THE PATTERN OF SALIVARY GLAND TUMOURS AMONG PATIENTS ATTENDING ORL AND MAXILLOFACIAL SERVICES AT MUHIMBILI NATIONAL HOSPITAL

John Masago

MMed (Otorhinolaryngology) Dissertation
Muhimbili University of Health and Allied Sciences
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By

John Masago

A Dissertation Submitted in (partial) Fulfilment of the Requirements for the Degree of Master of Medicine in Otorhinolaryngology of Muhimbili University of Health and Allied Sciences

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CERTIFICATION

The undersigned certifies that they have read and hereby recommends for acceptance by the Muhimbili University of Health and Allied Sciences a dissertation entitled **"*The pattern of salivary gland tumours among patients attending ORL and Maxillofacial services at Muhimbili National Hospital*"**, in (partial) fulfilment of the requirements for the degree of Master of Medicine of the Muhimbili University of Health and Allied Sciences.

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Dr Edwin Liyombo

(Supervisor)

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Date

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Date

DECLARATION AND COPYRIGHT

I, **Dr. John Masago**, declare that this **dissertation** is my own original work and that it has not been presented and will not be presented to any other University for a similar or any other degree award.

Signature……..... **Date**…….

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DEDICATION

I wish to dedicate this work to my beloved parent, Laurencea Masago, my wife Angel and My Son Erick for their love, understanding, encouragement and moral support in my life

ABSTRACT

SUMMARY

Introduction: Salivary gland neoplasm constitutes about 10% of all head & neck neoplasm which represent 3% of all neoplasm of the body. The diseases contribute to significant morbidity worldwide while its epidemiology in Tanzania remains sparse. There was paucity of information regarding salivary gland tumours in our setting; therefore it was important to conduct this study to describe our experience on salivary gland tumours, associated co-morbidities and treatment outcome in patients attending Muhimbili national hospital.

This study was carried out to find the prevalence and the frequency of malignancy among salivary gland neoplasms, their histological types, age and sex distribution of the patient.

Objective: The study aimed at determining the pattern of salivary gland tumours among patients attending Otorhinolaryngology and Maxillofacial services at Muhimbili National Hospital.

Method: This was a hospital based cross-sectional study that was conducted in the departments of the Otorhinolaryngology and Maxillofacial at Muhimbili national hospital involving all patients with a clinical diagnosis of Salivary gland tumours. Study was carried out on a total number of 276 patients of salivary neoplasms of different age groups. Data was collected by history taking, physical examination and the necessary investigations using a pre-tested coded questionnaire and analyzed using SPSS statistical

computer software version 20.0. The study took a period of six months from July to December 2016 with an estimated cost of 1,500,000 TShs.

Results

Among 276 study participants 156 (56.5%) were males and 120 (43.5%) were females. Their age ranged from 0 to 90 years with mean age of 49.47 years, SD ±15.7. Most of them 69 (28.6 %), were in the age group of above 60 years.

Most of them 31 (26.1 %), were in the age group of40-49 and 60+ years. The prevalence obtained was higher among males, 64 (55.1%) salivary gland tumours occurred in men and 52 (44.8%) occurred in women, P=0.76 which is not statistically significant. The parotid gland was the most commonly affected site (75%) and the submandibular and sublingual were the least affected sites (7.5%).

Among 116 patients with SGT, 76 (66%) had malignant type and 40 (34%) benign type. Both benign and malignant SGT tumours had male preponderance. The most common benign histology was pleomorphic adenoma which was high in males (28.1%) compared to females(25.0%), and the common malignant histology was mucoepidermoid carcinoma,(23.4%) in males and (28.9%) in females. The tumours affected men more commonly, particularly the 40-49 age group, but these differences were not statistically significant (p= 0.07).

Conclusion.

Majority of salivary gland tumours in our setting were malignant type and mucoepidermoid carcinoma being the most occuring histological type while Pleomorphic adenoma was the mostly frequent encountered benign type and both had male preponderance mostly seen at the age of 40 years and above. Majority of patients with malignant tumours presented late to the hospital therefore there is a need for advocacy for early health seeking behaviour to the community and early detection of the disease by health personnels in the primary health centers hence prompty referal to otorhinolaryngology specialists for definitive management.

Contents

CERTIFICATION iii
DECLARATION AND COPYRIGHT iv
ACKNOWLEDGEMENTS v
DEDICATION vi
ABSTRACT vii
SUMMARY vii
ABBREVIATIONS xii
DEFINITION OF TERMS xiii
LIST OF TABLE xiv
LIST OF FIGURE xv
CHAPTER ONE 1
1.0 INTRODUCTION AND BACKGROUND 1
1.1 Salivary gland tumours 1
1.2.1 Classification of salivary gland tumors 2
1.2.2 Benign epithelial tumors 2
1.2.3 Benign nonepithelial tumors 3
1.2.4 Tumorlike lesions 4
1.2.5 Malignant Salivary Gland Tumors 4
1.2.6 Aetiology and Associated risk factors 5
1.2.7 Pathophysiology 5
1.2.8 Presentation 6
1.2.9 Physical examination 7
1.2.10 Investigation 7
1.2.11 Staging 7
1.2.12 Treatment 8
1.3 LITERATURE REVIEW 9
1.4 STATEMENT OF THE PROBLEM 13
1.5 STUDY RATIONALE 14
1.6 RESEARCH QUESTIONS 15

CHAPTER TWO 16
2.0 OBJECTIVES 16
2.1 Broad objective 16
2.2 Specific Objectives 16
CHAPTER THREE 17
3.0 METHODOLOGY 17
3.1 Study Area 17
3.2 Study design 17
3.3 Study duration 17
3.4 Study population 17
3.5 Inclusion criteria 18
3.6 Exclusion criteria 18
3.7 Sampling procedure 18
3.8 Sample size calculation 18
3.9 Data collection technique 18
3.10 Data handling and analysis 19
3.11 Reproducibility 20
3.12 Ethical considerations 20
3.13 Study limitations 20
3.14 Study mitigations 20
CHAPTER FOUR 21
4.0 RESULTS 21
REFERENCES 31
Appendix 1 35
Consent form: English version 35
Consent form: Swahili version 37
Appendix 2 39
Questionnaire and clinical examination form (English version) 39
Questionnaire and clinical examination form (Swahili version) 42

ABBREVIATIONS

ACC-Adenoidcystic Carcinoma

AJCC-American Joint Committee on Cancer

CT-Computed Tomography

ENT-Ear, Nose and Throat

FNAB-Fine Needle Aspiration Biopsy

FNAC-Fine Needle Aspiration Cytology

MEC-Mucoepidermoid Carcioma

MD-Medical Doctor

MDM2- Mouse Double Minute 2

MMED-Master of Medicine

MNH-Muhimbili National Hospital

MUHAS-Muhimbili University of Health and Allied Sciences

ORL-Otorhinolaryngology

PA-Pleomorphic Adenoma

SGT-Salivary Gland Tumour

SPSS-Statistical Package for Social Sciences

TNM- Tumor, Nodes, Metastases

UICC-International Union for Cancer Control

VEGF-Vascular Endothelial Growth Factor

WHO-World Health Organization

DEFINITION OF TERMS

Gland: An organ in an animal's body that synthesizes a substance such as hormones, saliva for the release into the cavity inside the body or its outer surface or into the bloodstream.

Otorhinolaryngology: is the study of ear, nose, and throat conditions or ENT. It is also referred to as Otolaryngology–Head and Neck Surgery or otorhinolaryngology.

Maxillofacial; a surgical specialty which involves the diagnosis, surgery and adjunctive treatment of diseases, injuries and defects involving both the functional and aesthetics aspects of the hard and soft tissues of the oral and facial region.

Salivary gland; Any of the various glands that secrete saliva into the oral cavity.

Tumour: A mass of diseased cells that might become a lump, or ulcerate and cause illness.

LIST OF TABLE

Table 1. Dermographic distribution of study participants……21
Table 2. Age and sex distribution among patients with salivary gland tumours……..22
Table 3. Histopathological types of salivary gland tumors……..26

LIST OF FIGURE

Figure 1. Distribution of salivary gland tumors……23
Figure 2.Distribution of Benign SGT tumors by site of origin……...24
Figure 3. Distribution of malignant SGT by site of origin……...25

CHAPTER ONE

1.0 INTRODUCTION AND BACKGROUND

The salivary glands are exocrine glands, glands with ducts that produce saliva. The glands are divided into major and minor salivary gland categories. The major salivary glands are the parotid, the submandibular, and the sublingual glands. The minor glands are dispersed throughout the upper aerodigestive submucosa (ie, palate, lip, pharynx, nasopharynx, larynx, parapharyngeal space). (1, 2, 3)

1.1 Salivary gland tumours

Salivary gland tumours (SGTs) represent an uncommon heterogeneous group of neoplasms with complex clinicopathological characteristics. (4, 5) However, they are important in head and neck pathology due to the relative difficulty in their diagnosis, management and unpredictable clinical course. The prevalence of these tumours varies between studies, but has been estimated to make up about 3–10% of all head and neck tumors, with an estimated annual incidence throughout the world ranging from 0.05 to 2 new cases per 100,000 population. (6)

Tumours of many different origins can arise in the salivary glands. Some authors suggest that the histopathology of these neoplasms is more complex and diverse than any other site in the body (7). The World Health Organisation (WHO) proposed the first histological classification of salivary gland tumours in 1972 (8). Many studies have been performed in order to describe the epidemiology of benign and malignant salivary gland tumours.(5-7,10,11) Due to advances in the understanding of the aetiology and behaviour of these tumours as well as their wide morphological diversity, the WHO published the third and last edition of this classification in 2005. (12) The incidence, prevalence, age, gender, anatomical distribution and survival rates varies between different parts of the world(7,10) and is not necessarily representative of the population of Tanzania. To our knowledge there is only one study published in the literature conducted in a Tanzanian population which involved two hospital settings MNH & KCMC.

