Addis Ababa University

College of Health Sciences and School of Medicine

Department of Pathology

Morphological patterns of neoplastic and non-neoplastic salivary gland lesions in Tikur Anbessa specialized Hospital, Addis Ababa, Ethiopia, over a 5 year period, July 2015 to June 2020

July 22, 2020

Declaration of Principal Investigator

I the undersigned, Demis Abate agree to accept all responsibilities for the scientific and ethical conduct of this thesis entitled "**Morphological patterns of neoplastic and non-neoplastic salivary gland lesions in Tikur Anbessa specialized Hospital, Addis Ababa, Ethiopia, over a 5 year period, July 2015 to June 2020**

The Thesis is my original work and was not prepared by others. All resources and materials used for this research have been dully acknowledged. I was communicating and providing timely progress report to my advisor and seek the necessary advice, comment and approval in the course of this work.

Demis Abate Mekonnen (MD), Final Year Pathology Resident:

_____ _____

Signature Date

Approval of Advisor:

The Student had worked on this research and fulfilled all the requirements and hence hereby can submit the thesis to the Department of Pathology, Tikur Anbessa Specialized Hospital, School Of Medicine, College of Health Sciences, Addis Ababa University.

Dr. Mahlet Arayaselassie (MD, Assistant professor of pathology)

_____ _____

Signature Date

A Thesis Proposal submitted to the Department of Pathology, College of Health Sciences and School of medicine, Addis Ababa University in Partial fulfillment of the requirements for the Specialty Diploma in Pathology.

Investigator: Demis Abate (MD, Pathology resident)

Advisor: Dr. Mahlet Arayaselassie (MD, Assistant professor of pathology)

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Abbreviations

ACC: Acinic cell carcinoma

AdCC: Adenoid cystic carcinoma

ASIR: Age-specific incidence rate

ASMR: Age-specific mortality rate

Ca Ex-Pa: Carcinoma ex-pleomorphic adenoma

MEC: Mucoepidermoid carcinoma

PA: Pleomorphic adenoma

PAC: Polymorphous adenocarcinoma

SGLs: Salivary gland lesions

SGTs: Salivary gland tumors

TASH: Tikur Anbessa Specialized Hospital

WHO: World Health Organization

I. Abstract

Introduction: Salivary gland tumors account for < 1% of all tumors and about 4% of all epithelial neoplasms in head and neck region, and can display a remarkable range of morphological diversity between different tumor types. The objectives of this study were to analyze, compare and contrast the demographic and morphological data of neoplastic and non-neoplastic salivary gland lesions seen at Tikur Anbessa Hospital, Pathology department.

Materials and Method: This was a descriptive, retrospective study of the salivary gland lesions diagnosed from July 2015 up to June 2020 from the Tikur Anbessa Hospital, Department of Pathology archive. These were analyzed for age, gender, anatomical location of the tumors and morphological typing. The salivary gland tumors were classified according to the 2017 WHO classification system.

Results: From a total of 378 cases reviewed, 339 files had complete medical records fulfilling the study criteria. Of the 339 cases, 180 (53.1%) of the study subjects were females with an F: M ratio of 1.13:1. The commonest age group for both neoplastic and non-neoplastic salivary gland lesions was in the 3rd and 4th decades but spans a broad age range (2nd to 6th decades of life). 143 (42.2%) of the cases were non-neoplastic while the remaining 185 (54.6%) cases were neoplastic. Eleven (3.2%) cases were diagnosed as normal glands. Majority of the salivary gland neoplasms were benign tumors, accounting for 111 (60%).

Among from the 143 non-neoplastic 76 (53.1%) were sialadenitis. More than half of the sialadenitis, 47 cases (61.8%) were constituted by chronic non-specific sialadenitis followed by obstructive sialadenitis with sialolithiasis and lymphoepithelial sialadenitis, 7 cases (9.2%) each. The most frequently affected anatomic location was the submandibular glands (62%) followed by the parotids (23.4%).

Out of the 111benign tumors, PA was the most frequently occurring benign neoplasm with 99 cases (89.2%). The mean age of occurrence being 36.9 years and an F:M ratio of 1.4:1. The commonest site of occurrence was the parotids 36 (32.4%). The second most common benign tumor were myoepithelioma and basal cell adenoma containing 3 cases (2.7%) each, both located in the major salivary glands, mainly the parotids and the submandibular glands.

Of the malignant tumors, 40 (58.8%) were females and 30 (44.2%) were males with an F:M ratio of 1.33:1. The mean age was 42.5 years. Mucoepidermoid carcinoma 23 (33.3%) cases was the commonest salivary gland cancer followed by 21 cases of adenoid cystic carcinoma (30.4%), 6 cases of acinic cell carcinoma (8.8%) and 3 cases of adenocarcinoma, NOS (4.4%). 78 (42.4%) cases occurred in the parotid, 40 (21.7%) cases arose from the palate and 25 (13.6%) of the cases originated from the submandibular glands. Four cases of lymphomas, 3 cases of primary squamous cell carcinomas and a single case of high grade sarcoma were reported.

Conclusion: Non-neoplastic lesions and tumors of the salivary glands show a slight geographic variation. In our study, pleomorphic adenomas were the most frequent salivary gland tumors similar to other African, Brazilian and Asian studies, but significant variation form studies done in Croatia. Sialadenitis was the second commonest lesion obtained which was in agreement to

most literatures in African and Caribbean nations. In our study, Warthin tumor was the fourth most frequently identified benign salivary gland tumor which was in contradictory to most of the literatures.

1. Introduction

Salivary glands are exocrine organs comprising three pairs of major glands (parotid, submandibular, and sublingual) and about 500 to 1000 lobules of minor glands distributed in the submucosa of the oral cavity. The seromucinous glands of the nasal cavity, larynx, and bronchi, although not producing saliva by definition, are histologically similar to the minor salivary glands and share a similar repertoire of neoplasms. The normal adult parotid gland weighs 15 to 30 g. The superficial and deep lobes are separated by the facial nerve. Most salivary gland tumors arise from the superficial lobe and present as facial swellings. Tumors occurring in the deep lobe often expand through the parapharyngeal space, manifesting as pharyngeal swelling [1].

The accessory lobe of the parotid gland, situated adjacent to Stensen duct and separate from the main body of the parotid gland, is found in 21% of normal subjects [2]. Tumors arising in this lobe often present as mid-cheek masses [3]. About 20 lymph nodes and randomly distributed lymphoid aggregates are normally present in the parotid gland, with the latter component representing the mucosa-associated lymphoid tissue (MALT) [4]. Conventional types of nodal lymphoma occurring in intraparotid lymph nodes may present clinically as a tumor of the parotid gland. Conversely, salivary gland tissues can be found in intraparotid, paraparotid, and cervical lymph nodes and are believed to give rise to Warthin tumor and other salivary gland tumors in lymph nodes mimicking metastatic disease [5].

The submandibular and sublingual glands weigh approximately 7 to 15 g and 2 to 4 g, respectively. Unlike in the parotid gland, no lymph node or large nerve courses through the parenchyma, although lymph nodes are normally present adjacent to the submandibular gland. Minor salivary glands can be found in the lateral margins of the tongue, lips, buccal mucosa, palate, and glossopharyngeal area. Among them, the palate is the predilection site for salivary gland neoplasms. Heterotopic salivary gland tissue can occur in the soft tissues of the neck. It typically presents as a draining sinus and/or asymptomatic nodule of the neck along the lower anterior sternocleidomastoid muscle, often with cutaneous involvement [6].

Salivary gland lesions (SGLs) represent clinical and morphological diversity, which is a difficult task for histopathological interpretation [7].

The major salivary glands are enveloped by a thin fibrous capsule, except the sublingual gland, where the capsule is incomplete. The salivary lobules consist of variable proportions of serous and mucous cells. The parotid gland is exclusively serous, the submandibular gland mixed seromucinous, and the sublingual gland predominantly mucous; the minor glands are seromucinous or predominantly mucous depending on location.

Salivary glands are tubuloacinar exocrine glands. The acini are the secretory units situated at the terminus. The secretion reaches the oral cavity via the conducting unit, consisting of intercalated, striated, interlobular, excretory, and salivary ducts. Preservation of the lobular architecture is an important feature favoring the diagnosis of a non-neoplastic process over a tumor. The entire

glandular structure is a two-tiered organization that comprises luminal (acinar and ductal cells) and abluminal cells (myoepithelial and basal cells). The secretory acini and the intercalated ducts are wrapped by myoepithelial cells. The striated ducts and the subsequent conducting units are lined by simple or pseudostratified columnar epithelium that gradually transforms into stratified squamous epithelium in the salivary duct, and they are surrounded by basal cells.

1.1. Background of the study

SGTs constitute < 1% of all tumors and about 4% of all epithelial neoplasms in head and neck region [7]. These comprise a wide variety of benign and malignant neoplasms, non-neoplastic lesions which exhibit a difference in biological behavior. Non-neoplastic lesions range from an inflammatory disorder of infectious, granulomatous, or autoimmune etiology to obstructive, developmental, and idiopathic disorders. These often clinically present as tumors and may have pathological feature similar to some of the neoplasms [8].

Despite their rarity, salivary gland tumors (SGTs) can show a striking range of morphological diversity between different tumor types and sometimes within an individual tumor mass. In addition, hybrid tumors, dedifferentiation and the propensity for some benign tumors to progress to malignancy can confound histopathological interpretation. Major and minor salivary gland tumors differ in incidence, cell type, growth characteristics and method of treatment [9-11]. About 80% of the SGTs are found in the parotid gland, 10-15% in the submandibular gland. The majority of salivary gland tumors (80-85%) are of benign histology, with pleomorphic adenoma being the most common, [12] constituting 70% of benign tumors. The probability of malignancy is relatively inversely proportional to the size of the gland. Overall, benign tumors of the salivary glands tend to present somewhat earlier than malignant ones.

There are almost 40 named epithelial tumors in the 2017 WHO classification, it is evident that some tumors are very rare indeed and may be the subject of only a few case reports [13]. Pleomorphic adenoma (PA) is the most common among benign tumors. Mucoepidermoid carcinoma (MEC) is the most common among malignant tumors. Affected patients are between 15 and 70 years age group.

Hill (2002) studied 135 salivary gland tumors and noted that there were differences in prevalence between these lesions, depending on the anatomical site. The parotid gland, for example, showed a higher prevalence of MEC when compared to the submandibular gland [14].

In a multicenter study, in a total of 1,706 lesions diagnosed in pediatric patients, mucocele was more frequent (64%), and the most affected site was the lip (34.5%) and mandible (19.9%) [15].

Between 64% and 80% of all primary epithelial salivary gland tumors occur in the parotid gland with most located in the superficial (lateral) lobe; 7-11% occur in the submandibular glands; less than 1% occur in the sublingual glands and 9-23% occur in minor glands [16].

