in Pakistan from 1995-2002 indicated that two-thirds of the OC cases were discovered at advanced stages. Distant metastasis was observed in 65% of cases at the time of diagnosis [20].
According to one retrospective study done in Ethiopia on primary malignant tumor of head and neck, nearly 2/3rd of patients were diagnosed late (stage III and IV) [44]. Another similar hospital based study from 2010–2015 depicted that most of HNC patients (61.0%) were diagnosed at stage III and IV, while only 29.5% diagnosed at stage I and II [7].
The study on patterns of primary oral and maxillofacial malignancies in Ethiopia from 2020 to 2022 showed that 65.7% of the patients were presented with stage IV and 11.7% with stage III. Almost half (49.1%) of study subjects were presented with locally advanced tumor size of T4a. Out of studied patients 8.6% of the patient had distance metastasis mainly to lung [36].

2.6. Conceptual Framework

Understanding the patterns of primary oral and maxillofacial malignancies should take into account various factors. By integrating these factors, a comprehensive conceptual framework can be developed as follow:

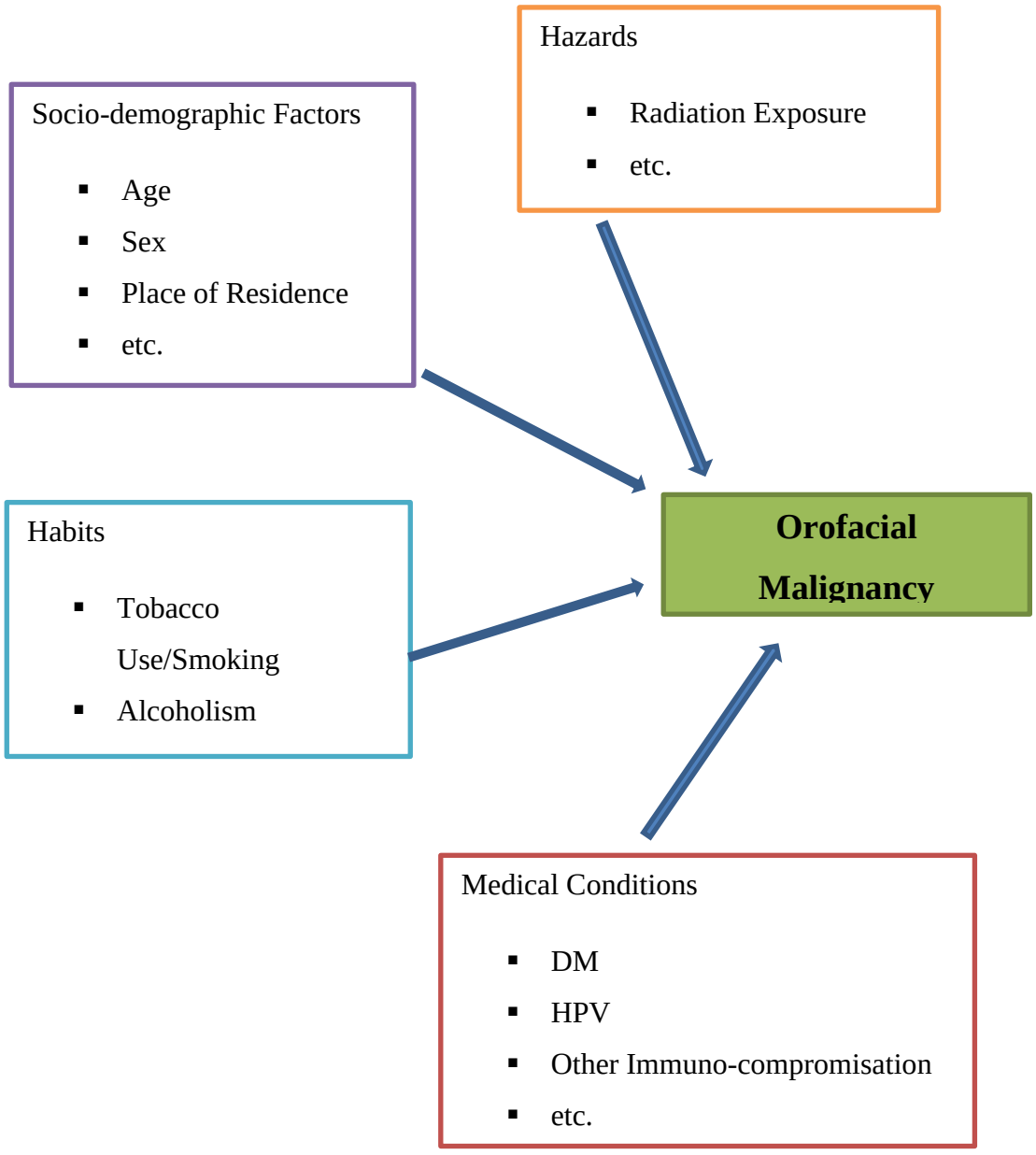


Figure 1: Conceptual framework for risk factors of orofacial malignancy

CHAPTER THREE

3.1. OBJECTIVES

3.1.1. General Objective

- To assess the prevalence and presentation patterns of oral cancers among patients who visited Jimma university medical center.

3.1.2. Specific Objectives

- To determine the socio-demographic distribution of primary orofacial malignancy in JMC from September 11, 2018 to September 10, 2023.
- To determine the histopathologic variants of primary orofacial malignancies at JMC, 2023.
- To identify the primary sites of primary orofacial malignancies at JMC, 2023.
- To assess factors associated with primary orofacial malignancies at JMC, 2023.
- To identify stage at presentation of these malignancies at JMC from September 11, 2018 to September 10, 2023.
- To describe the types of treatment given for these malignancies at JMC from September 11, 2018 to September 10, 2023.

CHAPTER FOUR

4. METHODS

4.1. Study Area and Period

The study was conducted at Maxillofacial Unit of JMC, found in Jimma town, Oromiya regional state, Ethiopia. JMC is governed by Ethiopian Federal Ministry of Health (FMOH). The hospital provides services to 15 million people with more than 1600 staff's members, 32 intensive care units, and 800 beds. It is the biggest center where specialized clinical services are given to peoples from southwestern Ethiopia. It provides services for approximately 15,000 inpatient and 160,000 outpatient attendances in a year. From these OMFS is one of the JMC departments, which serve community in-patient and outpatient. OMF has 20 beds for in patient unite and one operation room table with four senior surgeon and a total of more than 20 staffs including both supportive and health professionals. JMC is a pioneer in starting oral and maxillofacial surgery residency. This hospital is chosen for this study as it is the biggest center in this part of Ethiopia and is among a few centers in the country where oral and maxillofacial surgery services are rendered [45].

The study was conducted in month October, 2023.

4.2. Study Design

A cross-sectional study was conducted. Medical records of patients presented to JMC with a primary orofacial malignancy between September 11, 2018 and September 10, 2023 was reviewed.

4.3. Population

4.3.1. Source Population

All patients treated in JMC Maxillofacial unit; within a period of five years from September 11, 2018 to September 10, 2023.

4.3.2. Study Population

All the patients with primary oral and maxillofacial malignancy that were seen and treated from September 11, 2018 to September 10, 2023

4.4. Inclusion and Exclusion Criteria

4.4.1. Inclusion Criteria

All cases of histopathologically confirmed primary orofacial malignancies seen at JMC, OMFS department between September 11, 2018 and September 10, 2023

4.4.2. Exclusion Criteria

The exclusion criteria were:

- ✧ Inconclusive diagnosis.
- ✧ Re-excised surgical samples (repeated cases).
- ✧ Medical records with incomplete documentation and
- ✧ Other cranio-facial malignancies: eye tumors and facial skin tumors.

