



ADDIS ABABA UNIVERSITY
COLLEGE OF HEALTH SCIENCE,
SCHOOL OF MEDICINE
DEPARTMENT OF SURGERY
PLASTIC AND RECONSTRUCTIVE SURGERY UNIT



The Pattern of Head and Neck Cancers of the Oral cavity, Nasal cavity and Paranasal Sinuses, and Salivary Glands at ALERT Comprehensive Specialized Hospital, Addis Ababa, Ethiopia: Retrospective Cross-sectional Study

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A Research Thesis to be submitted to Addis Ababa University postgraduate studies, College of Health Science, Department of Surgery, in partial fulfillment of the requirement for a certificate of specialization in Plastic and Reconstructive Surgery.

Title: The Pattern of Head and Neck Cancers of Oral cavity, Nasal cavity and Paranasal Sinuses, and Salivary Glands at ALERT Comprehensive Specialized Hospital, Addis Ababa, Ethiopia: Retrospective Cross-sectional Study

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December 2023

Addis Ababa, Ethiopia

APPROVAL OF THE EXAMINING BOARD

This thesis by **Dr. Reyad Adem** is accepted in its present form by the board of examiners satisfying the thesis requirement for the specialty certificate in Plastic and Reconstructive Surgery.

Title of the Project: The Pattern of Head and Neck Cancers of Oral cavity, Nasal cavity and Paranasal Sinuses, and Salivary Glands at ALERT Comprehensive Specialized Hospital, Addis Ababa, Ethiopia: Retrospective Cross-sectional Study

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Acknowledgements.

I want to begin by voicing my gratitude to Allah, the All-Powerful, who provided me with the fortitude and resolve necessary to carry this task through to the end.

Second, I would like to express my sincere appreciation to the Plastic and Reconstructive Surgery Unit at Addis Ababa University's College of Health Sciences for offering me with this remarkable opportunity to carry out the study.

My heartfelt admiration is also extended to Dr. Abraham G/Egziabher, my advisor, for his insightful guidance, comments, and suggestions during the entire process, from the creation of the proposal to the finalization of the final report of the study.

I would also like to acknowledge the administrative staff of ALERT Comprehensive Specialized Hospital, particularly the Research Directorate, as well as all of the staff of the plastic surgery unit, OPD, Card room, and liaison office, for granting me to access patient data and for their assistance during data collection.

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ABSTRACT

Background: Despite substantial clinical advancements that make it possible for early detection and treatment, head and neck cancers (HNCs) continue to be a major public health problem worldwide, resulting in significant morbidity and mortality. Head and neck cancers account for around 5% to 7% of all cancer cases worldwide, exhibiting significant epidemiologic variability across geographical areas.

Objectives: The primary objective of this study is to determine the patterns of head and neck cancers of the oral cavity, nasal cavity, paranasal sinuses, and salivary glands at ALERT Comprehensive Specialized Hospital Plastic Surgery unit, between May 1, 2015 to May 1, 2023.

Methods: Retrospective cross-sectional chart review of all patients with diagnosis of head and neck cancers seen at ALERT comprehensive specialized hospital, Plastic surgery unit, during the study period who fulfill the inclusion criteria was done. The data was cleaned, coded, entered to SPSS version 26 software and analyzed.

Result and Discussion: A total of 101 patients with HNC of the oral cavity, salivary glands, and nasal cavity/paranasal sinuses were documented during a period under review. Charts of 76 patients were chosen for analysis. Male patients constitute 68.4% of all patients. The mean age of the study participants was 45.5 ± 19.68 SD. Patients with oral cancers were 47 years old on average. Addis Ababa had the highest proportion of patients (30%), followed by the Southern Region (27.5%). Lip and oral cavity cancers account for 63.2% of the total cases, followed by salivary gland malignancies (30.3%). SCC is the most frequent histologic type (54%), followed by adenoid cystic carcinoma (10.5%) and mucoepidermoid carcinoma (9.2%). Tobacco usage, consumption of alcohol, and chat chewing were the most frequently noted risk factors. About 27.5% of patients had cervical lymph node metastases, and Half of the patients were diagnosed with advanced-stage disease at presentation.

Abbreviations and acronyms

ALERT- All African Leprosy Research and Training Center

AJCC- American Joint Committee on Cancer

EBV- Epstein-Barr virus

HNC- Head and neck cancer

HNSCC- Head and neck squamous cell carcinoma

OC/OP SCC- Oral cavity/ oropharyngeal squamous cell carcinoma

OSCC- oral cavity SCC

MEC- mucoepidermoid cancer

TASH- Tikur-Anbessa Specialized Hospital

FNA- fine needle aspiration

BCC- basal cell carcinoma

US- Ultrasound

CT- Computer Tomography scan

MRI- Magnetic Resonance Imaging

RND- Radical neck dissection

MRND- Modified radical neck dissection

SND- Selective neck dissection

INTRODUCTION

1.1. Background

Cancer is the leading cause of mortality and an essential impediment to improving life expectancy in every country in the entire globe. Overall, the global burden of cancer incidence and mortality is constantly rising. Cancer claimed the lives of an estimated 10 million people globally in the year 2019. There is a broad variation in survival worldwide, and the causes for disparities in outcomes are multifactorial which presumably include disparities in the accessibility of early recognition and effective therapies, along with potential variations in risk factor exposure patterns.(da Cunha et al., 2023) Despite considerable clinical improvements that allow for early detection and treatment, head and neck cancers (HNCs) continue to be a serious public health problem worldwide, resulting in substantial morbidity and mortality. (Sung et al., 2021)

Head and neck cancers (HNC) encompass a diverse group of malignancies that arise from the oral cavity, nasal cavity, paranasal sinuses, nasopharynx, oropharynx, larynx, and hypopharynx. Head and neck squamous cell carcinoma (HNSCC) is the most common histologic type of HNC and it is the sixth most common cancer worldwide. About 53,000 new cases of HNSCC and 10,860 deaths from HNSCC were reported in the United States in 2019. HNC risk factors include smoking and alcohol use, EB virus infection (nasopharyngeal carcinoma), and HPV infection, particularly for oropharyngeal cancer.(Kangwen Guo et al., 2021)

The trends of head and neck cancer incidence differ considerably globally depending on cancer subtype, geographic location, age, sex, and socioeconomic status; with a higher incidence in African-Americans, males, senior citizens, and patients from low socioeconomic status ((Kangwen Guo et al., 2021); (Simard et al., 2014)). The wide variation in the worldwide incidence and mortality from HNC is mainly attributed to variations in exposure to the major environmental and behavioral risk factors. These risk factors are tobacco consumption (both smoked and ‘smokeless’), betel nut chewing, heavy alcohol consumption, and certain viral infections like human papillomavirus (HPV) and Epstein-Barr virus infections. There may be a genetic susceptibility to these environmental agents, which is compounded by various cultural dietary products high in nitroso compounds and volatile nitrosamines such as salted fish, hot spices, and certain preserved foods. Ultraviolet radiation is the most common risk factor for cancer of the lip, especially of the lower lip, irrespective of racial differences and skin complexion.