1.2.1 Classification of salivary gland tumors

Tumors of the salivary glands may be broadly categorized into benign neoplasms, tumorlike conditions, and malignant neoplasms.(6,11). Most (70%) salivary gland tumors (SGTs) originate in the parotid gland. The remaining tumors arise in the submandibular gland (8%) and in the minor salivary glands (22%). Although 80% of parotid gland tumors are benign, slightly more than 50% of tumors of the submandibular gland and 60-80% of minor SGTs are found to be malignant.(12)

1.2.2 Benign epithelial tumors

1.2.2.1 Pleomorphic adenoma

Pleomorphic adenomas (benign mixed tumors) are the most common tumors of the salivary gland and are most often located in the tail of the parotid gland. When found in the minor salivary glands, the hard palate is the site most frequently involved, followed by the upper lip.

These tumors were termed pleomorphic because of the epithelial and connective tissue components that compose them in varying degrees. Their gross appearance is a round, smooth mass with a thin, delicate, incomplete capsule. Pleomorphic adenomas (benign mixed tumors) are the most common benign SGTs, comprising 85% of all salivary gland neoplasms.(12)

1.2.2.2 Warthin tumor (ie, papillary cystadenoma lymphomatosum, cystic papillary adenoma, adenolymphoma)

Albrecht first recognized this tumor in 1910, and Warthin later described it in 1929. In gross appearance, it is a smooth, soft, parotid mass. It is well encapsulated when located in the parotid gland and contains multiple cysts. Malignant transformation has not been observed. All patients with this tumor survive, and the recurrence rate is 5%. The Warthin tumor tends to be bilateral (10% of cases) and is usually found in the major glands, as are most other types.(13,14)

1.2.2.3 Intraductal papilloma

Intraductal papilloma (IDP) is a small, tan, fairly smooth lesion that is usually found in the submucosal layer. IDP of the minor salivary gland is a rare lesion that has been described only in various case reports.(14)

1.2.2.4 Oxyphil adenoma (oncocytoma)

Duplay first described the oncocytic tumor in 1875. Oncocytomas of the salivary glands are very uncommon. They rarely, if ever, occur in the minor salivary glands. Such neoplasms occur more often in women than in men, with a female-to-male ratio of 2:1. Patients are older than 50 years, and the superficial lobe of the parotid gland is the most commonly reported location. Oncocytomas manifest as small (< 5 cm in diameter), firm, slow-growing, spherical masses. Bilateral oncocytomas of the parotid glands have been described. These tumors recur if excision is incomplete.(14)

1.2.3 Benign nonepithelial tumors

1.2.3.1 Hemangiomas

Hemangiomas are the most common SGTs in children and usually involve the parotid gland. Less often, they may involve the submandibular gland. These vascular tumors may be distinguished from vascular malformations by their presence early in life, rapid growth phase in children aged approximately 1-6 months, and gradual involution over 1-12 years. The typical presentation is an asymptomatic, unilateral, compressible mass. Gross examination reveals a dark red, lobulated, unencapsulated mass. (14)

1.2.3.2 Lymphangioma (cystic hygroma)

Lymphangiomas are most commonly located in the head and neck region of infants and children. They are believed to be due to lymphatic sequestration of primitive embryonic lymph ducts that undergo irregular growth and canalization. They are spongy, multiloculated masses with a yellowish or bluish surface and are formed by endothelial-lined spaces. More than 50% manifest at birth, and 80% manifest by age 2 years. Usually, they manifest as painless masses that may involve parotid glands, submandibular glands, or both. Diagnosis is made based on clinical findings..(14)

1.2.3.3 Lipoma

Lipoma tumors are relatively uncommon in a major salivary gland. They derive from fat cells and appear grossly as smooth, well-demarcated, bright-yellow masses. These tumors manifest as soft, mobile, painful masses and peak in the fifth and sixth decades of life, with a male-to-female ratio of 10:1. They are slow-growing tumors with an average diameter of 3 cm. Treatment is surgical excision. (14)

1.2.4 Tumorlike lesions

1.2.4.1 Necrotizing sialometaplasia

Necrotizing sialometaplasia may easily be mistaken for a malignant tumor because it presents as a single, unilateral, painless or slightly painful lesion on the hard palate. However, it is a benign, self-healing lesion of the minor salivary glands that is seen in adults older than 40 years and is 2-3 times more common in men than in women. Although the etiology is unknown, it may represent a reparative process in response to ischemic necrosis of salivary tissue. A biopsy helps to rule out a malignant process.(14)

1.2.4.2 Lymphoepithelial hyperplasia (Mikulicz disease, sicca complex, chronic punctate sialadenitis)

This disorder can manifest as a diffuse enlargement of all or part of the parotid gland, or it may manifest as a discrete mass. Lymphoepithelial hyperplasia is more frequent in females than in males, and its peak incidence is in the fourth and fifth decades of life. Occasionally, both parotid glands are involved. The growth of this tumor is slowly progressive, and it gives rise to pain around the ear or the retromandibular area. (14)

1.2.5 Malignant Salivary Gland Tumors

The world health organization has classified malignant salivary gland tumours into, malignant epithelial tumors, benign epithelial tumors, soft tissue tumors, hematolymphoid tumors, and secondary tumors (i.e. a tumor which has metastasized to the salivary gland from a distant location) (14)

1.2.6 Aetiology and Associated risk factors

The etiology of salivary gland neoplasms is not fully understood. Two theories predominate: the bicellular stem cell theory and the multicellular theory.

1.2.6.1 Bicellular stem cell theory

This theory holds that tumors arise from 1 of 2 undifferentiated stem cells: the excretory duct reserve cell or the intercalated duct reserve cell. Excretory stem cells give rise to squamous cell and mucoepidermoid carcinomas, while intercalated stem cells give rise to pleomorphic adenomas, oncocytomas, adenoid cystic carcinomas, adenocarcinomas, and acinic cell carcinomas. (18)

1.2.6.2 Multicellular theory

In the multicellular theory, each tumor type is associated with a specific differentiated cell of origin within the salivary gland unit. Squamous cell carcinomas arise from excretory duct cells, pleomorphic adenomas arise from the intercalated duct cells, oncocytomas arise from the striated duct cells, and acinic cell carcinomas arise from acinar cells. Recent evidence suggests that the bicellular stem cell theory is the more probable etiology of salivary gland neoplasms. This theory more logically explains neoplasms that contain multiple discrete cell types, such as pleomorphic adenomas and Warthin tumors. (18)

1.2.7 Pathophysiology

The histogenesis of SGTs is based on the salivary gland unit (see the image below). According to the multicellular theory of SGTs, pleomorphic adenomas originate from the intercalated duct cells and myoepithelial cells; oncocytic tumors originate from the striated duct cells; acinic cell tumors originate from the acinar cells; and mucoepidermoid and squamous cell tumors originate from the excretory duct cells. (15,18)

Studies that look at the neovascularization in salivary gland neoplasms have revealed factors that increase angiogenesis and are important in the progression of salivary gland neoplasms. Vascular endothelial growth factor (VEGF) is expressed by over half of

salivary gland carcinomas tested and is correlated with clinical stage, recurrence, metastasis, and survival. (18)

1.2.8 Presentation

The clinical presentation of a salivary gland neoplasm depends upon its specific site of origin and the extent of involvement of adjacent organs. Patients with a tumor of a major salivary gland typically present with a painless mass or swelling of the parotid, submandibular, or sublingual gland. The presence of a parotid mass in combination with signs or symptoms indicative of facial nerve paralysis, Pain, ulceration, fixation to surrounding tissues and lymph nodes involvement is generally indicative of a malignant rather than a benign tumor. (20)

Minor salivary gland tumors arising within the oral cavity may present with a painless submucosal mass or mucosal ulceration in the palate, lips, or buccal mucosa, with an appearance similar to sialometaplasia (squamous metaplasia of salivary glands) or squamous cell carcinoma. Symptoms due to more advanced minor salivary gland tumors are a function of the location of the tumor and can include nasal obstruction, congestion, vision changes, or trismus when present in the nasal cavity or maxillary sinus. Minor salivary gland tumors involving the nasopharynx usually present at an advanced stage; invasion of the skull base, intracranial extension, or involvement of cranial nerves is common. (20)

Most patients with salivary gland neoplasms present with a slowly enlarging painless mass. A discrete mass in an otherwise normal-appearing gland is the norm for parotid gland neoplasms. Parotid neoplasms most commonly occur in the tail of the gland. Submandibular neoplasms often appear with diffuse enlargement of the gland, whereas sublingual tumors produce a palpable fullness in the floor of the mouth. (20)