4.5. Sample Size and Sampling Procedure

4.5.1. Sample Size Determination

Sample size was calculated using formula for single and finite population, unknown population:

$\mathbf{n = z^2 p(1 - p)/E^2 = (1.96)^2 * 0.5 * (1-0.5) / (0.05)^2 = 384}$

Where:

n is the required sample size;

z is the desired confidence level of 95%, i.e.,1.96;

P is the estimated proportion or anticipated prevalence (i.e., 50%); **1-p**

E is the margin of error to be tolerated, i.e., 0.05;

The minimum sample size required was 384 since the total population is unknown and this sample size might also be adjusted if the total population is <10,000. Over the five years period (from September 11, 2018 to September 10, 2023), there were total of 7800 patients seen at OMFS unit of JMC, out of which 201 were primary malignancy of orofacial region. Therefore out of all 201 patients that fulfilling eligibility criterion was sampled.

4.5.2. Sampling Procedures

From log book/registration books of maxillofacial units, the medical record numbers of all 201 patients diagnosed with primary oral and maxillofacial malignancies between September 11, 2018 and September 10, 2023 was collected. Then their charts were retrieved from card room and 194 patients were finally selected for the study. Seven cards were not included in the study, because two were missing and the remaining five contains inadequate information.

4.6. Data Collection Tools and Procedures

4.6.1. Data Collection Tools

A structured questionnaire was used to extract relevant data on patient demographics, clinical presentation, tumor characteristics, and treatment modalities, from medical records of patients treated for primary oral and maxillofacial malignancies in the past 5 years (2018 - 2023) at maxillofacial units of JMC.

4.6.2. Data Collection Procedures and Criteria for Completeness of Medical Records

Retrospective review of medical records was done. These records were reviewed by 6 dental professionals, with supervision of 2 OMFS residents.

Completeness of the medical records was dictated based on the following criteria. The records were labeled complete if they possess adequate of the following information:

1. Pertinent history including the chief complaints, detailed information on character, duration, size of present illness, associated risk factors or habits, and comorbidities.
2. Physical Examination: characteristics of the lesion, examination results of local, regional and distant sites
3. Histopathology: conclusive result of biopsy or FNAC
4. Management given to the patient

4.7. Data Quality Management

A week prior to the data collection, two session training was given for the data collectors and supervisors on the quality of data anticipated and the way of gathering data from medical records. The questionnaires were pre-tested on similar settings prior to the actual data collection by the data collectors. The necessary adjustments were made after the pre-test. At the end of each day, the collected data was checked by the supervisors for the accuracy and completeness and

corrected for the coming days. The principal investigator was made blind to the raw data prior to analysis.

4.8. Variables

4.8.1. Dependent Variables

- Primary orofacial malignancy.

4.8.2. Independent variables

The independent variables include age, sex, residence area, alcohol intake, smoking, khat chewing, DM, AIDS, UV radiation exposure, chemotherapy treatment and poor oral hygiene.

4.9. Data Processing and Analysis

The collected data was tallied, organized, cleaned, coded and entered into Microsoft excel and Epidata version 3.1 to create a data set and calculate frequencies and percentages for different variables. Finally, the data set was exported to SPSS version 23.0 IBM program for analysis.

Bivariate and multivariable logistic regression was used to assess the significance and strength of the association between the independent and dependent variables. First univariate analysis was performed, depending on normality, to assess any associations between variables and determine SD. Those factors that showed association at p-value < 0.25 in the univariate analysis was transferred into multivariate logistic regression to overcome the effect of cofounding variable. Then multivariate logistic regression model was created, using a backwards elimination technique, until all variables had p values of <0.05. A p-value of 0.05 or less was used as the cut-off level for statistical significance. The final results were presented using charts, graphs, figures and tables.

4.10. Ethical Consideration

Ethical clearance was obtained from Research and Ethics Committee of Jimma University (JU) and permission was received from the JMC board before the study was conducted. Patients' name was excluded from checklist to guarantee confidentiality of the information.

4.11. Dissemination of Results

The finding of this study will be submitted to Jimma university postgraduate office, college of medical science, oral and maxillofacial department of school of dental medicine and to Jimma medical center. The finding will make available in JU Library Catalog and on JU website. It will also present on national and international scientific conferences and also published on reputable journals.

4.12. Limitation of the Study

The required information was not complete since the study was based on secondary data. There was a missing of history sheet, biopsy paper and radiographs. Some of the patient's cards were left at old card room and couldn't be found. Lack of proper/adequate published research on oral and maxillofacial malignancy is also another limitation.

4.13. Operational Definitions

Primary oral and maxillofacial region malignancy: In this study primary oral and maxillofacial malignancy includes those malignant lesions that arise from the epithelial, mesenchymal and hematolymphiod tissues in the orofacial regions based on WHO disease classifications.

CHAPTER FIVE

5. RESULTS

5.1. Characteristics of the Study Population

According to reports obtained from patients' files in the registration of Departments of Maxillofacial Surgery in Jimma Medical Center, the following results have been revealed. During the five-year period 7,800 patients visited OMFS unit of JMC among which 201 cases were diagnosed with Orofacial Malignancy (Figure 2). In other words, the prevalence of primary orofacial malignancy was 2.6% in the study area. Out of total 201 primary oral and maxillofacial malignancy case records, five were found incomplete while another two were missing, therefore excluded from the study, leaving 194 cases included in the study.

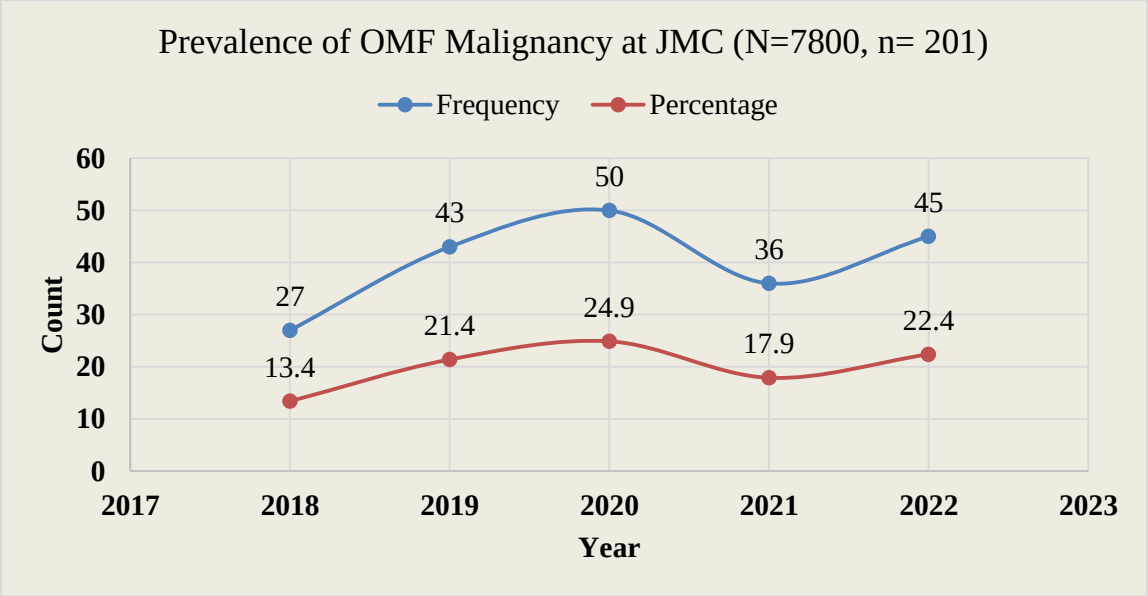


Figure 2: Proportions of Primary OMF Malignancy from Year 2018 - 2023

The overall mean age of the study participants was 41.81 (SD± 15.911, range of 10 to 73 years) with male to female ratio of 2.46:1. The mean age of male and female differ significantly (P = 0.009) and was 43.69 (SD±15.367) and 37.18 (SD±16.414) years, respectively (Refer Table 1). Majority of patients were aged above 40 years (n = 108, 55.7%), while only 12.4 % (n= 24) were

under the age of 20 years. The peak occurrence was between 41 and 60 years comprising 42.3% followed by 21 to 40 years (33%) and older than 61 year (12.4%) (Figure 3).