Chronic trauma to the oral mucosa from poor restorations and prostheses, as well as poor oral hygiene with a consequent heavy bacterial load in the mouth, are also reemerging as significant risk factors. It's also shown that some industrial occupational exposure to wood dust, asbestos, textiles, and leathers is associated with an increased risk of HNSCC. (Gupta et al., 2016).

By far the most commonly reported site of HNSCC in Sub-Saharan Africa was the oropharyngeal/oral cavity. From the existing studies, it is difficult to establish the roles of risk factors in HNSCC incidence in Sub-Saharan Africa. Still, the majority of patients did not use tobacco or alcohol.(C. E. Faggons et al., 2015).

1.2 Statement of the problem

Head and neck cancers (HNCs) continue to remain a significant public health burden worldwide, with the current and future estimated burden shifting to less developed regions, which may be less equipped to deal with this increasing burden. The HNCs continue causing significant mortality and morbidity despite significant clinical advances enabling their early diagnosis and treatment. This needs urgent attention from policymakers through the effective implementation of cancer control policy with population-based interventions (Gupta et al., 2016). A majority of HNC patients are diagnosed at an advanced stage (stage III and stage IV), to whom multimodality treatment is recommended, which is even more difficult to access in less developed countries (K. Guo et al., 2021). Worldwide, head and neck cancer (HNC) accounts for more than 550,000 occurrences and 300,000 deaths each year and is associated with a dismal 5-year overall survival rate of 40% to 50%.(Ilona Argirion et al., 2019) HNC is the seventh most frequent cancer in the world and causes significant morbidity and mortality, with approximately 900,000 new cases and half a million deaths reported annually. (Marwa Ahmed Balila Gebril et al., 2022)

According to GLOBOCON 2020, in Africa, an estimated 1.1 million new cases and 711,429 deaths occurred due to neoplasms in 2020.Cancer of the lip and oral cavity, nasopharynx, and salivary glands combined accounts for 2.64% of all cases (Sharma et al., 2022). In sub-Saharan and Southern Africa, HNC was the fourth most common cancer, while it ranks third in Western Africa (I. Argirion et al., 2019; M. A. B. Gebril et al., 2022). A ten-year retrospective cross-sectional study done in Lagos Nigeria, to assess the epidemiological patterns of head and neck cancers has shown that 1083 cases of head and neck malignancies were recorded. A female: male ratio of 1.01:1 was reported with a mean age of 39.6 years. The oral cavity was the most affected anatomic site (21.2%, 230/1083).

Malignant epithelial tumors accounted for 72% (779/1083) of cases seen. Carcinomas were the most common histological variant seen (67%, 726/1083), and squamous cell carcinoma accounted for 58% (421/726) of carcinomas recorded. Oral cavity malignancies (21.8%, 118/540) were the most common (O. A. Erinoso et al., 2016).

A cross-sectional retrospective study conducted to provide baseline data on the epidemiology of HNCs among patients treated at the National Cancer Institute (NCI) in central Sudan from 2016 to 2020 revealed that of the 9475 new cancer patients during the study period, 1033 (11%) had HNCs. The average age of adult patients was 54.5 years. The most common HNC sites were the nasopharynx (25.3%), hypopharynx (22.8%), and oral cavity (22.2%). Carcinoma was the most common diagnosis (87.6%), followed by lymphoma (5.6%). Most patients' tumors were at a locally advanced (22%) or metastatic stage (47%) at the time of presentation (M. A. B. Gebril et al., 2022).

There is no comprehensive national cancer registry system in Ethiopia. The only source of data on such rare cancers is hospital-based satellite studies though it does not tell the true burden. In Ethiopia, different hospital-based studies have shown increasing incidence and mortality rates from cancers in general, probably due to an increase in population size and changing lifestyles.

A systematic analysis done to evaluate the national cancer burden and trend has shown that over the last two decades in Ethiopia, there were an estimated 53,560 new incident cases, and 39,480 cancer-related deaths (Awedew et al., 2022).

Another retrospective study done at Black Lion Specialized Hospital, Oncology Center, Ethiopia from 2010 to 2015; found that of 8,580 patients who visited the oncology center, 834 patients were diagnosed with HNCs (9.7%) (Tefera et al., 2019).

1.3. Significance of the Study

The wide variation in the incidence and mortality from HNC, as well as the increasing incidence in developing countries, is mainly attributed to variations in exposure to the major environmental and behavioral risk factors; such as tobacco consumption (both smoked and 'smokeless'), the chewing of areca nut (betel nut), heavy consumption of any form of alcoholic beverage and infection with 'high risk' human papillomavirus (HPV) (Sung et al., 2021). It is not only the increasing burden and mortality associated with HNC, since mostly the disease arises from physiologically and aesthetically critical areas of our body, some surgical excision that could be done will have a significant impact on the patient's quality of life.

Some of the risk factors that are associated with the majority of the cases are modifiable and can be the basis for preventive measures, especially in a country like ours where those advanced treatments are hardly found. Early diagnosis and intervention could also not only improve mortality associated with the disease but also the morbidity of treatment from some extensive surgery required to treat advanced-stage disease. The absence of a national cancer registry makes it difficult to know the true incidence and impact of HNC in Ethiopia. This study will help to provide baseline information for health policymakers to plan for the future development of a national cancer registry and to draw possible community-based preventive measures for head and neck cancers in particular.

2. LITERATURE REVIEW

Worldwide, head and neck cancer (HNC) accounts for more than 878,348 new cases and more than 444,347 deaths in 2020 throughout the world, and the 5-year overall survival rate is a dismal 40% to 50%. HNC is the eighth most common cancer in the world, and the highest incidence is observed in South and Southeast Asia. (Sung et al., 2021) (I. Argirion et al., 2019) A total of 53,000 new cases and 10,860 HNC-related mortality were observed in the U.S. in 2019. According to the estimation of the World Health Organization, 439,000 mouth and oropharynx cancers will be observed in 2030. This study also shows that there are increasing disparities in the incidence trend and survival rate of head and neck cancers depending on race, age, sex, and socio-economic status: higher incidence and mortality rate in black, male, and senior citizens with poor socio-economic status. (K. Guo et al., 2021)

The most common histologic subtype of HNC is head and neck squamous cell carcinoma (HNSCC), accounting for more than 90% of all cases. Even though HNSCC accounts for 5-10% of all new cases of cancer in Northern America and Europe, there is a broad geographic disparity in the incidence and anatomic distribution of HNSCC globally, owing essentially to demographic differences in tobacco and alcohol consumption behaviors, which play a role in the development of nearly 80% of all HNSCC diagnosed internationally. Though the overall prevalence of HNC is decreasing in industrialized nations due to lower smoking rates, there has been a recent increase in HPV infection-related instances of oropharyngeal SCC. (N. Vigneswaran & M. D. Williams, 2014)