Females are more frequently affected, but there is some gender variation according to the tumor type. The average ages of patients with benign and malignant tumors are 46 and 47 years, respectively, and the peak incidence of most of the specific types is in the sixth and seventh decades [16]. Among all patients, the most common tumor type is PA, which accounts for about 50% of all tumors. Warthin's tumor is second in frequency among benign tumors. In most large studies MEC is the most common malignant tumor [16].

Benign tumors may be present for months to several years before coming to clinical attention, while cancers more often come to attention promptly, there are no reliable criteria to differentiate benign from malignant lesions on clinical grounds, and histopathologic evaluation is essential [17].

SGTs proved most difficult because they arise from or differentiate toward the same cell lines: epithelial and myoepithelial cells results in considerable overlap at all levels where these cells can undergo a variety of metaplastic changes [18].

Data concerning the global incidence of salivary gland cancers in the world are incomplete. Malignant neoplasms of salivary glands are extremely rare, the figures range from 0.05-2/100,000 population. The highest number of new cases come from Croatia, where there are 1.8/100,000 new cases of this type of cancer found in men [19]. Cancer of the salivary glands account for about 0.3% of all cancers worldwide [20] and is considerably more common in females than in males (ratio worldwide is 1.5:1) [21], although the proportion varies according to the histological type of tumor [22]

In both sexes, the highest number of salivary gland cancers are found in the European and North American population. Compared with Africa, the proportion is 40:6, whereas for Asia it is 40:1 [23].

According to the 2015 Addis Ababa Cancer registry, there were a total of 433 newly diagnosed cancer cases (210 females and 223 males) with an ASIR of 0.6 (males) and 0.7 (females) [24]. Salivary gland cancer is the 10^{th} most common cancer in Gondar and North-Western Ethiopia (2.2%) [25]. The incidence of salivary gland cancers in TASH is 13 % of all head and neck cancers [26]. Approximately 53,000 new salivary gland cancers (almost 24,000 in females and over 29,000 in males) were diagnosed worldwide in 2018, the lifetime risk of getting salivary gland cancer is 0.06 (0.07% in males, and 0.05% in females) and over 22,000 patients died from cancers of salivary gland in 2018 [20].

Since, there are very limited studies in Ethiopia done on these tumors, the aim of the present study is to determine the frequency as well as morphological patterns of salivary gland lesions, in Black Lion Hospital, Addis Ababa, Ethiopia.

1.2. Significance of the study

As mentioned earlier, data from the literature shows difference in the relative frequencies of the various neoplastic and non-neoplastic salivary gland lesions. Several reports on this topic from different parts of the world showed difference in geographic prevalence among the neoplastic and non-neoplastic lesions. Since there is limited information in the literature about the prevalence of the neoplastic and non-neoplastic salivary gland lesions in Ethiopia, the objective of the current study is to establish the frequency and type of the various neoplastic and non-neoplastic salivary gland lesions diagnosed in biopsy and FNA (for non-neoplastic lesions only) specimens in Tikur Anbessa Specialized Hospital (TASH) from July 2015 to June 2020. This study also aims to compare the results with those found in similar studies done in different parts of the world. This work will also serve as a reference for other studies in the future.

2. Literature Review

During 2018, 52,799 new cases of salivary gland cancers were diagnosed worldwide, 23,543 (44.58%) of whom were female and 29,256 (55.42%) were male. In general, the global ASIR of salivary gland cancer was 0.5 in women and 0.7 in men per 100,000 population. There were also 22,176 deaths from salivary gland cancer, 8,736 (39.39%) of whom were female and 13,440 (60.61%) were male. The global ASMR of salivary gland cancer was 0.03 (0.03 in males and 0.02 in females) [20].

A retrospective study of 268 cases was conducted in the Department of Histopathology and Morbid Anatomy, Muhimbili University College of Health Sciences, Uganda, over a period of 10 years (from 1979 to 1988). 43.3% were males and 56.7% were females with a male to female ratio of 1:1.3 for all tumors. The majority of the patients (90.8%) were seen between the 2^{nd} -6^{th} decades with mean age in female (37.8 years) and male (38.4 years) patients, except for male patients with malignant tumors who were somewhat older (mean: 44.5years) than their female counterparts (mean: 41.6years). Forty-six (46%) of the cases were malignant and 54% were benign tumors with malignant to benign ratio of 1:1.18. Excluding the seven cases with unrecorded sex, there was a female predominance in both malignant (52.4%) and benign (60.4%) tumors. Although there was a slightly preponderance of parotid tumors (34%), the distribution is similar to that of submandibular (33.2%) and minor salivary glands (32.8%). Of the latter site, about 50% (43 tumors) arose from the palate. Other locations of minor glands included, cheek, (17), lip (4), tongue (7), retromolar region (6) and maxillary sinus (4). In seven intraoral tumors, the site was not exact. More than half of the tumors from the parotid (54%) and those from minor glands (53%) were diagnosed as malignant. Noticeably, no involvement of sublingual gland was recorded in this series. The most frequent histological diagnosis was PA (73.8% of all benign tumors). The second most common benign tumor was myoepithelioma (11.2%), followed by basal cell adenoma (6.2%). The most affected site for benign tumors was the submandibular gland (43%). The parotid (29%) and minor glands (28%). No Whartin's tumor was found in this series. Adenoid cystic carcinoma (AdCC) was the most encountered malignant (29%) tumor and was second (13.4%) after PA in a whole series. Fifty percent of AdCC originated from minor glands of the oral cavity. It was followed by MEC (20.3%), and acinic cell carcinoma (ACC) (13.1%). Only 22% of all malignant tumors arose from the submandibular gland, whereas, 40% and 38% of malignant tumors were from the parotid and minor salivary glands, respectively [27].

Another study conducted in the Department of Pathology, University of Zagreb School of Medicine, University Hospital Dubrava, Croatia from 1985-2009. Over a period of 25 years, 779 patients with salivary gland tumors were evaluated, 392 males (50.3%) and 387 females (49.7%). The mean age of the patients was 52 years (range, 1-93 years). The average age of patients with benign tumors was 50 years and 56 years for patients with malignant tumors. There was no difference in age between males and females. The most common site was the parotid gland (65.3%), followed by the minor salivary glands (27.2%). There were 51 (6.6%) tumors of the submandibular gland and only seven tumors of the sublingual gland (0.9%). 72.8% tumors occurred in the major salivary glands. Overall there were 64.2% benign and 35.8% malignant tumors. Among tumors of the parotid tumors, two-thirds were benign and the rest were malignant (383 vs. 126); PAs were predominant (66.8%), followed by Warthin's tumor (22.8%).

Among the malignant tumors of the parotid gland, 32.5% were MECs, 15.9% AdCCs, 13.5% carcinoma ex-pleomorphic adenomas (Ca Ex-Pa) and 10.3% ACCs. In the submandibular gland, there were 30 (58.8%) benign and 21 (41.2%) malignant tumors. No benign tumors were found among the seven sublingual gland tumors. Among the benign tumors of the submandibular gland, pleomorphic adenomas were predominant (93.4%). One case of sebaceous adenoma and one case of inverted ductal papilloma were found in the submandibular gland. Of the malignant tumors of the submandibular gland, AdCC was the most common histological type (42.8%), followed by MEC (23.8%), Ca Ex-PA (14.3%), and adenocarcinoma NOS, (9.5%). In the sublingual gland, all tumors were malignant, 3 were MECs, 3 were AdCCs, and one was Ca Ex-PA. Of all minor salivary gland tumors, 87 (41.0%) were benign and 125 (59.0%) were malignant. The palate was the most frequent site (52.8%), followed by the maxillary sinus (17%), and the buccal mucosa (10.4%). Of the benign tumors of the minor salivary gland, 96.7% were PAs and among the malignant tumors, 49.6% were AdCCs, followed by MECs (14.4%), and Ca Ex- PAs (9.6%). Tumor histology was dependent on anatomic localization. Benign tumors were frequent in the lip (64.3%) and palate (53.6%), while malignant tumors were predominant in the maxillary sinus (97.2%), the rest being from rare sites (nasal cavity mucosa, upper and lower gingiva, tongue and ethmoid sinus). All nine benign tumors of the lip were PAs, seven of which were in the upper lip. Among the malignant tumors of the lips, four were in the lower lip. The most frequent tumors of the palate were PAs (53.6%) and AdCCs (21.4%). AdCC was the most common minor salivary gland tumor of the maxillary sinus and PA was the most common tumor of the buccal mucosa, lip, and parapharynx [28].

A 24 years retrospective and observational study was done at the State University of Maringa, Brazil by Sesenta Junior et al. on epidemiological profile of salivary gland lesions, between 1995 and 2018. Of the 3,127 biopsies performed, 381 (12.1%) were SGLs. 337 (88.5%) were non-neoplastic lesions, 27 (7%) benign neoplasms, and 17 (4.5%) malignant neoplasms. There was a slight preference for women, as 49% of cases were diagnosed in men and 51% in women. Regarding age, the second and third decades of life were the most affected, with 33% and 18.7% of cases, respectively. For ethnicity, 269 were Caucasians (71%), 69 blacks (18%), 38 mulattoes (10%) and only 5 yellow (1%). Mucocele was the most common lesion (70.6%), followed by pleomorphic adenoma (6.56%), oral ranula (5.77%), sialadenitis (3.93%), sialolithiasis (3.14%), salivary duct Sjogren syndrome (0.52%); ACC (0.26%), polymorphous adenocarcinoma (PAC) (0.26%), canalicular adenocarcinoma (0.26%) and ductal papilloma (0.26%) [29].

A Prospective Study done on epidemiological and histomorphological patterns of SGTs in Faculty of Medicine and Biomedical Sciences (FMBS) of the University of Yaoundé, Cameroon over a period of 11 years spanning from January 2000 to December 2010 and included a total of 275 files in the study. Females were 154 (56%) and males 121 (44%) of the sample. There was an increase in the number of cases per year as from 2007, with a peak in 2009 being 45 cases. Fifty eight tumors were malignant (21.1%) while 217 were benign (78.9%). The mean age of the patients was 37.44 years with extremes of 1 and 84 years. Mean age was 46.9 years with extremes of 18 and 79 years in the patients with malignant tumors versus 34.9 years with extremes of 1 and 84 years in those with benign tumors. The study obtained the sequence of 135:109:30 for parotid, submandibular and accessory salivary glands respectively, thus giving a parotid/submandibular gland ratio of 1.23. PA (60.36% of benign tumors and 47.7% of all tumors) was the most frequent benign tumor. The cystic AdCC was the most frequent malignant

tumor (31%), followed by the MEC (22.4%), and adenocarcinoma (19%). There were 30 cases (20%) of accessory salivary gland involvement, of which 20% were malignant tumors. The palate (66.7%), the cheek (30%) and the lips (3.3%) were the sites affected most by accessory salivary gland tumors. There were 54 inflammatory pseudo tumors, representing 24.8% of benign tumors and 19.6% of the sample [30].

