A 20-YEAR HISTOPATHOLOGIC AUDIT OF ORAL AND MAXILLOFACIAL DISEASES AT TWO REFERRAL CENTRES IN NAIROBI, KENYA (2001-2020)

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List of abbreviations

FNAC:	Fine Needle Aspiration Cytology
HIV/AIDS:	Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome
HPV:	Human Papillomavirus
ICD-10:	International Classification of Diseases-Tenth Revision
KNH:	Kenyatta National Hospital
KNH-UoN ERC:	Kenyatta National Hospital-University of Nairobi Ethics and Research Committee
OSCC:	Oral Squamous Cell Carcinoma
OMFDs:	Oral and Maxillofacial Diseases
OMFLs:	Oral and Maxillofacial lesions
OMF:	Oral and Maxillofacial
SPSS:	Statistical Package for Social Sciences
UoNDH:	University of Nairobi Dental Hospital
WHO:	World Health Organization

Definition of terms

Oral and maxillofacial lesions: Refers to pathologies affecting the hard and soft tissues of the oral cavity, jaws and the face.

Histopathology: The study and diagnosis through examination of alterations in tissues and or cells associated with a disorder by viewing processed specimens using a microscope.

Categories: A class or division of items regarded as having particular shared characteristics.

Disease: a disorder of structure or function in a human, often affecting a specific anatomical location with specific symptoms and not simply a direct result of physical injury.

Malignancies: Dysmorphic proliferation of tissues with potential for continuous autonomous growth and ability to infiltrate adjacent tissues and metastases to distant organs.

Oral squamous cell carcinoma: A malignant epithelial neoplasm affecting tissues of the oral cavity.

Benign tumours: Dysmorphic proliferation of tissues with potential for continuous autonomous growth.

Odontogenic tumours: A group of lesions, benign or malignant, that originate from remnants of epithelium, ectomesenchyme or mixed cells associated with teeth development.

Ameloblastoma: a benign locally aggressive odontogenic tumor of epithelial origin with unlimited growth capacity but also a high potential for malignant transformation as well as metastasis.

Data base: an organized collection of structured information, usually controlled by a database management system and typically stored electronically in a computer system.

Oral cancer: Malignant lesions that forms in tissues of the oral cavity or the oropharynx.

Cyst: An abnormal fluid (a gaseous, liquid, or semisolid substance) filled cavity in the body lined by an epithelium or a capsule.

Demographics: The study of statistical characteristics of populations and the different groups that make them up such as the size, growth, age, gender, income, and education

Trends: a general direction in which something is developing or changing

ANOVA: a type of statistical test used to determine statistically significant difference between two or more categorical groups by testing for differences of means using variance

Statistically significant: The claim that a result from data generated by testing or experimentation is likely to be attributable to a specific cause. A high degree of statistical significance indicates that an observed relationship is unlikely to be due to chance.

Abstract

Background: Oral and maxillofacial lesions occur widely across the Kenyan population, yet few long-term studies on the different lesions have been done based on confirmed tissue histopathology. The occurrence of such lesions in the population is associated with significant morbidity and mortality due to the effects of disease on vital orofacial structures that affects functions like nutrition, respiration and the special senses such as vision and hearing.

Generally, the occurrence of oral and maxillofacial lesions has been reported to fluctuate in the Kenyan population and elsewhere in the world. However, these local studies have been done over a limited duration, mostly in single centers. The knowledge of current trends and patterns of such lesions in the population is essential in establishing the burden of diseases and guiding oral health authorities and clinicians creating appropriate policies and decisions.

Broad Objective: The broad objective of this study was to describe the range, trends and patterns of oral and maxillofacial diseases and disorders confirmed by histopathological diagnosis at two centers in Kenya from the year 2001 to year 2020.

Study population: This study investigated histopathology records from the oral pathology department at the University of Nairobi Dental Hospital (UoNDH) and the pathology unit at the Kenyatta National Hospital (KNH). These facilities are the largest referral centers for the management of oral and maxillofacial diseases in Kenya.

MATERIAL AND METHODS:

STUDY DESIGN: This was a retrospective descriptive study.

DATA ANALYSIS: Data were analyzed using SPSS version 25.0 software. The data were presented in frequencies and percentages for categorical data and means and standard deviations for continuous data. The results were analyzed using a 95% Confidence Interval (CI) and p – value < 0.05 was considered significant.

RESULTS: There were 15,319 histopathological records analyzed in this study. The study reported 5020, (32.8%) malignant tumours as the most prevalent, while among other more common major categories of lesions included adaptive lesions 2191, (14.3%), Benign soft tissue neoplasm 1466, (9.6%), Cystic lesions 1391, (9.1%) and Odontogenic tumours 1288, (8.4%). The entire age range was 0.1 – 99.0 years. The occurrence of the lesions generally fluctuated over the study period without a statistically significant variation. A remarkable number of patients below 40 years (26.5%) were noted to have oral squamous cell carcinoma. The general peak of ameloblastoma was noted to be in the 2nd and 3rd decade while that of oral squamous cell carcinoma was in the 5th and 6th decade.

The gender distribution showed overall female predilection with a male: female ratio of 1:1.1. The commonest lesions recorded were oral squamous cell carcinoma 2928, (9.1%), ameloblastomas 913, (6.0%) with tobacco and alcohol use as the known inherent risk factors in the local population.

CONCLUSION

The baseline data on the occurrence of OMFDs in the study showed an overall female (52.4%) gender predilection with a male (52.1%) preponderance of advanced age among malignancies having been noted. The OSCC (58.3%) was the commonest malignancy while the ameloblastoma (70.88%) was the commonest benign tumor. The peak of OSCC was in the 6th and 7th decades while amelolastomas peaked in the 2nd and 3rd decades. A general increase in the trend of SCC cases despite fluctuations, an increasing burden of OSCC among the young population aged below 40 years (26.5%) with 18-year-olds having highest frequency was observed. The mandible and tongue were the most affected surgical sites.

CHAPTER ONE: INTRODUCTION AND LITERATURE REVIEW

1.1 Introduction and background

There are diverse types of lesions encountered in the oral and maxillofacial region. The World Health Organization (WHO) noted that oral diseases in the year 2017 affected an estimated 3.5 billion people globally including an estimated 400 million African people. These diseases are associated with an economic burden with reduced productivity of the affected population and increased costs of treatment, severe pain, social isolation, facial disfigurement before and occasionally after surgery and even death.[1]

Oral and maxillofacial diseases(OMFDs) continue to cause significant mortality and morbidity in Africa and their effective management require oral health care policies informed by realistic evidence of the dynamic patterns and trends of the existing pathologies.[1] A Kenyan 5-year audit by Dimba et al. (2007) on OMFDs in a major referral center reported that over half the sample population (53.83%) had tumours of the orofacial region, The study reported a remarkable number of malignant cases with up to 10.3% of oral squamous cell carcinoma (OSCC) noted among those aged below the age of 40 years.[2]

Gathece et al. (2015) in a country wide oral health survey reported that among adults, ulcerations (8.2%) were the most prevalent oral mucosal lesions while leukoplakia (6.7%) and lichen planus (5.5%) formed part of the most common lesions. Among children, the oral mucosal lesions were seen in 3.2 % of the population and the most prevalent oral mucosal lesion was ulceration (1.5%).[3] A few other isolated Kenyan studies have reported their findings on the patterns of different types of oral and maxillofacial (OMF) lesions including an audit on ameloblastomas by Vilembwa et al. (2008), reactive lesions by Awange et al. (2008), osteosarcomas by Chindia et al. (2000) and Guthua et al. (2020) as well as OSCC by Onyango et al. (2004).

The determination of high-risk groups among the demographics based on age, gender, location, site of lesion in a population allows integration of realistic and evidence guided oral health policy monitoring.[4] The established pattern of disease among the demographics of the lesions may point to the associated risk factors among different subgroups thus guiding strategies in treatment and prevention.[5]

The added knowledge of the frequencies of such conditions is useful in guiding the differential

diagnosis by establishing new variations in patterns of disease distribution locally.[5] There are limited epidemiological or laboratory-based studies of OMF conditions that have been done in Kenya as is the case in most of sub-Saharan countries. Data are, however, emerging from African countries which adds to the body of knowledge from Asia, America and Europe.[5-9]

Histopathology refers to the study and diagnosis through examination of alterations in tissues and or cells associated with a disorder by viewing processed specimens using a microscope.[10] It is an essential part of the diagnostic process which supplements the clinical and imaging data of OMFDs. Cytopathology refers to the study of cells using a microscope, the commonly used method is the fine needle aspiration cytology (FNAC) which involves collection of a sample using a narrow-gauge needle (25-22) for microscopic examination.[11] FNAC has a role in screening of superficial and deep-seated paediatric lesions and the modality is reported as safe, accurate, rapid, minimally invasive and cost effective.[12,13] Majority of oral and facial lesions are biopsied routinely and such information will be useful in studies established patterns of occurrence and distribution of the pathologies.

Updated data bases of OMFDs are essential in monitoring changing disease patterns. Until the development of an oral health survey report of 2015 by the ministry of health, the Kenya health information system of 2014 inadequately captured oral diseases.[7] While the survey done across the country explored the different oral diseases and conditions, the study did not capture the comprehensive data of OMFDs. A further comprehensive study of orofacial diseases is necessary in enriching the database as well as determining the disease burden which may guide informed oral health policy decisions.

It will be important to explore the range of diseases, trends and patterns seen in the already established burden of OMFDs diseases over a longer duration and compare the findings with earlier studies as well as the findings of the oral health policy by Gathece et al. (2015) among other local and regional studies to enrich the understanding of OMFDs.[2,3] The study will involve evaluating pathology reports from two centers of oral and maxillofacial surgery (OMFS) in Kenya.

1.2 Literature review

A few Kenyan studies have reported trends and patterns of occurrence of different OMFDs. Onyango et al. (2004) studied OSCC records in a single referral centre in Nairobi over a 20-year period where it was reported that oral cancer did not show change in pattern or an increase in frequency in the population since the early 1970's despite the emergence of Acquired Immunodeficiency Syndrome and lifestyle changes in the population.[20] A general decline in malignancies was reported without much variation in oral cancer from the beginning of the study to the end in 2004. Kamau et al. (2011) in a study about oral and maxillofacial malignancies with emphasis on sarcomas reported that OSCC and its variants were the commonest malignant pathologies corroborating the findings by Dimba et al. (2007). The occurrence reported fluctuations involving a sharp decline at the beginning of the study then an increase to compare with the count at the beginning towards the last year of the study in 2009. Malignant glandular neoplasms were the 2nd commonest malignant lesions while malignant melanoma, odontogenic carcinomas and sarcomas followed in that order. [78]

Similar studies have been done locally and other parts of the world. These were retrospective, census type of studies which reported varied categories of OMFDs prevalent in different populations. Saleh et al. (2017) for example reported predominance of orofacial malignancies in the study population which compared to local literature by Dimba et al. (2007). [2,21] Other studies have corroborated low prevalences of malignant maxillofacial lesions in their population including an Iranian study by Moridani et al. (2014). Alhindi et al. (2019), however, reported a majority of benign tumours in an Arabian population. The studies also reported fluctuations in the occurrence of the maxillofacial diseases. The Kenyan study by Onyango et al. cited above indicated a decline in malignant OMFDs while Kamau et al 2011 reported fluctuations in their occurrence, a subject of further interest in our study among other possible trends in other disease categories. [4,20, 65]

The Onyango et al. (2004) and Dimba et al. (2007) studies were done when the Human Immunodeficiency Virus pandemic was thought to influence the pattern of distribution particularly the increased number of malignancies.[2,20] Most of the studies have also been done for a limited duration involving specific lesions or categories in single study centers. Further comprehensive investigation of oral maxillofacial lesions will be essential to elucidate the range, trends and patterns of distribution of maxillofacial conditions in the local population.

OMFDs are a variety of hereditary and acquired conditions occurring in the oral cavity and the face due to a wide range of aetiological agents.[16] These lesions exhibit different trends and patterns in the diverse global populations. The diagnosis of these lesions includes clinical as well as radiographic investigations. The data from histopathological records, therefore, can be used to establish the prevalence of these lesions and the different demographics from which high risk populations can be determined.[4]

1.2.1 Clinical presentation of OMFDs

Orofacial cancers usually present as swellings with or without ulcerations. Associated symptoms include Pain, bleeding, paraesthesia, pus discharge and malodor when necrosis, ulceration and infection set in as well as cachexia and dysphagia usually in advanced stages.[18] Infiltration into adjacent tissue and subsequent metastasis is a key characteristic of malignant neoplasms. On the other hand, benign tumours are expansile masses which exhibit a slow progressive growth causing pressure effects on adjacent tissues. They commonly present as swelling in a majority of the cases with associated signs and symptoms including mobile teeth with or without extractions. Pain, purulent discharge and paraesthesia have been reported in few cases.[19]

A retrospective study by Onyango et al. (2004) in Kenyatta National Hospital based on pathology records established that oral cancer cases comprised of 3.6% of the population.[19] This study sampled 22, 788 cases of malignancies out of which 821 cases were noted to have had oral cancer. The occurrence of OSCC exhibited a fluctuation ranging from 1.5% to 7% of the total cases of malignancies, a small male predominance was reported while the peak age was noted at the 6-7th decades with the commonest site having been the tongue while the maxilla and mandible were also significantly affected.[19] Several studies have corroborated the finding of that tongue is the preferred anatomic location for OSCC, while the buccal mucosa, palate and floor of the mouth have been reported as significantly affected. [2,18,20, 21]

The prevalence of benign tumours is higher in the mandible than the maxilla as seen in several studies. [2,22] The parotid is the most preferred site for most salivary gland tumours, and more so benign salivary gland lesions. A female predominance has been shown in some studies while a few studies have reported a higher male dominance.[16,23,24] The pleomorphic adenoma has been reported as the commonest tumour while the Warthin's tumour, adenoid cystic and mucoepidermoid carcinomas form other more frequent lesions according to several studies. [24,25,26]

A 6-month histopathologic study done by Muange et al. (2014) between 2008 and 2009 reported that the prevalence of OSCC had a similar male preponderance of 1.6:1 with the tongue commonly affected.[18] The peak age was the 6th-7th decades and the poorly differentiated type (48.8%) was the commonest histopathological lesion while stage IV disease (52.4%) was the commonest clinical presentation. A variation of the peak age in other parts of the world where the 5th -6th decades have been shown as the peak in south, east and west Africa.[24,38,51]

An audit of oral diseases through histopathological reports by Dimba E.A.O. et al. (2007) found that malignant tumours were the most prevalent lesions. In the study oral facial tumours formed the majority of diseases at 53.83% (583 cases) with the peak of benign tumours having been seen in the 3rd decade. The ameloblastoma was the commonest benign tumour (50.23%, n= 109) exhibiting a young male preponderance and predilection to the mandible. Vilembwa et al. (2008) in clinical diagnosis and histopathology of ameloblastomas at two Kenyan maxillofacial centers reported a mean age of 29.9years for the male and 30.5years for female with no significance in gender difference.[19] The most prevalent locations of non-odontogenic tumours included the cheek, then maxilla, mandible and the tongue.[16]

Patients have a tendency to present late to referral centers in the Kenyan setting. A Kenyan study on ameloblastoma reported 44.4 months as the mean duration of first presentation for males and 46.3 months for females.[19] Ameloblastoma is a locally invasive benign epithelial tumour of odontogenic origin which occurs in the jaws. The preferred site from local studies have shown the mandible (93.5%) especially the posterior mandible as the commonest site, then the maxilla (6%)forms the 2nd prevalent site with the majority in the anterior region while very few (1%), have been reported in soft tissues.[2,19] The malignant ameloblastoma is rare, local studies have reported only 6% as malignant variants of ameloblastoma.[19]