Cancer is becoming more prevalent in Africa as a result of aging and population growth, as well as a rising number of risk factors that accompany a shift in the economy, such as smoking, being overweight or obese, inadequate physical activity, and contraceptive practices. According to United Nations population forecasts, Africa's population is expected to grow by 50% between the year 2010 and the year 2030 (from 1.03 billion to 1.52 billion) and by 90% for those older than 60 years (from 55 million to 105 million), the age group in which malignancy becomes increasingly prevalent. (Jemal et al., 2012) A retrospective study done in Sudan from 2016 to 2020 shows that head and neck cancer accounts for around 11% of all new cancer diagnoses of whom 74.2% were adults. The mean age of diagnosis was 55 years and around 60% of patients were male. The most common HNC sites were the nasopharynx (25.3%), hypopharynx (22.8%), and oral cavity (22.2%). The most common histologic subtype was carcinoma (87.6%), followed by lymphoma (5.6%). The majority of the patients presented with either locally advanced (22%) or metastatic disease (47%) as initial presentation. (M. A. B. Gebril et al., 2022).

A hospital-based institutional research study done in Tanzania between 2012 and 2013 to determine the pattern and prevalence of HNC found that HNC accounted for around 3% of all cases. Males were affected twice as often as females. The average age of patients at the time of diagnosis was 51 years. The commonest affected anatomical site was the nasal and paranasal sinuses (23.9%) followed by the larynx (20%). Carcinoma was responsible for 94% of head and neck malignancies, with squamous cell carcinoma being the most common (74%). Lymphoma (2%) was the least common histologic variant seen. (Mwansasu et al., 2015).

A ten-year retrospective cross-section study done at two teaching hospitals in Nigeria has shown that the incidence of head and neck cancer was approximately 99 cases/year within the state with similar prevalence among females and males and mean age of diagnosis of approximately 40 years. The commonest subsites affected were the oral cavity (21.2%) and the commonest histologic variant was squamous cell carcinoma (58%) (O. A. Erinoso et al., 2016). A review of the literature on the incidence of head and neck squamous cell carcinoma in Sub-Saharan African countries over a 20-year period revealed that the oropharyngeal and/or oral cavity were the most common sites resulting in more than 90% of all cases. The mean or median age of patients varied from country to country with the lowest in Kenya (37 years) and the oldest in Ghana (58 years). An exclusive study of HIV-infected patients with HNSCC in Kenya found that the average age was 37. In a population of OC/OP SCC from Congo, the youngest mean age was 46 years. The male-to-female ratio is also variable among Sub-Saharan African countries ranging from; 0.5:1 in Congo to 4:1 in South Africa. In general, males were 2.3 times more likely than females to develop OC/OP SCC. The mandibular or maxillary alveolar ridge was the most frequently involved OC/OP subsite (13%), followed by the tongue (10%). Eleven percent of patients had the degree of differentiation described. The percentages of carcinomas that were well-differentiated, moderately differentiated, and poorly differentiated were 42%, 37%, and 25%, respectively. About 4.8% of all cases had SCC of the nasopharynx, nasal cavity, or paranasal sinuses. Laryngeal SCC was diagnosed in 4.5% of all patients, while hypopharyngeal SCC was found in just 0.8% of all instances. In 862 patients with relevant data, 43% used smoking and 42% utilized alcohol, with reported usage varying considerably and being more common in laryngeal SCC than oropharyngeal/oral SCC. (C. E. Faggons et al., 2015)

In a country like Ethiopia, where there is no proper national cancer registry system, knowing the true incidence and/or pattern of let alone the rare pathologies such as head and neck cancers, but other common malignancies, is challenging.

A systematic analysis of the national cancer burden and trend in Ethiopia over the last two decades revealed an estimated 53,560 new occurrences and 39,480 fatalities due to cancer. Between 2010 and 2019, the cancer incidence, mortality, and disability-adjusted life years, all increased by 32%, 29%, and 19%, respectively. (Awedew et al., 2022)

A review of pathology specimens from the University of Gondar Specialized Comprehensive Hospital between 2014, and 2015 discovered that 16.7% of the cases were malignant, with head and neck squamous cell carcinoma accounting for 9.4% and salivary gland malignancies representing 2.2% of the cases.(Tefera et al., 2016) A hospital-based retrospective study done to review the epidemiology of primary head and neck cancer in Black Lion Specialized Hospital, Oncology Center, Ethiopia from 2010 to 2015 found that out of 8,580 patients visited the oncology center, 834 patients were diagnosed with HNCs (9.7%). The median age at diagnosis was 46 with a male-to-female ratio of 2:1. Oral cavity and oropharynx cancer is the commonest in both sexes. The prevalence of salivary gland malignancy is relatively equal in both males and females. Squamous cell carcinoma was the most common histologic type accounting for 91.3% of all HNCs. Mucoepidermoid carcinoma was the most frequently diagnosed salivary gland malignancy with a prevalence of 32.5% (Tefera et al., 2019)

3. OBJECTIVES

3.1. General Objectives

- To assess the patterns of head and neck cancers of the lip and oral cavity, nose, paranasal sinuses, and salivary glands over the past 8 years (from May 2015 to May 2023) at ALERT Comprehensive Specialized Hospital, Plastic Surgery Unit, Addis Ababa Ethiopia.

3.2. Specific Objectives

- To determine the patterns of head and neck cancers concerning the anatomic site of origin
- To estimate the gender and age distribution of patients with HNCs
- To identify common histologic types of head and neck cancers in patients with HNC diagnosis
- To determine risk factors and stage of the disease at presentation in patients with HNCs

4. METHODOLOGY

4.1 Study Area and Study Period

4.1.2 Study Area

The study was conducted at ALERT Comprehensive Specialized Hospital, plastic surgery department. The hospital is located in Addis Ababa, Ethiopia. It was opened in 1932 and was originally for the treatment of leprosy; the All-Africa Leprosy Rehabilitation and Training Center (hence the acronym). Currently, the hospital has expanded to include multiple specialties. It is a teaching institution for plastic and reconstructive surgery affiliated with Addis Ababa University. ALERT hospital serves as few and biggest national referral centers for plastic surgery cases, including head and neck malignancies.

4.1.3- Study Period

- September 1, 2023 to October 30, 2023.

4.2- Study Design

- Hospital-based retrospective cross-section chart review

4.3. Source Population.

- All patients who were seen and/or treated at the plastic and reconstructive surgery unit, from May 1, 2015 to May 1, 2023.

4.4. Study Population.

- All Patients with a histologic diagnosis of head and neck cancers seen from May 1, 2015, to May 1, 2023, at ALERT comprehensive specialized hospital, plastic, and reconstructive surgery department who fulfilled inclusion criteria.