Minor salivary gland tumors have a varied presentation, depending on the site of origin. Painless masses on the palate or floor of mouth are the most common presentation of minor salivary neoplasm. Laryngeal salivary gland neoplasms may produce airway obstruction, dysphagia, or hoarseness. Minor salivary tumors of the nasal cavity or paranasal sinus can manifest with nasal obstruction or sinusitis.Lateral pharyngeal wall

protrusions with resultant dysphagia and muffled voice should raise suspicion of a parapharyngeal space neoplasm. (20)

1.2.9 Physical examination

Physical examination of salivary gland masses should occur in the context of a thorough general head and neck examination. Note the size, mobility, and extent of the mass, as well as its fixation to surrounding structures and any tenderness. Perform bimanual palpation of the lateral pharyngeal wall for deep lobe parotid tumors to assess for parapharyngeal space extension. Bimanual palpation for submandibular and sublingual masses also reveals the extent of the mass and its fixation to surrounding structures. Pay attention to surrounding skin and mucosal sites, which drain to the parotid and submandibular lymphatics. Regional metastases from skin or mucosal malignancies may manifest as salivary gland masses. Also, the cervical lymph node basin should be palpated to assess for metastatic disease from a primary lesion of the salivary glands.CN VII should be assessed carefully to identify any weakness or paralysis. Facial nerve palsy usually indicates a malignant lesion with infiltration into the nerve.(20)

1.2.10 Investigation

Fine needle aspiration cytology (FNAC) is an investigation frequently used. The diagnostic yield of FNAC can be quite good with large study series showing sensitivity up to 85% and specificity up to 99% (15, 17). However, reports of other studies are far from ideal, and thus controversy as to the usefulness of FNAC still persists. It is safe to say that the role of FNAC mainly lies in preoperative patient counseling and surgical planning. In the case of a malignant FNAC result, the patient can be better prepared in terms of the extent of surgery, higher potential complications, and need for neck dissection or postoperative radiotherapy.(19)

1.2.11 Staging

Salivary gland cancers are staged according to the Seventh Edition of the American Joint Committee on Cancer (AJCC) Cancer Staging Manual and the International Union for Cancer Control (UICC) Tumor, Nodes, Metastases (TNM) system, where the primary tumour (T) is staged according to size, extraparenchymal extension, and direct invasion.

Regional lymph node involvement (N) staging is dependent on the size and location of the metastatic lymph nodes. The detection of distant metastasis is designated as M1. The overall cancer stage is derived from the combination of these three factors. (21)

1.2.12 Treatment

Surgery is the mainstay of treatment for salivary gland tumours. In the case of parotid gland tumours, superficial parotidectomy with facial nerve dissection and preservation is the standard diagnostic procedure. This operation is also therapeutic in cases of benign or small malignant tumours limited to the superficial lobe of the gland. Studies in the past have found enucleation of benign tumours to be associated with an unacceptably high chance of tumour recurrence especially for pleomorphic adenomas.(19) However, several recent studies have suggested that a more limited resection in the form of extracapsular dissection where the pleomorphic adenoma is resected only with a cuff of normal glandular tissue offers better postoperative cosmetic result and lower incidence of Frey's syndrome without an increase in the incidence of tumour recurrence and facial nerve injury. (15, 18-20).

1.3 LITERATURE REVIEW

Salivary gland tumors constitute an uncommon, heterogeneous group of neoplasms that vary considerably in their anatomic site of origin, histology, and biologic behavior. Both benign and malignant salivary gland tumors are classified according to the 2005 World Health Organization system.(26)

In a study done in Chile, salivary gland tumours prevalence was 15.24 per 100.000 and the incidence was 2.51 per 100,000. Forty one point nine percent of the tumours occurred in men and 58.1% occurred in women. One hundred and ninety six tumours 70.3% were benign and 29.7%were malignant. Of the benign tumours, 80 (40.8%) occurred in men and 59.2% occurred in women. Of the malignant tumours, 44.6% occurred in men and 55.4% in women. (30)

As the results in this study indicated, the age of patients was in the range of 9-80 years. This finding is similar to those reported by Ansari in Iran, Otoh et al (10) in Nigeria, Al-Khateeb and Ababneh in north Jordanians and Li et al(6) in China. In this study, also the mean age of affected patients by malignant salivary gland tumors was 52 years, while it was 41 years for patients with benign salivary gland neoplasms. This result has been supported by studies performed by Ansariin Iran, de Oliveira et al (5) in Brazil, Lukšić et al (7) in Croatia and Spiro et al (27) in United States of America. The results of these studies have shown that patients with malignant salivary gland neoplasms are older than patients with benign tumors.(5,7,8,26-28)

WHO and other reports (8)and in the study done in Chile, female patients are overall more affected than men, although there are some studies that report higher prevalence's in men (7,12,). According to current results, there was a slight female predominance in salivary gland neoplasms (male/female: 1/1.04). This was similar to de Oliveira et al (5) and Dhanuthai et al.studies in Brazil and Thailand. However, Otoh et al (10) and Tian et al (6) have reported more male predilection in salivary gland neoplasms in Nigeria and China. The more frequency of Warthin's tumor in china populations may describe these different results. (6,12,26)

Anatomically, the parotid gland is the most frequent site of salivary gland tumors, accounting for approximately 80 to 85 percent of these tumors.(26, 28) About three-fourths of parotid lesions are benign and approximately 25 percent are malignant.(28) Less frequently, salivary gland tumors originate in the submandibular, sublingual, and minor salivary glands, which are located throughout the submucosa of the mouth and upper aerodigestive tract. (28) In contrast to tumors arising in the parotid, 40 to 45 percent of submandibular gland tumors, 70 to 90 percent of sublingual gland tumors, and 50 to 75 percent of minor salivary gland tumors are malignant.

Neoplasm of salivary gland may occur at any age, Marshall and Miles (1974) showed malignant tumours usually appear in later age group but may be seen in the adolescents by studies done by Shafiquil et al (36) showed the highest number of patients were in the 5th decade which correlate with other studies. (6,24) Regarding the sex distribution of different neoplasms, benign parotid tumours was more common in male (M: F= 1.8:1). Malignant parotid neoplasms was also more common in male (M: F= 1.8:1). Among the malignant submandibular neoplasms, 50% were in male. Among the benign minor salivary gland tumour, (66.67%) were male and (33.33%) were female.(36)

It is reported that mesenchymal tumours account for 1.9% to 5% (30) of all salivary gland tumours. Takahama *et al*. (30) reported in their series of 600 cases that 95% of the tumours were of epithelial origin, while the remaining 5% were of non-epithelial origin. The majority of the cases in the present review were of epithelial origin (92.8%) with only 19 cases (6.8%) of non-epithelial origin, which is slightly different than the other reports.(30)

In Finland and Israel during the 10-year study period, 1,444 cases of SGTs of epithelial origin were managed in the Helsinki center, 444 in Oulu and 330 in TAU. The estimated annual incidence of salivary gland tumours was 10.3 per 100,000 population in Helsinki, 5.7 in Oulu, and 3.3 in TAU. In Helsinki, the benign tumors accounted for 1,217 cases and the malignant tumors for 227, yielding a benign-to-malignant ratio of 5.4:1. In Oulu, 389 cases were benign and 55 cases were malignant, yielding a ratio of 7.1:1. In TAU, 220 of the 330 SGTs were benign and the rest were malignant, yielding a ratio of 2:1.

Pleomorphic adenoma (PA) and adenoid cystic carcinoma (ACC) were the most common benign and malignant tumors, respectively, in all the three centers. Warthin tumor and mucoepidermoid carcinoma were the second most common benign and malignant tumors, respectively.(24) The study which reports the largest salivary gland tumor series from Turkey indicates in the present salivary gland tumor series, malignancy rate is 31.0 %.(31)

In Africa, only few studies on salivary gland tumors have been reported, mainly in Kenya, Tanzania, Congo, Uganda and Nigeria. The prevalence of salivary gland tumors in these countries ranges from 2.8% to 10% of all head and neck tumors (32-34), the parotid gland is the commonest site in 46.5% to 60% of the cases. (33) The commonest benign tumor is the pleomorphic adenoma, (34) while the commonest malignant tumor is the adenoid cystic carcinoma.

In a study done in Nigeria, Out of 1688 cases of maxillofacial tumors seen within the study period, 135 patients (8%) had SGTs of which 62 were males and 73 were females, male to female ratio was 1:1.2. The age range was 2.5 years to 80 years. Most patients (80.7%) were between 21-60 years old. Fewer SGTs (28.9%) were benign than malignant (71.1%). The most common SGT was adenoid cystic carcinoma (ACC) with a relative prevalence of 35.5% followed by pleomorphic adenoma (PA) (27.4%) and mucoepidermoid carcinoma (MEC) (21.4%).(29) The major salivary glands (parotid and submandibular) accounted for 82 SGTs (60.7%) while the rest 53 (39.3%) occurred in minor salivary glands.(29) In Kenya salivary gland tumours formed 20.2% of all tumours and tumour-likelesions of the oro-facial region.(33)

In Tanzania the study done by Masanja et al revealed that salivary gland tumours occurred with a relative frequency of 6.3% out of all other tumours and tumourlike lesions in the oro-facial region, which is in agreement with several other studies (8, 33). However, this is in contrast to findings from Kenya where they were seen to occur with a higher relative frequency (35).