There are different social and cultural habits which have been linked to the occurrence of different oral lesions, these include *toombak* snuffing among the Sudanese,[28] *shammah* and qat chewing among the Yemenis,[29] *shisha* and cigarrete smoking among the Egyptians.[30]. In the study, Saleh et al. (2017) also noted the *"shammah''* associated malignancies depicted certain trends over years in the increases and decrease though not having been statistically significant.[21] The cystic lesions reported in a local study comprised of the majority (68.10%) having been of odontogenic origin. Salivary gland diseases, infections, reactive and autoimmune lesions formed 26.60% of the cases

examined.[15]

In the East African region, an early study between 1989 to 1999 reported a high number of malignant lesions having been 50.5% and 74.83% in Uganda and Tanzania respectively.[22,31] The occurrence of OMFDs may be influenced by geographical region, the environment, lifestyle as well as genetic makeup. Studies done elsewhere show variable outcomes. Histopathological studies at the University of Srinakharinwirot in Thailand analyzed 701 cases among which males were less affected (38.4%) than females (61.4%). In the study, patients had a mean age of 40years.[32] The mandible was the most prevalent site of hard swellings while the preferred site for soft tissue lesions was the buccal mucosa. The six commonest pathologies included lichen planus, mucocele, radicular cyst, fibroma, dentigerous cyst and pyogenic granuloma.[32]

The prevalence of the different lesions across different geographical areas has been varied. Most studies have, however, reported similar trends among the top five prevalent lesions. Despite a higher frequency reported of malignant lesions in early local studies in east Africa by Kamulegeya et al. (2008) the general picture was that benign lesions formed the majority in most studies.[15, 33,34] A 6-year retrospective study on OMF (2003-2009) in Tanzania equally reported a higher prevalence of benign tumours (56.2%) while the malignant counterparts were at 7.9%.[22] Adaptive/ reactive lesions formed a majority of these conditions as reported in studies. Alhindi et al. (2019) from an analysis of 1, 218 cases in Jeddah Saudi Arabia, noted that a majority were benign lesions consistent with our local studies. The commonest reactive lesion from that study was a fibro epithelial polyp.[4] Other studies have reported similar findings.[8,22,23] Cystic lesions have been reported in high incidences in several studies, the radicular and dentigerous cysts constituted the commonest odontogenic cysts in that order. Besides a local study, other studies have corroborated this finding.[2,4,9] In a similar study in an Austrian adult population, Kelloway et al. (2014) reported fibrous dysplasia as the most common OMF lesion.[36]

Inflammatory lesions such as the periapical granuloma have been shown to exhibit high frequencies in most regional and international reviews of oral pathology.[4,37] Other epithelial pathologies such as pyogenic granuloma and peripheral giant cell granulomas have equally been reported.[37] Tooth alterations are variably reported in high incidences as well as mucoceles. However, these lesions may be underreported locally due to failure of submission of the samples for histopathology. Franklin et al. (2006) who analyzed 6,666 cases over a 30-year duration

reported tooth pathology in the United Kingdom as the second most prevalent pathology.[9] There are limited studies on the pattern of tooth abnormalities in our population.

1.2.2 The epidemiology of oral and maxillofacial conditions

Different OMFDs exhibit varying distribution in different groups of the population. Oral mucosal pathology for example may be seen in between 25 and 50% of the population according to Andreasen et al.[40] A local oral health survey in 2015 reported a higher prevalence of mucosal lesions in adults (20.8%) than in children (3.2%).[3]

Jaw cysts are benign lesions which have been broadly classified by the WHO in 2017 as odontogenic or non-odontogenic cysts. A male predilection with the mandible as the most frequent site has been reported in several studies.[16,12,41] The anterior maxilla has been reported in the literature as another preferred site.[5,42] This high occurrence among males may be associated with the generally poor oral hygiene among males as compared to females. Dental trauma involving the pulp which accounts for 3.6% of our local population may equally contribute to a sequala leading to the development of radicular cysts. Males are more likely to be involved in high-risk activities including interpersonal violence, sports, falls or even risky driving more likely to predispose them to OMF trauma than female counterparts as reported in other studies (Siber et al,2015).[43] Dental trauma has been reported by Gassner et al. (2003) to be more common (49%) than bone injuries (25%) being the second common after soft tissue injuries (58%) during daily life and play accidents.[44]

The odontogenic cysts are then further categorized as inflammatory and developmental while the non-odontogenic as developmental cysts. The radicular cyst has been reported as the most frequent cyst in most studies whence the dentigerous cyst and mucocele form part of most frequent cysts.[16] The keratocystic odontogenic cyst (OKC) peaks in the 2nd to 4th decades and have a mean frequency of about 7.8% among jaw cysts with a preferred location of the angle- ascending mandible region.[53] It is unique due to its high recurrence, aggressive nature, histological features including friable infiltrative epithelium and associated patched gene mutation. It was categorized as a developmental odontogenic cyst in 2017 from the odontogenic keratocystic tumour, a benign odontogenic tumour in WHO classification of 2005.[45]

A Kenyan study by Micha et al. (2012) cysts of the jaws and cyst-like lesions reported the commonest cyst as the OKC (28%) followed by dentigerous cysts (25%) while the nasopalatine

duct cysts (19%) was noted as the third most common. While several studies have reported radicular the cyst as the commonest cyst, it was noted to have been the 4th commonest (15%) in the population. The calcifying odontogenic cyst was less common forming 4% of the cases. [2,4,9,46]

Oral manifestations of the human immunodeficiency virus (HIV) infections may serve as an early guide to the diagnosis, indicators of disease progression or a marker of the immune status. The most prevalent HIV infection/AIDS manifestation among patients is oral candidiasis while earlier studies have reported high prevalent of Kaposi's sarcoma.[11]

Reactive lesions are equally found in the oral cavity tissues as they are exposed to various injurious stimuli such as foreign material including ill-fitting dentures, calculus or plaque. These lesions may be pedunculated or sessile. Sangle et al. (2018) reported a high prevalence of traumatic fibromas and tissue hyperplasia and significant high female preponderance (63.9%).[7] A local study by Awange et al. (2009) on oral mucosal reactive localised inflammatory hyperplastic lesions over a 14-year period reported a prevalence of 10.6% in the population. The commonest subtypes were fibrous epulis (38.7%), then pyogenic granuloma (28.3%). A female predominance (73.2%) was seen in the histopathological subtypes with the most preferred site having been reported as the gingivae (77.2%) followed by the tongue (8.4%).[47]

Malignant odontogenic tumours include ameloblastic carcinoma which is categorized as a primary intraosseous carcinoma. The sclerosing odontogenic carcinoma, an epithelial tumour exhibiting stromal sclerosis is also part of this malignant group.[48] Sarcomas of the neck and the head are rare as confirmed in a local study by Chindia et al. (2000). The Kaposi's sarcoma (39%) was reported as the most prevalent, perhaps associated with the burden and disease prognosis of HIV infection at the time. The osteosarcoma (23%), rhabdomyosarcoma (21%) and fibrosarcoma (13%) equally formed the commonest lesions. Other rare sarcomas included the chondrosarcoma (2%) while at 1% were the malignant fibrous histiocytoma and dermatofibrosarcoma protruberans.[49] Kamau et al. (2011) in a 10-year retrospective histopathologic study, however, noted that the commonest sarcoma was the osteosarcoma (29.7%), which was followed by Kaposi's sarcoma (28.7), fibrosarcoma (18.8%) and rhabdomyosarcoma (9.9%). The study reported a fluctuation of sarcomas with a peak in the third decade where up to 70% were seen below 40 years.[47]

There are few local epidemiological or laboratory-based studies which have been done to depict the incidence of the conditions in our country. In the year 2018, the estimated number of lip and

oral cavity cancer cases worldwide was reported as 4 per 100, 000 people while the number of oral cancer cases in the year 2003 was estimated as 2% of all malignancies.[1,50] The local studies by Onyango et al. (2004) reported that oral cancer frequency was 2-3% with minimal annual variation. Muange et al. (2014) reported a 1:1.6 female to male ratio with a peak incidence of 6^{th} – 7^{th} decades which is at least a decade later than other parts of the world.[38,39, 51]

1.2.3 Aetiology of maxillofacial lesions

Maxillofacial lesions have a diverse range of hereditary and acquired etiologies depending on the nature and progression of each disease. The varied diseases in the oral facial region can broadly be classified as hereditary or acquired lesions.[52] Unlike hereditary lesions, acquired lesions are absent at birth and occur in one's lifetime usually due to environmental factors which may interact with genetic predisposition.[18] These lesions include infectious, reactive, autoimmune, cystic, congenital, potentially neoplastic and neoplastic categories of disease. Neoplasms of the orofacial region may be broadly categorized as benign or malignant. Neoplastic pathologies of the jaws can be grouped into odontogenic and non-odontogenic tumours based on the tissue of origin (WHO classification, 2017).[10,16]

Causative factors associated with malignancy are frequently modifiable such as alcohol consumption, tobacco chewing and smoking, unhealthy oral habits as well as environmental exposures.[18,26,53] Gathece et al. (2015) reported that the local populations have generally a history of tobacco use more prevalent in rural areas with more males likely to smoke (34.4%) as compared to females (8.4%). A similar trend but less prevalence of smoking is seen in urban areas where males (33.7%) smoked more than females (6.4%).[3]

Most patients require availability of prompt professional services to avert the consequences when suffering these diseases. Reactive lesions are usually a tissue response in adapting to chronic irritation or minor trauma.[34] Invasion of nonspecific microorganisms into the inflamed tissues may play a role while chemicals including drugs and hormones as well as radiation has been reported as likely etiologic agents.[34,35]

Dental alterations have been shown to originate from trauma to developing tooth such as dilacerations and ankylosis as well as hormonal and genetic causes such as for microdontia and

macrodontia.[54,55,56] Infectious conditions usually have established causative agents which may commonly be of viral, bacterial and fungal origin. The oral cavity is rich in microorganisms which are equally unique. Infections may be as common as the odontogenic infections caused by the staphylococcus and the streptococcal groups of bacteria or rare infections like actinomycosis caused by the actinomyces species of bacteria which may clinically be confused with a malignancy but histologically distinguished particularly by the presence of Sulphur granules.[57]

Diseases of the oral maxillofacial region have been associated different genetic mutations. Studies have shown different genetic alterations including point mutations, deletions, rearrangements or amplification in most malignant neoplasms. These lead to amplification of excitatory pathways or rearrangement of genes causing inhibition pathways to be inactivated ultimately affecting gene products which then lead to disease. The k-ras and p53 are some of the commonest gene alterations seen in the pathogenesis of oral cancer.[58] Premalignant lesions and oral carcinomas have been shown to exhibit deletions of chromosomes, poorly differentiated variety of tumours exhibit 4q, 8p, 11q, 13q, 18q and 21q while 3p, 5q and 9p chromosomal deletions are seen in well differentiated tumours. The OSCC of the head and neck has been shown to commonly have chromosomal imbalance of 9p.[59] Chromosomal deletions in 9p21–22 have shown in nearly a third of all head and neck cancers which have been associated with mutation of cyclin dependent kinases and tumour suppressor genes which play a key role in the cell cycle regulation. [60]

Viruses such as the Human papilloma viruses (HPV) have been linked with epithelial dysplasia and OSCC. The HPV 16 and 18 contain E6 and E7 oncoproteins which bind to p53 and the retinoblastoma and impair their role in apoptosis or DNA repair.[61] Genetic alterations have been strongly associated with OSCC reported below 40yrs of age.[62] The Epstein Bar Virus has been shown to complement a chromosome responsible for dysregulation of the c-myc oncogene which causes Burkitt's lymphoma.[63]

Odontogenic tumours are lesions originating from the epithelium of odontogenic origin that remains entrapped in the jaws or within adjacent soft tissues. Loss of suppressor genes as well as mutations leading to activation of oncogenes is postulated as key in the development of these tumours. There are specific products of oncogenes which have been linked with the cell differentiation and proliferation leading to neoplasia including growth factors like Platelet-Derived Growth Factor and Fibroblast Growth Factor. The involvement of Ret, HER-2, specific kinases,

transcription factors which include Myc and signal transducers such as Ras have equally been reported.[56] Mutations in p53 with or without associated mutation of negative inhibitor protein MDM2 as well as retinoblastoma gene mutation have been shown in ameloblastoma.[64] Genetic mutations play a key role in oral and maxillofacial lesions including cystic lesions particularly the OKC which has been associated with the human patched gene mutation.[45] The interaction of the genetic predisposition with environmental factors is central to the genesis of these lesions. Given the scarce capacity for curative strategies, preventive approaches may be more effective in low resource settings such as Kenya.

1.2.4 Gender prevalence

Female persons have been noted to have high prevalence of OMF conditions.[9,21] The sociocultural practices including exposure to etiologic agents and a longer life expectancy may explain the pattern.[21] This has been shown in many studies. Jones et al. (2006) in a 30-year study reported a male to female ratio of 0.9:1. Saleh et al. (2017) equally reported in 6-year similar retrospective study a male to female ratio of 1:1.3.[21] Torabi-Parizi et al. (2017) in a 20-year study done among children and adolescents equally reported a similar pattern with male to female ratio of 1:1.1.[37] Other studies have reported male population with a higher prevalence of oral and maxillofacial lesions while some specific lesions show strong predilection to a particular gender. Malignant tumours, odontogenic tumours and epithelial lesions have been reported to have higher frequencies in males.[4,42.]

Salivary gland pathologies commonly seen include pleomorphic adenomas, polymorphous low-grade adenocarcinoma, mucoepidermoid carcinomas, adenocarcinomas, adenoid cystic carcinomas and mucoceles. Males have been reported to have higher incidence of high-grade tumours in some studies while females have been shown to develop salivary gland lesions at a younger age but also shown to exhibit a higher prevalence of benign lesions.[65,66] A higher incidence of pleomorphic adenomas among males compared to their female counterparts was reported by Okoh et al. (2005). Mucoepidermoid carcinoma is reported as the commonest salivary gland malignancy in some populations.[66,67] However, it has been reported to have no gender predilection in some studies.[67] Most studies concur that females have a higher disease burden of salivary gland diseases.[66-68]

1.2.5 Age predilection

The average age as reported from local studies by Dimba et al. (2007) for benign tumours showed a peak in the 3rd decade with a predominance of men at a younger age while malignant tumours peaked in the 6th decade. Different age groups exhibit different patterns of lesions. Advanced age has been associated with malignant OMFDs as seen in the peak of OSCC from the 5th to the 7th decade depending on the geographical area[18, 20]. In the study of children and adolescents below 18 years, Torabi-Parizi et al. (2017) reported 10.2% of patients with OMF lesions.[37] Other studies have reported different prevalences in children including 13% and 6.6 % in Brazil, 12% in America, 8.2% in the United Kingdom and 25% in Nigeria.[33,69-71] The vast majority of the pathologies in this paediatric group were benign with inflammatory and reactive lesions forming the highest frequency.[72] Kamulegeya et al. (2011) in Uganda reported that benign neoplasms were more prevalent in a similar population in the age group which ranged from 0 to 16 years. [31]

1.2.6 Prevalence of specific conditions in paediatrics

Prosdócimo et al. (2018) in a 75-year study, retrospectively examined 2408 paediatric cases where they reported salivary gland lesions as the most prevalent particularly the mucocele then reactive lesions and finally odontogenic cysts.[73] The dentigerous cyst formed the 2nd commonest then fibrous dysplasia followed in that order. Among tumours, Lima et al. (2008) reported not only more prevalent benign tumours but also benign odontogenic tumours, particularly the odontomas were the most prevalent tumour in the paediatric population.[72]

The occurrence of ameloblastoma in the below 20-years-old age group may mimic odontogenic cysts. Early detection is key to avoid significant morbidity caused by delayed diagnosis. Butt et al. (2012) in a study noted that there was a higher frequency (81.5%) among the 15-19-year-olds compared to the below 10-14-year-olds (18.5%). The study showed no gender predilection and no cases of ameloblastoma were seen below 10-years of age in the 13-year retrospective study.[74]