A 10 years retrospective study was done in the Pathology department of the San Fernando Teaching Hospital, Trinidad and Tobago between the periods January 2005 to June 2015. A study sample of 85 resections were reviewed and analyzed. The mean age of the patients reviewed was 46.8 years with a range of 6–72 years showing a slight male preponderance of 1:1.2. Benign neoplastic lesions were the most common 53 (62.4%) of all the resections performed, followed by non-neoplastic lesions 25 (29.4%) such as sialadenitis, cysts or normal glands. Malignant neoplasms made up the minority with only 7 cases. There were no documented sublingual gland lesions [31].

Another study was done on 371 cases in the Department of Pathology, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana, between the year 2009 and 2016. The mean age was 37 years (6 months to 88 years). One hundred and sixty-seven cases were males while 204 were females with male to female ratio of 1:1.22. There was female preponderance in inflammatory, tumor-like as well as benign lesions; however there was a slight reversal of this in the malignant lesions (with 1.14:1 male to female ratio). Most of the cases of the salivary gland specimens reviewed were from the major salivary glands with the parotid gland recording the highest frequency of 193 cases (52%). One hundred and fifty five cases (41.8%) were from submandibular gland while the sublingual recorded the lowest number of 5(1.3%). The minor salivary glands recorded 10 cases (2.7%) while 8 cases (2.1%) were unspecified. The commonest types of lesions seen in the salivary gland were grouped as benign with a total of 167 cases (45%). Primary malignant cases were 103 cases (27.8%) and inflammatory and tumor- like cases were 86 cases (23.2%). While 4 cases (1.1%) were metastatic, 11 cases (2.9%) were normal. The representation of these entities in the various glands shows similar pattern with a slight variation. Parotid gland recorded the highest number of benign cases, 106 (54.9%). A high number of cases, 59 (38.1%) from the submandibular were inflammatory and tumor-like. All the cases in the sublingual glands were inflammatory and tumor-like. In the minor salivary gland, there were more malignant cases than benign ones (4 out of 10) [32].

Retrospective study of 124 cases of salivary gland tumors was conducted in the Department of Pathology, Federal University of Santa Catarina, Brazil from 1995 to 2016. A total of 124 salivary gland tumor cases were identified. 81 (65.3%) were benign and 43 (34.6%) were malignant. Of the benign tumors, PA was the most common (91.3%). Of the malignant tumors, adenocarcinoma NOS was the most common (25.5%), followed by AdCC, MEC, and Ca Ex-PA (8 cases each, 18.6%). The most common site was the parotid gland (57.2%), followed by the minor (29%), submandibular (11.2%), and sublingual glands (2.41%). Regarding the benign tumors, 48 occurred in the parotid gland, 22 in the minor salivary glands, and 11 in the submandibular gland, while 23, 14, and 3 malignant tumors were identified in the same locations, respectively. Only malignant tumors affected the sublingual glands, with 3 cases. Among the minor SGTs, the palate was the most common site, accounting for 17.7% of all cases, followed by the lip (5.6%). Patient age was available in 117 cases. The ages ranged from 14 to

94 years. Among benign tumors, the average was 41.3 years, with the highest prevalence in the third decade. Among malignant tumors, the patient average was 54.3 years, with a higher prevalence in the fifth decade. Regarding the distributions by gender, 54.8% and 45.2% of all neoplasms occurred in women and men, respectively. Among benign tumors, 56.7% occurred in women and 43.2% in men. Among malignant tumors, 51.1% occurred in women and 48.8% in men [33].

A retrospective study was conducted on salivary gland tumors diagnosed at the Department of Oral Pathology, Shahid Beheshti University of Medical Sciences, Tehran, Iran from March 2000 to March 2015. Of the 45,429 biopsies conducted over 15 years, 6065 (13.3%) cases were oral and maxillofacial lesions, and 937 (15.4%) of these had tumoral diagnoses. Of the 937 tumoral cases, 184 (19.6%) cases were SGTs. The overall frequencies of benign and malignant tumors were 35.3% and 64.7%, respectively. PA was the most frequently occurring tumor, comprising 60 cases, 32.6% of all tumors and 92.3% of benign neoplasms. MEC was the most frequently occurring malignancy and the second most common tumor, representing 27.1% of all tumors and 42.01% of malignant tumors. There were 41 cases of AdCC (22.2% of all tumors), which made it the third most frequent tumor and the second most common malignant tumor (34.4% of malignant tumors). Tumors were more frequently reported in minor salivary glands (73.9%), particularly the palate with 89 (48.4 %) cases, followed by the parotid (14.6%). Eight cases of intraosseous MEC (16% of all MECs and 4.3% of all cases considered) were identified in this study, and these cases mainly affected women (62.5%) and particularly the posterior of the mandible (5 cases) for patients with a mean age of 40.5 years. Interestingly, all cases of ACC were diagnosed during the second decade of life. In terms of gender, 111 (60.4%) cases were female and 73 (39.6%) cases were male. Benign tumors showed a slight predilection for males (53.8%), whereas malignant tumors showed a predilection for females (72.9%). The peak ages of incidence were the fourth and sixth decades of life with mean ages of 41.2 and 45.5 years for benign and malignant tumors, respectively [34].

A descriptive cross-sectional study was conducted in Pathology Department of Bannu Medical College, Bannu, KPK, Pakistan from January, 2011 to December, 2015 on histopathological patterns of SGTs. Out of a total of 78 patients with salivary gland tumors, the ratio of male to female was 1.2:1. The mean age of the sample was 31.22 ±11.23 years and range was from 13 to 58 years i.e., 45 years. The common age group in benign tumors was 21-30 years, in 46 (69.69%), followed by 31-40 years, 13 (19.69%) 10-20 years in 4 (6.06%) cases, whereas in malignant tumors the most common age group was 41-50 years in 9 (75%) and 51-60 years in 3 (25%) cases. Major salivary gland tumors were 59 (75.64%) and minor salivary gland tumors were involved in 19 (24.35%) cases. Out of 59 major salivary glands, parotid was involved in 48 (82.35%) followed by submandibular gland in 11 (14.10%) cases, whereas out of 19 minor salivary glands, palate was commonest site involved by 13 (16.66%), followed by buccal mucosa 03 (3.84%) cases. Amongst these salivary gland tumors, benign were 66(84.61%) and malignant 12(15.38%). Out of 66 benign tumors, PAs were 57 (73.87%) followed by monomorphic adenoma 5(6.41%), Warthin tumor 2(2.56%), myoepithelioma and hemangioma 1(1.26%) in each case. Out of 12 malignant tumors MEC was in 5(6.41%), followed by AdCC in 3(3.84%), ACC in 2(2.56%), malignant mixed tumor and large duct adenocarcinoma 1(1.28%) in each case [35].

Ito et al. conducted a retrospective study of salivary gland tumors in Brazilian population in the Department of Pathology, Londrina Cancer Institute, Parana state, Brazil, from 1972 to 2001. Out of total of 496 cases of major and minor salivary glands analyzed, 335 (67.5%) were benign and 161 (32.5%) malignant. The most common site was the parotid gland with 336 cases, followed by the minor salivary glands (113 cases) and submandibular gland (47 cases). No tumors of the sublingual gland were found. Among the minor salivary gland tumors, the palate was the most frequent location (67%), followed by the lips (10%). Regarding the benign tumors, 256 occurred in the parotid gland, 42 in the minor salivary glands and 37 in the submandibular gland, while the corresponding values of the malignant tumors were 80, 71 and 10, respectively. The peak incidence of all patients with salivary gland tumors was in the fifth decade. Benign tumors were slightly predominant in females (58.5%), while 52.2% of the malignant tumors occurred in males. The peak incidence for patients with benign tumors was in the fifth decade. However, for patients with malignant tumors the peak incidence was in the seventh decade. It was observed that females were more frequent in the fifth decade, while males in the seventh decade. PA was the most frequent tumor with 269 cases, comprising 54.2% of all tumors and 80.3% of the benign salivary gland tumors of our series. MEC, 67 cases, was the second most common, and the most frequent malignancy, representing 13.5% of all tumors and 41.6% of the malignant tumors. Warthin's tumor (WT) was the third most frequent tumor with 42 cases (8.5% of all tumors) and the second most common benign tumor (12.5% of the benign tumors). Analyzing only parotid tumors, PA was the most frequent followed by Warthin tumor. AdCC was the fourth most frequent neoplasm (7.9%), and the second largest group of the malignant tumors with 39 cases (24.2%). According to the location, 198 (73.6%) cases of PA were located in the parotid gland, 38 (14.1%) in the minor salivary glands and 33 (12.3%) in the submandibular gland. MEC were also more common in the parotid gland (56.7%) followed by the minor salivary glands (37.3%) and submandibular gland (6%). On the other hand, the majority of AdCC was located in the minor salivary glands (71.8%) followed by the parotid gland (20.5%) and submandibular glands (7.7%). All cases of Warthin tumor occurred in the parotid gland. Considering the gender of the patients, 56.7% of PA arose in females. On the contrary, MEC were more frequent in males (58.2%). Warthin tumors were also predominant in males (male to female ratio of 2:1). Regarding AdCC, it was observed a similar incidence with 20 cases in females and 19 cases in males [36].

A study was carried out on histopathological patterns of SGLs from June 2015 to May 2018 in the department of Pathology, JLN Medical College and associated Group of Hospitals, Ajmer region, India. Out of a total 121 cases, 53 cases (43.80%) were diagnosed as non-neoplastic lesions and 68 cases (56.2%) as neoplastic lesions. Chronic sialadenitis was the commonest non neoplastic salivary gland lesion accounting for 23 cases (43.39%) followed by mucocele 15 cases (28.84%). Among all salivary gland lesions, pleomorphic adenoma was the single commonest lesion with 44 cases (36.36%). In neoplastic lesions, benign tumors were far ahead in frequency than malignant with 54 cases (79.41%). Out of total 54 cases of benign neoplastic lesions, PA was the commonest, (44 cases, 81.4%) followed by Warthin's tumor (7 cases, 13%). Warthin's tumor was found exclusively in parotid gland with M:F ratio 6:1 Out of total 14 malignant neoplastic lesions, MEC was the most common malignant salivary gland tumor (7 cases, 50%) followed by AdCC (3 cases, 21.42%). The peak incidence of non-neoplastic lesions was observed in 2nd and 3rd decades with mean age 27.09±13.62 years. Benign tumors were common in 3rd and 4th decades (mean age 37.26±13.69 years), whereas malignant tumors were commonest

in 6th decade (mean age 53.57±12.67 years). Male predominance was seen in overall salivary gland lesions with exception in non-neoplastic lesions in which the male to female ratio was 1:1.21. The male to female ratio of benign neoplastic lesions was 1.45:1 and in malignant neoplastic lesions was 1.33:1. In site wise distribution of lesions, out of 121 cases overall commonest site involved was parotid with 62 cases (51.24%). Non-neoplastic lesions were more commonly seen in submandibular gland (47.17%) followed by minor salivary glands (32.08%). Neoplastic lesions were most commonly distributed in parotid gland (75%), followed by submandibular gland (20.6%) and minor salivary glands (4.4%), in decreasing order of frequency [37].