Data of studies indicated that the most common site of occurrence for salivary gland tumors is parotid (45.9%) and then minor salivary glands (41.5%). After that,

submandibular gland (12.2%) and sublingual gland (0.4%) are affected. Among the minor salivary gland tumors, palate was the most frequent location accounting for 98% of the tumors. Other studies by Waldron et al. in USA, Tilakaratne et al. in Sri Lanka, Kayembe and Kalengayi in Congo (38) Ito et al. (10) in Brazil, and Subhashraj in India (39), had reported the same result for the site of malignancies in salivary gland tumors. (37)

Histologically, the most common type of benign salivary gland tumor is the pleomorphic adenoma, which comprises about half of all salivary tumors. Other rarer benign salivary gland tumors include Warthin tumor, basal cell adenoma, and canalicular adenoma. The most common malignant salivary gland tumors are mucoepidermoid carcinoma and adenoid cystic carcinoma, which together comprise approximately one-half of all malignant salivary gland tumors. (4, 37)

1.4 STATEMENT OF THE PROBLEM

Tumours of the salivary glands form one of the most heterogeneous groups of oncological pathology. They constitute a substantial proportion of all tumours of the oro-facial region. Salivary gland neoplasm constitute 10%of all head and neck tumours.

In Muhimbili national hospital salivary gland tumours are among the diseases seen in the ORL and Maxillofacial departments.Salivary gland tumours in the parotid or submandibular glands usually present as an enlarging painless mass and hence raise little concern to seek for medical attention. This may be associated with neurological symptoms such as facial nerve paralysis or pain if the tumour is malignant.

Patients with salivary gland tumours present late in the referal hospitals due to its painless presentation symptoms.Due to late stages at diagnosis of the disease treatment becomes challenging and most of them end up with complications like facial nerve paralysis or malignant transformation of benign tumor. This is a problem that needs to be addressed in order to maximise the effectiveness of treatment. Very little documented information about SGTs is known in our setting.

Insufficient knowledge on the disease by the health personnels in the primary heatlh care centres is another challenge which lead to delayed refferral to higher centers that can manage the disease making most patients be seen with signs of metastasis.

SGTs constitute a significant cause of morbidity in most of African countries. Prognosis correlates most strongly with clinical stage,emphasizing the importance of early diagnosis.Optimal initial surgery minimizes the risk of local reccurence,hence the risk of distant metastases reduced with early diagnosis and intervention.

1.5 STUDY RATIONALE

This study aimed in establing the prevalence of salivary gland tumours in our setting in which little is currently known.The only study which was done in Tanzania was conducted at Maxillofacial department, this study was conducted in both Otorhinolaryngology and Maxillofacial departments and hence reveals the reality of the burden and morbidity in our setting.

The results of this study has established the prevalence of the salivary gland tumours, clinical presentation, common histopathological types, site of involvement and the stage at diagnosis in our setting. Clinical-pathologic presentation of different salivary glands tumours has been known and this will help in arriving at the correct clinical diagnosis and treatment planning in our hospital and to the other lower level health facilities. The knowledge on salivary glands tumours will expand to health workers and the findings of this study has provided a baseline data for the occurrence of the salivary glands tumours among Tanzanian population.

The information obtained from this study has formed the corner stone for educating the health personnels who see patients in the primary health care centers, on early diagnosis and referring patients to higher centers for further management. However, the information has also to be used to educate the society on early seeking of treatment so as to reduce the deliterous effects of the tumours to the society and nation at large.

Theseresults will also form a platform for further studies on salivary gland tumours in our setting and the information gained from this study shall be submitted to the Ministry of Health, Community Development, Gender, Elderly and Children for use in planning community-based health education programmes and provision of manpower, medical supplies and equipments to the health facilities.

This study was also done as partial fullfillment of my Masters of Medicine degree in ORL at MUHAS.

1.6 RESEARCH QUESTIONS

1. What is the prevalence of salivary gland tumours among patients attending otorhinolaryngology and maxillofacial services at MNH?

2. What gender and age which is more affected?

3. What are the sites of origin, histological types and stages at diagnosis among patients with salivary gland tumours attending ORL and maxillofacial services at MNH?

CHAPTER TWO

2.0 OBJECTIVES

2.1 Broad objective

To determine the pattern of salivary gland tumors among patients attending ORL and Maxillofacial services at MNH from June to December 2016.

2.2 Specific Objectives

1. To describe age and sex distribution among patients with salivary gland tumours.
2. To determine the sites of origin of salivary gland tumors.
3. To describe histopathological types of salivary gland tumors.

CHAPTER THREE

3.0 METHODOLOGY

3.1 Study Area

This study was conducted at the clinics and wards of ORL and Maxillofacial departments at MNH. Muhimbili National Hospital is situated in Ilala Municipality. The hospital serves as a tertiary referral and teaching hospitals for MUHAS. It has a capacity of 1500 beds and serves about 1000 out-patients per day. It receives the patients referred from all over the country. This hospital has the largest **ORL** and Maxillofacial departments which both provide inpatients and outpatients services to an approximately 1600 patients per month. The department of ORL two wards; male and female with bed capacity of 64.The outpatient clinic in ORL operates for five days in a week with an average of 60 patients per day, 70 new cases per week and 4 admissions per day. The department of maxillofacial has two wards for male and female with a total bed capacity of 68 ,The outpatients clinic are conducted five days a week with daily average of 100 patients and about 5 admission per day.

3.2 Study design

Hospital based descriptive cross-sectional study.

3.3 Study duration

The study was conducted for 6 months from 1st July 2016 to 31st December 2016.

3.4 Study population

The study population included all the outpatients and inpatients with ORL and Maxillofacial problem(s) presented at the clinics and in the wards at MNH during the months of July to December 2016.

3.5 Inclusion criteria

All patients who received ORL and Maxillofacial treatment at MNH study whom gave a written informed consent.

3.6 Exclusion criteria

All patients who did not consent to the study.

3.7 Sampling procedure

Convinient sampling was used whereby all patients who met the inclusion criteria were included in the study

3.8 Sample size calculation

From the study done in Tanzania Salivary gland tumours constituted 6.3% (44) of all oral-facial tumours and tumour like lesions.

The sample size for a finite population was calculated as follows;-

$$n = \frac{Z^2\ p(100-p)}{\varepsilon^2}$$

n= Sample size

ε= Margin of error (for this study 3% is considered)

P= 6.3% Current Prevalence of Salivary gland tumour study done in Tanzanian population) (44)

Therefore from the formula above, the required sample size is 251 patients.

Adjusting for the non-response rate which is 10%, the sample size for this study will be **276** patients.

3.9 Data collection technique

This was done by the principle investigator and the specialists working at ORL/Maxillofacial wards and clinics. All patients who attended ORL and maxillofacial clinics and wards were screened for salivary gland tumours and those who gave consent were recruited.

Demographic information i.e. age, sex, address, phone number, presenting symptoms, duration, were obtained from the patient through thorough history taking and relevant physical examination for the head and neck was performed to determine the site and the results recorded in the questionnaire and clinical examination forms. Patients with clinical features which were not suggesting salivary gland tumors were treated accordingly while those with clinical features suggesting salivary gland tumour underwent further investigations to confirm the disease and staging. Fine needle aspiration cytology were done by a pathologist to all patients with salivary gland tumours and the results followed after two weeks. Tissue biopsy were taken from patients with clinical diagnosis of salivary gland tumor who have ulcerative lesions and to those that the cytology results had have been uncomfirmative and recommended tissue biopsy to obtain histopathologic type of tumour. The tissue biopsy were taken by the principle investigator in collaboration with the specialists from both ORL and Maxillofacial clinic and wards. Immediately after obtaining the tissues, they were be put into a special container filled with 10% formalin of volume at least ten times the tissue volume, clearly prelabelled with patients' identifications (patient's name, hospital registration number, age, sex and the name of clinic or ward number) The tissue specimens were then transferred to the Central Pathology Laboratory (CPL) in the Histopathology unit at MNH together with histological laboratory investigation request forms containing patient's particulars (similar to those on a container),details of clinical examination, clinical diagnosis, and clinical stage of the tumor. Histopathology reports were followed up and recorded in a questionnaire according to patients' identifications.
Data collection tools were English structured questionnaires with a Swahili version, clinical examination forms, cytology gun, and biopsy forceps.

3.10 Data handling and analysis

Filled questionnaires at ORL clinics were collected by the principal researcher and/or research assistant daily from the respective clinic room. Data quality check for inconsistence was done on daily bases to ensure that incomplete and missing data are identified and corrected and/or discarded as required.

All collected information were confidentially handled both physically and electronically by the principal researcher. Data entry, cleaning and analysis was done using the SPSS 20.0 software with help of a biostatistician**.** The results are presented in frequency tables, cross tabulations and figures. Chi-square test has been used to compare proportions and P value of less than 0.05 was considered statistically significant

3.11 Reproducibility

For the purpose of avoiding variations, the clinical assessments and diagnosis of the patients were made by the principal investigator, specialists and residents at clinics, wards of ORL and maxillofacial departments.