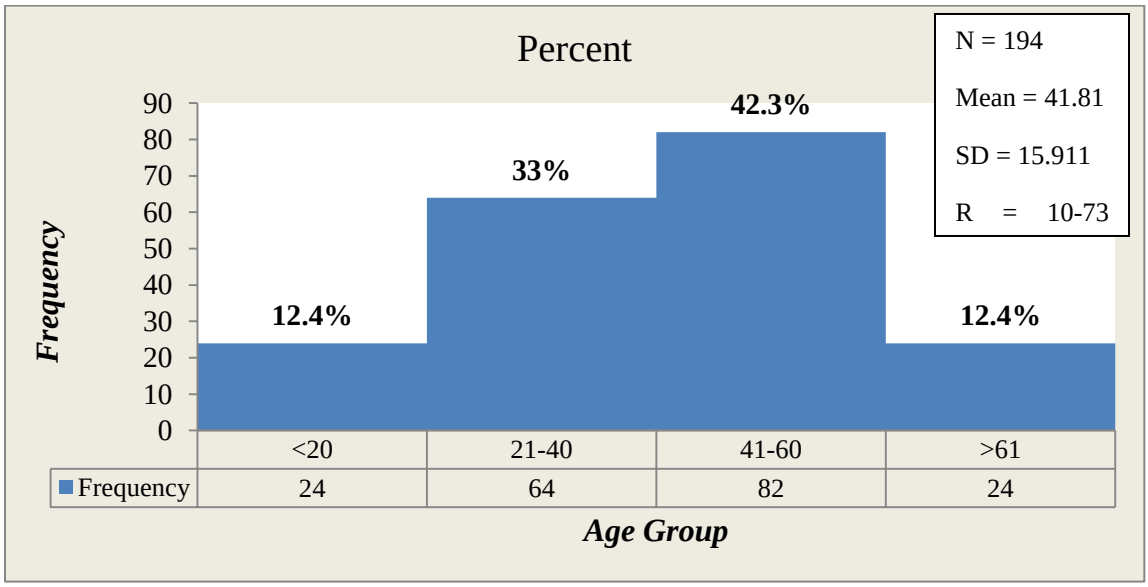


Figure 3: Distribution of primary OMF malignancy by age groups of the patient, 2023

According to this study most of patients were from Oromiya region (74.2%), followed by Southern Nation (20.6%) and other regions accounts for 5.2%, i.e., 4.6% from Gambella and other 0.5% cases from Somali region (Table 1 and Figure 4).

Table 1: Characteristics of the study subjects at Maxillofacial Unit of JMC, 2023 (n = 194)

Variables	Frequency (%)	Mean Age±SD (Min. - Max.)	Ratio	t-test for Equality of Means		
				Sig. (2-tailed)	95% CI for Mean	
					Lower	Upper
Gender						
Male (M)	138 (71.1)	43.69±15.367 (10 - 73)				
Female (F)	56 (28.9)	37.18±16.414 (15 - 70)				
M & F	194 (100)	41.81±15.911 (10 - 73)	2.46:1	0.009	1.611	11.408
Residential Setup						
Urban	101 (52.1)	41.23±15.752 (14 - 72)				
Rural	93 (47.9)	42.44±16.144 (10 - 73)				
Urban & Rural	194 (100)	41.81±15.911 (10 - 73)	1.09:1	0.597	-5.732	3.305
Place of Residence (Region)						

Oromiya	144 (74.2)	43.50±15.826 (10 - 73)			40.89	46.11
Southern	40 (20.6)	37.43±15.016 (14 - 65)			32.62	42.23
Others[$]	10 (5.1)	35.00±17.010 (15 - 60)			22.83	47.17
Total	**101 (100)**	**41.81±15.911 (10 - 73)**	**14.4:4:1**	**0.038***	**39.56**	**44.06**

* The statistical significance for regions is calculated using one-way ANOVA; $ Others indicate one patient from Somali and nine patients from Gambella Region. SD = Standard Deviation; CI = Confidence Interval.

With respect to residential set-up, majorities (52.1%) of these patients are from the urban and 47.9% are from the rural area (Table 1 and Figure 4). There is a difference in residential set up among residential areas (Pearson Chi-Square Tests (X^2) = 11.818; P-value < 0.008). The mean age is also significantly differ between residential setups (p = 0.038; 95% CI = 39.56, 44.06) (Table 1).

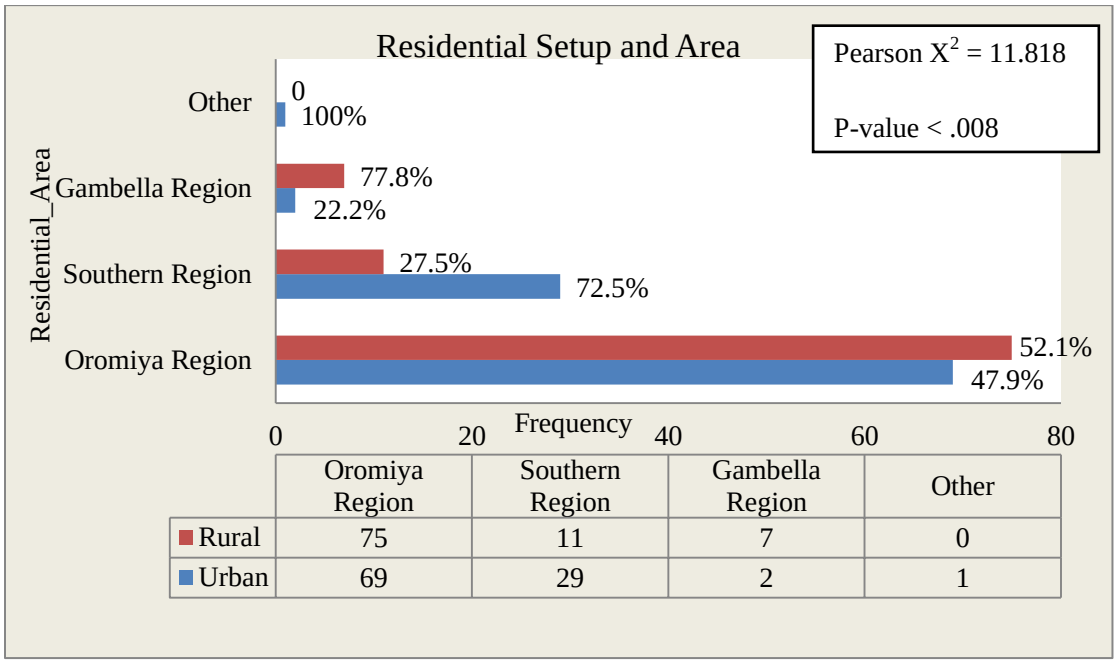


Figure 4: Distribution of Subjects based on their residential setup and region, JMC, 2023

5.2. Histologic Variants of the Lesion

Table 2 show the age and gender distribution of tissue of origins and histologic types of primary orofacial malignancies. Out of total of 194 study cases, 163 (84.0%) were carcinomas, 27 (13.9%) were sarcomas and the remaining 4 (2.1%) were lymphomas. Patients with diagnosis of carcinoma (mean age = 44.42±14.766 years, range: 14 to 73) was significantly older than those

of sarcoma (mean age = 29.30±15.516 years, range: 10 to 60) and lymphoma (mean age = 20.00±3.742 years, range: 16 to 25) with p-value of 0.000 and 0.004 respectively (Table 2).