Malignant lesions form small percentages in most studies thus (1.12%) in Saudi Arabia[21]and 1.2% in Brazil.[72] Among these, Burkitt's lymphoma has been reported as one of the commonest. Similar studies in Africa have reported equally high frequencies of Burkitt's lymphoma, (Omoregie et al. (2014)).[75] According to the literature the general paediatric malignancies represent less than 1% of all diagnoses.[9] The rhabdomyosarcoma accounts for 3-4% of all neck cancers affecting the paediatric population and 35% of head and neck cancers, making it the commonest soft tissue

malignancy in paediatric and young adults in the general populaaation.[76]

Saleh et al. (2017) in a retrospective study of histopathological specimens OMF pathologies in Saudi Arabia reported a predominance of malignant lesions where the mean age in the population was 46.8±23.4 yrs. [21] Fierro-Garibay et al. (2010) noted a comparatively older age group while a younger mean age has been noted in other studies.[33-36,77] Generally, the paediatric population forms less than 10% of the histopathology cases, a variation on the upper end may be seen due to the inclusion criteria.[72] Different age groups have been used in different studies ranging from an upper age of 14, 15, 16, 17 to 18 years. Also, the scope of oral or oral and maxillofacial, study period, genetic and geographical background may bring in a challenge when comparing the reports across the different populations. [69]

Sarcomas have a high morbidity and mortality and their prevalence in our local population is about 18.98% of all other malignancies with a peak age in the 3rd decade where 70% is seen below 40years of age as reported by Kamau et al. (2013).[78] The mandible and the maxilla form the most common sites of sarcomas while among the subtypes, the osteosarcoma and Kaposi's sarcoma formed the most frequent types (59%). Fibrosarcoma (19%) and rhabdomyosarcoma (10%) equally affect significant populations.[78,79] The preferred site of osteosarcoma was reported as the mandible by Guthua et al. (2020) and the mean age of occurrence was similar to that in the study by Kamau et al. (2013).[80] Other studies done elsewhere in the world confirm the rarity of sarcomas such that the most frequent subtypes vary in other populations. Okoh et al. (2018) in Nigeria reported malignant fibrous histiocytoma and fibrosarcoma as the most common with the 2nd decade as the mean age of occurrence.[79]

1.2.7 Trends of Oral and maxillofacial diseases

The OMF pathologies have been associated with high morbidity, while most malignancies are equally associated with high mortality. The commonest presentation among the patients with OMF conditions seeking healthcare is at advanced stages which significantly affects the outcome. Oral malignancies have been reported as more common in previous studies over a decade ago. The high prevalence of malignancies of the orofacial region may be associated with the rise of OSCC cases in which the commonest presentation is stage IV disease. Studies have reported alcohol intake and tobacco chewing to have been linked to the high prevalence of the lesions locally.[18, 20] A late

presentation of benign lesions has been equally reported locally.[19] There is, therefore, need to investigate comprehensively the burden of OMF conditions in our population over several centers and for a longer duration to inform the full range, patterns and trends of orofacial diseases in our set up. The detection of OSCC rather than epithelial dysplasia or stage IV disease of OSCC as the commonest presentation in our population, may be a reflection of delayed diagnosis and poor referral which may require education to both patients and general practitioners to adopt early detection and histopathological diagnosis to improve the chances of survival after management.[21]

The present study explored the range, trends and patterns of OMFDs under 13 disease categories based on classification by Jones et al. (2006) and Lima et al. (2008).[9, 72] These included**;** reactive lesions, cysts, bone pathologies**,** odontogenic tumours, mucosal pathology**,** benign soft tissue neoplasms, malignant tumours, tooth abnormalities, infections, salivary gland diseases, normal tissues and dentition, other pathologies and inconclusive diagnoses. This information should bridge the gap of knowledge needed by healthcare persons and clinicians in the effective delivery of services to target groups as well as monitor and help refine the effectiveness of existing healthcare policies in our institutions.

1.3 Problem statement

Evidence based decisions of prevention and management of OMFLs require reliable data bases derived from consistent research. Studies have shown fluctuations in occurrence of some OMFDs including a general decline reported by Onyango et al. (2004).

OMFLs contribute significantly to the growing burden of Non Communicable Diseases affecting developing countries such as Kenya. The WHO estimated a population of 3.5 billion in 2017 to have oral diseases where a significant portion is seen in developing countries

With a historical emphasis on infectious disease research, the morbidity and mortality caused by the OMFLs is poorly documented. Progressively disfiguring orofacial lesions is a presentation noted locally as reported by Muange et al. (2009), advanced oral cancer is often fatal with poor

prognosis particularly when surrounding vital structures including the airway and oropharyngeal structures, radical resection of the same is equally associated with significant morbidity.

There is paucity of data and limited studies exploring the range, trends and patterns of oral and maxillofacial diseases from an audit of histopathological records. There is no current long term comprehensive local study addressing OMFDs in our local population.

1.4 Justification of the study

The only comprehensive Kenyan study on oral and maxillofacial diseases was done in 2001 to 2004 by Dimba et al. while Kamau et al. (2011) in a 10-year clinical pathological study reported fluctuations in the occurrence of oral malignancies. Local studies report oral squamous cell carcinoma was the most popular oral malignancy. The occurrence of OMFLs locally and elsewhere in the world has been shown to have fluctuations in the study populations. There is a knowledge gap in the existence of a current comprehensive literature on data base depicting the range, current trends and patterns of distribution of OMFDs

The study will give a better understanding to clinicians and students on the different OMFDs in our local population based on site, gender and age groups as well as allow comparison to other studies done elsewhere in the world. An audit of the histopathology samples will reveal gaps, emphasize on the need of timely sampling of oral and maxillofacial lesions for histopathology diagnosis and the need to keep updated data bases in the different hospitals. The results may guide future policy formulation including optimal care to high risk groups as well as monitoring of management of head and neck diseases based on the demographics and predilections.

1.5 Study objectives

1.5.1 General objectives

To identify the trends and patterns of oral and maxillofacial diseases and disorders based on pathology records in two major referral centers of oral and maxillofacial surgery over 20 years

1.5.2 Specific Objectives

1. To determine the range of oral and maxillofacial pathologies in the KNH and UoNDH diagnostic referral laboratories.
2. To determine sociodemographic, age of disease presentation in categories and anatomic sites of oral and maxillofacial lesions.
3. To determine the trends and patterns of occurrence in different categories and common diseases of OMFDs

1.6 Variables

TABLE 1: SOCIODEMOGRAPHIC AND INDEPENDENT VARIABLES AND THEIR MEASURES.

Sociodemographic Variables	Measures
Age	Years
Gender	Male, Female
Year of Biopsy collection	Exact Year Date

TABLE 2: DEPENDENT VARIABLES AND THEIR MEASURES

Variable	Measures
Diagnosis	Histopathological type of lesion
Disease Categories	Number of Biopsies
Site	Code and site by name ICD-10

CHAPTER TWO: MATERIALS AND METHODS

2.1 Study design and sites

The study was a retrospective descriptive study based on pathology records at the University of Nairobi Dental Hospital (UoNDH) and the Kenyatta National Hospital (KNH). The study involved the use of data from histopathology laboratory records from the two largest referral oral and maxillofacial centers in Nairobi, Kenya. These centers are referral hospitals and receive patients from all over the country. The two hospitals are located in the City of Nairobi a few kilometers from the central business district.

All the specimens received at the division of oral pathology and oral medicine were analyzed and their information stored in the histopathological records from where data was obtained. Fine needle aspirate cytology biopsies which receive mainly lesions in the paediatric oncology as well as salivary and lymph node biopsies was equally considered, however it was noted that the records from the year 2001- 2009 was not available hence excluded from the study.

The study involved all histopathological records whose biopsy samples of oral and maxillofacial region that were analyzed by histopathology in the two centers from 1st January 2001 to 31st December 2020.

2.2 Study population

2.2.1 Study population

The study involved all patients records whose biopsy samples of oral and maxillofacial region were analyzed by histopathology in the two centers from 1st January 2001 to 31st December 2020.

2.2.2 Study design

The study design was a retrospective and a census type of study, all histopathological records of oral and maxillofacial diseases over the 20-year in the two referral centers was considered.

2.2.3 Inclusion criteria

All cases recorded in the histopathology and cytology records in the period between 1st January 2001 and 31st December 2020 and reviewed by certified pathologists.

2.2.3 Exclusion criteria

Specimens with diagnosis other than oral and maxillofacial diseases and disorders

Specimens with significantly missing data at collection including age, gender, diagnosis or site.

2.3 Data collection instrument and techniques

2.3.1 Data collection

The information was obtained from clinicopathological laboratory records from the UoNDH and KNH. A census was conducted to retrieve records from the archives whereupon the number of OMFDs diagnosed was recorded together with the corresponding biodata including the age, sex, site of the lesion as per ICD-10. The diseases were categorized into major categories based on Lima et al. (2008) and Jones et al. (2006) et al. (see Appendix II). A data extraction tool in excel sheet (see Appendix III) was then used for the data collection. The patient records were reviewed for errors then entered using Microsoft Excel for quality control.

2.3.2 Data analysis and presentation

Once data entry was done, 15% of the records were sampled for errors to ensure accuracy. The data set was also checked for any logical or typographical errors. Data were described using frequencies and percentages for categorical data while means and standard deviations were used for continuous data. These results were presented in either tabular or graphical format.

Descriptive statistics were applied to continuous data such as age. Thereafter Pearson's Chi-square test were used to test the bivariate associations between categorical data of the disease factors and socio-demographic variables while analysis of variance was used to test the significant difference between proportions. Multiple Logistic Regression was used for multivariate analysis. For each predictor variable the unadjusted odds ratio, 95% confidence interval and p – value < 0.05 were used to test the statistical significance of results. All the variables that are statistically significantly associated with disease factors in presentation at the bivariate stage ($p<0.05$) were considered together using binary logistic regression.

All statistical tests were determined at 0.05 statistical level of significance ($p < 0.05$) and a Confidence Interval (CI) of 95%.

CHAPTER THREE: RESULTS

3.1 Sociodemographic features

3.1.1 The range and age distribution of OMFDs

During the 20 year-period, there were 15, 319 histology specimens processed at the UoNDH (5,606) and KNH (9,713) pathology departments were considered. Overall reviewed records were 15, 469. Few incomplete records were noted. A total of 150 incomplete records was noted to have significantly missing details of diagnosis (65) or age and gender or site (85). The fine needle aspiration cytology data was missing from the year 2001 to 2009. The incomplete records (150) and the fine needle aspiration cytology records were excluded at the beginning of data analysis. (Fig. 1)

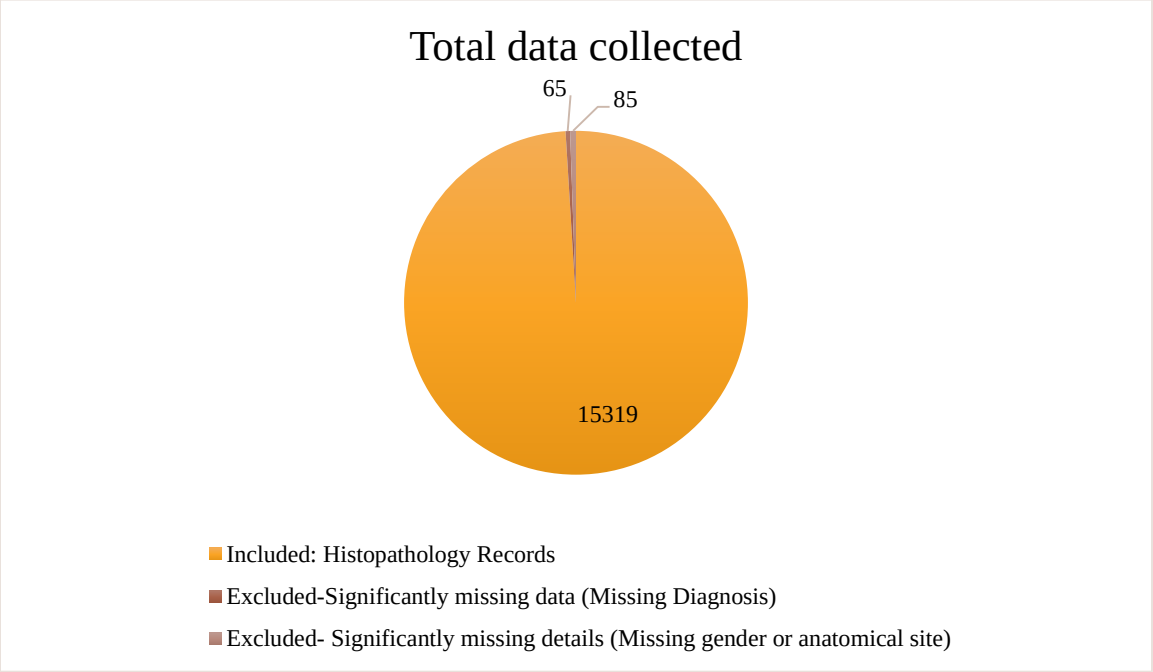

FIGURE 1: DATA COLLECTED OF OMFDS

The range of OMFDs was grouped into categories as follows: malignant tumours (n =5020,32.8%) were the most common followed by adaptive/reactive lesions at (n = 2191,14.5%). Other diseases are as shown below. (Table 3).

TABLE 3: DISTRIBUTION OF DIAGNOSIS OF OMFDS ACCORDING TO MAJOR CATEGORIES

OMFD Categories	Frequency (n)	Percentage
Malignant tumours	5020	32.8%
Adaptive/Reactive lesions	2191	14.3%.
Benign soft tissue neoplasm	1466	9.6%
Cystic lesions	1391	9.1%
Odontogenic tumours	1288	8.4%
Other pathologies	1203	7.9%
Bone pathologies	978	6.4%
Salivary gland disease	874	5.7%
Epithelial disorders/Mucosal pathology	499	3.3%
Infections	118	0.8%
Tooth abnormalities	5	0.0%
Normal tissues and dentition	99	0.6%
Inconclusive diagnosis	187	1.2%

The age range of patients from whom biopsy specimens were obtained was from 0.1 – 99.0 years with a mean age of (*M* = 35.9, *SD* = 20.2), a mode age of 18.0 years and a median age of 32.0 years. Comparison of the participants' age quartiles showed an interquartile range of 33.0 ranging from 18 to 51 years with Tukeys hinges for the box plot. The majority (66.9%) of cases were between 10 – 49 years of age. There were relatively few patients presenting with the oral and maxillofacial diseases below the age of 9 years and above the age of 70 years (Fig.2)

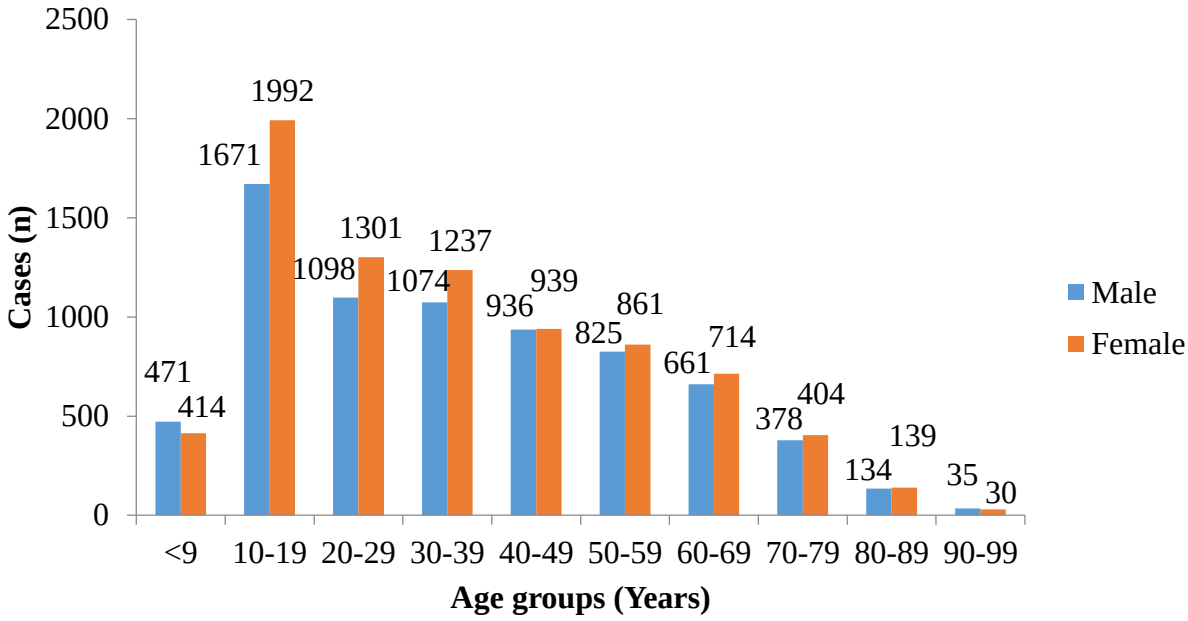

FIGURE 2: DISTRIBUTION OF OMFDS BY GENDER AND AGE GROUPS (*N* = 15319)

3.1.2 Site distribution of major OMFDs

Among the diagnoses, the recorded site distribution showed that the mandible at 2589, (16.9%) was the most commonly affected oral maxillofacial site followed by tongue 1311, (8.6%) and maxilla 1272, (8.3%). Other anatomical sites included a list of many isolated regions including the scalp, conjuctiva, eyelid, oropharynx, post nasal space and other extra oral sites which were excluded for comparison purposes of previous studies. Their further analysis in the future may bring in a robust analysis of distribution of OMFDs which may not be within the scope of the study. (Table 4).