3.12 Ethical considerations

Ethical clearance was sought from Muhimbili University of Health and Allied Health Sciences (MUHAS) Senate of Research and Publications committee. Participant or guardian of the participant were given an informed consent and be allowed without coercion to consent or to not. Confidentiality of the information was observed and ensure no breach of information. Unauthorized party was not allowed to access information without permission. For patients younger than 18 years informed consent were obtained from their parents or guardians. Patients who cannot read and/or write had their finger prints obtained. Those that declined to participate in the study will be resumed to get the treatment.

3.13 Study limitations

The limitations of participants to refuse to participate in this study was anticipated and rectified not to jeopardize the study.

3.14 Study mitigations

The above limitations were mitigated by explaining clearly to the participants on the benefit of doing this research, but also having knowing that ,estimated sample size of the participants was adjusted to 90% response rate, making a maximum sample size of 276 participants.

CHAPTER FOUR

4.0 RESULTS

Table 1

1 Dermographic distribution of study participants

Variable	Salivary gland tumours		Total
	yes	no	
Age group			
<=19	9(7.8)	3(1.9)	12(4.3)
20-29	12(10.3)	10(6.2)	22(8.0)
30-39	11(9.5)	25(15.6)	36(13.0)
40-49	31(26.7)	29(18.1)	60(21.7)
50-59	22(19.0)	45(28.1)	67(24.3)
60+	31(26.7)	48(30.0)	79(28.6)
Gender			
Male	64(55.2)	92(57.5)	156(56.5)
Female	**52(44.8)**	**68(42.5)**	**120(43.5)**
Total	116(100)	160(100)	276(100)

This study constituted 276 participants 156 (56.5%) were males and 120 (43.5%) were females. Their age ranged from 0 to >60 years with mean age of 49.47 years, SD ±15.7. Most of them 69 (28.6 %), were in the age group of above 60 years.

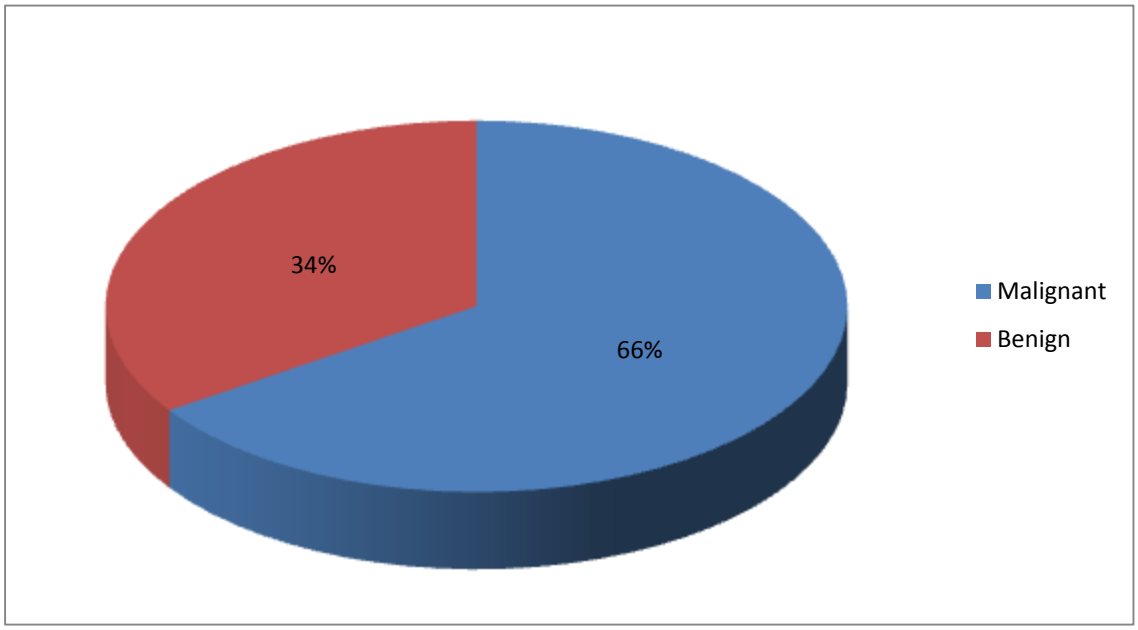
Table 2

2. Age and sex distribution among patients with salivary gland tumours

Age	Male	Female	Total
<=19	6(9.4)	3(5.8)	9(7.8)
20-29	5(7.8)	7(13.5)	12(10.3)
30-39	5(7.8)	6(11.5)	11(9.5)
40-49	18(28.1)	13(25.0)	31(26.7)
50-59	11(17.2)	11(21.2)	22(19.0)
60+	19(29.7)	12(23.1)	31(26.7)
Total	64(100)	52(100)	116(100)

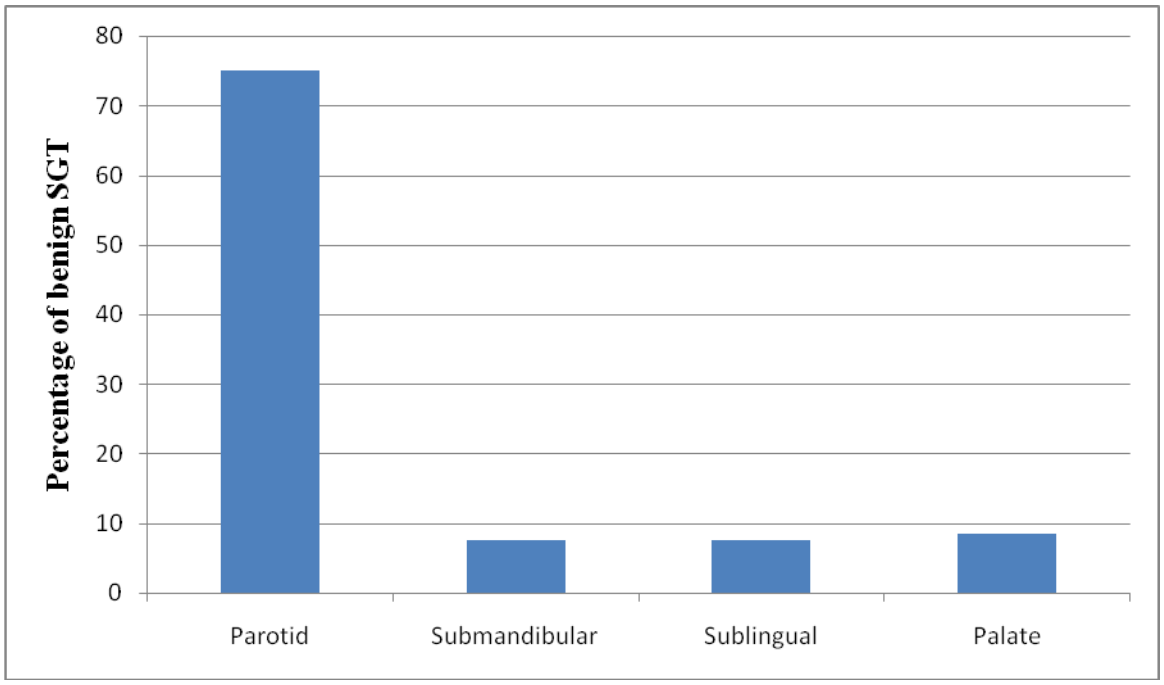
The majority of tumors (26.7%) were in the 40-49 years and the least common affected age was less than (19%) in the 50-59 years age groups.(P value 0.02) which is statistically significant. The tumours affected men more commonly, 64 (55.1%) salivary gland tumours occurred in men and 52 (44.8%) occurred in women, P=0.76 which is not statistically significant.

Figure 1.Distribution of salivary gland tumours



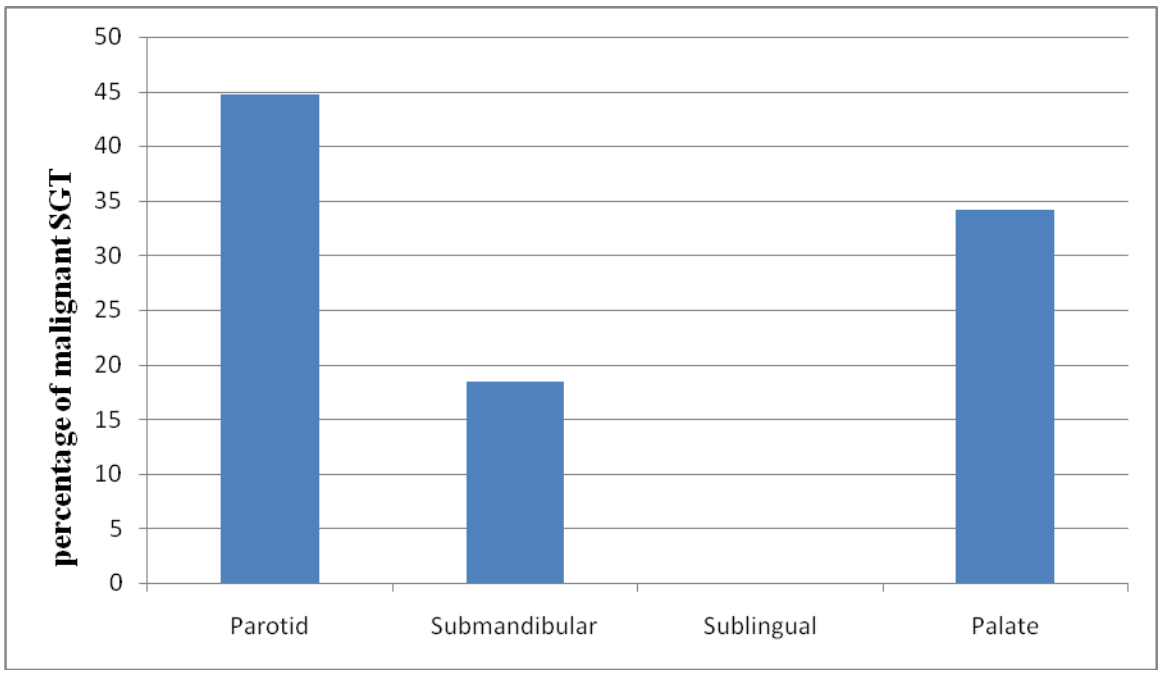
Among 116 patients with salivary gland tumours, malignant salivary accounted for 66% and benign 34%.