SCC was the most common specific histology followed by MEC and osteosarcoma corresponding to 59.5%, 16% and 9.3% of cases respectively. From overall salivary gland malignancies (55 cases), MEC was the most common (47.27%) followed by AdCC comprising 25.5 %. SCC was frequently found in males (65 versus 32 in females) with the peak age of occurrence at 41–60 age-groups (Table 2).

Table 2: Distribution HNCs patients by their histological type at JMC from 2018 to 2023

Tissue of Origin (n, %)	Mean age ± SD(R)	One-way ANOVA	Lesion[$]	n (%)	Age Group (years)				Gender		
					<20	21-40	41-60	>61	M	F	M:F
Carcinomas (163, 84%)	44.42±14.766 (14-73)	***P* = 0.000**; df = 2; F= 16.609	SCC	97 (59.5)	4	22	58	13	65	32	2.0:1
			Ameloblastic Ca.	2 (1.2)	0	1	1	0	2	0	-
			Sclerosing Odont. Ca.	4 (2.4)	0	2	2	0	4	0	-
			Ghost Cell Odont. Ca.	2 (1.2)	0	1	1	0	2	0	-
			ACC	3 (1.8)	0	1	2	0	3	0	-
			MEC	26 (16)	3	16	2	5	20	6	3.3:1
			AdCC	14 (8.6)	0	10	4	0	12	2	6:1
			Ca. Ex-PA	12 (7.4)	2	2	4	4	8	4	2:1
			Papillary Ca.	1 (0.6)	1	0	0	0	1	0	-
			Mucosal Melanoma	2 (1.2)	0	0	0	2	2	0	-
Sarcomas* (27, 13.9%)	29.30±15.516 (10-60)		ST Sarcoma	6 (3.1)	4	0	2	0	6	0	-
			Chondrosarcoma	2 (1.0)	1	1	0	0	1	1	1:1
			Osteosarcoma	18 (9.3)	5	7	6	0	11	7	1.6:1
			Ewing Sarcoma	1 (0.5)	1	0	0	0	0	1	-
Lymphoma* (4, 2.1%)	20.0±3.742(16-25)		Lymphoma	4 (2.1)	3	1	0	0	1	3	0.3:1
All patients (194)	**41.81±15.911 (10-73)**			**194**	**24**	**64**	**82**	**24**	**138**	**56**	**2.46:1**

* Patients with a diagnosis of sarcoma and lymphoma were younger than those with carcinoma: p = 0.000 (CI 7.88, 22.37) & p = 0.004 (CI 6.77, 42.06) compared to carcinoma group, using one-way ANOVA & Turkey's HSD Post Hoc Tests.

M = Male; F= Female; R = Range; SD = Standard deviation; ST = Soft Tissue; CI = Confidence Interval; SCC = Squamous cell carcinoma; Ca. = carcinoma; ACC = Acinic cell carcinoma; MEC = Mucoepidermoid carcinoma; AdCC = Adenoid cystic carcinoma; Ca. Ex-PA = Carcinoma Ex Pleomorphic Adenoma; Malign. = Malignant; Odont. = Odontogenic.

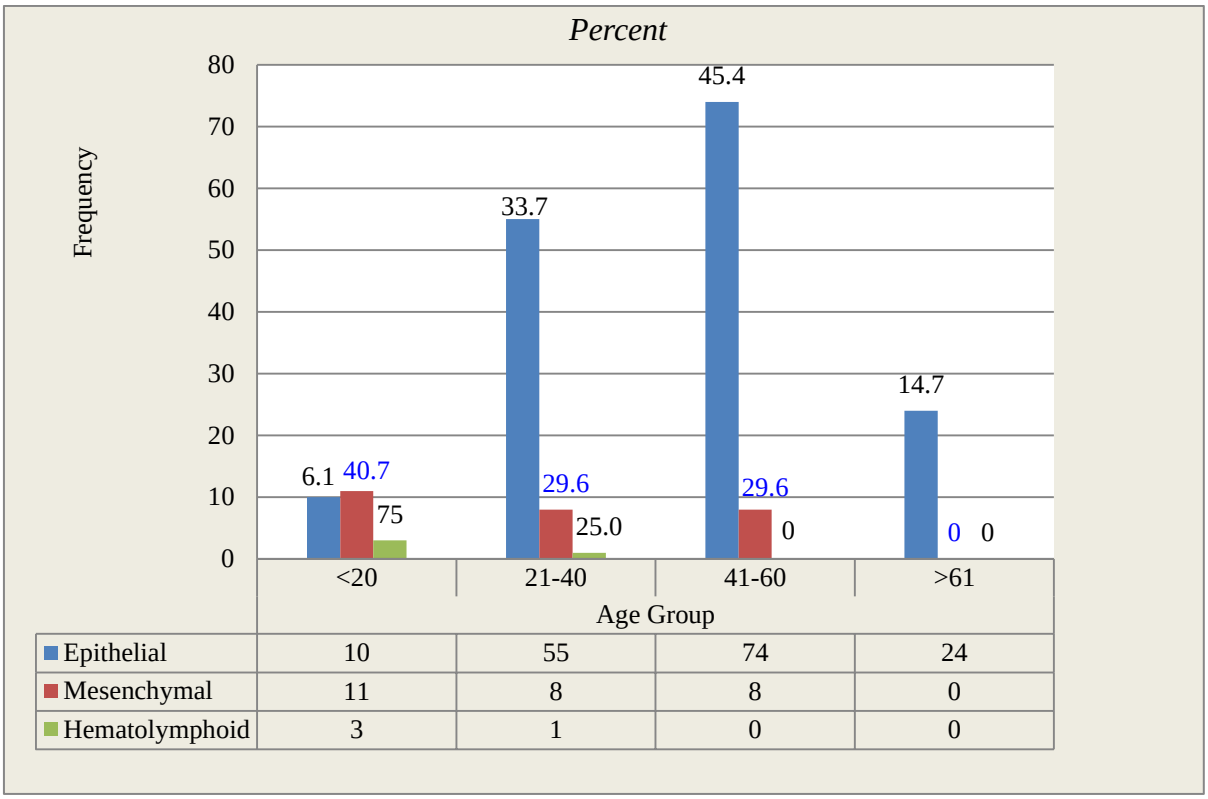
Table 3 shows the age variation among different lesions of primary orofacial malignancies. The statistical analysis showed that mean age for SCC (47.54±13.454 years) is significantly differ from mean ages for Soft tissue sarcoma (27.67±21.360 years), osteosarcoma (31.67±14.213 years) and lymphoma (20.00±3.742 years) with p-value of 0.039, 0.001 and 0.009 respectively.