TABLE 4: COMPARISON OF DESCRIPTIVE STATISTICS OF THE MOST COMMON ORAL AND MAXILLOFACIAL SITES AMONGST PATIENTS (N = 15319).

		Gender n (%)		Age (Years)	
Anatomical Site	*n* (%)	Male	Female	Range	*M* ± *SD*
Mandible	2589 (16.9)	1282 (8.4)	1307 (8.5)	0.1 – 95.0	36.1 ± 20.1
Tongue	1311 (8.6)	614 (4.2)	667 (4.4)	0.1 – 99.0	36.0 ± 20.6
Maxilla	1272 (8.3)	611 (4.0)	661 (4.3)	0.3 – 98.0	35.1 ± 19.4
Palate	1021 (6.7)	501 (3.3)	520 (3.4)	0.1 – 98.0	36.2 ± 20.2
Buccal mucosa, retromolar	968 (6.3)	449 (2.9)	519 (3.4)	1.0 – 92.0	34.2 ± 19.6
Lip	894 (5.8)	435 (2.8)	459 (3.0)	0.5 – 90.0	35.3 ± 19.7
Gingiva, alveolus	815 (5.3)	372 (2.4)	443 (2.9)	1.0 – 96.0	33.2 ± 18.7
Nose	764 (5.0)	343 (2.2)	421 (2.8)	0.2 – 98.0	37.4 ± 21.0
Major salivary gland	633 (4.1)	302 (2.0)	331 (2.1)	0.5 – 89.0	37.3 ± 21.2
Orbit	313 (2.0)	131 (0.9)	182 (1.1)	1.0 – 95.0	37.5 ± 20.8
Others	4739 (30.9)	2216 (14.5)	2523 (16.4)	0.1 – 99.0	36.3 ± 20.6
Total	15319 (100)	7286 (47.6)	8033 (52.4)	0.1 – 99.0	35.9 ± 20.2

M; Mean, *SD*; Standard Deviation

There were no outliers in the data, as assessed by inspection of the boxplot. A Kolmogorov-Smirnov test for normality of age at the major categories showed some degree of normality. (Fig. 3)

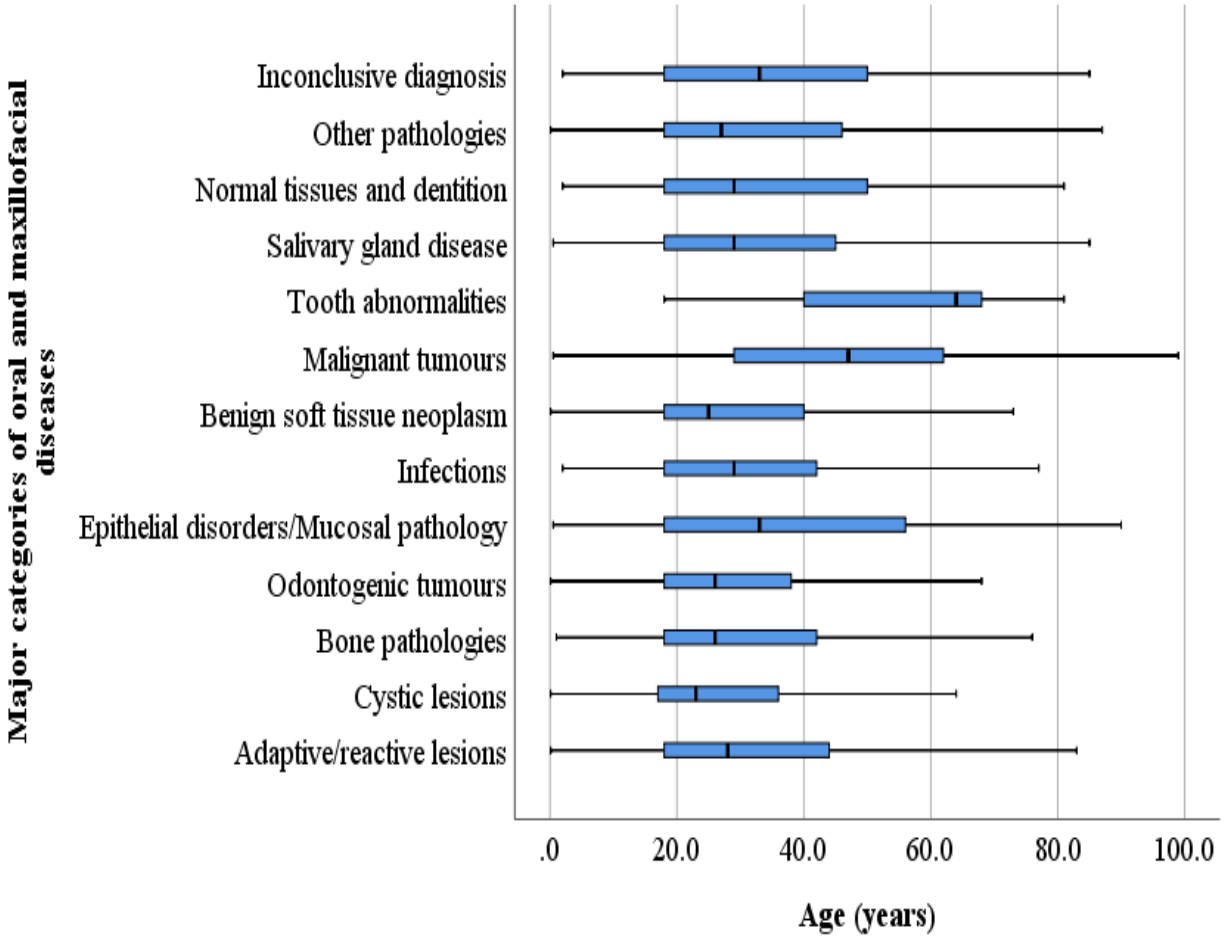

FIGURE 3: COMPARISON OF AGE DISTRIBUTION OF MAJOR ORAL MAXILLOFACIAL DISEASE CATEGORIES.

3.2.3 Sociodemographic trends – gender distribution of OMFDs

The overall Male: Female ratio was 1:1.1. There were higher frequencies of males in malignancies while females showed higher frequencies in most other categories as shown below. (Fig. 4).

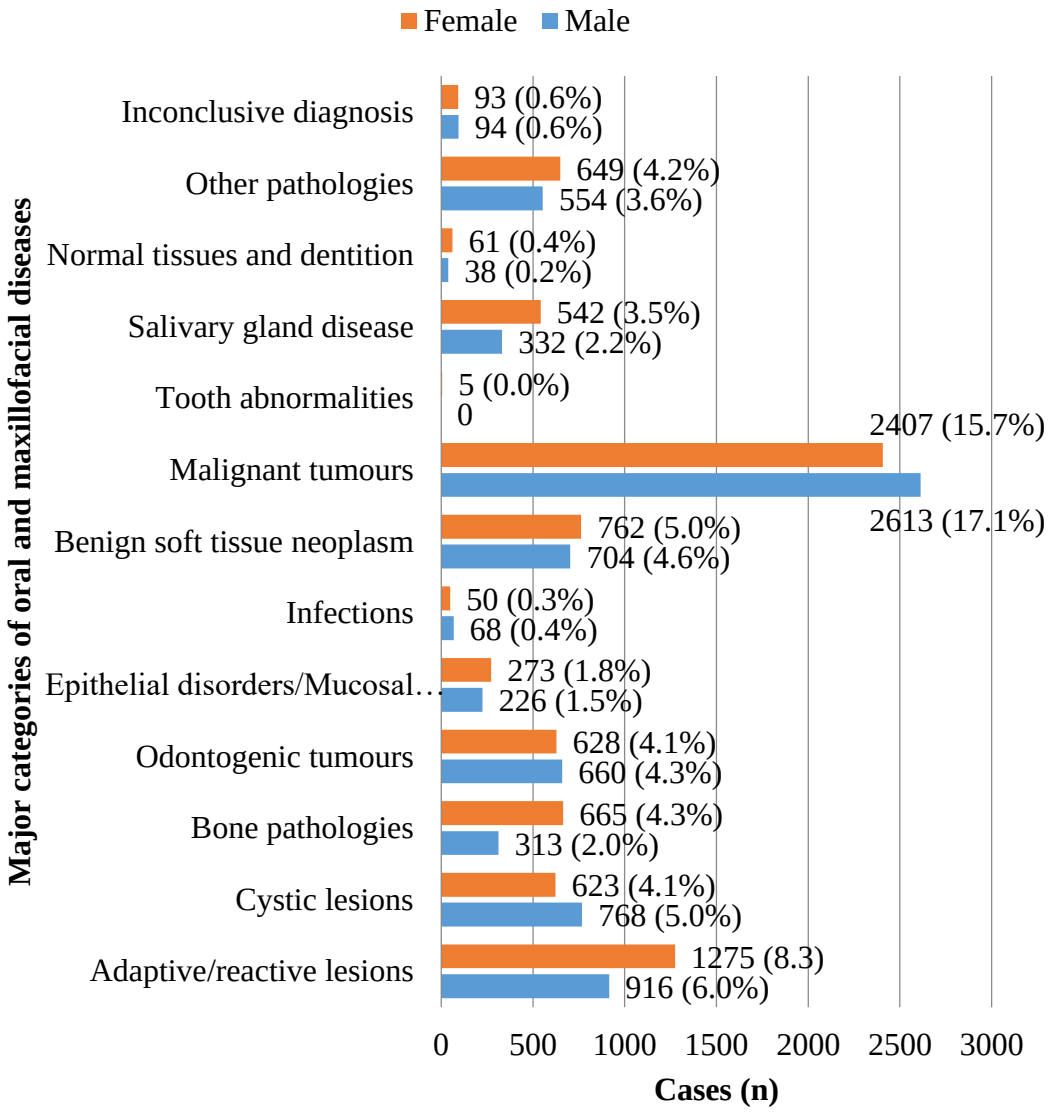

FIGURE 4: GENDER DISTRIBUTION OF MAJOR CATEGORIES OF ORAL AND MAXILLOFACIAL DISEASES BY GENDER (*N* = 15319).

3.2 Inferential statistics for sociodemographic data

The oral and maxillofacial diseases presented across an entire age range from 0.1years to 99.0 years. Malignancies were seen in more advanced age (45.7 +/- 20.8) years than the other diseases. Females showed higher frequencies in adaptive, bone pathologies, mucosal disorders, salivary gland disease and benign soft tissue neoplasms. The number of records on tooth abnormalities were too low which may reflect low rate of submission for histopathological diagnoses (Table 5).

TABLE 5: COMPARISON OF DESCRIPTIVE STATISTICS FOR MAJOR CATEGORIES OF OMFDS. (N = 15319).

Maxillofacial Disease Categories	*n* (%)	Gender n (%)		Age (Years)	
		Male	Female	Range	*M* ± *SD*
Adaptive/ reactive lesions	2191 (14.3)	916 (6.0)	1275 (8.3)	0.1 – 99.0	32.1 ± 18.0
Cystic lesions	1391 (9.1)	768 (5.0)	623 (4.1)	0.1 – 96.0	27.3 ± 16.9
Bone pathologies	978 (6.4)	313 (2.0)	665 (4.3)	1.0 – 94.0	30.6 ± 17.5
Odontogenic tumours	1288 (8.4)	660 (4.3)	628 (4.1)	0.1 – 95.0	30.3 ±16.0
Epithelial disorders/ Mucosal pathology	499 (3.3)	226 (1.5)	273 (1.8)	0.5 – 90.0	37.7 ± 20.6
Infections	118 (0.8)	68 (0.4)	50 (0.3)	2.0 – 87.0	32.7 ± 19.1
Benign soft tissue neoplasm	1466 (9.6)	704 (4.6)	762 (5.0)	0.1 – 99.0	29.4 ± 18.1
Malignant tumours	5020 (32.8)	2613 (17.1)	2407 (15.7)	0.5 – 99.0	45.7 ± 20.8
Tooth abnormalities	5 (0.0)	0	5 (0.0)	18.0 – 81.0	54.2 ± 25.1
Salivary gland disease	874 (5.7)	332 (2.2)	542 (3.5)	0.5 – 95.0	32.6 ± 18.6
Normal tissues and dentition	99 (0.6)	38 (0.2)	61 (0.4)	2.0 – 81.0	34.1 ± 19.5
Other pathologies	1203 (7.9)	554 (3.6)	649 (4.2)	0.1 – 94.0	32.2 ± 19.5
Inconclusive diagnosis	187 (1.2)	94 (0.6)	93 (0.6)	2.0 – 85.0	35.7 ± 19.3
Total	15319 (100)	7286 (47.6)	8033 (52.4)	0.1 – 99.0	35.9 ± 20.2

M; Mean

SD; Standard Deviation

Analysis of variance (ANOVA) test was applied to determine if there were statistically significant differences in age means among the 13 categories of OMFDs based on classification by Lima et al. (2008) and Jones et al. (2006). The ANOVA test showed a statistically significant differences in mean age amongst the 13 categories ($F = 179.332$, $df = 12, 15306$, $p < .001$). (Table 6).

TABLE 6: ANALYSIS OF VARIANCE (ANOVA) OF AGE MEANS AMONG THE MAJOR MAXILLOFACIAL DISEASE CATEGORIES OF ORAL AND MAXILLOFACIAL DISEASES (N = 15319).

				95% Confidence Interval for Maxillofacial Disease Mean		ANOVA		
Categories	*n*	*M*	*SD*	Lower	Upper	*F*	*df*	*p*
Adaptive/ reactive lesions	2191	32.1	18.0	31.3	32.8	179.332*	12, 15306	< .001
Cystic lesions	1391	27.3	16.9	26.4	28.2			
Bone pathologies	978	30.6	17.5	29.5	31.7			
Odontogenic tumours	1288	30.3	16.0	29.4	31.2			
Epithelial disorders/ Mucosal pathology	499	37.7	20.6	35.9	39.5			
Infections	118	32.7	19.1	29.2	36.2			
Benign soft tissue neoplasm	1466	29.4	18.1	28.5	30.4			
Malignant tumours	5020	45.7	20.8	45.1	46.2			
Tooth abnormalities	5	54.2	25.1	23.1	85.4			
Salivary gland disease	874	32.6	18.6	31.4	33.9			
Total	15319	35.9	20.2	35.6	36.2			

Analysis of variance (ANOVA) test was applied. df; degrees of freedom. * $p < .05$

A multinomial logistic regression test was applied to determine the association between age and

the major categories of OMFDs. The statistical significance predicted a 1-year increase in the age leading to 2.4% increase in odds of having a malignant tumor. There were no outliers in the data, as assessed by inspection of the boxplot and the assumption for multicollinearity was not violated. (Table 7).