4.5. Inclusion and Exclusion Criteria

4.5.1. Inclusion Criteria

- All patients with clinical and histologic diagnoses of cancers of the head and neck (Lip and oral cavity, nasal cavity and paranasal sinuses, and salivary glands) whose charts were complete.

4.5.2. Exclusion Criteria

- Incomplete records
- Those patients with benign histologic diagnosis.
- Patients with HNC arising from the cutaneous part, hypopharynx, larynx, and thyroid anatomic subsites
- None Ethiopian Citizens

4.6. Sample Size determination and sampling technique

- All patients with diagnosis of specified HNC who fulfilled the inclusion criteria were included

4.7. Data Collection Instruments and Techniques

- Medical record numbers of all patients with the histologic diagnosis of the specified HNC were first retrieved from Operation Theatre, Plastic Surgery wards, and OPD logbooks, and Liaison office admission lists. The patient's medical charts were retrieved from record room, using medical record numbers. A pilot study done on 10% of charts and few adjustments of the questionnaire were made depending on the available information on the patient's records. Data was collected by using a semi-structured questionnaire on EpiData version 4.

4.8. Variables

4.8.1. Dependent Variables

- Head and neck cancer (Histologic types, Anatomic sites and Clinical stage)

4.8.2. Independent Variables

- Age
- Sex
- Address
- Duration of complaint
- Tobacco smoking
- Alcohol consumption
- Radiation

4.9. Operational Definitions

➤ **Head and Neck Cancers-**

The definition of head and neck cancers varies across different scientific literatures and textbooks. Many textbooks and research journals define HNC as malignant tumors of the Upper aerodigestive tract, Sinonasal cavities, Salivary glands, and Thyroid(Chung, 2019; C. Faggons et al., 2015; Marwa Ahmed Balila Gebril et al., 2022). To address this inconsistency and ambiguity in nomenclature, as well to standardize statistical reporting, World Health Organization (WHO)- International Classification of Disease (ICD-10) for oncology defined Head and neck cancers as a diverse group of malignancies that involve head and neck regions such as lip and oral cavity, hypopharynx, nasopharynx, nasal cavity and middle ear, Paranasal sinuses, larynx, salivary gland tumors and other ill-defined region of the head and neck. (O. Erinoso et al., 2016; Gormley et al., 2022)

- Oral cavity- from lip mucocutaneous junction anteriorly to the junction of hard and soft palate and circumvallate papillae posteriorly
- Radical neck dissection (RND)- removal of lymph nodes from level I-V and Sternocleidomastoid muscle (SCM), Internal Jugular vein (IJV), and Spinal accessory nerve (SAN).
- Modified RND- removal of lymph node levels described for RND with preservation of at least one of the three non-lymphatic structures
- Functional neck dissection- all three non-lymphatic structures are preserved
- Selective neck dissection (SND)- when one or more lymph node levels which primarily removed in RND are spared.
- Elective neck dissection- neck dissection done for clinically node-negative (N0) HNC
- Therapeutic neck dissection- type of neck dissection done for HNC with positive neck nodal disease
- Clinically node-negative (cN0)- No palpable lymph node on examination or enlarged (>1cm) lymph nodes on imaging studies like the US, CT/scan, or MRI.
- Wide local excision- removal of the tumor with margins of healthy-looking surrounding tissues in all dimensions depending on international guidelines recommendation
- Tumor size- the greatest diameter of the tumor

4.10. Data Quality

Pilot study was done, the data collection format (semi-structured questionnaire) was cross-matched with available information on records and the questionnaires were rearranged as necessary. The collected data were recorded on EpiData version 4 software. Daily completeness of the data was cross-checked. All the data was collected by the principal investigator

4.11. Data Analysis.

After completion of data collection, data were exported from EpiData version 4 to SPSS version 26 software. The data were processed and checked for completeness, clarity, and consistency. Descriptive statistical analysis using numbers, percentages, means and ranges were done. The association was measured by using P- value with a 95% confidence interval.

4.12. Ethical Consideration

Ethical clearance was obtained from Addis Ababa University and ALERT Hospital Ethical Clearance Committee and an official letter was submitted to the unit to secure permission. Therefore, informed consent for the study was not taken from the study subjects. The principal investigator will make sure that the confidentiality of the information will be assured in such a way that no disclosure of any name of the patient, or the health care provider will be made about the finding.

4.13. Dissemination Plan

The results of the study with their respective discussions, interpretations, and recommendations will be disseminated to TASH, the School of Medicine, Surgery Department, ALERT Hospital Plastic and Reconstructive Surgery Unit, and any policy-making body to whom the result may apply. Finally, there will be a plan to publish in national or international journals.

5. RESULT

5.1. Demography of the Patients

During the period under review; a total of 101 patients with a diagnosis of Head and Neck cancers specifically from anatomic subsites of the oral cavity, nasal cavity and paranasal sinuses, and salivary glands were found recorded in different hospital registration books. From a total of 101 patients, medical charts of 15 patients were lost and 10 charts were found to be incomplete. The remaining 76 patients were selected for analysis.

Males account for 68.4% (52) of the patients in the study, while females account for 31.6% (24), with a male-to-female ratio of 2.2:1 (Fig.1). The mean age of the study participants was 45.5 ± 19.68 SD with a range of 1 to 86 years. The majority of the patients (43.4%) are between the ages of 41 and 60 years. Those under the age of 20 account for 13.2% (10), while those aged 61 and above account for 22.4% (17). (Table 1, Fig-2)

The majority of the patients were from Addis Ababa 23 (30.3%), followed by Southern Region 21 (27.6%), and Oromia Region 18 (23.7%) (Table 2)