A 5 years retrospective study was conducted on the histological patterns of non-neoplastic and neoplastic SGLs from January 2011 to 2015 December in the Department of Pathology, Sri Venkata Sai Medical College & Hospital, Mahabubnagar, Telangana, India. A total of 55 specimens of salivary gland specimens were reviewed. Out of 55 cases, 40 (72.27%) cases are neoplastic and 15 (27.27) cases are non-neoplastic. Among 40 neoplastic lesions, 30 (75%) cases are benign, and 10 (10%) cases are malignant. Most common benign tumor of salivary glands is PA followed by Warthin's tumor. Most common malignant tumor of salivary glands is MEC followed by AdCC. Affected patients are between 15 and 70 years age group. Predominantly females are affected (with female to male ratio of 1:0.5). A maximum number of cases are seen in parotid gland constituting, 37 cases (67.27%) followed by submandibular gland constituting 14 cases (25.45%). A maximum number of cases are seen in 41-50-year age group followed by 51-60-year age group [38].

Another 1 year retrospective study was done at Pathology Department, GMERS Medical College and Hospital, Sola, Ahmedabad, India on histomorphological aspects of non-neoplastic and neoplastic lesions of salivary glands in 2019. In this study, total of 66 salivary gland specimens were reviewed. Out of 66 cases, 22(33%) cases are non-neoplastic and 44 (67%) cases are neoplastic. Among 44 neoplastic lesions, 42(95%) cases are benign and 02 (5%) cases are malignant. Chronic sialadenitis is the most common non-neoplastic lesion. Most common benign tumor of salivary glands is PA followed by Warthin's tumor. The MEC was the only recognized malignant tumor followed by undifferentiated malignant tumor. The mean age found was 39.5 years with affected patients are between 3 and 72 years age group. Predominantly males are affected with male to female ratio of 3.4:1. A maximum number of cases are seen in parotid gland constituting 45 cases (68.18%) followed by submandibular gland constituting 21 cases (31.81%). Out of 45 (68.18%) cases of parotid tumors, 7 (15.5%) cases of non-neoplastic, 36(80%) cases of benign and 2 (4.44%) cases of malignant lesions finding out. Out of 21 (31.81%) cases of Submandibular gland tumors, 15 (71.42%) cases of non-neoplastic, 6 (28.57%) cases of benign lesions finding out. Salivary gland tumors studied were seen in the wide age group ranging from 3 years to 72 year. Most of the tumors were seen in middle age group with mean age of 39.5. Overall, 77.27% of cases in the study were male with 22.72% female cases. A maximum number of cases are seen in 21-30 year age group followed by 51-60-year age group [39].

A prospective descriptive hospital-based study was carried out at Al-gomhori Teaching Hospital in Republic of Yemen, Sana'a in 2019. A total of 140 cases of salivary gland files were studied, 64 cases (45.7%) were males, and 76 cases (54.3%) were females, male to female ratio was

0.8:1. The age of patients ranged from 3 to 82 years, with mean age for both gender of 40. 09 ±21.149. The majority of patients (79%) were over the age of 20 years. The peak age of occurrence (35.7%) was between the fourth and sixth decades of life. The most common disease of salivary glands was tumors, accounting (43.6%), followed by, cysts and sialolithiases, accounting 20.7% and 20.0 % respectively. The less common disease were sialadenitis and sialadenosis, accounting 12.9% and 2.9% respectively. Of salivary gland tumors, 61 cases were reported, 26 cases (42.6%) were males and 35 cases (57.4%) were females, male to female ratio was 0.7:1. Thirty-eight cases (62.3%) of salivary gland tumors were malignant and 32 cases (37.7%) were benign. Of malignant tumors, 38 cases were reported, 18 cases (47.4%) were males and 20 cases (52.6%) were females. Male to female ratio was 0.9:1. The majority of patients (89.4%) were over the age of 40 years. The peak occurrence (60.5%) was in between 4^{th} and 6^{th} decades of life. Squamous cell carcinoma was the most common type, accounting (50.0%), followed by AdCC and MEC (15.8% and 10.5% respectively). The less common types were, Ca Ex-Pa, ACC and lymphoma accounting 7.9% for each one. More than 92 percent of salivary gland malignancies found on the major salivary glands, 45.7% of these were found on the parotid glands, 31.4% on the submandibular gland and 22. 9% on the sublingual glands. Of benign tumors, 23 cases were reported, 8 cases were males and 15 cases were females, male to female ratio was 0.5:1. The majority of patients (70%) were found between the 3^{rd} and 6^{th} decades of life. PA was the commonest type, accounting (78.3%), followed by Whartin's tumor and hemangioma accounting (13.0% and 8.7% respectively). Thirteen cases of benign tumors (59.1%) were found on the major salivary glands and 9 cases (40.9%) on the minor salivary glands. Ninety two percent of benign tumors of the major salivary gland's tumors were located on the parotid glands, 53.8 % of these tumors were PA, 23. 1% were Warthin tumors and 15. 4 % were hemangioma. Of cystic lesion, 29 cases were reported, 11 cases (37.9%) were males and 18 cases (62.1%) were females, male to female ratio was 0.6:1. The majority of patients (96.5%) were found between the 1^{st} to 4^{th} decades of life, the peak age of occurrence (58.6%) was in the 1^{st} and 2^{nd} decades of life. Ranula and mucocele were reported, accounting 75.9% and 24.1% respectively. Sublingual glands were the most affected sites (75.9%). Of the 28 cases of sialolithiases seen, 14 cases were males and 14 cases were females, male to female ratio was 1:1. More than 90% of patients were found over the age of 20 years. Patients on the middle age were commonly affected (78.6%). Submandibular gland was the most common affected site (89.3%), followed by parotid glands (10%). Of 18 cases sialadenitis reported, 13 cases (72.2%) were males and 5 cases (27.8%) were females, male to female ratio was 2.6:1. Patient age ranged from 3 to 82 years with mean age of 42. Sialadenosis was the least common type (4 cases were reported) accounting 2. 9% of all salivary gland disease. All cases were found in female patients [40].

A research was conducted on histopathologically diagnosed SGTs to look at the prevalence and demographic distribution of salivary gland tumors at the Komfo Anokye Teaching Hospital, Ghana from 1999-2010. The total number of salivary gland tumors were 121. Male to female ratio was 1.75:1. Out of the total of 34 salivary malignancies seen, male to female ratio was 1.8:1. Malignant tumor was 28.1% while 71.9% were benign. Mean age for malignancy was 53.5 years and that for benign was 35.5 years. A total of 77 salivary tumors were seen in males and 22(29.3%) were malignant. In females, out of the 44 cases, 12 (26.0%) were malignant. The parotid was the commonest location of all salivary gland tumors. The submandibular gland had

more malignant tumors, representing 47.4%. A total of 10 out of 38 tumors in the right parotid were malignant, representing 26% as against a total of eight out of 22 cases of the minor salivary glands being malignant, (36%). Six cases of the minor salivary gland malignancies representing 75% were located on the palate. PA was the commonest SGT, constituting 50% of total salivary gland tumors and 69% of all the benign salivary gland tumors. Warthin's tumor constituted 3.3% of all salivary tumors. The commonest malignant tumor was Adenoid cystic carcinoma, which was 13.22% [41].

One retrospective study was conducted on pattern of salivary gland tumors in Ethiopia and non-Western countries in the Department of Pathology, Addis Ababa University, over a period of ten years from 1990-1999 inclusive. Of all SGTs, parotid gland accounts for 43.2% followed by submandibular gland for 25% and the rest of all minor salivary glands contribute for 31.9%. Out of 176 tumors, 117 were reported to be benign and 59 were malignant. PA forms 58.5% of all tumors [42].

3. Objective of the study

3.1. General objective

- The general objective of this study was to assess the pattern of morphological (microscopic) diagnosis of salivary gland lesions in Tikur Anbessa Hospital from July 2015 to June 2020.

3.2. Specific objectives

The specific objectives were to

- Analyze the relative frequency of individual SGLs
- Classify salivary gland lesions for therapeutic implication
- Describe the epidemiological patterns SGLs (the prevalence and frequency of non-neoplastic and neoplastic salivary gland lesions) with particular references to age, gender, anatomical site and its incidence

4. Methodology

4.1. Study setting

This study was conducted at Black Lion (Tikur Anbessa) specialized teaching Hospital. Tikur Anbessa (Black Lion) Specialized Hospital is located in Addis Ababa at Lideta sub-city opposite to Immigration office of Ethiopia. It is the teaching hospital of the Addis Ababa University and the largest referral hospital in the country with over 700 beds, and serves as a training centre for undergraduate and postgraduate medical students, dentists, nurses, midwives, pharmacists, medical laboratory technologists, radiology technologists, and others who shoulder the responsibilities to solve the health problem of the community and the country at large.

4.2. Study design and period

The study was a retrospective descriptive study where data was retrieved from the archives of the department of pathology registered from July 2015 up to June 2020.

4.3. Study population

All patients whose salivary gland biopsy and FNAC (for non-neoplastic lesions only) specimens were submitted to the department in the study period from July 2015 to June 2020 which fulfilled the inclusion criteria.

4.4. Eligibility criteria

4.4.1. Inclusion criteria

- Cases of SGLs
- Complete medical records (demographic data, clinical history and if any, imaging findings and previous pathology reports) of patients
- All cases with definitive and unambiguous morphological diagnoses

4.4.2. Exclusion criteria

- Cases with descriptive diagnoses
- Recurrent salivary gland tumors
- Cases with salivary gland-type diagnoses of other organs

4.5. Data management and analysis

4.5.1. Data collection procedure

Surgical biopsy request papers and cytopathology requisitions (for non-neoplastic lesions only) were retrieved from the department archives registered from July 2015 to June 2020 using an appropriate data collection tools. Demographic, clinical, radiologic descriptions and final microscopic diagnoses were collected.

4.5.2. Study variables and data analysis

4.5.2.1. Independent variables

- Anatomical site (location) of the lesions
- Age of the patient
- Gender of the patient

4.5.2.2. Dependent variables

- Morphological diagnoses of the lesions
- Behavior of the tumor (non-neoplastic and neoplastic, benign and malignant)

These variables were subjected for data analysis and the data feeding and analysis was done using the software package SPSS (Statistical Packages of Social Sciences) version 25.0.

4.6. Ethical considerations

Ethical permission was sought from the Department of Pathology, College of Health Sciences, School of Medicine, Addis Ababa University. Names of patients or their chart numbers were not described in the study to keep the confidentiality of the patients.

5. Results

From a total of 378 cases reviewed, 339 files have complete medical records fulfilling the criteria of the study. The rest 39 cases were excluded due to incomplete relevant demographic and clinical data as well as being descriptive diagnoses.

5.1. Mode of diagnosis

Among the 339 cases, 277 were biopsies and 62 were FNA cases of non-neoplastic salivary gland lesions (Fig. 1).