Table 3: Age distributions and Post Hoc Turkey's Tests with Multiple Comparisons for SCC

Lesion types	N	Mean Age±SD (Range)	Post Hoc Turkey's Tests & Multiple Comparisons for SCC				
			Mean Difference	Std. Error	Sig. (2 tailed)	95% CI for Mean	
						Lower	Upper
SCC	97	47.54±13.454 (14-73)	-	1.366		44.82	50.25
ST Sarcomas	6	27.67±21.360 (10-55)	19.869	8.720	**.039**	5.25	50.08
Osteosarcoma	18	31.67±14.213 (17-60)	15.869	3.350	**.001**	24.60	38.73
Lymphoma	4	20.00±3.742 (16-25)	27.536	1.871	**.009**	14.05	25.95
ACC	3	42.67±3.055 (40-46)	4.869	1.764	1.000	35.08	50.26
MEC	26	37.62±17.337 (17-70)	9.921	3.400	.062	30.61	44.62
AdCC	14	38.64±10.051 (28-55)	8.893	2.686	.462	32.84	44.45
Ca.-Ex-PA	12	43.42±19.332 (15-65)	4.119	5.581	.992	31.13	55.70
Other Variants	14	36.86±16.774 (15-66)	10.679	4.483	.216	27.17	46.54
Total	194	41.81±15.911 (10-73)		1.142		39.56	44.06

SD: Standard deviation; CI = Confidence Interval; SCC = Squamous cell carcinoma; Ca. = carcinoma; ACC = Acinic cell carcinoma; MEC = Mucoepidermoid carcinoma; AdCC = Adenoid cystic carcinoma; Ca. Ex-PA = Carcinoma Ex Pleomorphic Adenoma; ST = Soft Tissue; Malign. = Malignant; Odont. = Odontogenic. Others variants includes Ameloblastic carcinoma, Sclerosing Odontogenic carcinoma, Ghost Cell Odontogenic carcinoma, Papillary carcinoma, Malignant Mucosal Melanoma.

According to our study distribution by tissue of origin was different depending on age group (Pearson $X^2 = 43.223$; $P < 0$ .000). Most of carcinomas were diagnosed in older adults (41- 60 years) accounting for 74 cases (45.4%) followed by age groups of young adults (21-40 years) accounting for 33.7%, while 75% of sarcoma cases were in adolescents followed by young adults (25%) age groups (Figure 5).



	<20	21-40	41-60	>61
Epithelial	10	55	74	24
Mesenchymal	11	8	8	0
Hematolymphoid	3	1	0	0

Figure 5: Distribution of Orofacial Cancer's tissue of origin by patient's age at JMC, 2023

5.3. Primary Sites of the Orofacial Malignancies

On analyzing patterns of primary HNC by subsite we discovered that oral cavity (52.6%), salivary gland sites (28.9%), maxillary sinus (11.3%) and mandible (10.3%) were the commonly affected anatomic sites by primary HNCs. Tongue was the commonly affected oral cavity sub-site making up 27.4% (n=28) followed by hard palate comprising 23.5 % (n=24), buccal mucosa and alveolar ridges contributing 11.8% (n=12) each (Table 4).

Gender distribution of oral and maxillofacial malignancy varies with involved subsite (Pearson $X^2 = 4.560$; $P< 0.803$), but not significantly differ. In majority of the sites male predominate with a minimum male to female ratio of 1.25:1 in cancers of maxillary sinus and maximum of 5:1 in the FOM malignancy. There were no gender predilection seen in buccal mucosa, oropharynx and nasal cavity sites (Table 4).

Table 4: Anatomic and Gender Distribution of Orofacial Malignancies from 2018 to 2023

Primary Site Of Lesion			Frequency (%)	Gender		
				Male	Female	M:F Ratio
Oral Subsites (102, 52.6%)	Mucosa (81, 79.4%)	Oral Tongue	28 (27.4)	22	6	3.7:1
		Buccal Mucosa	12 (11.8)	6	6	1:1
		FOM	6 (5.9)	5	1	5:1
		Alveolar Ridge	12 (11.8)	8	4	2:1
		Retro-Molar	6 (5.9)	4	2	2:1
		Hard Palate	7 (6.9)	4	3	1.3:1
		Lips	10 (9.8)	8	2	4:1
	Minor SGs (21, 20.6%)	Buccal Lining	4 (3.9)	2	2	1:1
		Palate	17 (16.7)	13	4	3.25:1
	Total		**102 (52.6)**	**72**	**30**	**2.4:1**
Mandible			**20** (**10.3**)	15	5	3:1
Maxilla			**6** (**3.1**)	4	2	2:1
SGs Sites (56, 28.9%)	Major SGs (30, 53.6%)		30 (53.6)			
	Minor SGs (25, 44.6%)	Buccal Lining	4 (16)			
		Palate	17 (68)			
		Maxillary Sinus	4 (16)			
	Intra-parotid LN (1, 1.8%)		1 (1.8)			
	Total			43	13	3.3:1
Maxillary Sinus			**18** (**9.3**)	10	8	1.25:1
Facial STs*			8 (4.1)	6	2	3:1
Oropharynx			2 (1.0)	1	1	1:1
Nasal Cavity			2 (1.0)	1	1	1:1
Neck			1 (0.5)	1	0	------
Total			**194** (**100.0**)	**138**	**56**	**2.46:1**

* excluding the skin; FOM = floor of the mouth; SGs = Salivary Glands; LN = lymph nodes (Lymphoma); STs = Soft Tissues. Pearson $X2 = 4.560$; $P < 0.803$

5.4. Factors Associated With Orofacial Malignancy

Out of 194 patients analyzed, 92 (47.4%) had history of exposure to known predisposing factors among which 34 (37%) exposed to more than one factors (24 alcohol with tobacco and 10 uses other factors combinations). This study shows that 34 (37%) patients smokes (alone or combined with other factors), 41 (44.6%) consume alcohol (alone or in combination), 20 (21.8%) chew Khat (alone or in combination) and 7 (7.6%) cases were immuno-compromised (four cases of retroviral infections (RVI) and three cases of diabetic mellitus (DM)) (Table 5).

Table 5: Frequency, age and gender distributions of risk factors for orofacial cancer at JMC, 2023

Factor Types	Frequency (%)	Mean Age±SD	ANOVA/ t-Test*	Age-Set		X^2-test	Age Groups				X^2-test**	Gender		X^2-test
				<= 40	> 40		< 20	21-40	41-60	> 61		M	F	
Predisposition Status														
No	102 (52.6)	36.41±16.287	***P* = 0.000**	59	43	x^2= 15.915	2	37	33	10	x^2= 21.5	60	42	x^2= 15.8
Yes	92 (47.4)	47.79±13.178	CI (-15.606, -7.158)	27	65	df = 1 ***P* = .000**	2	27	49	14	60 df= 3 ***P*= .000**	78	14	75 df= 1 ***P*= .000**
All patients	194	41.81±15.911		86	108		24	64	82	24		138	56	
Factor Types														
Tobacco Use	10 (10.9)	58.00±5.375	***P* = 0.000**	0	10	x^2= 13.642	0	0	6	4	x^2 = 51.3	8	2	x^2= 8.195
Alcoholism	17 (18.5)	46.12±15.708		7	10	df = 6	0	7	8	2	76	15	2	
Khat Chewing	10 (10.9)	45.00±10.812	CI (45.06, 50.52)	2	8	***P* = 0.034**	0	2	8	0	df = 18	9	1	df= 6
Poor Oral Hygiene	14 (15.2)	42.71±12.156		4	10		2	2	10	0		9	5	
Immunosuppression	7 (7.6)	41.29±7.973		3	4		0	3	4	0	***P* = 0.000**	7	0	***P*= 0.224**
Tobacco & Alcohol	24 (26.1)	43.29±10.170		11	13		0	1 3	9	2		20	4	
Other Combinations	10 (10.9)	65.70±6.183		0	10		0	0	4	6		10	0	
Total	**92 (100)**	**47.79±13.178**		**27**	**65**		**2**	**27**	**49**	**14**		**78**	**14**	

* One-way ANOVA/Independent T-test, among the mean age values of different factor types or Predisposition status respectively; ** Pearson Chi square test, variation in age-set/age group/gender among different predisposition status/factor types. CI = Confidence Interval.