TABLE 7: MULTINOMIAL LOGISTIC REGRESSION FOR ASSOCIATION BETWEEN AGE AND THE MAJOR MAXILLOFACIAL DISEASE CATEGORIES. (N = 15319).

Maxillofacial Disease Categories		*B*	*SE*	Wald	*df*	*p*	Exp(B)	95% Confidence Interval for Exp(B) Lower	Upper
Adaptive/reactive lesions	Intercept	2.805	.159	312.147	1	.000			
	Age	-.010	.004	6.662	1	.010	.990	.982	.998
Cystic lesions	Intercept	2.820	.162	304.612	1	.000			
	Age	-.026	.004	40.222	1	.000	.974	.967	.982
Bone pathologies	Intercept	2.138	.165	166.859	1	.000			
	Age	-.015	.004	12.316	1	.000	.986	.977	.994
Odontogenic tumours	Intercept	2.443	.163	225.906	1	.000			
	Age	-.016	.004	14.616	1	.000	.985	.977	.992
Epithelial disorders/Mucosal pathology	Intercept	.796	.180	19.482	1	.000			
	Age	.005	.004	1.332	1	.248	1.005	.996	1.014
Infections	Intercept	-.175	.241	.530	1	.467			
	Age	-.008	.006	1.801	1	.180	.992	.980	1.004
Benign soft tissue neoplasm	Intercept	2.656	.161	271.314	1	.000			
	Age	-.018	.004	20.666	1	.000	.982	.974	.990
Malignant tumours*	Intercept	2.312	.157	217.445	1	.000			
	Age	.024	.004	39.703	1	.000	1.024	1.017	1.032
Tooth abnormalities	Intercept	-5.608	1.294	18.791	1	.000			
	Age	.044	.023	3.859	1	.049	1.045	1.000	1.092
Salivary gland disease	Intercept	1.834	.167	119.950	1	.000			
	Age	-.009	.004	4.182	1	.041	.992	.983	1.000
Normal tissues and dentition	Intercept	-.482	.257	3.534	1	.060			
	Age	-.004	.006	.461	1	.497	.996	.983	1.008
Other pathologies	Intercept	2.199	.163	181.049	1	.000			
	Age	-.010	.004	6.001	1	.014	.990	.982	.998

Multinomial Logistic Regression was applied
The reference category is: Inconclusive diagnosis.
* $p < .05$

3.3.1 Common disease entities

3.3.1.1 Age trends in squamous cell carcinoma

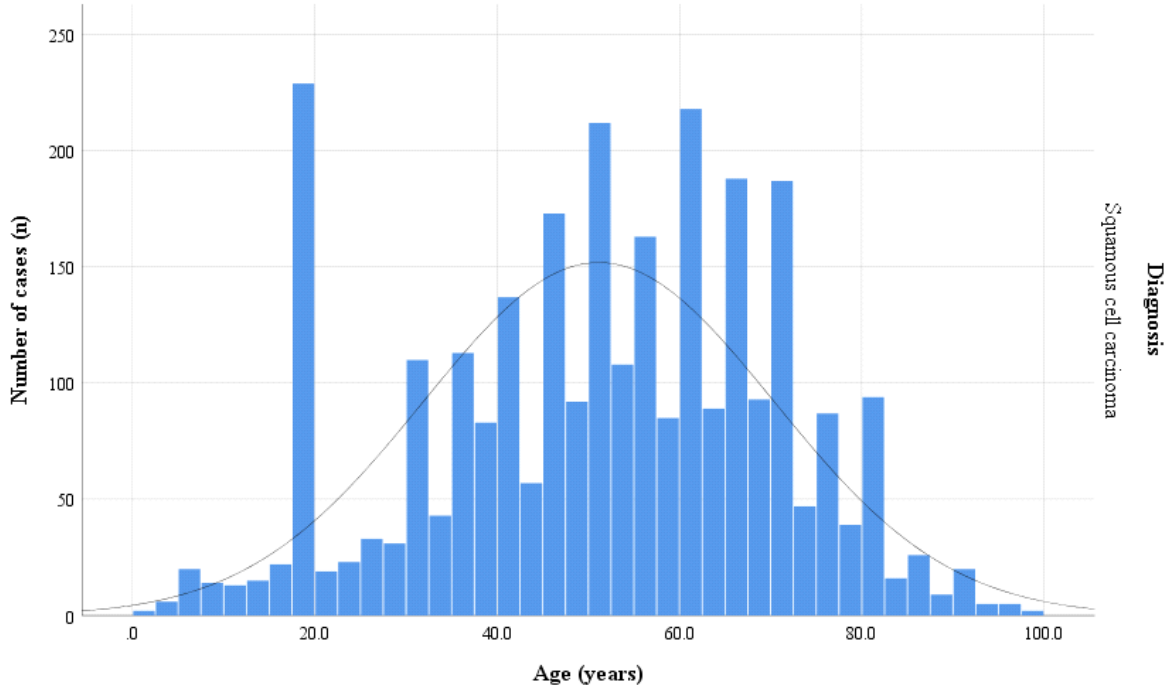

FIGURE 5: AGE DISTRIBUTION OF SQUAMOUS CELL CARCINOMA

Squamous cell carcinomas (n = 2928) constituted 58.3% of the total number of malignancies (n = 5020). The percentage drops only slightly to 56.5% with exclusion of the paediatric group (n= 92). A peak of SCC was seen at 18 years of 222 (7.6%) while the young people below 40 years constituted 776 (26.5%) of the oral squamous cell carcinoma. The mean age was (M = 51.1, SD = 19.2) with a median age of 53.0, a mode age of 18.0 years, the minimum age was 1.0 and maximum age of 90.0 years. An overall peak of the SCC cases was seen in the 5th and 6th decades, however, when the peak of 18 years was left out it was seen to shift to 6th and 7th decade as shown in Fig. 5.

3.3.1.2 Age trends in ameloblastoma

Ameloblastoma was the second commonest lesion in the study after oral squamous cell carcinoma. It constituted 70.88% of odontogenic tumors and 24.5% of all the benign tumours. The patients

mean age was (M = 31.8, SD = 15.7) with a median age of 28.0, a mode age of 18.0, a minimum age of 2.0 and maximum age of 90.0 years. The peak age of ameloblastoma was generally 2nd to 3rd decade with an isolated peak at 18 years of 140 (15.3%) cases as shown in Fig. 6

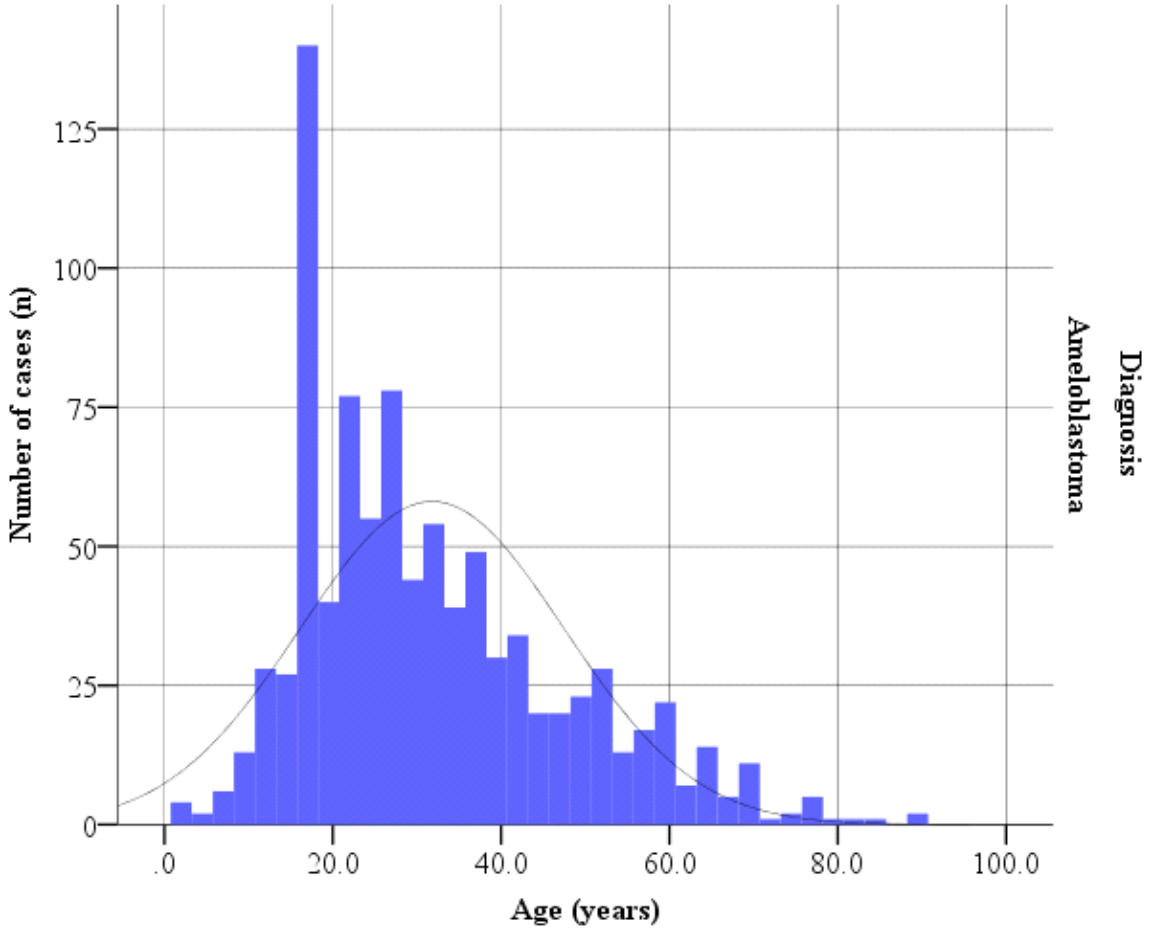

FIGURE 6: AGE DISTRIBUTION OF AMELOBLASTOMA

The most common lesions when observed for trends depicted fluctuations. The oral squamous cell carcinoma sustained higher frequencies throughout the study period. (Fig. 7)

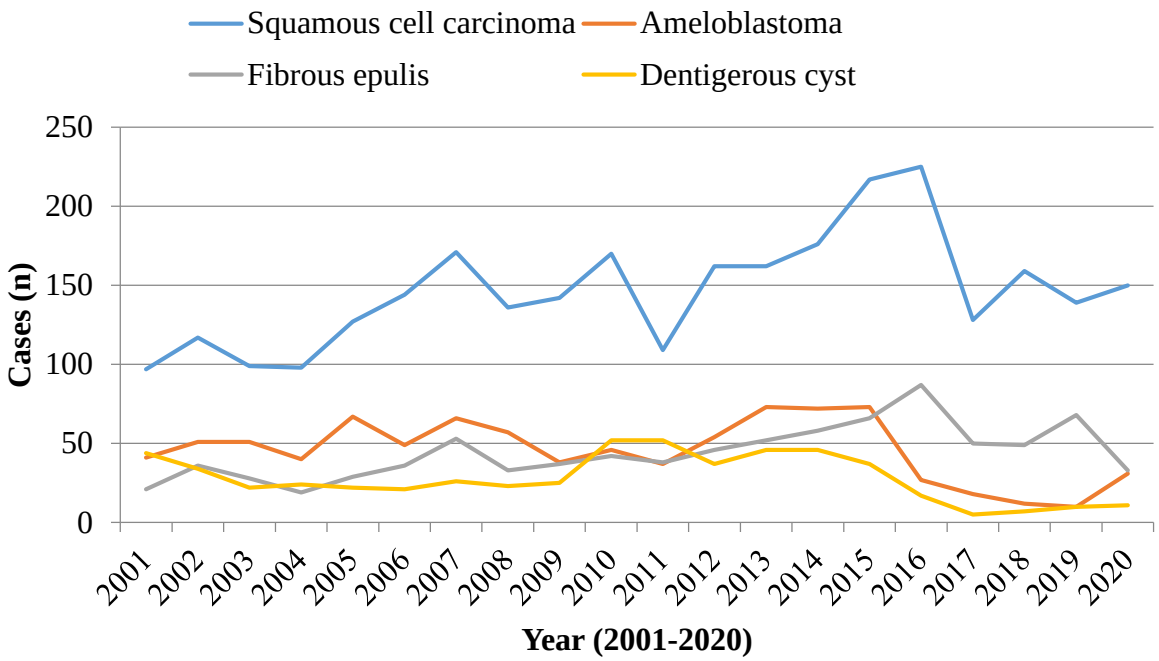

FIGURE 7: Frequencies of the most commonly affected oral maxillofacial surgical sites over time (2001 – 2020)

The 20-year distribution of the data among the paediatric age below 18 years showed a generally slight increase in frequencies of SCC with fluctuations having sustained higher frequencies. The range of frequencies over the years were comparable for the fibrous epulis, ameloblastoma and dentigerous cyst, a general increase was note for the former two while a general decrease noted for the dentigerous cysts. The highest peak was seen in the year 2015 and 2016. Fig. 8

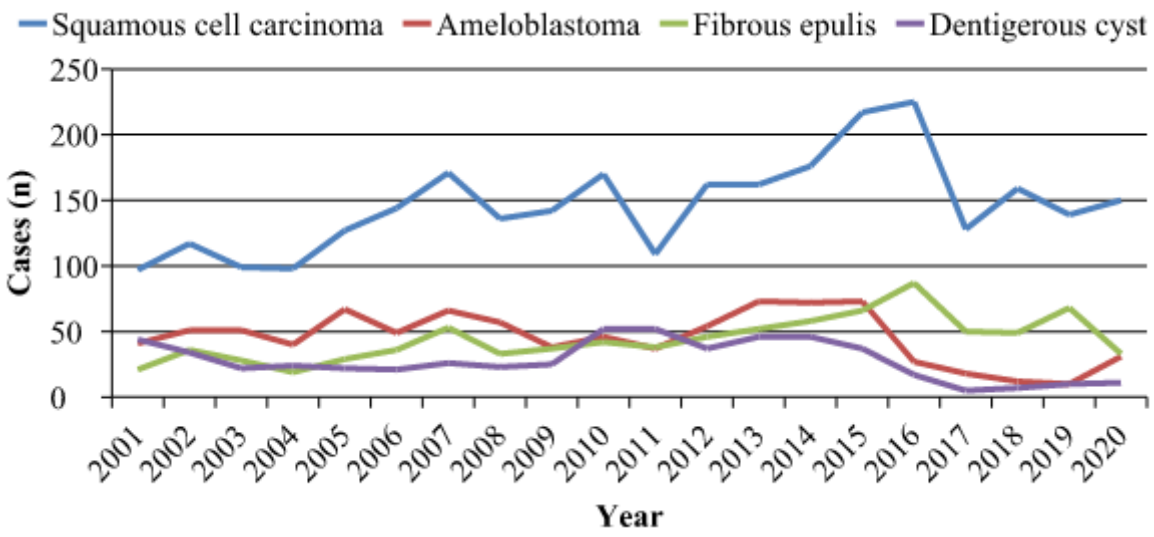

FIGURE 8: Frequencies of the most commonly affected OMFDs below 18years over time (2001 – 2020)

3.3.2 Inferential statistics for common oral and maxillofacial diseases

3.3.2.1 The most common oral maxillofacial diagnosis

Among the diagnoses, from the total cases diagnosed during the study period, Squamous cell carcinoma (n = 2928, (19.1%) was the most common diagnosis followed by Ameloblastoma 913, (6.0%). The gender distribution showed a male predominance in the squamous cell carcinoma (Table 8).

TABLE 8: COMPARISON OF DESCRIPTIVE STATISTICS OF THE MOST COMMON ORAL AND MAXILLOFACIAL DIAGNOSIS AMONGST PATIENTS (N = 15319).