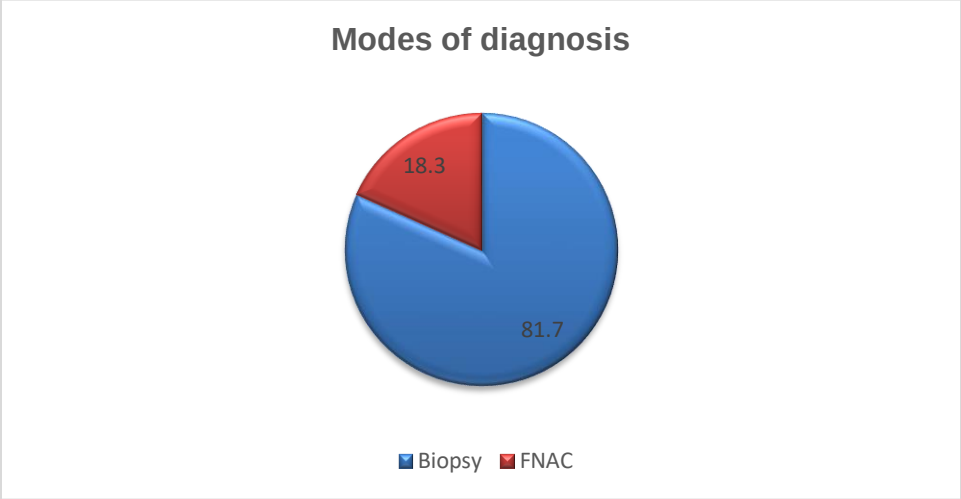

Figure 1 showing the of mode of diagnosis

5.2. Patient characteristics

Of the 339 cases, 180 (53.1%) of the study subjects were females while the remaining 159 (46.9%) males (Fig. 2) with an F: M ratio of 1.13:1. The minimum age was 1 year and the maximum was 75 years.

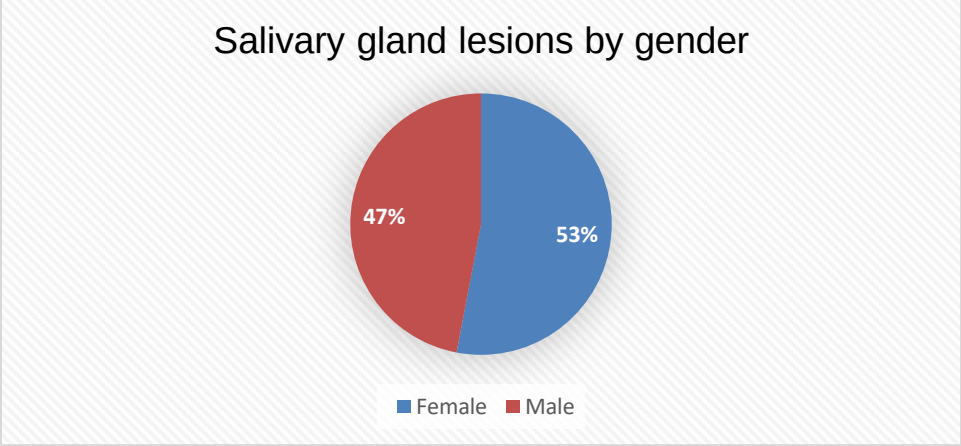

Figure 2 Salivary gland frequency by gender

The overall mean age was 36.2 years. The mean age for benign tumors, malignant tumors and non-neoplastic lesions was 36.9, 42.5 and 36 years respectively (Table 1). The commonest age group for both neoplastic and non-neoplastic salivary gland lesions was in the 3rd and 4th decades but spans from 2nd to 6th decades of life (Fig. 3).

Most of the patients (93.8%) in the non-neoplastic salivary gland lesions were seen between the 1st and 6th decades. There was a slight male predominance with M: F ratio of 1:0.9. The minimum age was 1 year and the maximum age was 75 years

Table 1 Mean, range and standard deviation

	Age (years)			
	Minimum	Maximum	Mean	Std. Deviation
Benign SGTs	4	75	36.9	14.9
Malignant SGTs	10	71	42.5	16.8
Non-neoplastic SGLs	1	75	36.2	17.5

Figure 3 Distribution of benign SGLs by age group

5.3. Nature, site and morphological patterns of salivary gland lesions

Among the 339 cases studied, 143 cases were non-neoplastic lesions while 185 cases were neoplastic (Table 2 and Fig. 4). A total of 11 cases (3.2%) were diagnosed and reported as normal glands.

Regarding the anatomical distribution, 220 cases arose from the major salivary glands while the remaining 119 subjects originated in the minor salivary glands (Fig. 5).

Table 2 Nature of salivary gland lesions

	N=180	Percent
Benign tumors	110	61.1
Malignant tumors	70	38.9

Among the major salivary glands, the parotid glands were affected most harboring 116 (52.7%) of the lesions. Hundred cases (45%) developed in the submandibular glands. The sublingual glands were the least affected with only 2. One case arose from the parotid and submandibular ducts each (Table 3).

	N=220	Percent
Parotid glands	117	53.2
Submandibular glands	100	45.0
Sublingual glands	2	.9
Parotid and submandibular glands	1	.5

Table 3 Distribution of lesions in major salivary glands

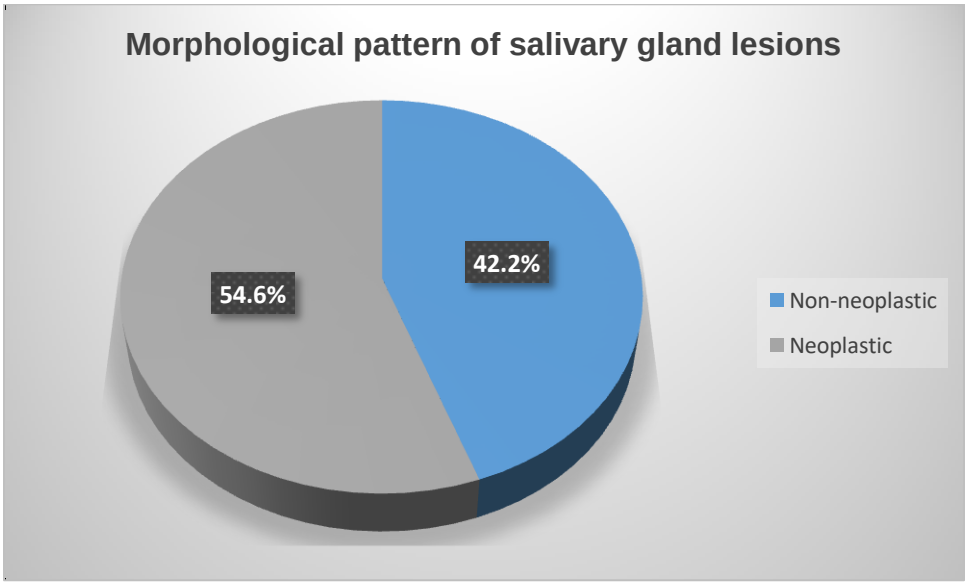

Figure 4 Nature of salivary gland lesions

The palate was the most frequent site of minor salivary gland involvement where 42 cases (35.3%) of the minor salivary gland lesions arose. Minor glands of the face, lip, buccal mucosa,

neck, periauricular area and the paranasal sinuses were also the preferred locations (Fig. 6). The lower lip was affected by non-neoplastic lesions (10) but tumoral cases were diagnosed in the upper lip (4). No non-neoplastic lesions were reported in the upper lip and vice versa. Overall, the parotids, the palate and the submandibular glands are the most commonly affected sites accounting for 78 (42.4%), 40 (21.7%) and 25 (13.6%) cases respectively (Table 4 and Fig. 7).

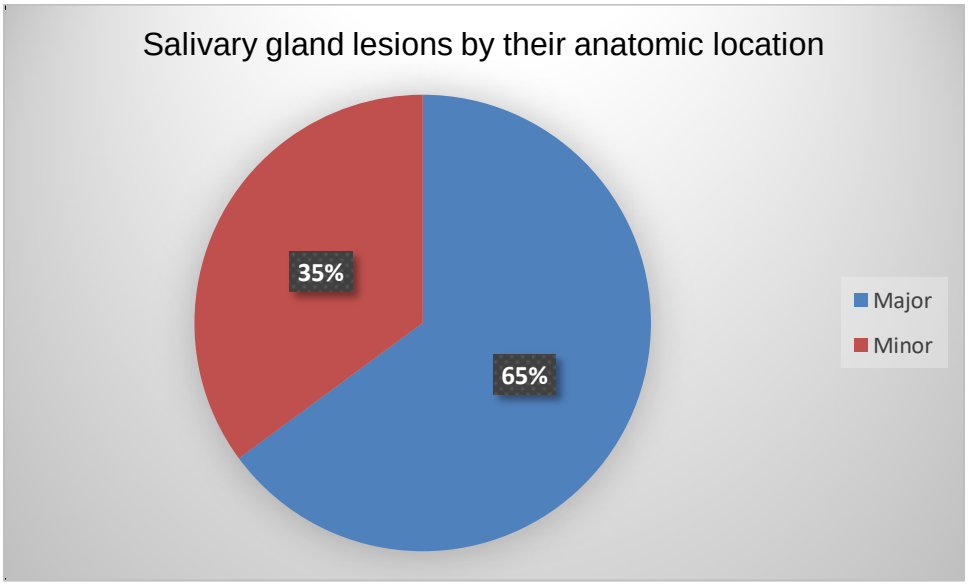

Figure 5 Frequency of SGLs by anatomic location

Out of the 143 non-neoplastic salivary gland lesions, 76 (53.1%) were sialadenitis followed by 32 sialadenosis cases (22.4%) and 19 cases of mucocele (13.3%). Benign cystic lesions, oral cavity ranula and chronic sclerosing polycystic adenosis in decreasing frequency were 11, 5 and 1 respectively (Fig. 8). More than half of the sialadenitis (47) were constituted by chronic non-specific sialadenitis followed by obstructive sialadenitis with sialolithiasis and lymphoepithelial sialadenitis with 7 cases each (Table 5). Approximately 90% of the benign cystic lesions of the salivary glands were made up of lymphoepithelial cysts accompanied by a single case of lymphatic cyst (10%).