Figure 2: Distribution of Benign salivary gland tumors by site of origin



The parotid gland was the most commonly affected site (75%) and the submandibular and sublingual were the least affected sites (7.5%).

Figure 3: Distribution of malignant Salivary gland by site of origin



The most affected site by malignant SGT was the Parotid gland (44.7%) and the least affected was the submandibular 18.4% whereas the sublingual gland was not affected.

Table 3. Histopathological types of salivary gland tumors

	Gender		Age group			
Histology	**Male**	**Female**	**0-20**	**21-40**	**41-60**	**61+**
Benign tumours						
Chronic Sialolithiasis	1(1.6	3(5.7)	0	1(1.6)	2(4.0)	1(3.5)
Myoepithelioma	2(3.1)	0	0	2(4.1)	0	0
Pleomorphic adenoma	18(28.1)	13(25.0)	5(55.6)	11	13(26.0)	2(6.9)
Warthin's tumour	1(1.6)	2(3.9)	0	0	1(2.0)	2(6.9)
Malignant tumours						
Adenocarcinoma	7(10.9)	3(5.8)	0	2(7.1)	7(14.0)	1(3.5)
Adenoidcystic carcinoma	11(17.2)	6(11.5)	3(3.3)	3(10.7)	7(14.0)	4(13.8)
Carcinoma ex pleomorphic adenoma	1(1.6)	4(7.7)	0	0	3(6.0)	2(6.9)
Mocoeidermoid carcinoma	15(23.4)	15(28.9)	1(11.1)	4(14.3)	12(24.0)	13(44.8)
Squamous cell carcinoma	6(9.4)	2(3.8)	0	1(3.6)	4(8.0)	3(10.3)
Others	2(3.2)	4(7.6)	0	4(14.3)	1(2.0)	1(3.5)

The most common benign histology was pleomorphic adenoma which was high in males (28.1%) compared to females (25.0%), and the common malignant histology was mucoepidermoid carcinoma,(23.4%) in males and (28.9%) in females.The tumours affected men more commonly, particularly the 40-49 age group, but these differences were not statistically significant (p= 0.07).

Discussion

Among the 276 participants 156 (56.5%) were males and 120 (43.5%) were females. Their age ranged from 0 to 90 years with mean age of 49.47 years, SD ±15.7. Most of them 69 (28.6 %), were in the age group of above 60 years.

The age range was from 10 to >60 years, with the majority of tumors (26.7%) in the 40-49 years and (19%) in the 50-59 years age groups. (P value 0.02) which is statistically significant

The percentage of SGT was high in age 60+ (29.7%) in males and (26.7 %) in females, followed by 40-49 (28.1%) in males and 26.7 % in females. The least common affected age was < 19 yrs in females. The average age for men and women was 49.48 ± 15.4 and 47.43 ± 15.3 years respectively. The average age at which benign tumours were diagnosed was of 49.47 ± 19.2 years while malignant tumours were diagnosed at an average age of 49.2 ± 15.9 years, similar to what have been reported by other studies (6,7,8,11,12,28).The differences between age of appearance of malignant and benign tumours were statistically significant (p=0.03).

Among 116 patients with SGT, 76 (65.5%) had malignant type and 13(44.8%) were in the age group 60 years and above. Majority 13 (26.0%) of those with benign type were in the age group of 41-60 yrs. Both benign and malignant SGT had male preponderance.

The tumours affected men more commonly, 64 (55.1%) salivary gland tumours occurred in men and 52 (44.8%) occurred in women, P=0.76 which is not statistically significant. According to the WHO and other reports (5,8,26) and in agreement with the present results, female patients are overall more affected than men, although this and some other studies report higher prevalence's in men (7,8,9,10,11).

Major salivary glands were affected more than minor glands, especially the parotid gland (59.7%), followed by palatine glands (15.5%). Similar results are described in the majority of studies on SGTs. (5, 7, 8,11,12,15,30)

The parotid gland was the most commonly affected site by benign SGT n=28 (41.9%) followed by the palatal salivary glands and the submandibular gland. Among the 40 benign tumors, 33 (62.8%) were pleomorphic adenoma..

Among the (n=76) malignant tumors, (n=64) were located in the parotid gland, and n=34 (59.7%) were malignant. Generally the parotid gland was the most commonly affected gland (59.7%) by both benign and malignant tumors followed by the Palate (15.5%) and the submandibular (12.0%) glands respectively. This is similar to the findings reported by Cho *et al*. (11). In their study, the parotid gland was the most commonly affected gland with 83.3% of the cases, followed by the submandibular gland with 17.7% of the cases.

The most frequent location of this lesion was the parotid, submandibular and minor palatal salivary glands respectively, similar to that which has been reported in other studies (6-9,13,15,24).

Fifteen point five percent of the tumours in the minor salivary glands were located in the palate. Eighteen of them were malignant and 4 were benign. While this suggests that malignant neoplasms are more common than benign neoplasms in the minor salivary glands of the palate, the difference was not statistically significant. These findings are consistent with those reported in the literature (5, 6, 8, 12).

When analysing the SGT by histological type, the most prevalent neoplasm was the pleomorphic adenoma (62.8%), followed by mucoepidemoid carcinoma,then adenoidcystic carcinoma. Most of the pleomorphic adenomas were found in females, which was statistically significant (p= 0.007). Similar results have also been found by other authors (7,8). One case of Warthin tumour was found in males, which has also been reported by other series (7-9) In relation to mucoepidermoid, the present series have shown a male gender predilection.

The mucoepidermoid carcinoma represented the second most common tumour and was the most frequent malignant neoplasm, followed by the adenoid cystic carcinoma and adenocarcinoma. These results are similar to previous series (6,7,10,13,).In this study High prevalence was seen in mucoepidermoid carcinoma,n= 30 (39.5%) which affected

all sites mostly the parotid followed by, n=18 (23.7%) adenoid cystic carcinoma which mostly affected the submandibular gland, n=8 (10.5%) were squamous cell carcinoma and n=4 (5.3%) were Carcinoma x pleomorphic adenoma.

Adenoid cystic carcinoma was most prevalent SGT in males compared to females, which are in contrary to several present studies which show predilection to females. The predominance of adenoid cystic carcinoma has been described in studies conducted in Congo, Tanzania, Croatia and Nigeria. (7,10,29,33,38) In contrast, studies conducted in Iran, Brazil, Jordan, the USA,(11,12,14) the United Kingdom and Italy report a greater frequency of mucoepidermoid carcinoma than adenoid cystic carcinoma, whereas similar distribution between these two types of SGTs has been reported in China, Finland and Mexico.(6,24) These findings suggest geographic variation in the frequency of malignant SGTs. Other observed benign SGT histologies were, Warthin tumor, Chronic sialolithiasis, Myoepithelioma, and for malignant SGT SCC, Acinic cell carcinoma, Nodular KS, Myoepithelial carcinoma, Carcinoma (NOS) were observed in one or two cases.

Conclusion

Salivary gland tumours are uncommon neoplasms that usually arise in the major or minor salivary glands but have proven to be a public health problem which commonly affects people above forty years of age. The disease is more prevalent among males than the females with the Parotid gland being commonest affected. Pleomorphic adenoma and mucoepidermoid carcinoma were the most common benign and malignant tumours reported in this study respectively. All of the tumours arising from minor salivary glands were malignant, so special care must be taken when these glands are affected.

Recommendation

Health education to the community through social media, and outreach services on symptoms of the disease and on importance of early health seeking behaviour for early detection of the disease and proper management, so as to avoid the deliterous effects of the disease to the patient, community and nation at large.

Health education to the health personnels in the primary health centers on early diagnosis of SGT and prompt referring patients to higher centers for further management.

Early interventions should be considered when suspecting salivary gland tumor to avoid histological types that have higher risk of metastasis: high-grade mucoepidermoid carcinoma, squamous cell carcinoma (SCC), anaplastic tumours and carcinoma ex pleomorphic adenoma

The earlier cancer is detected the better are the chances of cure and complete recovery. Self-examination by each and every one of us will go a long way in detecting cancer at the early stage.

Regular medical checkup is advised for both the sexes to detect the tumour in early stages.