		Gender n (%)		Age (Years)	
Diagnosis	*n* (%)	Male	Female	Range	*M* ± *SD*
Squamous cell carcinoma	2928 (9.1)	1637 (10.7)	1291 (8.4)	1.0 – 99.0	51.1 ± 19.2
Ameloblastoma	913 (6.0)	476 (3.1)	437 (2.9)	2.0 – 90.0	31.8 ± 15.7
Fibrous epulis	881 (5.8)	352 (2.3)	529 (3.5)	0.1 – 98.0	31.5 ± 17.7
Dentigerous cyst	561 (3.7)	250 (1.6)	311 (2.1)	0.1 – 81.0	28.1 ± 17.3
Pyogenic granulomas	464 (3.0)	167 (1.1)	297 (1.9)	1.0 – 87.0	30.2 ± 16.8
Inflammation	457 (3.0)	249 (1.6)	208 (1.4)	1.0 – 99.0	34.7 ± 17.1
Lipoma	424 (2.8)	224 (1.5)	200 (1.3)	1.0 – 94.0	32.7 ± 19.1
Pleomorphic Salivary adenoma	402 (2.6)	149 (1.0)	253 (1.6)	2.0 – 98.0	35.1 ± 17.6
Mucocele	328 (2.1)	148 (1.0)	180 (1.2)	0.5 – 78.0	23.4 ± 16.6
Ossifying fibroma	231 (1.5)	103 (0.7)	128 (0.8)	4.0 – 92.0	45.6 ± 19.7
	10076 (65.8)				

M; Mean, *SD*; Standard Deviation

An ANOVA test was applied to determine if there were differences in age among the most common oral maxillofacial diagnosis. There were no outliers in the data as assessed by inspection of the box plots. A Kolmogorov-Smirnov test for normality of age amongst the most common diagnosis showed some degree of normality ($p > .05$). The Levene's test showed homogenous data. ($p > .05$). The ANOVA test showed a statistical significance in the characteristic mean ages amongst the oral maxillofacial diagnoses (F = 106.939, df = 26, 10049, p < .001) (Table 9)

TABLE 9: ANALYSIS OF VARIANCE (ANOVA) FOR COMPARISON OF AGE MEANS AMONG THE MOST COMMON ORAL MAXILLOFACIAL DIAGNOSIS (N = 15319).

				95% Confidence Interval for Mean				ANOVA		
Diagnosis	*n*	*M*	*SD*	Lower	Upper	Min.	Max.	*F*	*df*	*p*
Squamous cell carcinoma	2928	51.1	19.2	50.4	51.8	1.0	99.0	106.939*	2, 10049	<.001
Ameloblastoma	913	31.8	15.7	30.8	32.8	2.0	90.0			
Fibrous epulis	881	31.5	17.7	30.4	32.7	0.1	98.0			
Dentigerous cyst	561	28.1	17.3	26.7	29.6	0.1	81.0			
Pyogenic granulomas	464	30.2	16.8	28.7	31.7	1.0	87.0			
Inflammation	457	34.7	17.1	31.7	35.1	1.0	99.0			
Lipoma	424	32.7	19.1	33.0	36.3	1.0	94.0			
Pleomorphic salivary adenoma	402	35.1	17.6	33.4	36.9	2.0	98.0			
Mucocele	328	23.4	16.6	21.6	25.2	0.5	78.0			
Oral Keratinocyte Carcinoma	301	30.1	17.9	28.1	32.1	6.0	95.0			
Ossifying fibroma	231	45.6	19.7	43.0	48.2	4.0	92.0			

Analysis of variance (ANOVA) test was applied. df; degrees of freedom. * $p < .05$

The Pearson Chi-Square test of independence was applied to determine the independence of oral maxillofacial diagnosis and gender. The diagnosis and gender variable levels were mutually exclusive and the study groups were independent. The Pearson Chi-Square test showed a statistically significant association between the diagnosis and gender ($X^2 = 268.028$, $df = 26$, $p < .001$). It can, therefore, be inferred that the patients' diagnoses and gender were clinically correlated in the entire population.

3.3.3 Inferential statistics on the most common oral maxillofacial surgical sites

Analysis of variance (ANOVA) was applied to determine if there were differences in age means among the most common oral maxillofacial sites. There were no outliers in the data as assessed by inspection of the box plots. A Kolmogorov-Smirnov test for normality of age amongst the most common diagnosis showed some degree of normality ($p > .05$). The Levene's test of homogeneity of variances showed a non-statistically significant difference in variances of age among the diagnoses ($p > .05$). The ANOVA test showed a statistically significance in mean age amongst the oral maxillofacial sites (F = 3.533, df = 10, 15308, p < .001) (Table 10).

TABLE 10: ANALYSIS OF VARIANCE (ANOVA) FOR COMPARISON OF AGE MEANS AMONG THE MOST COMMON ORAL MAXILLOFACIAL SITES (N = 15319).

				95% Confidence Interval for Mean				ANOVA		
Diagnosis	*n*	*M*	*SD*	Lower	Upper	Min.	Max.	*F*	*df*	*p*
Mandible	2589	36.1	20.1	50.4	51.8	0.1	95.0	3.533*	10, 15308	<.001
Tongue	1311	36.0	20.6	30.8	32.8	0.1	99.0			
Maxilla	1272	35.1	19.4	30.4	32.7	0.3	98.0			
Palate	1021	36.2	20.2	26.7	29.6	0.1	98.0			
Buccal mucosa, retromolar	968	34.2	19.6	28.7	31.7	1.0	92.0			
Lip	894	35.3	19.7	31.7	35.1	0.5	90.0			
Gingiva, alveolus	815	33.2	18.7	33.0	36.3	1.0	96.0			
Nose	764	37.4	21.0	33.4	36.9	0.2	98.0			
Major salivary gland	633	37.3	21.2	35.6	38.9	0.5	89.0			
Orbit	313	37.5	20.8	21.6	25.2	1.0	95.0			
Others	4739	36.3	20.6	29.5	38.4	0.1	99.0			
Total	15319	35.9	20.2	35.6	36.2	0.1	99.0			

Analysis of variance (ANOVA) test was applied.

df; degrees of freedom.

* $p < .05$

A Pearson Chi-Square test of independence was applied to determine the independence of oral maxillofacial sites and gender. The sites and gender variables levels were mutually exclusive and the study groups were independent. The Pearson Chi-Square test showed a no statistical significant association between the sites and gender (X^2 = 15.957, *df* = 10, *p* = .101).

A Pearson Chi-Square test of independence was applied to determine the independence of oral maxillofacial diagnoses and gender.

Comparison of the patients' mean age among the oral maxillofacial surgical sites showed a statistically significant difference in age means. (*F* = 3.533, *df* = 10, 15308, *p* < .101).

Comparison of the patients' mean age among the disease diagnosis showed a statistically significant difference in age means. (*F* = 103.240, *df* = 27, 15291, *p* < .001).

Comparison of the patients' mean age among the 13 categories showed a statistically significant difference in age means (*F* = 179.332, *df* = 12, 15306, *p* < .001).

3.4 OMFDs patterns in specific patient age groups

3.4.1 OMFDs patterns in patients below 40 years

TABLE 11: DISTRIBUTION OF MOST COMMON ORAL MAXILLOFACIAL DISEASES FOR PATIENTS BELOW AGE 40 YEARS.

Categories	*n*	*%*
Squamous cell carcinoma	776	8.4
Oral Keratinocyte Carcinoma	239	2.6
Kaposi's sarcoma	153	1.7
Anaplastic carcinoma	120	1.3
Carcinoma(NOS)	58	.6
Inflammation	292	3.2
Lipoma	274	3.0
Pleomorphic salivary adenoma	261	2.8
Haemangioma	133	1.4
Ossifying fibroma	90	1.0

The Squamous cell carcinoma (n = 776), was the most common disease in the age group below 40 years. This forms 26.5% of all OSCC (n=2928). The ameloblastoma (n =668), was the second commonest while mucosal hyperplastic lesions (fibrous epulis, n = 620) and dentigerous cyst, (n = 437), were among the most common diseases. Lipoma (n =274) was the most common benign soft tissue mesenchymal tumor while mucocele (n = 285) was the commonest salivary gland disease followed by pleomorphic salivary adenoma (n = 261). (Table 11).

3.4.2 OMFD patterns in patients below 18 years

The squamous cell carcinoma (n = 314), was the most common lesion. The fibrous epulis (n=277), the dentigerous cyst (n = 234), ameloblastoma (n = 5.0) and mucocele (n=167) were the other more common OMFDs in that order. (Table 12)

TABLE 12: COMPARISON OF DESCRIPTIVE STATISTICS OF THE MOST COMMON OMFDS IN CASES OF PATIENTS BELOW 18 YEARS OF AGE BY GENDER AND AGE (N = 4408).

		Gender n (%)		Age (Years)	
Diagnosis	*n* (%)	Male	Female	Range	*M* ± *SD*
Squamous cell carcinoma	314 (7.1)	177 (4.0)	137 (3.1)	1.0 – 18.0	15.8 ± 4.2
Fibrous epulis	277 (6.3)	129 (2.9)	148 (3.4)	0.1 – 18.0	13.9 ± 4.6
Dentigerous cyst	234 (5.3)	125 (2.8)	109 (2.5)	0.1 – 18.0	13.6 ± 4.3
Ameloblastoma	220 (5.0)	130 (2.9)	90 (2.0)	2.0 – 18.0	15.3 ± 3.6
Mucocele	167 (3.8)	72 (1.6)	95 (2.2)	0.5 – 18.0	11.4 ± 5.2
Inflammation	151 (3.4)	88 (2.0)	63 (1.4)	1.0 – 18.0	14.8 ± 4.4
Pyogenic granulomas	146 (3.3)	59 (1.3)	87 (2.0)	1.0 – 18.0	14.2 ± 4.8
Lipoma	113 (2.6)	61 (1.4)	52 (1.2)	1.0 – 18.0	15.7 ± 4.6
Oral Keratinocyte Carcinoma	94 (2.1)	47 (1.1)	47 (1.1)	6.0 – 18.0	14.4 ± 3.1
Chronic sinusitis	81 (1.8)	36 (0.8)	45 (1.0)	1.5 – 18.0	13.3 ± 5.0
Epidermoid cyst	75 (1.7)	33 (0.7)	42 (1.0)	2.0 – 18.0	14.2 ± 3.7
Kaposi's sarcoma	75 (1.7)	44 (1.0)	31 (0.7)	0.5 – 18.0	12.8 ± 6.7
Radiation Cystitis	75 (1.7)	37 (0.8)	38 (0.9)	0.1 – 18.0	12.4 ± 6.0
Pleomorphic sarcoma/adenoma	74 (1.7)	25 (0.6)	49 (1.1)	2.0 – 18.0	15.4 ± 3.9

M; Mean
SD; Standard Deviation

The distribution of lesions among different anatomical sites showed the mandible, tongue and maxilla to be the most preferred sites. The site of lesion may be attributed to the exposure of aetiological factors. (Fig. 9)

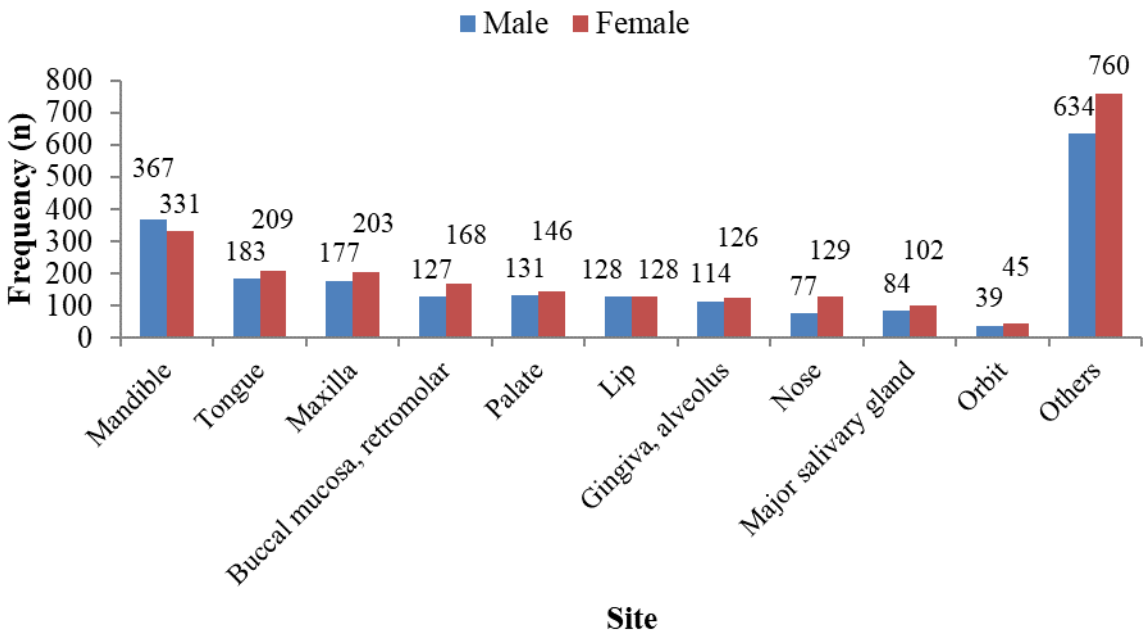

FIGURE 9: COMPARISON OF FREQUENCIES OF MAXILLOFACIAL DISEASES SITE DISTRIBUTION ACCORDING TO GENDER

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The 20-year distribution of the data among the paediatric age below 18 years showed fluctuations with the OSCC having sustained higher frequencies. The range of frequencies over the years were comparable for the fibrous epulis, ameloblastoma and dentigerous cyst. The highest peak was seen in the year 2015 and 2016. (Fig. 10)

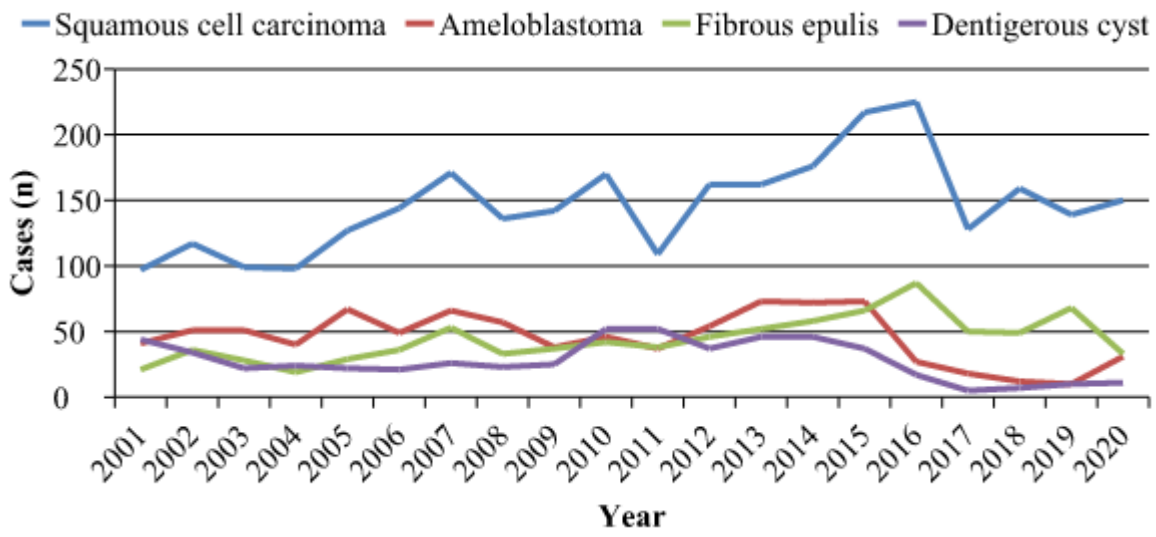

FIGURE 10: Frequencies of the most common OMFDs below 18 years over time (2001 – 2020)

The SCC showed a general increase over the period of study with variations in fluctuation the highest peak is seen in the year 2015. The Ameloblastoma showed fluctuations with variations among the years with a general decline towards the last five years of study. There was minimal change in the occurrence of fibrous epulis and dentigerous cyst with fluctuations over the years.