Significant difference was seen among male and female with respect to predisposition status (Pearson X^2 = 15.875; *P* = 0.000). A higher number of exposures were among males (85%) than females (25%) with ration of 5.6:1 (See Figure 6). However, no significant difference was seen among genders with respect to risk factor types (Pearson X^2 = 8.195; *P* = 0.224) (Table 5).

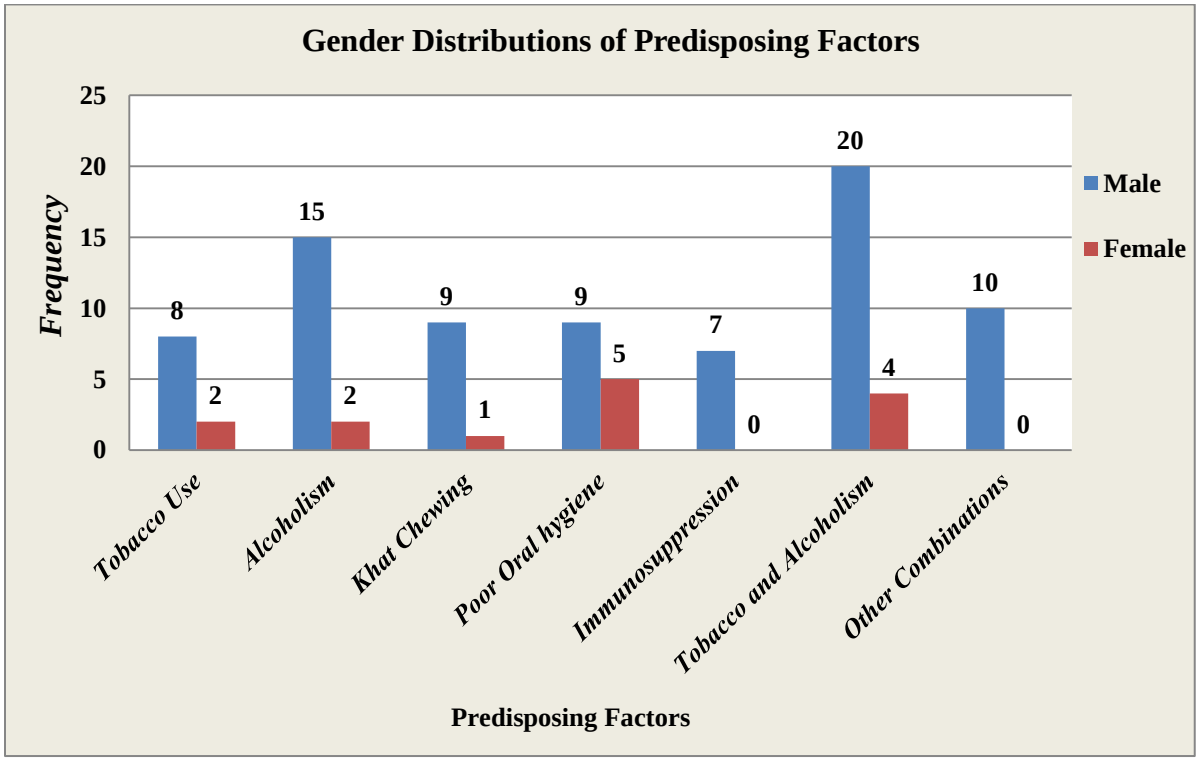


Figure 6: Gender Distribution of Predisposing Factors among Study Subjects, JMC, 2023

There was a significant difference among oral site with respect to predisposition status and factor types (*P* = 0.000 & *P* = 0.025 respectively). Oral cavity site (n= 54, 58.7%) has highest predisposition history among other sites (Table 6).

Table 6: Risk factor status and types for primary sites of orofacial malignancy, JMC, 2023

Parameter	Primary Sites, n (%)					Total	X^2 Tests
	Oral Mucosa	Mandible	Maxilla	Salivary Glands	Maxillary Sinus		
Predisposition Status							
No	27 (30.3)	10 (11.2)	4 (4.5)	34 (38.2)	14 (15.7)	89 (49.2)	X^2= 30.359 df= 8 ***P*** <
Yes	54 (58.7)	10 (10.9)	2 (2.2)	22 (23.9)	4 (4.3)	92 (50.8)	
All Patients	81 (44.5)	20 (11.1)	6	56 (30.9)	18 (9.9)	181 (100)	

			(3.3)				***0.000***
Factor Types							
Tobacco Use	6 (11.1)	2 (20)	0	2 (9.1)	0	10 (10.9)	X^2=
Alcoholism	6 (11.1)	2 (20)	0	5 (22.7)	4 (100)	17 (18.5)	39.31
Khat Chewing	8 (14.8)	0	0	2 (9.1)	0	10 (10.9)	0
Poor Oral Hygiene	8 (14.8)	2 (20)	2(100)	2 (9.1)	0	14 (15.2)	df=
Immunosuppression	4 (7.4)	2 (20)	0	1(4.5)	0	7 (7.6)	24
Tobacco & Alcohol	14 (25.9)	2 (20)	0	8 (36.4)	0	24 (26.1)	
Other Combinations	8 (14.8)	0	0	2 (9.1)	0	10 (10.9)	***P*** <
Total	**54 (58.7)**	**10 (10.9)**	**2 (2.2)**	**22 (23.9)**	**4 (4.3)**	**92 (100)**	***0.025***

5.5. Stage at Presentation of Malignant Lesions

Table 7 shows the characteristics of orofacial lesions among patients seen at JMC during the study period. With respect to the size 38.7% of primary lesion was with locally advanced (T4 stage) at presentation. Majority of the patients, i.e., 145 (74.8%) were presented at late stage (stage III & IV) and only 8.8% were early presented (stage I & II). Unfortunately 9.8% of the cases had distance metastasis mainly to the lung (37%) followed by the brain (21%) at presentation.

Table 7: Characteristic of Orofacial Lesions at Presentation, 2023

Variables	Frequency (%)	Variables	Frequency (%)
T- Stage		**M - Status**	
T1	5 (2.6)	Non-metastatic Lesions	142 (73.2)
T2	12 (6.2)	Metastatic Lesions	19 (9.8)
T3	70 (36.1)	Unknown Status	33 (17.0)
T4	75 (38.7)	**Total**	**194** (**100.0**)
Unstage*	32 (16.5)	**Metastatic Site**	
Total	**194** (**100.0**)		
Stage at Presentation		Lung	7 (36.8)
Stage I	5 (2.6)	Liver	2 (10.6)
Stage II	12 (6.2)	Brain	4 (21)
Stage III	70 (36.1)	Bone	2 (10.6)
Stage IV	75 (38.7)	Lung and Bone	2 (10.6)
Unstaged*	32 (16.5)	Brain and Bone	2 (10.6)
Total	**194** (**100.0**)	**Total**	**19** (**100**)

**Unstaged lesions contains sarcomas, lymphomas and other 8 carcinomas*

5.6. Treatment Modalities for Primary Maxillofacial Malignancies

Surgery was the main mode of treatment used in 148 (76.3%) cases, followed by the modality combining surgery with radiotherapy in 69 (35.6%) cases. Other treatment modalities are shown in Figure 7.