Table 4 Anatomical distribution of salivary gland neoplasms

Salivary glands	Number of lesions	Percent (%)
Major		
Parotid	78	42.4
Submandibular	25	13.6
Sublingual	1	0.5
Minor		
Palate	40	21.7
Upper lip	4	2.2
Buccal mucosa	3	1.6
Cheek	4	2.2
Paranasal sinuses	7	3.8
Nasal cavity and nasopharynx	7	3.8
Tongue	3	1.6
Oral cavity	1	0.5
Retromandibular trigone	1	0.5
Other minor salivary glands	10	5.4

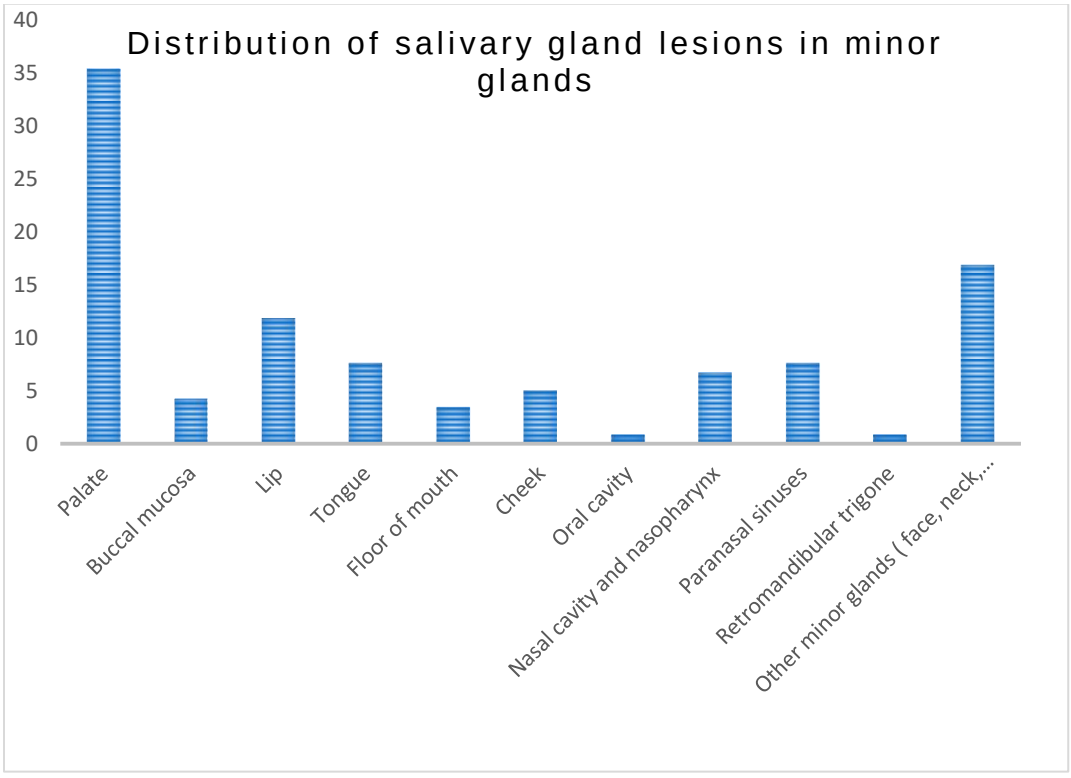

Figure 6 Frequency salivary gland lesions in the minor salivary glands

Table 5 Sialadenitis

	N=76	Percent
Chronic non-specific sialadenitis	47	62.7
Obstructive sialadenitis (sialolithiasis)	7	9.3
Acute suppurative sialadenitis	3	4.0
Acute on chronic sialadenitis	4	5.3
Granulomatous sialadenitis	2	2.7
Chronic sclerosing sialadenitis	6	8.0
Lymphoepithelial sialadenitis	6	8.0

One hundred and seven (107) patients (73.8%) of these non-neoplastic lesions reviewed were from the major salivary glands with the submandibular gland recording the highest frequency of 67 cases (62.6%) (Fig. 9).

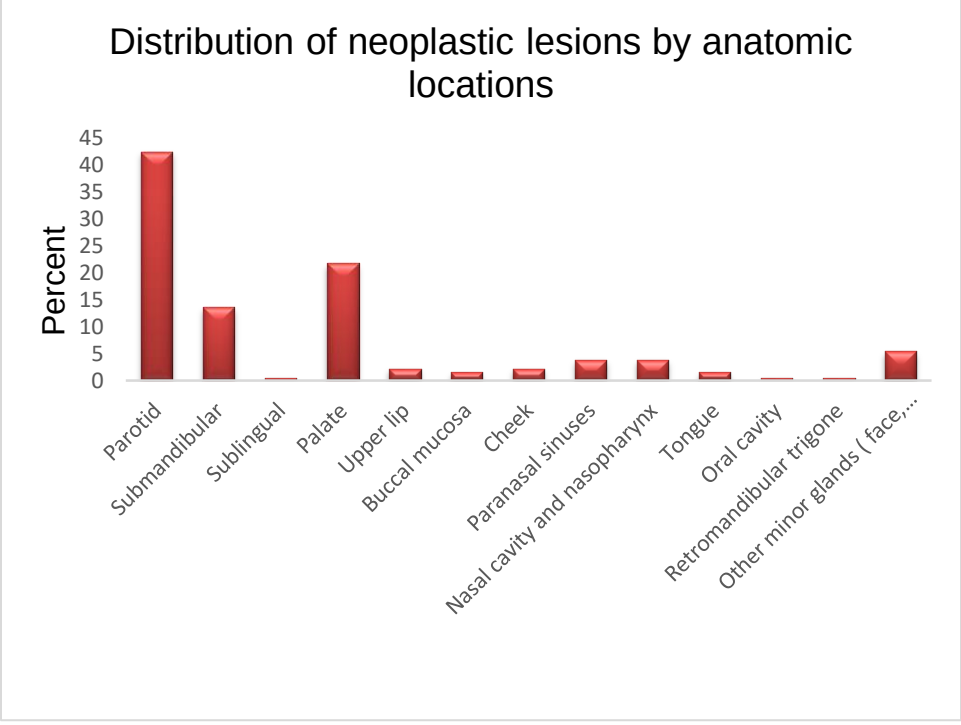

Figure 7 Anatomical sites of salivary gland neoplasms

Sialadenitis (47) was the commonest non-neoplastic lesion observed in the submandibular glands (Fig. 10). The lower lip was affected by non-neoplastic lesions but tumoral cases were diagnosed in the upper lip. No non-neoplastic lesions were reported in the upper lip and vice versa.