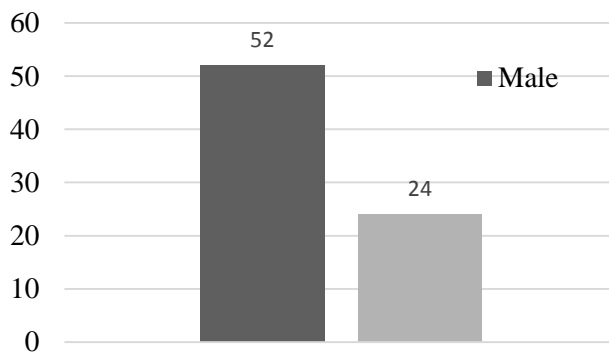


Figure 1. Sex of the patients

Table 1: Frequency of different age groups

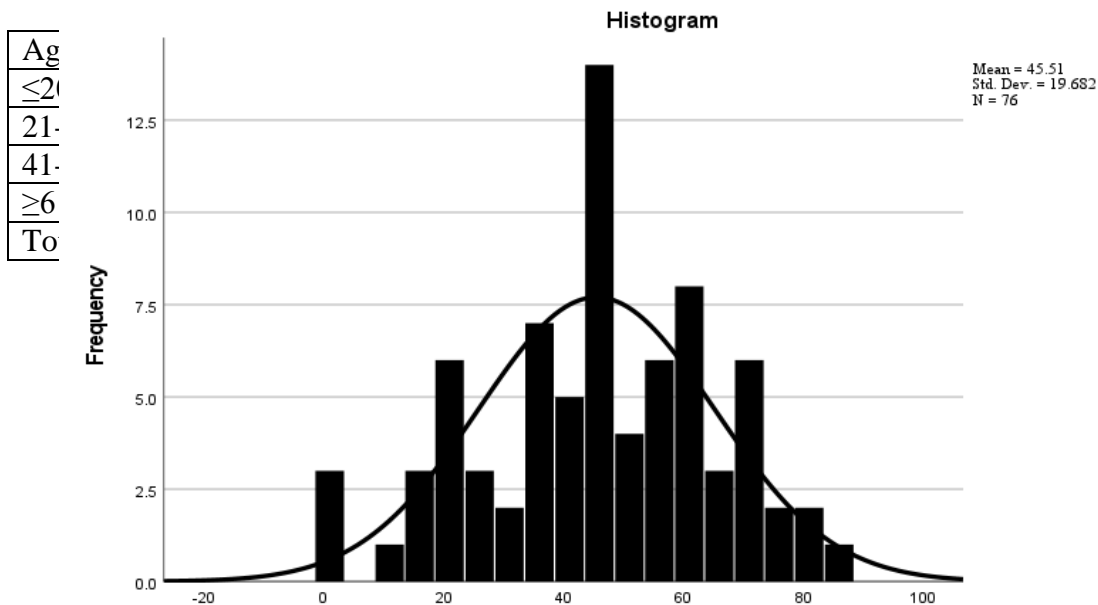


Figure 2. Distribution of age at diagnosis

Table 2: Address of the Patients of patients with Lip and oral cavity, nasal cavity and paranasal sinuses, and salivary gland cancers at Alert Hospital, Ethiopia, May 2015 to May 2023

Address	Frequency	Percent
Oromia	18	23.7
Harari	1	1.3
Amhara	6	7.9
SNN Region	21	27.6
Dire Dawa	2	2.6
Addis Ababa	23	30.3
Afar	2	2.6
Somali	3	3.9
Total	76	100.0

5.2. Clinical Presentation

The majority of the patients' initial complaints were swelling, ulceration, and/or bleeding (Table 3). At the initial visit, 22% of patients with parotid gland cancers showed signs of facial paralysis. Fifty-seven percent of patients presented with a complaint that had lasted more than a year (Fig 3). Only 7% of individuals seek medical attention within 6 months after the commencement of symptoms.

Table 3- Frequencies of different presenting complaints of patients with Lip and oral cavity, nasal cavity and paranasal sinuses, and salivary gland cancers at Alert Hospital, Ethiopia, May 2015 to May 2023

		Responses	
		N	Percent
Clinical presentation	Swelling	65	45.8%
	Dysphagia	5	3.5%
	Ulceration and/or bleeding	42	29.6%
	Discharge	4	2.8%
	Discoloration	5	3.5%
	Pain	8	5.6%
	Oral malodor	13	9.2%
Total		142	100.0%

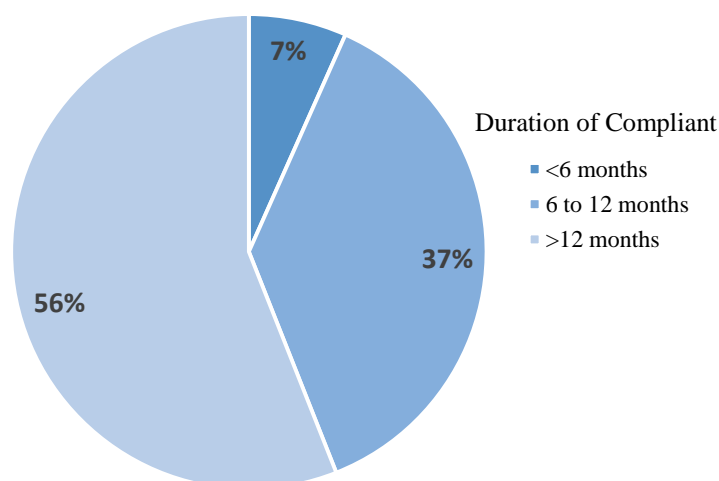


Fig 3. Frequency of total duration of complaint from symptom onset to hospital visit

5.3. Risk Factors

Approximately 48.7% of patients in the study had one or more risk factors for head and neck cancer. Among the indicated risk factors, cigarette smoking was observed in 31.6% of all patients, either alone or in conjunction with alcohol drinking and/or chat chewing. Among individuals with lip and oral cavity malignancies, 14.6% had recurrence after earlier surgery for similar lesions, while another 6.3% had xeroderma pigmentosum. Other risk factors, such as childhood extensive exposure to sunlight, oral hygiene status, occupational exposures, etc were not documented.

About 52.5% of patients with lip and oral cavity squamous cell carcinoma had a history of tobacco smoking, with concomitant chronic alcohol usage in 27.5%. Chat chewing is another common behavior, with 27.5% of all oral cavity SCC patients engaging in it.

5.4. Anatomic subsites and Tumor characteristics

The lip and oral cavity cancers are responsible for 63.2% (48) of the subjects of the study, followed by salivary gland cancers (30.3%). Only 6.6% (5) of the cases had malignancies of the nasal cavity and paranasal sinuses. Lip cancers constitute 39.5% (30) of all reviewed patients and 62.5% of all oral cavity lesions, with buccal mucosa and oral tongue accounting for 14.6% (7) and 12.5% (6) of cases, respectively. The Parotid gland had the highest rate of salivary gland malignancy, representing 78.3% of all salivary gland cancers. Submandibular and minor salivary gland cancers totaled 6.5% (5) of all cases. (See **table 4**)

The study also revealed that the median age of patients with lip and oral cavity cancers was 47 years. The youngest patient was one year old and the oldest was 86 years. Two third of patients with lip and oral cavity cancers are male with male to female ratio of 2:1.

At presentation, the diameter of the tumor measured clinically or on imaging as the greatest dimension was between 2 and 4 cm in 47.4% of the patients. Tumors with a diameter of more than 4 cm at presentation account for 40.8% of all. (Table 5) Patients having tumors with a depth of invasion of more than 4 mm, as determined by imaging and/or pathologic examination, account for 84.2% (64) of all study patients. About 82.5% of patients with OSCC had tumor depth of invasion of more than 4mm at diagnosis. (Table 5) There was a clinical extension of the tumor to adjacent structure(s) in 31.6% (24) of the studied patients.

Cervical clinical lymphadenopathy (LAP) or enlarged cervical lymph node(s) on preoperative imaging was detected in 42% (32) of patients on first visit. (See **Fig 4**) Among those with clinically positive cervical lymph node(s), only 2 patients had lymph node(s) with a diameter greater than 3cm.