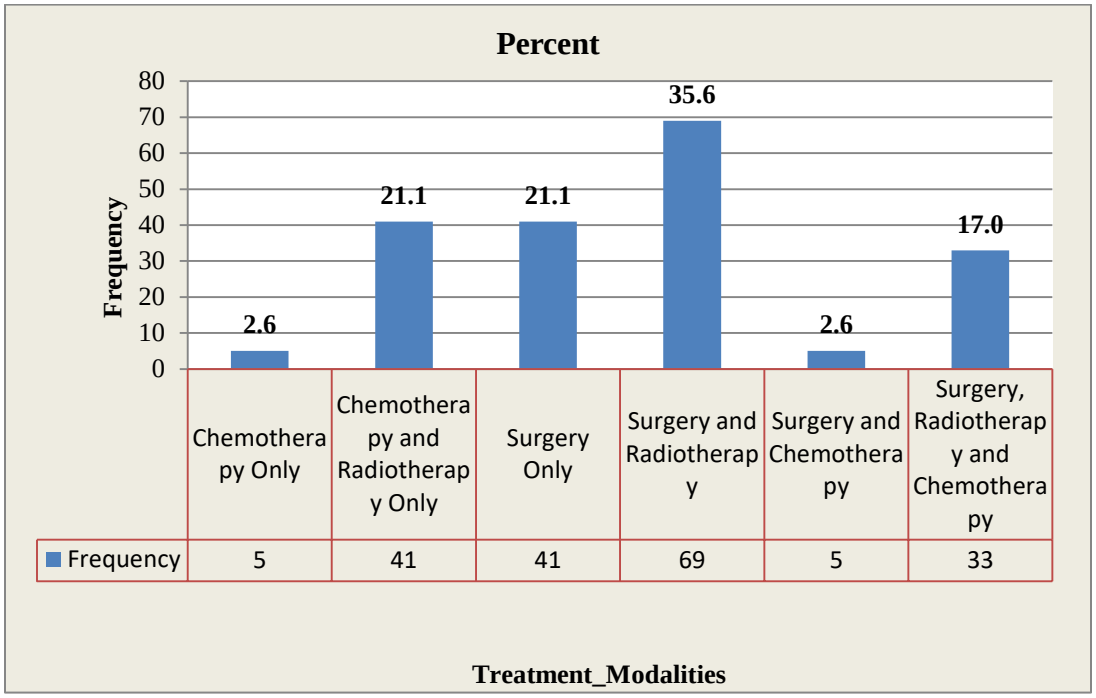


Figure 7: Treatment Modalities for Primary Orofacial Malignancy at JMC, 2023

CHAPTER SIX:

6. DISCUSSIONS

This study showed an overall male preponderance with a male to female ratio of 2.46:1, which falls within the range found in Ethiopia, Tanzania, Uganda, Zimbabwe, Ghana, India and Europe where a male to female ratio range from 1.3 to 2.63:1 [7,17,19–21,27–30,44,46]. Various sites of oral and maxillofacial region show difference in male to female ratio. Oral mucosa site in this study show a male to female ratio of 2.4:1 which is almost similar to worldwide estimation 2:1 and result from southeastern Iran with 2.74:1ratio [24]. However it is slightly higher than study at Black Lion hospital with ratio of 1.72:1 [30]. This might be explained by the fact that the predisposition in this study was greater among men than women (Pearson $X^2 = 15.875$; $P < .000$).

The mean age of the subjects was 41.81 ±15.911 years, which corresponds to a study done in Japan with mean age of 42 years [39] and in Nigeria (mean age of 42.2 years) [26]. It is also similar with other studies done in Ghana (mean age of 45.08 years) [27], and in Ethiopia[7,30,44] with mean age from 44.56 to 46.66 years. The prevalence of the primary OMF cancer rose with increasing age until it peaked in the age group 40 to 60 years (42.3%). This is in accordance with other studies in Ethiopia by Tefera et al. (40.5%), Chala et al. (43.4%), Girma (40.5%) and Abdulmenan (41.6%) [7,30,36,44]. It also parallels other studies in Zimbabwe and Ghana [27,28]. In contrast to this finding, the research done in western Iran, reported that the highest risk group was >60 years (60.2%) age groups [25]. Young adults (20 to 40 years) comprises the second commonly involved age groups with 33% of cases, which corresponds to Chala et al. (30.3%), Girma (34.3%) and Abdulmenan (27.3%) [30,36,44]. However, our finding disagree with others from Europe, Middle east and India in which old age groups (above 60 years) were the second frequently involved site [19,22,23]. This difference may be attributed to the higher percentage of people below 40 years, lower life expectancy and early exposure to risk factors in developing countries. Youngsters (<21 years) were 12.4% in our study, which is similar to a study done in Zimbabwe (11.7%) [28]**,** but slightly lower than study done in Nigerian tertiary hospital (20%) [26].

In the present study, most HNCs arose from the epithelial origin (84%) (); among that SCC was the commonest tumor type (59.5%). This is analogous to studies done in Ghana, Iran, India and

others [20,22,25,27] . However, the percentage (80.5%) is higher in our study, when compared to 72.0% at Black Lion hospital [7], 49.6% found in Ghana and nearly similar with Iran finding which was 77.5% [24]. Patients with diagnosis of carcinoma (mean age = 44.42±14.766 years, range: 14 to 73) was significantly older than those of sarcoma (mean age = 29.30±15.516 years, range: 10 to 60) and lymphoma (mean age = 20.00±3.742 years, range: 16 to 25) with p-value of 0.000 and 0.004 respectively. This is similar to finding from Ajayi et al., 2007 with $p< 0.01$ in both cases [26].MEC (16%) was the second most common variant in this study followed by osteosarcoma (9.3%) unlike study done at Black Lion hospital, where adenocarcinoma was the second most common specific histology [7]. Only 3.7% of the cases were Sarcomas according to the histopathology results, which is in line with a study done in Iran [24]**.** The direct and immediate contact of predisposing factors to the epithelial tissue of OMF region may be the reason for highest prevalence of carcinoma than sarcoma and lymphoma.

According to the site distribution of primary orofacial malignancy, this study found oral cavity (52.6%) and its oral tongue subsite (n=28, 27.4%) as the most common site (Table 4). Similarly, a study on the anatomical distribution of head and neck malignant tumors in Ghana [27] found the oral cavity to be the most common site for HNCs with a prevalence of 35.0% which is also similar to the findings in Arab countries, India and Ethiopia [22,23,25,30]. Primary malignancy of parotid gland (n=56, 28.9%) was the second most common site. This finding is somewhat different from the other studies, where a cancer of floor of the mouth was the second commonly involved site [37,54].

The etiology of orofacial malignancy is multifactorial in this study. About 47.4% of patient had risk factor like smoking, alcohol consumption, Khat chewing and immune compromising disease, which is consistent with epidemiological study done in this country [7,36]. Osman et al reported 49.8% toomback dipping and smoking in Sudan which is in line with this study [35]. Saman Warnakulasuriya et al, on the study of Global epidemiology of oral and or pharyngeal cancer, reported smoking and alcohol has 80% of association with cancer [31]. Freidrich et al (German) reported 66.9% of orofacial cancer cases were smoker [32]. The study shows that majority (n= 13, 54.2%) of the combined users of alcohol and smoking are in this age group which can be the reason for prevalence of OMF cancers in young adults, but needs further study.