TABLE 13: COMPARISON OF DESCRIPTIVE STATISTICS OF THE MOST COMMON ORAL AND MAXILLOFACIAL SITES IN PATIENTS BELOW 18 YEARS BY GENDER AND AGE (N = 4408).

		Gender n (%)		Age (Years)	
Site	*n* (%)	Male	Female	Range	*M* ± *SD*
Mandible	698 (15.8)	367 (8.3)	331 (7.5)	0.1 – 18.0	14.0 ± 5.0
Tongue	392 (8.9)	183 (4.2)	209 (4.7)	0.1 – 18.0	14.5 ± 4.6
Maxilla	380 (8.6)	177 (4.0)	203 (4.6)	0.3 – 18.0	14.5 ± 4.7
Buccal mucosa, retromolar	295 (6.7)	127 (2.9)	168 (3.8)	1.0 – 18.0	14.1 ± 4.9
Palate	277 (6.3)	131 (3.0)	146 (3.3)	0.1 – 18.0	13.9 ± 5.1
Lip	256 (5.8)	128 (2.9)	128 (2.9)	0.5 – 18.0	14.0 ± 4.9
Gingiva, alveolus	240 (5.4)	114 (2.6)	126 (2.9)	1.0 – 18.0	14.7 ± 4.7
Nose	206 (4.7)	77 (1.7)	129 (2.9)	0.2 – 18.0	13.6 ± 5.4
Major salivary gland	186 (4.2)	84 (1.9)	102 (2.3)	0.5 – 18.0	14.3 ± 4.6
Orbit	84 (1.9)	39 (0.9)	45 (1.0)	1.0 – 18.0	14.6 ± 4.7
Others	1394 (31.6)	634 (14.4)	760 (17.2)	0.1 – 18.0	13.9 ± 5.2
Total	4408 (100)	2061 (46.8)	2347 (53.2)	0.1 – 99.0	14.1 ± 5.0

M; Mean
SD; Standard Deviation

The mandible was the most common anatomical site of OMFDs followed by the tongue and maxilla. The occurrence of the lesions in this sites ranged from 0.1 to 18 years. The distribution of the anatomical sites has a clinical correlation to exposure factors leading to the diagnosis. (Table 13)

CHAPTER FOUR: DISCUSSION, CONCLUSSION AND RECOMMENDATIONS

4.1 Discussion

Data on the incidence and demographics of oral maxillofacial diseases (OMFDs) are necessary for the development of coherent health policies which should be effective in the management of diseases. The emergence of new diseases over the years which may be associated with changing lifestyles affect existing patterns of disease and hence treatment needs of the society. There is only one comprehensive study of OMFDs in the Kenyan population.[2] There are other specific studies on sarcomas, cysts and cyst-like conditions, adaptive lesions, benign tumours and ameloblastoma, OSCC which are also available.[18,19,78]

The analysis of variance for age means reported 1-year increase in age leading to 2.4% increase in odds of having a malignant tumor. Malignant lesions have elsewhere in the world been shown to occur at a higher age in the population.[4] A slight female gender predilection of OMFDs, which was statistically significant, was reported in the study with 1:1.1 male to female ratio, other previous studies have reported similar higher frequencies of female prepoderance.[4,9] Torabi-Parizi et al. (2017) in a 20-year study equally noted a similar gender ratio of occurrence of OMFDs. A few other studies have reported a female predilection associated with better health seeking behavior among women.[9,65.]

A male predominance of OMFDs has however been reported in other studies.[27,39] This study not only reported a statistically significant high prevalence of OMFDs among females but also higher frequencies of malignancies and cystic lesions in males, while females depicted a slight predominance of adaptive lesions, epithelial disorders and salivary gland diseases which was noted to have been statistically significant. This female gender predilection of oral maxillofacial lesions (OMFL) has been associated in other studies with higher life expectancy among females as well as better utilization of health services than their male counterparts. The benefit of advanced age with known pre-existing predispositions such as fibro osseous lesions as well as hormone associated adaptive lesions is equally a possible explanation.[9,35,85] While in certain geographical areas the use of tobacco products has been implicated,[4,42,66] a safer sociocultural profile including limited use of tobacco products and smoking locally among women may imply different predisposing etiologic factors locally which may be subject of another study.

There are different patterns of distribution of specific OMFDs in different populations. OSCC,

ameloblastoma, fibrous epulis and dentigerous cyst were reported as the most common lesions as enlisted from the categories of malignancies, benign odontogenic tumours, adaptive lesions and cysts respectively. Among malignancies the other common lesions included, anaplastic carcinoma, Kaposi's sarcoma, and malignant ex-pleomorphic adenoma. The male population showed a predominance in malignancies including the OSCC and odontogenic tumours, this predilection has been reported both locally,[4,82] and elsewhere in the world.[42]

Tumours of the oral and maxillofacial region were reported as the most common disease category. The average yearly relative frequencies of oral cancer in a 20-year histopathological Kenyan study has been reported as 1.5%.[20] In the present study, malignancies were reported as the commonest category, which is corroborated by other local studies.[2,20] Similar results have been reported in other parts of the world.[2, 21.] The most common lesion among the malignancies was the SCC(58.3%) which was in agreement with Dimba et al. (2007), followed by anaplastic carcinoma then adenoid cystic carcinoma of salivary glands. While the distribution of lesions has been shown to differ in geographical regions, this picture is largely corroborated in other east African countries and elsewhere in the world. In East Africa, earlier studies equally showed a high prevalence of malignancies with 74.83% and 50.5% in a Uganda and Tanzania respectively.[22,31] The proportion of malignancies (32.8%) was higher than reported in similar histopathological studies done in other parts of the world such as Kuwait (6.5%) and Jeddah - Saudi Arabia (5.8%).[4,21]

The use of tobacco and alcohol are the two main factors associated with oral cancer as reported by Muange et al. (2014), the higher rate of consumption may point to the male predominance. The consumption of tobacco products in Kenya is estimated at 17% among men while less than 1% among women as per the Kenya demographic Health survey of 2008-2009.[85] Different geographical distribution of OMFDs point at exposure of specific known aetiological agents. Smokeless tobacco uses especially *shammah,* a mixture of substances including tobacco placed in buccal cavity, has been implicated in other parts of the world such as south western parts of south Arabia.[21]

The OSCC has been shown to occur commonly above the age of 40 years.[24, 87] The peak in the study was seen generally in the 5^{th} - 6^{th} decades, when the peak of 18 years was not considered, the peak was noted to be in the 6^{th} and 7^{th} decade, which was consistent with studies which report OSCC as a malignancy seen at the age of 5^{th} to 7^{th} decade.[18, 21] The study also reported a remarkable

number of patients below the age 40 years at 19.1% of all lesions and 26.5% of all malignancies who were diagnosed during the period of study. Dimba et al. (2007) and Muange et al. (2014) noted that 10.30% and 13. 4% of OSCC cases occurred in patients below the age of 40. [4, 18]

A different isolated peak of OSCC was seen at 18-year-olds, which raises concern of key aetiological agents among the paediatric and the below 40-year group. This may point at an inherent aetiological risk exposure to this age group. However, this also happens at a time people come of age as majority complete high school with increased health seeking behaviour. OSCC especially oropharyngeal lesions have been associated with oncogenic HPV (16 and 18) with an increased incidence of viral promoted cancers among the HIV infected persons.[61, 86] Local studies have reported HIV infection to be estimated at 2% among the 15-17-year age group with up to 8% reported at age 23-24-age group years.[85] Tobacco consumption locally was reported to have been 13% among the 12-15-year.[88] Patient education on the role of certain known etiologic habits should play a central role in prevention of such lesions.

Local studies have shown the average initial occurrence of malignant lesions showed a comparative delayed age pattern with a mean age of 45.7 years compared to benign soft tissue tumours who had a mean of 29.4 years or benign odontogenic tumours with a mean of 30.3 years. The reported peak of ameloblastoma in the study was in the 2nd to 3rd decades with an isolated peak at 18 years. Vilembwa et al. (2008) reported the mean age of ameloblastoma as 29.9 years, this having been reported as the commonest odontogenic tumor.[19] Butt et al. (2012) in a study of ameloblastoma among the adolescents however reported a high frequency of ameloblastoma among the 15 -19-year-old group as compare to the 14-year-olds and below. Ameloblastoma can easily mimic odontogenic cysts in the early stages and may be easily missed out if not carefully examined. The eruption of the 3rd molar about this time is associated with different pathologies including cysts, infections, and neoplasms its eruption may contribute to the group peak of OMFDs in this group.[74]

Benign tumours are expansile neoplastic masses usually painless but may present with significant facial disfiguring especially at late presentation which is common locally[19]. They include the odontogenic tumours and benign soft tissue tumours in our grouping which formed the second biggest category. A male predominance was equally seen among benign tumours. Ameloblastoma was the commonest odontogenic tumour in the present study. The other more prevalent lesions

included ossifying fibroma and cemento ossifying fibroma. The findings are consistent with Butt et al. (2012) findings.[83] Other studies have reported similar results.[2,4]

The dentigerous, mucocele and epidermoid cysts were the commonest cysts in this category. Dimba et al. (2007) corroborated such findings with OKC as the most frequent subtype. [4] The dentigerous and OKC are developmental cysts from the embryonic remnants of the developing dental follicle. The propensity of dentigerous cysts to transform to cystic ameloblastomas (15-20%) requires that timely diagnosis and management is key in preventing possible complication.[86] The high number of dentigerous cysts as well as ameloblastomas in the local population may insinuate a possible delayed diagnosis and transformation which should be a subject of another study. Mucoceles are saliva filled encapsulated lesions which may be due to extravasation from the ducts or retention within the acini, trauma is a common aetiology of mucocele. While other studies have reported a higher percentage of mucoceles, failure to submit the lesions for histopathology due to the obvious diagnosis may be a reason for the difference in percentage in the local population. Males depict a higher proportion of patients with cysts. Poor hygiene habits or trauma associated with sports and conflicts may point to the male predilection among cystic lesions.[6]

Adaptive lesions are inflammatory lesions that occur as a result of continuous soft tissue irritation by a certain stimulus. Hormonal influence has been associated in the aetiology. Some studies have reported them as the most prevalent lesions.[9, 27, 39] The present study showed higher frequencies among the female population. The fibrous epulis and pyogenic granuloma were the commonest lesions as corroborated by findings by Awange et al. (2008), a similar picture reported by elsewhere. [8,22,23] The pyogenic granuloma is a vascular epulis associated with pregnant women where hormonal fluctuations in the setting of common irritants like plaque trigger the abnormal growth of the gingival tissue. The mean age was 32.1 years which may be a reflection of the female reproductive age. Epithelial and mucosal lesions form a high percentage of oral cavity lesions. These include ulcerative, inflammatory or even autoimmune lesions affecting the oral mucosa. Such lesions were found to affect more females than males. Better health seeking habits among females than males may be a possible reason for the gender disparity.[4]

Salivary gland diseases are pathologies which affect either or both the major salivary glands and minor salivary glands. The salivary gland pathologies were defined to include tumours, cysts and

other immune diseases. The salivary adenomas and particularly pleomorphic salivary adenoma form the commonest benign neoplasm while the adenoid cystic carcinoma form the commonest malignancy in our local population.[4] Females were reported to have higher frequencies of salivary disease.[6] Other common lesions reported in our population included mucocele and sialadenitis with few cases of Sjogren's disease among others. Some of these conditions are managed clinically or easily missed and the records may not reflect the true picture in the population since many resolve without any surgical intervention Failure of clinicians to diagnose may also be an associated challenge.

Infections are pathological changes on tissues associated with known microbes which may include bacteria, viruses or fungi. Males were reported to exhibit more infections than females. The mean age group was 32.7 +/- 19.1 years and associated factors may include risk habits among the different age groups particularly among the male population. Habits including smoking, poor oral hygiene resulting into periodontal disease may be associated with predisposition to infections.[43] Immunosuppressive conditions like diabetes and HIV infection are likely to predispose to infections from oral flora. *Staphylococcus viridans* and fusobacterium are a common etiologic agents of oral infections while Actinomycosis may be seen following trauma from the field and *Candida albicans* are likely to be seen in the immunocompromised. Notably, males are more affected by periodontal disease.[44,89] Some of these lesions are likely to be managed medically and hence less likely to end up in histopathology laboratory for diagnosis.[57] Inconclusive diagnoses may be as a result of inadequate tissue or poor sampling. Poor storage medium among other clinician and handling factors may be implicated. Rarely it may be an error by the pathologist.

In corroboration with the present study Lam-ubol et al. (2019) in their histopathological study in Thailand similarly reported the mandible as the most prevalent site of orofacial lesions.[32] Exposure to etiologic agents like tobacco products on buccal mucosa has been associated with specific predisposition of certain anatomical sites.[21] Females showed higher frequencies in all sites though not statistically significant. The occurrence of the orofacial lesions showed a fluctuation without much variation with peak increases in the year 2015 and 2016 from when a general decline was seen. The mean age of the lesions in the mandible was 36.1 +/- 20.1 years while the average age of the occurrence in the other common sites was in the 3rd decade. Vilembwa et al. (2008) reported a comparable mean age of occurrence of ameloblastoma, 30.2 +/- 14.1 years among females and

a mean of 29.9 years for the males. Onyango et al. (2004) and Muange et al. (2014) established that the tongue was the most preferred site of oral squamous cell carcinoma with the maxilla and the mandible forming significant proportions.[19,20]

The occurrence of orofacial lesions was observed for trends in the years of study for the most common lesions in the 4 most common categories. The distribution of the lesions in the 20 years including the OSCC, fibrous hyperplasia reactive lesions, ameloblastomas and dentigerous cyst revealed fluctuations over the years. Oral cancer was lowest in the earlier years of 2001 to 2004 with minimal fluctuation in the year 2002, a general increase was observed with a remarkable peak seen in the years 2014 to 2016 followed by a decline which showed minimal fluctuation in the last 3 years. Onyango et al. (2004) in a 20-year study reported a general decline in the occurrence of oral malignancies without much variation in the occurrence of OSCC despite the emergence of HIV infection and lifestyle changes in the population during the study period. [20] Ameloblastoma were noted to fluctuate without much variation upto the year 2015 when a progressive decline proceeded to the lowest occurrence at the end of the study. Dentigerous cyst depicted fluctuations from the beginning of the study without much variation up to the year 2015 where a general decline was observed. Fibrous epulis showed fluctuation without much variation with a peak in 2016 followed by a general decline. Similar studies elsewhere in the world by Saleh et al. (2014) have reported similar fluctuations with a general decline which was equally not statistically significant. [21]

A histopathology study makes use of key investigation necessary for management of oral and maxillofacial lesions. It thus provides a true burden of patients seeking health care services hence may be used to highlight high risk populations as well as a guide to policies which serve as a guide to optimal service delivery in institutions. [83] Being a retrospective study, there are errors which are beyond remedy such as missing details of patients including the proper site of lesion or accurate diagnosis.

4.2 Conclusion

1. The present investigation provides baseline data on the occurrence of OMFDs in the study population. Occurrence of OMFDs showed a gender predilection with females (52.4%) showing a slight predominance than males.

2. Malignancies (32.8%) were higher in males (52.1%) of a higher age (45.7 +/- 20.8 years) in our population. The malignancies and odontogenic tumours followed by reactive lesions and cysts were the most common lesions in the population. OSCC (58.3% of malignancies) and ameloblastoma (70.88% of odontogenic tumors), fibrous epulis and dentigerous cysts remain the most common lesions among the four commonest categories in the study population.

3. The peak of SCC was generally in the 5th and 6th decades while up on exempting the peak at 18 years it was noted to be in the 6th and 7th decades, the ameloblastoma was common in the 2nd and 3rd decades.

4. There was an increasing burden of SCC (26.5%) among the young population aged below 40 years with 18-year-olds reported as a high risk group possibly indicating suboptimal health seeking behaviour of the paediatric population.