REFERENCES

1. Ten Cate's Oral Histology, Nanci, Elsevier, 2013, page 275-276
2. Rosen EJ. Salivary Gland Neoplasms.http://emedicine.medscape.com/article/852373. 2002;
3. Illustrated Anatomy of the Head and Neck, Fehrenbach and Herring, Elsevier, 2012, p. 157
4. Xiao CC, Zhan KY, White-Gilbertson SJ, Day TA. Predictors of Nodal Metastasis in Parotid Malignancies: A National Cancer Data Base Study of 22,653 Patients. Otolaryngol Head Neck Surg 2016; 154:121.
5. de Oliveira FA, Duarte EC, Taveira CT, Maximo AA, de Aquino EC, Alencar RC, et al. Salivary gland tumor: a review of 599 cases in a Brazilian population. Head and neck pathology. 2009; 3:271-5.
6. Tian Z, Li L, Wang L, Hu Y, Li J. Salivary gland neoplasms in oral and maxillofacial regions: a 23-year retrospective study of 6982 cases in an eastern Chinese population. International journal of oral and maxillofacial surgery. 2010; 39:235-42.
7. Lukšić I, Virag M, Manojlović S, Macan D. Salivary gland tumours: 25 years of experience from a single institution in Croatia. Journal of cranio-maxillo-facial surgery. 2012;40:e75-81
8. Eveson JW, Cawson RA. Salivary gland tumours. A review of 2410 cases with particular reference to histological types, site, age and sex distribution. J Pathol. 2015; 146:51-8.
9. Eveson JW. Salivary tumours. Periodontol 2000. 2011;57:150-9
10. Otoh EC, Johnson NW, Olasoji H,Danfillo IS, Adeleke OA. Salivary gland neoplasms in Maiduguri, north-eastern Nigeria. Oral Dis. 2005;11:386-91
11. Ito FA, Ito K, Vargas PA, de Almeida OP, Lopes MA. Salivary gland tumors in a Brazilian population: a retrospective study of 496 cases. International journal of oral and maxillofacial surgery. 2005; 34:533-6.

12. Shishegar M, Ashraf MJ, Azarpira N, Khademi B, Hashemi B, Ashrafi A. Salivary gland tumors in maxillofacial region: a retrospective study of 130 cases in a southern Iranian population. Pathology research international. 2011;2011:934350
13. Barnes L, Eveson JW, Reichert P, et al. World health classification of tumours. Pathology and genetics of head and neck tumours. Lyon: IARC Press; 2005.
14. Ellis GL, Auclair PL. Atlas of tumor pathology. Tumors of the salivary glands. Washington DC: AFIP; 1995.
15. To VSH, Chan JYW, Tsang RKY, Wei WI. Review of Salivary Gland Neoplasms. ISRN Otolaryngol. 2012;2012:1–6.
16. Y. Y. P. Lee, K. T. Wong, A. D. King, and A. T. Ahuja, "Imaging of salivary gland tumours," European Journal of Radiology, vol. 66, no. 3, pp. 419–436, 2008.
17. S. R. Orell, "Diagnostic difficulties in the interpretation of fine needle aspirates of salivary gland lesions: the problem revisited," Cytopathology, vol. 6, no. 5, pp. 285–300, 1995.
18. Stenner M, Klussmann JP. Current update on established and novel biomarkers in salivary gland carcinoma pathology and the molecular pathways involved. *Eur Arch Otorhinolaryngol*. 2009 Mar. 266(3):333-41
19. K. H. Lam, W. I. Wei, H. C. Ho, and C. M. Ho, "Whole organ sectioning of mixed parotid tumors,"American Journal of Surgery, vol. 160, no. 4, pp. 377–381
20. Elledge R. Current concepts in research related to oncogenes implicated in salivary gland tumourigenesis: a review of the literature. *Oral Dis*. 2009 May. 15(4):249-54
21. American Joint Committee on Cancer Staging Manual, 7th ed, Edge SB, Byrd DR, Compton CC, et al (Eds), Springer, New York 2010.
22. Spuntarelli G, Santecchia L, Urbani U, Zama M. Minor salivary gland neoplasm in children. *J Craniofac Surg*. 2013 Mar. 24(2):664-7.
23. Ritwik P, Brannon RB. A clinical analysis of nine new pediatric and adolescent cases of benign minor salivary gland neoplasms and a review of the literature. *J Med Case Rep*. 2012 Sep 11. 6(1):287.
24. Bello IO, Salo T, Dayan D, Tervahauta E, Almangoush A, Schnaiderman-Shapiro A, et al. Epithelial salivary gland tumors in two distant geographical locations, Finland (Helsinki and Oulu) and Israel (Tel Aviv)

25. Pathology O. Clinicopathological analysis of salivary gland tumors over a 15-year period. 2016;30:1–7.
26. Tumours of the Salivary Glands. In: Pathology and Genetics of Head and Neck Tumours, Barnes L, Eveson JW, Reichart P, Sidransky D. (Eds), World Health Organization, Lyon 2005. p.209.
27. Spiro RH. Salivary neoplasms: overview of a 35-year experience with 2,807 patients. Head Neck Surg 1986; 8:177.
28. M. Guzzo, L. D. Locati, F. J. Prott, G. Gatta, M. McGurk, and L. Licitra, "Major and minor salivary gland tumors," Critical Reviews in Oncology/Hematology, vol. 74, no. 2, pp. 134–148, 2010.
29. Fomete B, Adebayo ET, Ononiwu CN. Management of salivary gland tumors in a Nigerian tertiary institution. Ann Afr Med. 2015;14(3):148–54.
30. Araya J, Martinez R, Niklander S, Marshall M, Esguep A. Incidence and prevalence of salivary gland tumours in Valparaiso , Chile. 2015.
31. Kızıl Y, Aydil U, Ekinci O, Dilci A, Köybaşıoğlu A, Düzlü M, et al. Salivary gland tumors in Turkey: demographic features and histopathological distribution of 510 patients. Indian J Otolaryngol Head Neck Surg
32. Silas O A, Echejoh G O, Menasseh A N, Mandong B M, Otoh E C. Descriptive pattern of salivary gland tumors in Jos University Teaching Hospital: A 10-year retrospective study. Ann Afr Med 2009;8:199-202
33. Masanja MI, Kalyanyama BM, Simon EN. Salivary gland tumours in Tanzania. West India Med J 2001; 50:62-5.
34. Hill AG. Major salivary gland tumours in a rural Kenyan hospital. Laryngoscope 1997; 107:127-80.
35. Onyango, J.E., Awange, D.O. and Wakiaga, J.M. Oral tumoursandtumour like conditions in Kenya. I Histological distribution. *East. Afr. Med. J.* 1995; **72:**560-563.
36. Shafiquil IM, Md Azharul Islam, Md Abdus Sattar, AFM Ekramuddula HI Al, Hadi. Malignant Salivary Gland Neoplasm - clinicopathological Study Mohammed Shafiqul Islam, Md Azharul Islam, Md Abdus Sattar, AFM Ekramuddula, Hossain Imam Al Hadi. Bangladesh J Otorhinolaryngol 2008; 14(1) 1-5. 14(1):1–5
37. Torabinia N, Khalesi S. Clinicopathological study of 229 cases of salivary gland

tumors in Isfahan population. Dent Res J (Isfahan)

38. Kayembe MKA, Kalengayi MMR. Salivary gland tumours in Congo (Zaire). Odontostomatol Trop[Internet].2002;25(99):1922.Availablefrom:http://www.ncbi.nlm.nih.gov/pubmed/12430
39. Subhashraj K. Salivary gland tumors: a single institution experience in India. Br J Oral Maxillofac Surg

Appendix 1

Consent form: English version

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES

DIRECTORATE OF RESEARCH AND PUBLICATIONS, MUHAS

INFORMED CONSENT FORM

ID-NO……..

Consent to Participate in a Study

Greetings! My name is Dr John Masago; I am working on this research with the objective of determining prevalence of salivary gland tumours among patients attending otorhinolaryngology and maxillofacial services at Muhimbili national hospital.

Purpose of the study

The study is conducted in partial fulfillment of the requirements for the degree of Master of Medicine in otorhinolaryngology of MUHAS. This study is aiming at determining prevalence of salivary gland tumours among patients attending otorhinolaryngology and maxillofacial services at Muhimbili national hospital.

You are being asked to participate in this study because you have particular knowledge and experiences that may be important to the study. Kindly please be honest and true for betterment of the results that could lead to better intervention and recommendations for future.

What Participation Involves

If you agree to join the study, you will be interviewed in order to answer a series of questions in the questionnaire prepared for the study. There after a thorough clinical examination of the head and neck will be done to you.

Confidentiality

I assure you that all the information collected from you will be kept confidential. Your name will not be written on any questionnaire or in any report/documents that might let someone identify you. Your name will not be linked with the research information in any way. All information collected on forms will be entered into computers with only the study identification number. Confidentiality will be observed and unauthorized persons will have no access to the data collected.

Risks

We do not expect that any harm will happen to you because of participating in this study.

Some questions could potentially make you feel uncomfortable. You may refuse to answer any particular question and may stop the interview at any time.

Right to Withdraw and Alternatives

Taking part in this study is completely voluntary. You can stop participating in this study at any time, even if you have already given your consent. Refusal to participate or withdrawal from the study will not involve any penalty.

Benefits

The information you provide and the clinical examination done to you will ascertain the prevalence, clinical and histological types, and site of origin of salivary gland tumors therefore aiding the decision to intervene. Those found with salivary gland tumors will be given appropriate management.