From these patients with a history of 85% were males and 68.7% had cancers of oral cavity (*p* =.025).

With respect to primary tumour size, T4 stage was observed in the majority (38.7%) patients, followed by T3 (36.1%), T2 (6.2%), and T1 (2.6%). This finding is comparable with the study done in Lahore, Pakistan, in which T4 stage was accounted for (57%) and only (2.5%) are T1 stage [25]. In our current study, 19 cases (9.8%) had distant metastasis mainly to lung. Ariyoshi et al found distant metastasis seen only in (1%) patients with orofacial cancer in Japan which is lower than this finding [40]. This might be due to late presentation of patients; lack of awareness and limited service in developing country.

A study done in head and neck cancer in Africa found that 64% mortality rate was reported in the developing world where cancer prognosis tends to be worse, due to late-stage presentation [10]. The present study supports the above statement, as close to three quarter of the cases (74.8%) was visited the medical center at a late stage (stage III and IV) of malignancy. Similar study in Ethiopia also prove the same [7].

Orofacial cancer is a deadly but forgotten disease in Ethiopia. Surgery was a main treatment modality in 148 (76.3%) cases, followed by surgery combined with radiotherapy in 69 (35.6%) cases which is similar to the study done in Sudan [41]. Delayed treatment for orofacial cancer in developing African countries including Ethiopia may be due to the limited oncologic service in government institutions and long waiting time.

To ensure quick response, early diagnosis of patients is very important. Primary health care professionals should have to have knowledge of early sign and symptoms of oral cancer in order to facilitate diagnosis and treatment before the disease become advanced.

CHAPTER SEVEN

7. CONCLUSION AND RECOMMENDATION

7.1. Conclusion

✧ The prevalence of primary orofacial malignancy was 2.6% among the total patients and the majority of them are histologically squamous cell carcinomas, commonly affecting older adult age groups (41–60 years) and males.

✧ The highest number of cases was the oral cavity and salivary gland cancers followed by maxillary sinus cancers.

✧ Even though the cause of orofacial cancer is multifactorial, smoking, immune compromising disease, khat chewing and alcohol were some of the identified risk factor in this study.

✧ Alcohol consumption, smoking and khat chewing were the most common predisposing factors.

✧ Nearly three-fourth of patients was diagnosed at a late stage of orofacial malignancy.

✧ Few patients had distance metastasis to mainly lung (37%) while brain and cervical vertebrae metastasis were also encountered.

✧ Surgery was the main means of treatment modality given to orofacial cancer patients.

7.2. Recommendations

We recommend the responsible body to collaborate with treating physician and community leaders, to increase awareness on burden of orofacial cancer.

Capacity building of health facilities and professionals at all levels in early diagnosis and timely referral as well as improving access to oral and maxillofacial service is recommended.
The higher number of OMF region cancers as well as predisposing factors among young adults should be a major concern as it these will result in damage to workforce and economy at large.

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ANNEX I: Check List

Jimma University

Institute Of Health Sciences

School Of Dental Medicine

Department Of Oral and Maxillofacial Surgery

This check list is designed to assess the Patterns of primary oral and maxillofacial malignancy among patients seen at JMC Maxillofacial unit during period from September 11, 2018 to September 10, 2023.

Instruction: Read each part of the checklist carefully and write "Code No." for appropriate response in the cell provided or write answer in given area.

Labeling: Date (E.C): ____/____/____ MRN: _____ Code №:_____ Data collector _____ Supervisor _____

Variables	**Category**	**Descriptions**	**Code**	
Age (in years): _____				
Sex:	Male(**1**); Female(**2**)			
Date of Visit/Admission (dd/mm/yy): _____/ _____/ _____				
Address:	Urban(**1**); Rural(**2**)			
	Oromiya (**1**); South Nations(**2**); Gambela(**3**); Benishangul(**4**)			
	Others (specify)(**5**) _____			
Predisposition	**Status:** No(**0**); Yes(**1**)			
	if Yes: Tobacco(**1**); Alcohol(**2**); Khat(**3**); Poor Oral Hygiene(**4**); Immuno-suppression (**5**); Tobacco & Alcohol(**6**); other combinations(**7**)			
	Others: Specify(**8**) _____			
C/C (with character, localization, duration): _____of _____ duration				
Pertinent Findings (Specify): _____				
Primary Site of Lesion	**Oral Cavity(01):** Oral tongue(**1**); Buccal mucosa(**2**); FOM(**3**); Alveolar ridge/gingiva(**4**); retro-molar (**5**); Hard palate(**6**); Lips(**7**); Minor SGs Sites: Specify(8) _____; Other Oral site: Specify(9)_____			

	Mandible(**02**): Anterior (**1**); Posterior (**2**)		
	Maxilla(**03**): Anterior (**1**); Posterior (**2**)		
	Salivary Gland(04): Parotid(**1**); Sub-mandibular(**2**); Sublingual(**3**); Minor SG(**4**)		
	Other: Specify(**05**) _____		
Size of lesion (cm): _____			
Dx by	Biopsy (**1**); FNAC (**2**)		
T-stage:	T1(**1**); T2(**2**); T3(**3**); T4(**4**); Unknown(**5**); Not Applicable(**6**)		
cTNM (8e)	Stage I(**1**); Stage II(**2**); Stage III(**3**); Stage IV(**4**); Unknown(**5**); Not Applicable(**6**)		
Metastasis	**Status:** No(**0**); Yes(**1**); Unknown(**2**)		
	if Yes (Specify sites): _____		
Origin	Epithelial(**1**); Mesenchymal(**2**); Hematolymphiod/Lymphoma(**3**)		
Specific Histology Variants	SCC(**1**); Ameloblastic ca.(**2**); Primary intraosseous Ca.(**3**); Sclerosing odontogenic ca.(**4**); Clear cell odontogenic ca.(**5**);Ghost cell odontogenic ca.(**6**); Odontogenic ca.(**7**); Odontogenic sarcoma(**8**); Soft tissue sarcoma(**9**); Chondrosarcoma(**10**); Osteosarcoma(**11**); Lymphoma(**12**); Adenocarcinoma(**13**); ACC(**14**); MEC(**15**); Papillary Ca.(**16**); AdCC(**17**); Ca. Ex Pleomorphic (**18**)		
	Other: Specify(**19**) _____		
Rx Profile	Not Treated (**0**); Radiotherapy Only(**1**); Chemotherapy Only(**2**); Chemoradiotherapy only(**3**); Surgery Only(**4**); Surgery with Radiotherapy(PORT)(**5**); Surgery with Chemotherapy(POChT)(**6**); Surgery, RT & ChT(POCRT)(**7**); Unknown(**8**)		
	If Operated: Date of operation (d/m/y) _____/_____/_____		
	Need reconstruction: No (**0**); Yes(**1**); Unknown (**2**)		

DECLARATION

I, the undersigned, declare that this thesis is my original work, has not been presented for degree in this or any other university and that all sources of materials used for the thesis have been fully acknowledged.

Name: _____

Signature: _____

Name of the institution: _____

Date of submission: _____

This thesis has been submitted for examination with my approval as University advisor

Name and Signature of the first advisor

_____

_____

Name and Signature of the second advisor

_____

_____