Histopathology from all 76 cases was reviewed. Squamous cell carcinoma is responsible for the majority (53.95%) of all histologic diagnoses; followed by adenoid cystic carcinoma and mucoepidermoid carcinoma, each accounting for 10.5% and 9.2% respectively. SCC is also the most frequent histologic subtype of lip and oral cavity cancers, accounting for 83.3%. (**Table-6**)

Nearly half (47.9% /23) of oral cavity cancer patients present with clinically palpable and/or enlarged cervical lymph node(s) at first visit. cases. Lip and oral cavity SCC is the most common

histologic type (26.3%) which presents with clinical cervical lymphadenopathy, followed by sarcoma and adenoid cystic carcinoma each accounting for 3.95%. There was one case of metastatic BCC. Cervical lymphadenopathy was observed in 30.4% of all patients with salivary gland malignancies. (See **Table 7**) The patterns of lymphadenopathy among the study population were ipsilateral in 75% (24) and bilateral in 25%.

Clinical staging of the cancers at presentation was also reviewed and half of the patients (50.1%) had advanced disease (stage IV and stage III) upon initial evaluation. Only 9.2% (7) present with stage I disease at initial diagnosis. (**Table-8**)

The presence of clinically suspected or confirmed distant metastasis on imaging was found in 3.9% (3) of the cases. Proven cervical lymph node metastasis from the primary tumor was confirmed in 27.6% (21). Approximately 34% of patients with clinically positive cervical lymphadenopathy were found to be reactive on post-operative histopathology analysis. All lymph node samples from elective neck dissection were also found to be free of malignancies. (**Fig.5**)

Table 4- Anatomic subsites cancers in patients with Lip and oral cavity, nasal cavity and paranasal sinuses, and salivary gland cancers at Alert Hospital, Ethiopia, May 2015 to May 2023

		Frequency	Percent (total cases)	Percent (Oral cavity)
Oral Cavity	Upper lip	9	11.8	18.8
	Lower lip	21	27.6	43.8
	Oral tongue	6	7.9	12.5
	Alveolar ridge/gingival mucosa	2	2.6	4.2
	Buccal mucosa	7	9.2	14.6
	Hard palate	3	3.9	6.3
	Total	48	63.2	100.0
Salivary Glands	Parotid	18	23.7	78.3
	Submandibular	3	3.9	13
	Minor	2	2.6	8.7
	Total	23	30.2	100
Nasal cavity & paranasal sinuses		5	6.6	
Total		76	100	

Table 5: Size of the tumor at presentation and depth of invasion

Tumor size		Frequency		Percent					
	≤2cm	9		11.8					
	2-4cm	36		47.4					
	>4cm	31		40.8					
	Total	76		100.0					
Depth of invasion * Lip and Oral cavity cancer Crosstabulation									
		Lip and Oral Cavity Cancers						Total	
		SCC		Sarcoma		BCC			
		N	%	N	%	N	%	N	%
Depth of invasion	<4mm	4	10	0	0	1	25	5	10.4
	≥4mm	33	82.5	4	100	3	75	40	83.3
	Not documented	3	7.5	0	0	0	0	3	6.3
Total		40	100	4	100	4	100	48	100

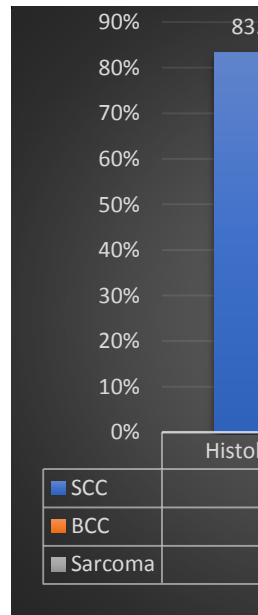
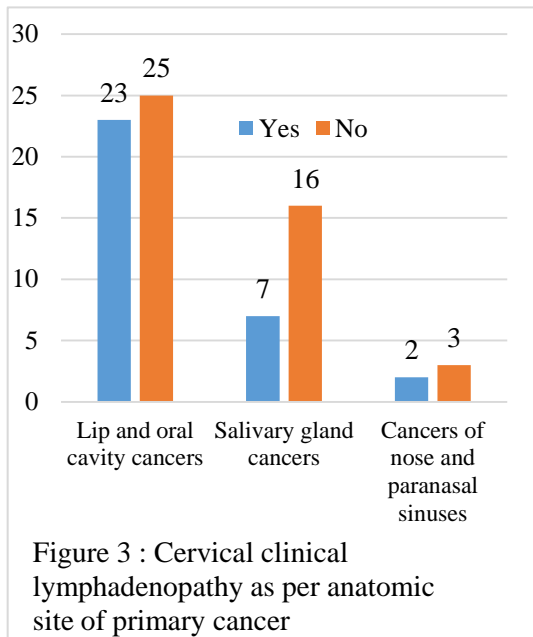


Table 6: Histologic features of head and neck cancers

	Histologic types	Frequency	Percent	Percent
Oral cavity	SCC	40	52.6	
	Sarcoma	4	5.3	
	BCC	4	5.3	
	Total	48	63.2	
Salivary gland malignancies	Mucoepidermoid Carcinoma	7	9.2	
	Adenocarcinoma	1	1.3	
	Adenoid cystic carcinoma	8	10.5	
	Acinic cell carcinoma	4	5.3	
	Mixed malignant tumor	1	1.3	
	Carcinoma Ex-pleomorphic adenoma	1	1.3	
	Malignant sialoblastoma	1	1.3	
	Total	23	30.3	
Nasal cavity and paranasal sinuses	Lymphoma	2	2.6	
	SCC	1	1.3	
	BCC	1	1.3	
	Nasal neuroblastoma	1	1.3	
	Total	5	6.6	
Total		76	100.0	