Who to Contact

If you ever have questions about this study, you should contact the Principal Investigator, Dr John Masago of Muhimbili University of Health and Allied Sciences, P. O. Box 65001, Dar es Salaam. Telephone +255-717 138 282, Dr Edwin Liyombo who is the supervisor of this study (Tel +255-715 283569) and Dr Enica Richard who is Co-Supervisor (Tel +255-754 307717)

If you ever have questions about your rights as a participant, you may call, Chairperson of the Senate Research and Publications Committee, Prof. Said Aboud, P. O. Box 65001, Telephone : 255 22 2152489 Dar es Salaam

Signature:

Do you agree?

Participant agrees …….. Participant does NOT agree …….

I ……. have read the contents in this form. My questions have been answered. I agree to participate in this study.

Signature of participant **……**

Signature of Research Assistant ……..

Date of signed consent …….

CHUO KIKUU CHA SAYANSI ZA AFYA MUHIMBILI KURUGENZI YA UTAFITI NA MACHAPISHO

Consent form: Swahili version

Namba ya utambulisho……

Ridhaa ya kushiriki kwenye utafiti

Hujambo! Ninaitwa Dkt.John Masago, nashughulika kwenye utafiti huu wenye lengo la kutathmini magonjwa uvimbe wa tezi za mate kwa wagonjwa wanaotibiwa katika Hospitali ya Taifa Muhimbilia. Utafiti huu unafanyika katika kutimiza sehemu ya matakwa ya shahada ya uzamili ya magonjwa ya masikio, pua na koo ya Chuo Kikuu cha Afya na Sayansi ya Tiba Muhimbili.

Uzito wa magonjwa ya uvimbe katika tezi za mate, dalili za magonjwa haya na tabia zake. Unaombwa kushiriki katika utafiti huu kutokana na upeo na ufahamu ulio nao ambavyo ni muhimu kwa utafiti huu. Tafadhali kuwa mkweli na muwazi kwa vile matokeo ya utafiti huu yanaweza akatoa maamuzi na mapendekezo ya baadaye.

Jinsi ya kushiriki

Ukikubali kushiriki katika utafiti huu, utasailiwa ili kuweza kujibu maswali toka kwenye dodoso lililoandaliwa kwa ajili ya utafiti huu. Baada ya usaili utafanyiwa uchunguzi wa kinywa na maeneo ya uso na shingo.

Usiri

Taarifa zote zitakazokusanywa kupitia dodoso zitaingizwa kwenye ngamizi kwa kutumia namba za utambulisho. Kutakuwa na usiri na hakuna mtu yeyote asiyehusika atakayepata taarifa zilizokusanywa

Hatari

Hatutegemei madhara yoyote kukutokea kwa kushiriki kwako kwenye utafiti huu.

Faida

Kama utakubali kushiriki kwenye utafiti huu taarifa utakazotoa zitatuwezesha kujua kiwango au ukubwa wa tatizo ambao ni muhimu katika uamuzi wa kuzuia au kupunguza tatizo. Watakaogundulika kuwa na meno yaliyooza au matatizo mengine ya,masikio, pua na koo, kinywa na meno watapewa tiba stahili.

Athari na kukitokea madhara

Hutegemewi kupata madhara yoyote kutokana na ushiriki wako katika utafiti huu. Baadhi ya maswali yanaweza yasikupendeze, unaweza kukataa kujibu swali lolote la aina hiyo naunaweza kuamua kusimamisha udahili wakati wowote.

Uhuru wa kushiriki na haki ya kujitoa

Kushiriki kwenye utafiti huu ni hiari. Unaweza kujitoa kwenye utafiti huu wakati wowote hata kama umeshajaza fomu ya ridhaa ya kushiriki utafiti huu. Kukataa kushiriki au kujitoa kwenye utafiti huu hakutaambatana na masharti yoyote.

Nani wa kuwasiliana naye

Kama una maswali kuhusiana na utafiti huu, wasiliana na Mtafiti mkuu wa utafiti huu, Dr John Masago wa Chuo Kikuu cha Tiba na Sayansi Shirikishi-Muhimbili, S. L. P. 65014, Dar es Salaam. Simu +255-717 138 282 au msimamizi wa utafiti huu Dkt. Edwin Liyombo (Simu: 0715 283 569) au msimamizi Dr Enica Richard (Simu ; 0754 307717)

Kama una swali kuhusu stahili zako kama mshiriki unaweza kumpigia simu Prof. Said Aboud, Mkurugenzi wa Utafiti na Machapisho, S.L.P 65001, Simu: 255 22 2152489 Dar es Salaam

Sahihi:

Je umekubali?

Mshiriki amekubali ……..... Mshiriki hajakubali …….....

Mimi ..... nimesoma maelezo ya fomu hii.

Maswali yangu yamejibiwa.Nakubali kushiriki katika utafiti huu.

Sahihi ya mshiriki……

Sahihi ya mtafiti msaidizi……

Tarehe ya kutia sahihi ya idhini ya kushiriki……..

Appendix 2

Questionnaire and clinical examination form (English version)
A study on salivary glands diseases among patients attending Muhimbili National Hospital

Questionnaire no……

Date of interview……

Sociodemographic data

1. Hospital Registration number……
2. Age in years. ( )
3. Gender: Male = 1, Female = 2 ( )
4. Place of domicile;

   District…….

   Region…….

   Tel…….
5. Category

   1. Outpatient
   2. Inpatient

   [ ]
5. Education level

   1. No formal Education
   2. Primary school
   3. Secondary school
   4. Post secondary

   [ ]
6. Marital status:

   1. Single
   2. Married
   3. Separated
   4. Divorced
   5. Widow
   6. Widower

   [ ]

Presenting symptoms

What is/are the main complaint(s) that has brought you to the hospital? Tick the appropriate

7. Swelling Yes = 1, No = 2 ( )

If Yes, Duration…….(in months)

10. Painless ( )

11. Painful ( )

12**.** Facial asymmetry ( )

13. Facial Pain ( )

14. Facial Numbness ( )

15.Cheek ulcer ( )

14. Ear discharge ( )

15. Ear ache ( )

16**.** Hearing loss ( )

17. Voice change ( )

18. Nasal discharging ( )

19. Difficulty swallowing ( )

20. Dry mouth (zerostomia) ( )

23. Others..(specify).....

24. When did the problem begin? ……..in months.

EXAMINATION OF THE HEAD AND NECK

A. site of the lesion (circle the appropriate)

Major salivary glands

1. Parotid gland Right Left

2. Submandibular gland Right Left

3. Sublingual gland Yes No

Minor salivary glands

4. Palate 1. Soft Plate 2. Hard palate 3.Soft and Hard Palate

5. Others……..

6. Facial examination findings

1. Asymetry
2. Infra orbital numbness
3. Facial ulceration
4. Trismus



HISTOPATHOLOGY

1. Cytological diagnosis

……

……

2. Histological diagnosis …….

Questionnaire and clinical examination form (Swahili version)
Dodoso kwa ajili ya utafiti juu ya magonjwa ya uvimbe katika tezi za mate katika hospitali ya Taifa Muhimbili

Nambari ya dodoso……

Tarehe ya kuhojiwa……

1. Nambari ya kuandikishwa hospitali…….

2. Umri wa mgonjwa katika miaka…….

3. Jinsia: kiume= 1, kike=2 ☐

4. Mahali unapoishi; Wilaya……Mkoa……

5. Kiwango cha elimu

    1. Hajasoma
    2. Elimu ya msingi
    3. Elimu ya sekondari
    4. Elimu baada ya elimu ya sekondari

☐

6. Hali kindoa:

    1. Hajaoa wala kuolewa
    2. Ameoa au ameolewa
    3. Wametengana
    4. Ameachika
    5. Mjane
    6. Mgane

☐

Matatizo yaliyokuleta hospitali

Je, unasumbuliwa na kitu gani katika tezi (weka alama ya tiki Panapohusika)

7. Uvimbe Ndio=1, Hapana=2

Kama Ndio;

Kwa muda gani…….(miezi)

10. Uvimbe Usio na maumivu ( )
11. Uvimbe wenye maumivu ( )
12. Kutolingana kwa pande za uso ( )
13. Maumivu ya uso ( )
14. Ganzi usoni ( )

15. Kidonda kwenye mashavu ( )
16. Maji maji/usaha kutoka masikioni ( )
17. Maumivu masikioni ( )
18. Kutokusikia ( )
19. Sauti kukwaruza ( )
20. Majimaji/usaha kutoka puani ( )
21. Uvimbe ndani ya kinywa ( )
22. Kukauka mate mdomoni ( )
23. Dalili nyinginezo (Taja)……..
24. Dalili kwa muda gani?.....

UCHUNGUZI KWA MGONJWA

A.Ugonjwa ulipoazia (Zungushia panapohusika)

Tezi kubwa za mate

1. Tezi chini ya sikio Kulia Kushoto

2. Tezi chini ya taya Kulia Kushoto

3. Tezi chini ya ulimi Ndio Hapana

Tezi ndogo za mate

4. Palate 1. Soft Plate 2. Hard palate 3.Soft and Hard Palate

5. Nyinginezo……

6. Uchunguzi waUso

    1. Kutolingana
    2. Ganzi
    3. Kidonda
    4. Trismus



VIPIMO VYA HISTOPATHOLOLOJIA

1. Matokeo ya cytolojia

……

2. Matokeo ya histolojia…….