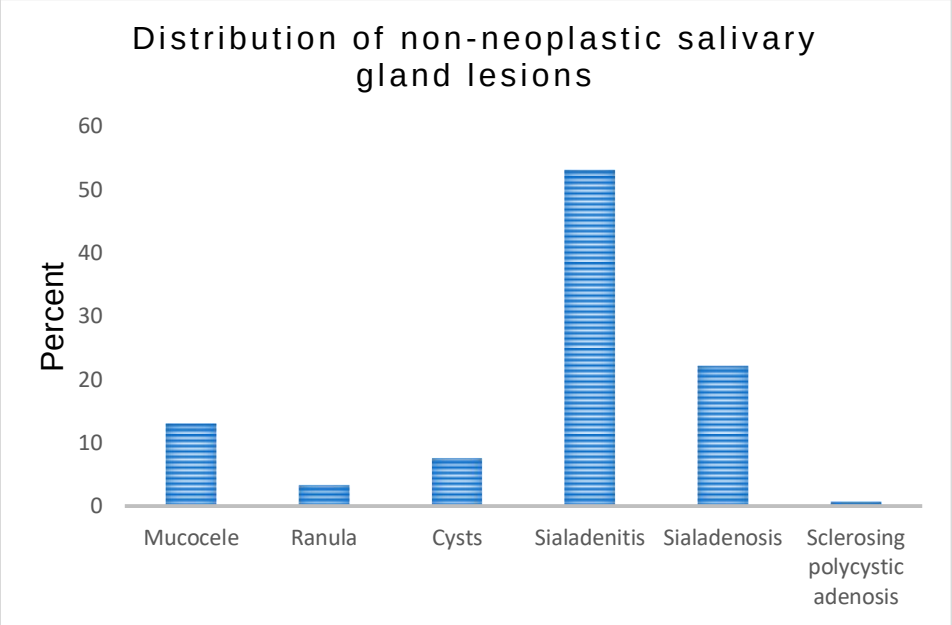

Figure 8 Frequency of non-neoplastic salivary gland lesion

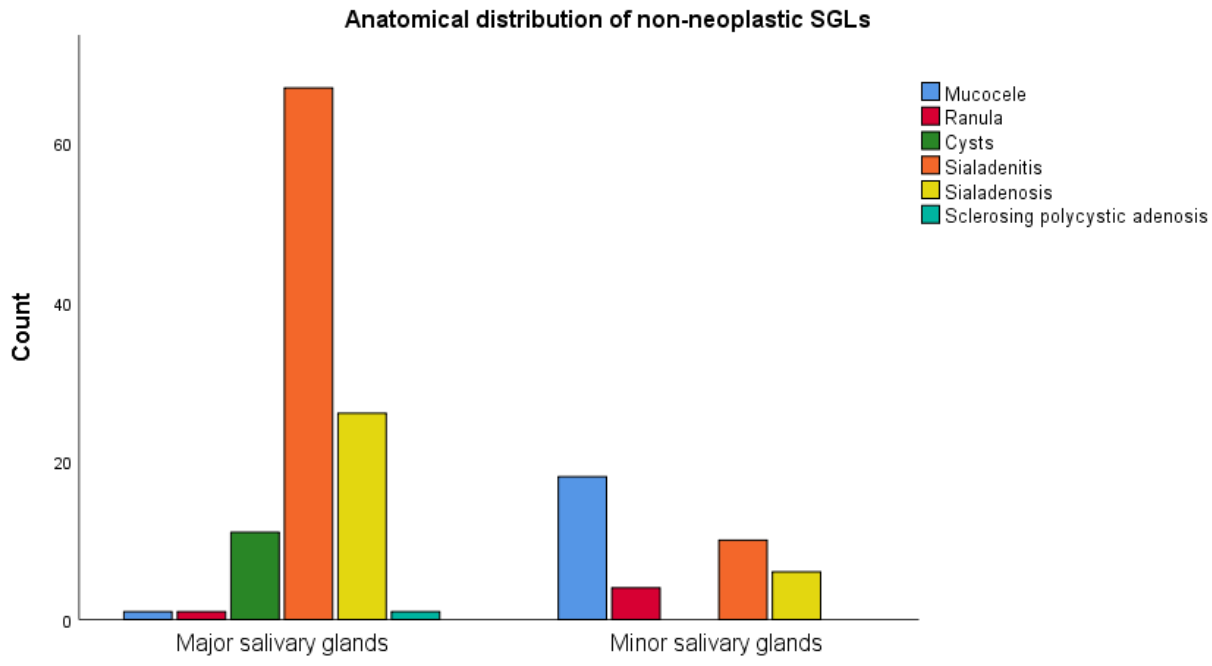

Figure 9 Anatomical distribution of non-neoplastic SGLs

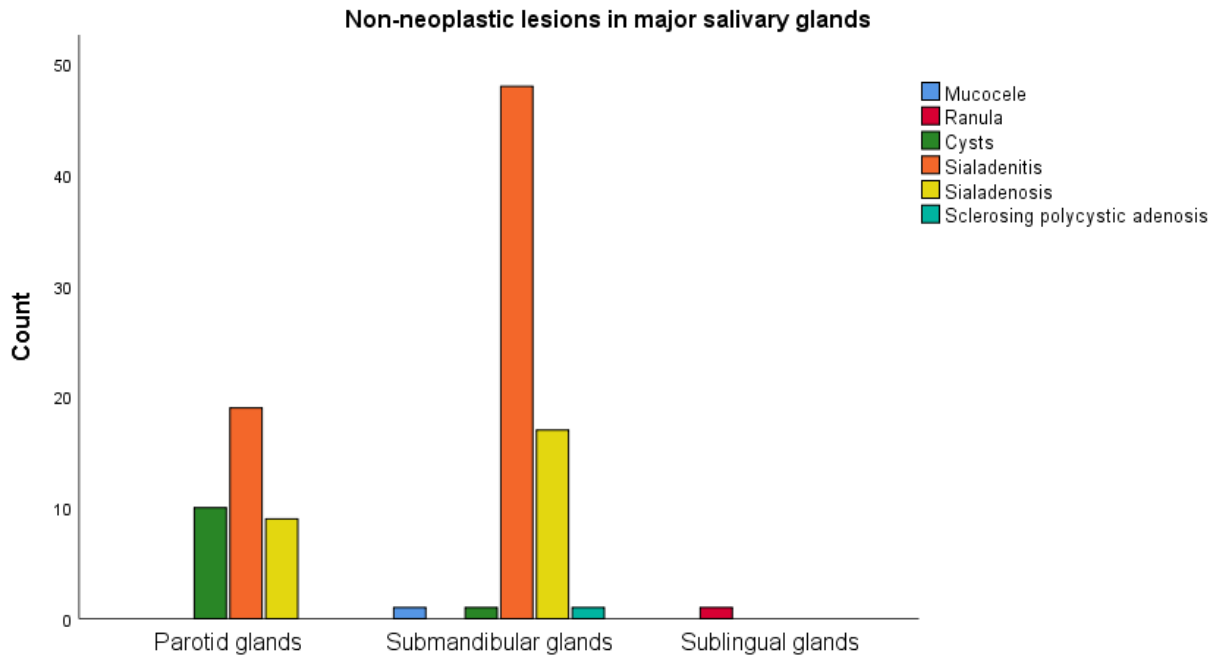

Figure 10 Non-neoplastic lesions in major salivary glands

Majority of the salivary gland neoplasms were benign tumors, accounting for 111 (60%) while the malignant epithelial tumors were 74 (40%) (Fig. 11).

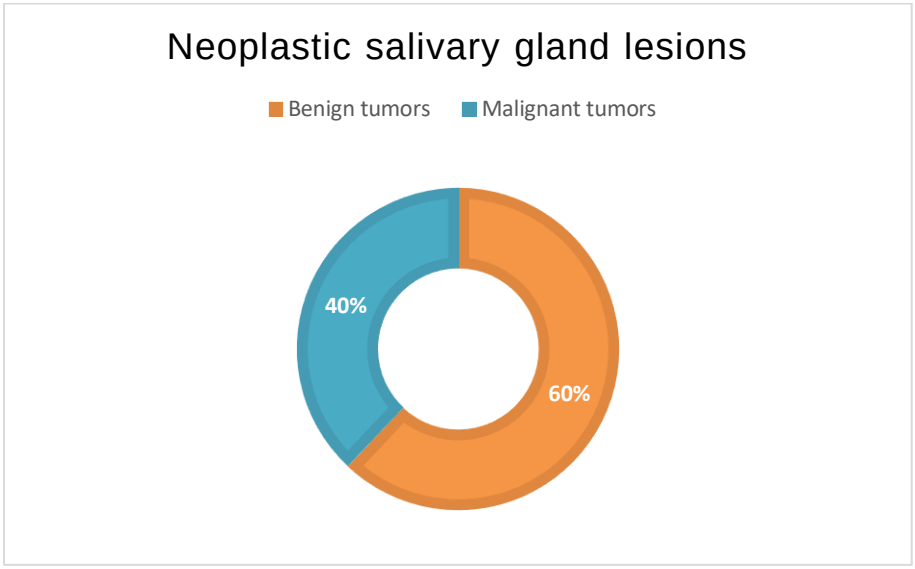

Figure 11 Frequency of salivary gland tumors

PA was the most frequently occurring benign neoplasm with 99 cases (89.2%) followed by myoepithelioma and basal cell adenoma containing 3 cases (2.7%) each. Two cases of Warthin

tumors and a single case of oncocytoma were seen. Three patients were diagnosed with benign mesenchymal tumors (1 sialolipoma, 1 neurofibroma and 1 cavernous lymphangioma) (Table 6).

Table 6 Benign neoplastic salivary gland tumors

	N=111	Percent
Pleomorphic adenoma	99	89.2
Myoepithelioma	3	2.7
Basal cell adenoma	3	2.7
Warthin tumor	2	1.8
Oncocytoma	1	.9
Sialolipoma	1	.9
Neurofibroma	1	.9
Cavernous lymphangioma	1	.9

The minimum and maximum ages for benign tumors were 4 years and 75 years respectively. These tumors were more frequently reported in the major salivary glands (55.9%) and 44.1% the minor salivary glands. Female preponderance was observed with an F: M ratio of 1.4:1. The minor salivary glands of the oral cavity, upper lip and paranasal sinuses, mainly the maxillary sinus were also commonly reported sites (Fig. 12).

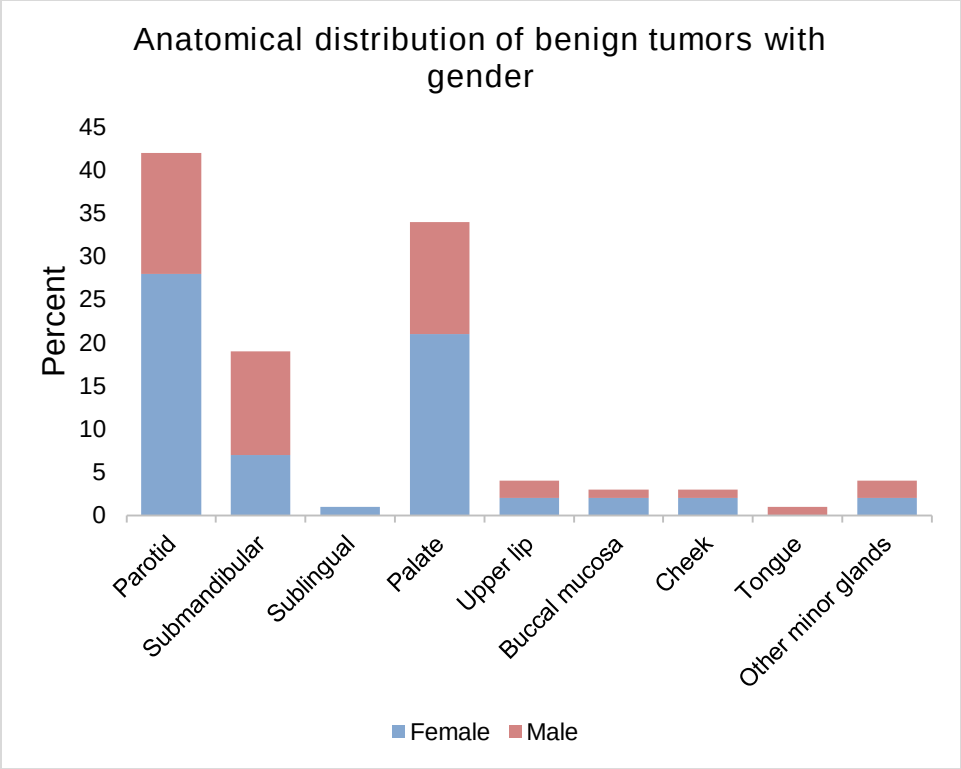

Figure 12 Anatomical distribution of benign tumors by gender

Out of 62 major salivary glands, parotid was involved in 42 (67.7%) followed by submandibular glands in 19 (30.6%) and finally the sublingual glands in 1. PA was the predominant benign tumor in all of the major glands. No other benign tumor was reported in the sublingual glands (Fig. 13).

Of the 49 minor salivary glands reviewed, 34 cases (69.4%) were located on the palates followed by the upper lip and other minor salivary glands of the face and oral cavity in 4 cases (8%) each. PA constituted 99% of the palate and 1% myoepithelioma. No other benign tumor was found in the remaining minor salivary glands apart from the pleomorphic adenoma (Table 7).

Table 7 Benign tumors in minor salivary glands

Minor glands	Pleomorphic adenoma	Myoepithelioma	Total
Palate	33	1	34
Buccal mucosa	3	0	3
Lip	4	0	4
Tongue	1	0	1
Cheek	3	0	3
Other minor glands (face, neck, periauricular area, mandible)	4	0	4
Total	48	1	49

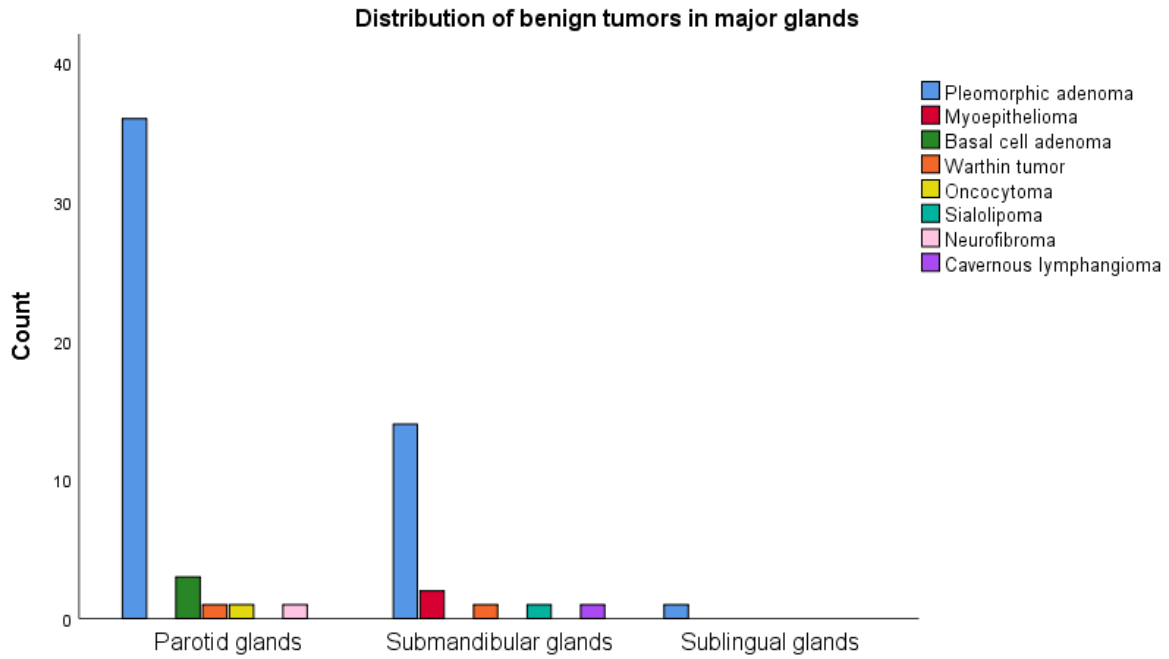

Figure 13 Distribution of benign tumors in major glands

Of the 69 malignant epithelial tumors, the commonest malignancy was mucoepidermoid carcinoma in 23 cases (33.3%) followed by 21 cases of adenoid cystic carcinoma (30.4%), 6 cases of acinic cell carcinoma (8.7%) and 3 cases of adenocarcinoma, NOS (4.3%). Three cases of squamous cell carcinoma, 3 cases of carcinoma ex-PA (1 high-grade MEC & 1 salivary duct

carcinoma were reported. One case of carcinoma ex-PA was reported without specification of the malignant component (Table 8).