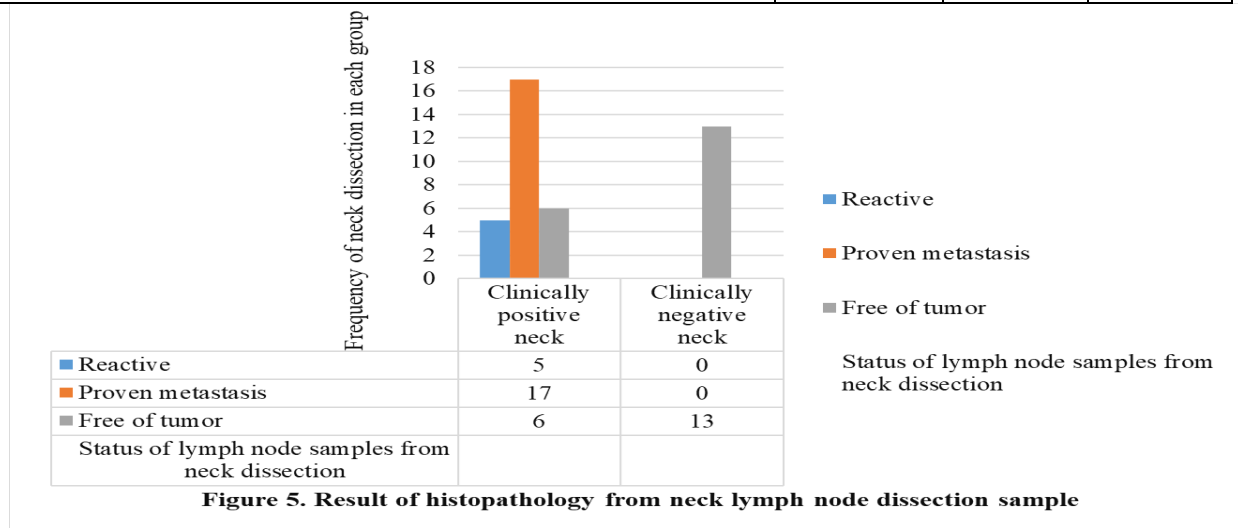


Table 7: Presence of clinical cervical lymphadenopathy according to anatomic sites and histologic subtypes

		Clinically palpable and/or enlarged Cervical Lymph node on neck imaging				Total
		Yes	%	No	%	
Lip and oral cavity cancers	SCC	20	41.7	20	41.7	40
	Sarcoma	3	6.3	1	2.1	4
	BCC	0		4	8.3	4
Total		23	47.9	25	52.1	48
Salivary Gland tumors	Mucoepidermoid Carcinoma	2	8.7	5	21.7	7
	Adenocarcinoma	1	4.4	0		1
	Adenoid cystic carcinoma	3	13	5	21.7	8
	Acinic cell carcinoma	1	4.3	3	13	4
	Mixed malignant tumor	0		1	4.4	1
	Carcinoma Ex-pleomorphic adenoma	0		1	4.4	1
	Malignant sialoblastoma	0		1	4.4	1
Total		7	30.4	16	69.6	23
Nasal cavity and paranasal sinuses	lymphoma	1		1		2
	SCC	0		1		1
	BCC	1		0		1
	Nasal Neuroblastoma	0		1		1
Total		2		3		5

Table 8: Clinical stage of the cancers at diagnosis

Clinical Stages	Frequency	Percent
Stage IVA	21	27.6
Stage III	17	22.4
Stage II	20	26.3
Stage-I	7	9.2
Others	11	14.5
Total	76	100.0

5.5. Provided Treatments

The primary malignancies of 96.1% (73) of the studied subjects were managed surgically. The remaining 3 patients were referred to oncology. Among those who underwent surgery, wide local excision with a clinically negative margin was possible in 86.3% (63) of patients. Only debulking surgery was possible in the remaining 13.7% (10). Neck dissection was done for a total of 41(56.2%) of surgically managed patients out of which 13 (31.7%) were elective/prophylactic. Functional neck dissection (Modified radical neck dissection-type III) was the most frequently performed neck dissection accounting for 58.5%.

5.6 Correlation Analysis

Cross-tabulation and Chi-square test were done to see if there is any association between advanced-stage disease (stage III & IV) at initial diagnosis and the patient's delayed health seeking after 12 months of symptom onset. (**Table 9**). The test showed that there is a statistically significant association between a delay in hospital visits of more than 12 months since symptom onset and the chance of having advanced-stage disease with a p-value of 0.03 (which is <0.05).

Table 9: Cross-tabulation of clinical stages of the disease and duration of complaint

Clinical stages * Duration of complaint Crosstabulation							
		Duration of complaint				Total	
		≤12 months		>12 months		N	%
		N	%	N	%		
Disease Stage	Early stages (I&II)	17	50.0%	9	21.4%	26	34.2%
	Advanced stages (III & IV)	13	38.2%	25	59.5%	38	50%
	Un staged	4	11.8%	8	19%	12	15.8%
Total		34	100%	42	100%	76	100%

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	6.818a	2	0.033	0.036		
Likelihood Ratio	6.873	2	0.032	0.036		
Fisher-Freeman-Halton Exact Test	6.663			0.036		
Linear-by-Linear Association	5.114b	1	0.024	0.028	0.017	0.010
N of Valid Cases	76					

a. 0 cells (0.0%) have an expected count of less than 5. The minimum expected count is 5.37.

b. The standardized statistic is 2.262.

Tumor size * Cervical LAP Crosstabulation					
			Clinically Cervical LAP		Total
			Yes	No	
Tumor size	≤2cm	Count	0	7	7
		% Of Total	0.0%	14.6%	14.6%
	2-4cm	Count	11	9	20
		% Of Total	22.9%	18.8%	41.7%
	>4cm	Count	12	9	21
		% Of Total	25.0%	18.8%	43.8%
Total		Count	23	25	48
		% Of Total	47.9%	52.1%	100%

Chi-Square Tests			
	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	7.558 ^a	2	.023
Likelihood Ratio	10.251	2	.006
Linear-by-Linear Association	4.594	1	.032
N of Valid Cases	48		
a. 2 cells (33.3%) have an expected count of less than 5. The minimum expected count is 3.35.			

The correlation between the size of the tumor; measured as the greatest diameter and the presence of clinically palpable cervical lymph nodes were tested for oral cavity cancers with the Pearson chi-square test. There was a significant association found with a likelihood ratio of 0.006 (level of significance 0.05).

6. DISCUSSION

Sub-Saharan Africa is experiencing a rapidly increasing burden of cancer-related morbidity and mortality. While annual deaths in the region resulting from human immunodeficiency virus (HIV), tuberculosis, and malaria are steadily declining, cancer-related deaths are projected to increase by 85% by 2030. Early cancer detection through screening, understanding of tumor biology and pathogenesis, as well as improved treatments and supportive care, have contributed to increasing cancer survivorship in developed countries. However, cancer patients in sub-Saharan Africa have largely not benefited from these advances and outcomes remain poor because of severely limited resources for diagnosis and treatment, as well as possible differences in the etiology and pathogenesis of cancer in this region. (C. Faggons et al., 2015) Understanding the pattern of HNC will have important implications for prevention and could form cancer management policies.

The definition of head and neck cancers varies across different scientific literatures and textbooks. Most textbooks and research journals define HNC as malignant tumors of the Upper aerodigestive tract, Sinonasal cavities, Salivary glands, and Thyroid (Chung, 2019; C. Faggons et al., 2015; Marwa Ahmed Balila Gebril et al., 2022). To address this inconsistency and ambiguity in nomenclature, as well to standardize statistical reporting, World Health Organization (WHO)-International Classification of Disease (ICD-10) for oncology defined Head and neck cancers as a diverse group of malignancies that involve head and neck regions such as lip and oral cavity, hypopharynx, nasopharynx, nasal cavity and middle ear, Paranasal sinuses, larynx, salivary gland tumors and other ill-defined region of the head and neck. (O. Erinoso et al., 2016; Gormley et al., 2022)

In this study, we evaluated the patterns of Head and neck cancers of the oral cavity, nasal cavity paranasal sinuses, and salivary glands at tertiary referral hospital. Other head and neck anatomic subsites were not included because they are not treated in our unit and most of them go to Hospitals with otorhinolaryngology service.