5. There was a general increase in the trend of SCC with fluctuations across the years which may reflect poor health seeking habits.

6. The mandible and tongue were the most preferred disease sites. The pattern of occurrence of other OMFDs showed fluctuation among the years of study without much variation.

4.3 Recommendations

1. There is need to keep updated comprehensive, clinical data bases in hospitals which serve to monitor the range, trends and patterns of the disease distribution locally and hence a guide to evidence based health policies for optimal service delivery. Further research on factors causing female predilection and high risk target groups is essential.

2. The increasing predisposition of malignancies (SCC) to the age group below 40 years, the peak at 18 years as well as male predisposition in our population require further research on aetiology and mitigation.

3. Clinicians need to keep high index of suspicion of OSCC on protracted ulcerated lesions in the 5th through the 7th decade while management protocols of ameloblastomas should

take into account curative intent due to the many productive years ahead from the 2nd or 3rd decade as seen in our local population

4. Health care policies which mitigate and expedite oral and maxillofacial disease care for the adolescent's local population will be of added advantage in reduction of cases in this group

5. Training of maxillofacial surgeons need to emphasize competencies in the surgical resection and reconstruction skills of lesions in the most affected regions of the mandible and tongue. With the high incidence of both skeletal and soft tissue OMFDs, there is a demand for surgical skills that would address diseases in theses anatomical sites.

4.4 Limitations of the study

Being a retrospective, the study may have been subject to errors in the records beyond our control. Data with grossly missing details were few and were eliminated before the analysis

The study is carried out in two centers in Nairobi and despite them being major maxillofacial referral centers, the data may not necessarily be reflective of the general population picture in the entire country.

The data on FNAC was incomplete for the 20 year-study with missing records from the 2001 to the 2009, consequently specific data on paediatric oncology like lymphomas may not be well represented, the study however provides essential information comparable with a majority of similar histopathological studies

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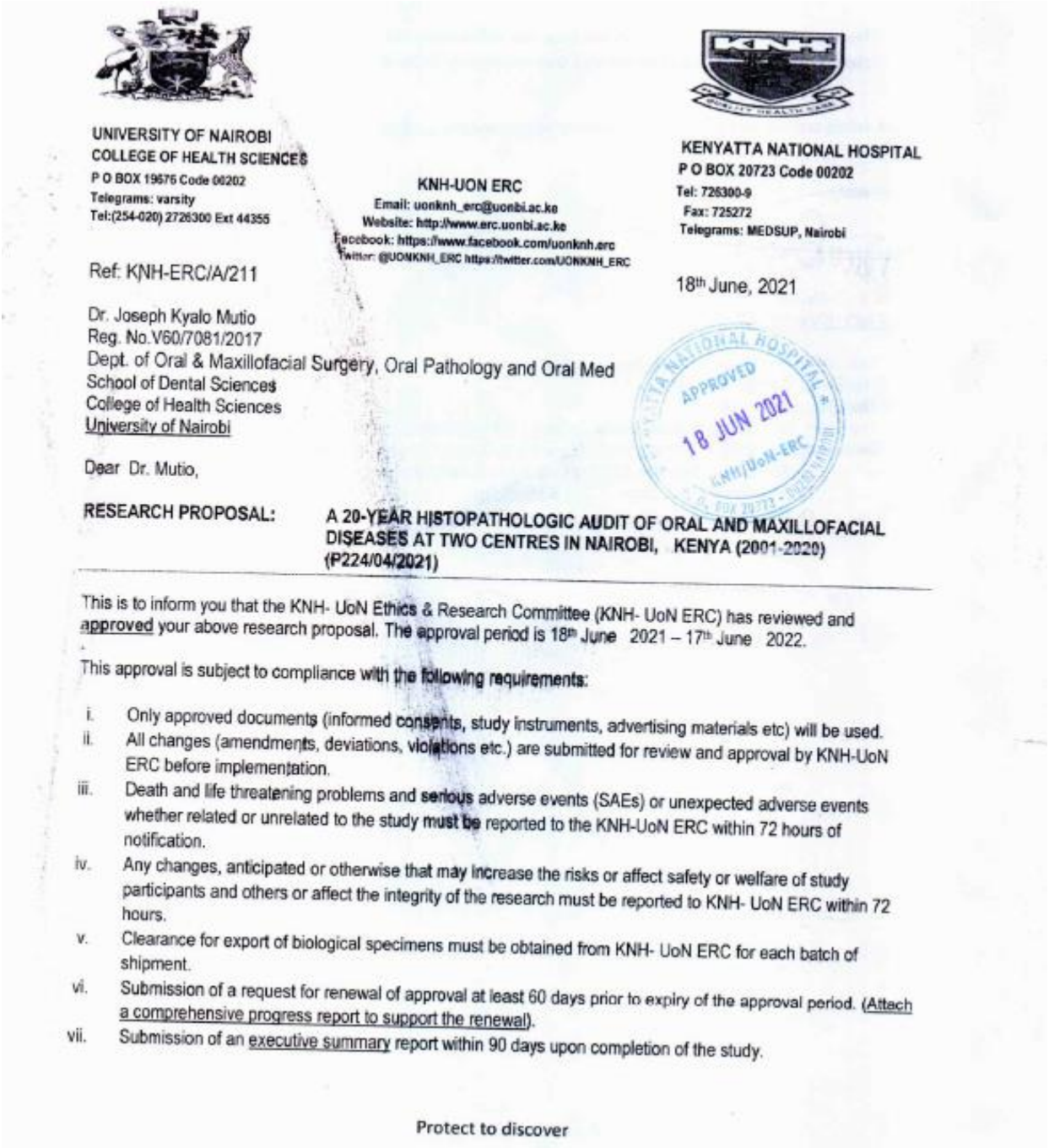
6.0 APPENDICES

6.1 Appendix 1: Ethical approval document (Ref no. P224/04/2021)

Adobe Acrobat Document



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18th June, 2021

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KENYATTA NATIONAL HOSPITAL APPROVED 18 JUN 2021 KNH/UoN-ERC

Dear Dr. Mutio,

RESEARCH PROPOSAL: **A 20-YEAR HISTOPATHOLOGIC AUDIT OF ORAL AND MAXILLOFACIAL DISEASES AT TWO CENTRES IN NAIROBI, KENYA (2001-2020) (P224/04/2021)**

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and approved your above research proposal. The approval period is 18th June 2021 – 17th June 2022.

This approval is subject to compliance with the following requirements:

i. Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
ii. All changes (amendments, deviations, violations etc.) are submitted for review and approval by KNH-UoN ERC before implementation.
iii. Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
iv. Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
v. Clearance for export of biological specimens must be obtained from KNH- UoN ERC for each batch of shipment.
vi. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (Attach a comprehensive progress report to support the renewal).
vii. Submission of an executive summary report within 90 days upon completion of the study.

Protect to discover

This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

For more details consult the KNH- UoN ERC website **http://www.erc.uonbi.ac.ke**

Yours sincerely,

PROF. M. L. CHINDIA
SECRETARY, KNH-UoN ERC

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The Senior Director, CS, KNH
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Supervisors: Prof. M. L. Chindia, Dept.of Oral & Maxillofacial Surgery, Oral Pathology and Oral Med. UoN
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Dr. Elizabeth Dimba, Dept. of Oral & Maxillofacial Surgery, Oral Pathology and Oral Med. UoN
Dr.Wambeti Njiru, Dept.of Oral & Maxillofacial Surgery, Oral Pathology and Oral Med. UoN

6.2 Appendix 2: NACOSTI approval (Research License Ref. No. 773981)

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REPUBLIC OF KENYA

NATIONAL COMMISSION FOR SCIENCE, TECHNOLOGY & INNOVATION

Ref No: 773981

Date of Issue: 25/August/2022

RESEARCH LICENSE

This is to Certify that Dr.. Joseph Kyalo Mutio of University of Nairobi, has been licensed to conduct research in Nairobi on the topic: A 20-YEAR HISTOPATHOLOGIC AUDIT OF ORAL AND MAXILLOFACIAL DISEASES AT TWO REFERRAL CENTRES IN NAIROBI, KENYA (2001-2020) for the period ending : 25/August/2023.

License No: NACOSTI/P/22/19713

773981

Applicant Identification Number

Director General
NATIONAL COMMISSION FOR SCIENCE, TECHNOLOGY & INNOVATION

Verification QR Code

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6.3 Appendix 3: Institutional Permission (KNH)

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KNH/R&P/FORM/01

KENYATTA NATIONAL HOSPITAL
P.O. Box 20723-00202 Nairobi

Tel.: 2726300/2726450/2726565
Research & Programs: Ext. 44705
Fax: 2725272
Email: knhresearch@gmail.com

Study Registration Certificate

1. Name of the Principal Investigator/Researcher
JOSEPH KYALO MUTIO

2. Email address: mejojoek@gmail.com Tel No. 0712337083

3. Contact person (if different from PI) SAMR

4. Email address: ..... Tel No. .....

5. Study Title
A 20-YEAR HISTOPATHOLOGIC AUDIT OF ORAL AND MAXILLOFACIAL DISEASES AT TWO CENTRES IN NAIROBI, KENYA (2001-2020)

6. Department where the study will be conducted (Histology)- Laboratory Medicine
(Please attach copy of Abstract)

7. Endorsed by KNH Head of Department where study will be conducted.

Name: MARY MUNGAI Signature [signature] Date 6/7/21

8. KNH UoN Ethics Research Committee approved study number P224/04/2021
(Please attach copy of ERC approval)

9. I JOSEPH KYALO MUTIO commit to submit a report of my study findings to the Department where the study will be conducted and to the Department of Medical Research.

Signature [signature] Date 02/07/2021

10. Study Registration number (Dept/Number/Year) Lab Medicine /176/2021
(To be completed by Medical Research Department)

11. Research and Program Stamp 0 JUL 2021

All studies conducted at Kenyatta National Hospital **must** be registered with the Department of Medical Research and investigators **must commit** to share results with the hospital.

6.4 Appendix 4: Institutional Permission (UoNDH)

Adobe Acrobat Document

University of Nairobi

Department of Dental Sciences

P.O. Box 19676-00202

Nairobi

Kenya

20 August 2021,

Dear Prof M.L. Chindia

Secretary, KNH-UON-ERC

RE: Dr. Mutio K. Joseph V60/7081/2017, Principal Investigator, Unit of Oral and Maxillofacial Surgery, Department of Dental Sciences

Research Topic: A 20-YEAR HISTOPATHOLOGIC AUDIT OF ORAL AND MAXILLOFACIAL DISEASES AT TWO REFERRAL CENTRES IN NAIROBI, KENYA (2001-2020)

You are hereby informed that the University of Nairobi, Department of Dental Sciences has no objection in availing access to patient's histopathological records at UoN Dental Hospital to the researcher for his dissertation study which is mentioned above and for which the proposal has been submitted to the KNH-UoN ERC.

Regards,

Dr. W.A. Odhiambo,

Chair of Department,

Dental Sciences.

Signature..... Date 20/8/2021

6.5 Appendix 5: Categories of oral and maxillofacial conditions/sites (ICD 10)[81]

C00-C14, C41.1, C43, C44, C46.2, C49.9, C79.5, C79.8: Malignant tumours involving the oral cavity, lip, and the pharynx

C31: Malignant tumours involving accessory sinuses

C76, C77: Malignant tumours involving of lymph nodes; Unspecified or Secondary

D10-11.9: Benign tumours involving the major salivary glands, mouth and pharynx

D14: Benign neoplastic lesions of the respiratory system and middle ear

D16.4, D16.5, D23.0: Benign neoplastic lesions involving the face, skull and articular cartilage

D37, D38.5: Neoplastic lesions of unknown behaviour of oral cavity

D00: Carcinoma in situ involving the oral cavity

D02.3: Carcinoma in situ lesion involving other parts of respiratory system

K00: Abnormalities of tooth development and eruption

K01: Teeth are which are embedded and impacted

K02: Dental decay

K03: Other pathologies involving the hard tissues of the teeth

K04: Diseases involving the tissues in the pulp and periapical region

K05: Gingival inflammation and diseases of the periodontium

K06: Other pathologies involving the edentulous alveolar ridge and the gingiva

K07: Anomalies involving the dentofacial region

K08: Other pathologies involving the teeth and their supporting structures

K09: Cystic lesions involving the oral region which are not classified elsewhere

K10: Other jaw diseases

K11 Diseases involving the salivary glands

K12 Inflammatory lesions of oral cavity like Stomatitis and related conditions

K13 Diseases involving the lips

K14 Diseases involving the tongue

Q38 Other congenital malformations involving the mouth, tongue and pharynx

Q10-Q18 Congenital malformations affecting the neck, face, eye and ear

6.6 Appendix 6: Major Categories of oral and maxillofacial diseases based on classification by Lima et al. (2008)[72] and Jones et al. (2006)[9]

The 13 Categories of oral and maxillofacial diseases

1. Adaptive/reactive lesions: Fibrous epulis, Inflammatory fibrous hyperplasia, hyperplasia, peripheral giant cell granuloma, parulis, focal fibrous hyperplasia, gingival hyperplasia, denture irritation hyperplasia, others.
2. Cystic lesions:
    a. Odontogenic cysts: Eruption, Dentigerous, Radicular, odontogenic keratocyst, Gingival cysts of adult & newborn
    b. Non odontogenic cyst: Nasopalatine cyst, Nasolabial cyst, Medial palatine,
    c. Dermoid/ epidermoid cysts, Thyroglossal duct cyst, Lymphoepithelial / branchial cysts
    d. others
3. Bone pathologies: Fibrous dysplasia, cherubism, exostosis, traumatic and aneurysmal bone cysts, central ossifying fibroma, cement osseous dysplasia, ossifying periostitis, osteomyelitis, Central giant cell granuloma, reaction bone tissue, others.
4. Odontogenic tumours: Ameloblastomas, ameloblastic fibroma, ameloblastic fibro-odontoma, peripheral odontogenic fibroma, adenomatoid odontogenic tumour, odontogenic myxoma, Odontoma, benign cementoblastoma, others.
5. Epithelial disorders/Mucosal Pathology: Unspecific inflammatory process, Recurrent aphthous ulcerations, Actinic cheilitis, Fibroepithelial hyperplasia, Papilloma, Irritative hyperkeratosis, Benign migratory glossitis, Traumatic ulcer, Fibroma, Fibrosis, Melanin pigmentation, Lichen planus, Melanocytic nevus, Mucositis, Verruca vulgaris, Amalgam tattoo, Hyperkeratosis and acanthosis, others
6. Infections: Actinomycosis, Paracoccidioidomycosis, leishmaniasis, Toxoplasmosis,

others.

7. Benign soft tissue neoplasms: Squamous Papilloma, lymphangioma, Giant cell fibroma, Haemangioma, Nevus, lipoma, common wart, congenital epulis, fibroma, neurofibroma, vascular hamartoma, others.
8. Malignant tumours: Squamous cell carcinoma, verruca's carcinoma, osteosarcoma, Rhabdomyosarcoma, fibrosarcoma, Langerhans cell histiocytosis, melanoma, Non-Hodgkin's lymphoma, Neuroblastoma, Basal cell carcinoma, others
9. Tooth abnormalities: Supernumerary, Amelogenesis imperfecta, Dentinogenesis imperfecta, microdontia, mesiodens, *Dens invaginatus*, twinning, fusion, germination, pulp nodules, root resorption, taurodontia, ankylosis, others
10. Salivary gland diseases: Ranula, Mucocele, sialadenitis, sialolithiasis, adenomatoid hyperplasia, myoepithelioma, Pleomorphic salivary adenoma, mucoepidermoid carcinoma, adenoid cystic carcinoma, Warthin's, others
11. Normal tissues and dentition: Normal lymph nodes, Pericoronal follicle, Healthy soft or Hard tissue.
12. Other pathologies
13. Inconclusive diagnoses

6.7 Appendix 7: Data extraction form

Serial number	Patient hospital number (de identified)	Lab code	Referral facility	Date of submission	Age	Gender	Site	ICD-10 code	Diagnosis	13 categories