This study reveals that the incidence of head and neck cancers among study groups was more common in males 68.4% (52) than females with the male to female ratio of 2,2:1. This finding is similar to the findings from multiple other studies. (Andreano et al., 2018; C. Faggons et al., 2015; Kangwen Guo et al., 2021; Mwansasu et al., 2015)

In our study, the mean age of study subjects was **45.5±19.68** SD with a range of 1 to 86 years. Most of the patients (43.4%) are between the ages of 41 to 60 years. Those younger than 20 years account for 13.2% (10) of all patients and about 22.4% (17) are 61 years or older.

This finding is almost the same as a similar study done at Tikur Anbessa Hospital which also stated the mean age of their patients to be 44.56 ± 16.47 with a peak prevalence in the 5th and 6th decades (41-60 years). (Tefera et al., 2019). The review study done in Sub-Saharan African countries also confirms a similar age distribution to our study with the mean or median age of HNSCC patients in the Sub-Saharan region ranging from 37 years in Kenya and 58 years in Ghana. (C. Faggons et al., 2015) However; the mean age of our patients is younger than what has been shown in different Western studies. (Andreano et al., 2018; Ribeiro et al., 2015; Nadarajah Vigneswaran & Michelle D Williams, 2014)

The duration of symptoms was analyzed and it showed that the majority of patients (56%) came with delayed presentation of more than a year. Delayed presentation is true for more concealed areas like the nasopharynx, oropharynx, or laryngeal cancers. Unlike our findings, lip and oral cavity cancers as well as salivary gland cancers are usually more likely to be detected early. (Chung, 2019) However; the finding in our study is similar to the study done in India. (Kulkarni, 2014)

Lip and oral cavity carcinomas account for 63.2% of our study subjects, the finding which is also similar to the study done in India, (Kulkarni, 2014), but contrary to the result of a similar study done in Tanzania and Sudan where sinonasal cancers were the most common. (Marwa Ahmed Balila Gebril et al., 2022; Mwansasu et al., 2015) Salivary gland malignancies were responsible for (30.3%). This is slightly similar to the finding from a study done in Cameroon (Sando et al., 2016), but much higher than the incidence reported in other studies. (Yoo et al., 2015)

The higher incidence of salivary gland cancers in our study is justified probably by the limited head and neck anatomic sites reviewed and the small number of patients in our study. Salivary gland malignancies involved the Parotid gland in 78.3% of the cases and were twice more common in men than females in this study group. This gender predilection is similar to the finding of a study done in Togo (Amana et al., 2014); but opposite to what is observed in other African studies. (Alsanie et al., 2022; Omitola et al., 2019; Parkins et al., 2021) In all these studies the most commonly involved gland is similar.

Squamous cell carcinoma is the most frequent histologic finding in our study accounting for 54% of all reviewed cases and 83.3% of all lip and oral cavity cancers. A similar pattern is also true in multiple other regional and international studies. (C. Faggons et al., 2015; Marwa Ahmed Balila Gebril et al., 2022; Mwansasu et al., 2015; Tefera et al., 2019).

From the oral cavity anatomic subsites involved, the lip contributed nearly two-thirds (62.5%) of the cases in this study. The incidence of OSCC among different anatomic subsites of the oral cavity is widely variable depending on demographic status, the most common site being the tongue in the U.S mainly smoking-related (Nadarajah Vigneswaran & Michelle D Williams, 2014), buccal mucosa is the most common site in Asian countries where the habit of betel nut chewing highly prevalent(Kulkarni, 2014; Shrestha et al., 2020). The difference in our study could be explained by probably a small number of patients.

Known head and neck cancer predisposing factors were found to be positive in nearly half of the patients in our study with tobacco smoking and chronic alcohol consumption the most frequently identified factors in patients with lip and oral cavity cancers. This observation is similar with multitude of other studies.(C. Faggons et al., 2015; Marwa Ahmed Balila Gebril et al., 2022; Kulkarni, 2014; Shrestha et al., 2020)

The result of our study also showed that 42.1% of the study subjects had clinically enlarged cervical lymphadenopathy among which 27.6% was proven to harbor metastasis from the primary tumor at initial presentation. This percentage is slightly lower than the finding from the population-based study done in China in which 38.6% of patients had confirmed pathological cervical lymph node metastasis. (Zhang et al., 2022)

Oral cavity cancers were found to be associated with a high incidence of cervical metastasis on presentation, compared to the other anatomic sites in our patients. Similar findings of early lymph node metastasis of oral cavity SCC were observed in other studies too. (Kangwen Guo et al., 2021; Gupta et al., 2016; Kulkarni, 2014)

In this study half of the patients were found to have advanced-stage disease (stage III & IV) at the time of diagnosis which is probably linked with delayed patient visits to health facilities as observed from the study. This presentation of head and neck cancer patients with advanced-stage disease is a common scenario observed in multiple other studies from the developing world. (Marwa Ahmed Balila Gebril et al., 2022; Kulkarni, 2014; Tefera et al., 2019)

7. STRENGTH AND LIMITATIONS OF THE STUDY

7.1. Strength of the Study

One major strength of this study is a long study period of 8 years, so as many patients as possible were tried to be included in the study in order to give the actual picture of the problem under study. The other is since the study is done at a national referral center for most of those cancers it will give the idea of disease distribution patterns in different regional states.

7.2. Limitations

- The study is retrospective, so it provides lower evidence compared with prospective studies and is prone to bias.
- Medical charts of approximately a quarter of the patients (24.8%) were either incomplete or lost and excluded from the study which could probably affect the result of the study.
- Some of the data planned to be gathered as part of the evaluation for the research question were missing from the retrieved charts which forced us to restructure our data collection tool.

8. CONCLUSION AND RECOMMENDATION

8.1. Conclusion

In conclusion, head and neck cancers of the lip and oral cavity, salivary glands, and nasal cavity/paranasal sinuses were more common in males than females with the highest incidence occurring in those 40 to 60 years of age. Oral cavity cancers account for the majority of the cases. Nearly one-third of patients present with proven cervical lymph node metastasis and half of the patients have advanced-stage disease at diagnosis. There was a significant delay between the onset of symptoms and the patient's arrival at our hospital. Surgery was the primary means of management for almost all patients.

8.2. Recommendation

To ALERT Comprehensive Specialized Hospital

- Digitalization of patient data for easy access and to avoid the problem of lost charts
- To take the role of leading larger, more inclusive, prospective studies that can be representative and can answer the question of why there is a delay between disease onset and final treatment as identified in this study

To researchers

- Disseminate the result of this study for those who may use the information
- Plan and undertake wider prospective studies

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