Among 38 major salivary glands reviewed, 32 cases (84.2%) were located in the parotids and 5 cases (13.2%) arose from the minor salivary glands. A single case was reported in both the parotid and submandibular glands. No malignancy was reported in the sublingual glands (Fig. 14).

Out of the 30 minor salivary glands, 14 cases (46.7%) were situated in the nasal cavity, paranasal sinuses and the nasopharynx together followed by 5 cases (16.7%) in the palate. The remaining cases were located at the minor salivary glands of the oral cavity and face (buccal mucosa, cheek, oral cavity & retromadibular trigone). The commonest malignant tumor in the minor salivary glands is adenoid cystic carcinoma accounting 53.3% followed by the MEC (23.3%) (Fig. 15).

Table 8 Malignant epithelial salivary gland tumors

Malignant epithelial tumors	N=69	Percent
Mucoepidermoid carcinoma	23	33.3
Adenoid cystic carcinoma	21	30.4
Acinic cell carcinoma	6	8.7
Basal cell adenocarcinoma	3	4.3
Adenocarcinoma, NOS	3	4.3
Salivary duct carcinoma ex-PA	1	1.4
High-grade mucoepidermoid carcinoma ex-PA	1	1.4
Polymorphous adenocarcinoma	2	2.9
Myoepithelial carcinoma	1	1.4
Epithelial-myoepithelial carcinoma	2	2.9
Intraductal carcinoma	1	1.4
Squamous cell carcinoma	2	2.9
Cystic squamous cell carcinoma	1	1.4
Undifferentiated carcinoma	1	1.4
Carcinoma ex-PA	1	1.4

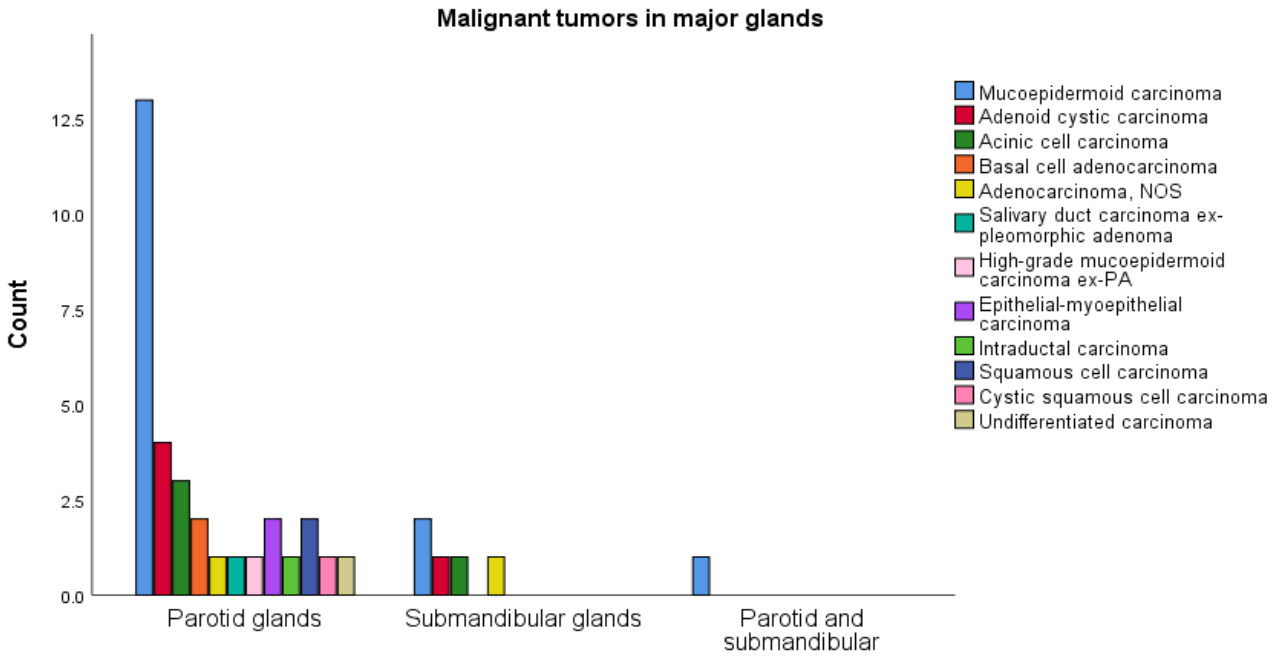

Figure 14 Distribution of malignant tumors in major glands

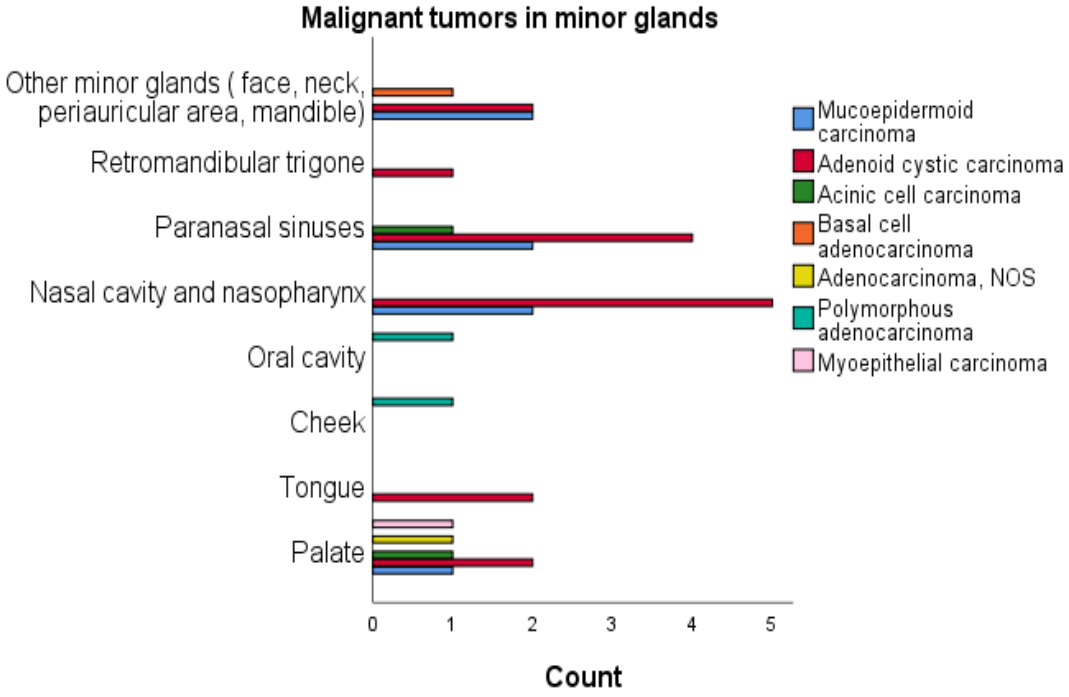

Figure 15 Distribution of malignant tumors in minor glands

Four cases (4) of hematolymphoid tumors (5.4% of all of the salivary gland lesions) were diagnosed in the salivary glands within study period. Two diffuse large B-cell lymphomas, one

case of Lymphocyte-rich Hodgkin lymphoma and 1 case of extranodal marginal zone B-cell lymphoma (MALT lymphoma).

A single case of high grade sarcoma was the only reported malignant mesenchymal tumor of the salivary gland (accounts 1.4% all salivary gland lesions).

Pleomorphic adenoma (33.1%) was the most frequently reported salivary gland lesion overall in this study period followed by sialadenitis (25.5%), mucoepidermoid carcinoma (7.6%) and adenoid cystic carcinoma (7%) (Table 9).

The most commonly encountered salivary gland tumor was pleomorphic adenoma which accounted about 56.3% of all the salivary gland neoplasms followed by mucoepidermoid carcinoma (13.1%) and adenoid cystic carcinoma (11.9%) (Table 10).

Table 9 Overall frequency of SGLs (tumors of similar differentiation are merged)

Salivary gland lesions	N=339	Percent
Pleomorphic adenoma	99	32.7
Sialadenitis	77	25.1
Mucoepidermoid carcinoma	23	7.6
Adenoid cystic carcinoma	21	7.0
Mucocele	12	4.0
Ranula	4	1.3
Benign cystic lesions	6	2.0
Sialadenosis	12	4.0
Sclerosing polycystic adenosis	1	.3
Acinic cell carcinoma	6	2.0
Basal cell neoplasms	5	1.7
Adenocarcinoma, NOS	3	1.0
Carcinoma ex-PA	2	.7
Polymorphous adenocarcinoma	2	.7
Myoepithelial neoplasms	4	1.3
Epithelial-myoepithelial carcinoma	2	.7
Intraductal carcinoma	1	.3
Squamous cell carcinoma	3	1.0
Undifferentiated carcinoma	1	.3
Warthin tumor	1	.3
Oncocytoma	1	.3
Mesenchymal tumors	4	1.3
Hematolymphoid tumors	5	1.7
Normal histology	6	2.0

Table 10 Overall frequency of epithelial salivary gland tumors

Epithelial SGTs	N=177	Percent
Pleomorphic adenoma	99	56.3
Mucoepidermoid carcinoma	23	13.1
Adenoid cystic carcinoma	21	11.9
Acinic cell carcinoma	6	3.4
Basal cell adenocarcinoma	3	1.7
Adenocarcinoma, NOS	3	1.7
SDC ex-pleomorphic adenoma	1	.6
High-grade MEC ex-PA	1	.6
Polymorphous adenocarcinoma	2	1.1
Myoepithelial carcinoma	1	.6
Epithelial-myoepithelial carcinoma	2	1.1
Intraductal carcinoma	1	.6
Squamous cell carcinoma	2	1.1
Cystic squamous cell carcinoma	1	.6
Undifferentiated carcinoma	1	.6
Myoepithelioma	3	1.7
Basal cell adenoma	3	1.7
Warthin tumor	2	1.1
Oncocytoma	1	.6

6. Discussion

In the present study, a total of 339 salivary gland specimens were evaluated. Nearly 82% of the cases were biopsy specimens. The majority of patients (42%) affected by salivary gland lesion were between the 3rd and 4th decades of life for benign tumors and 4th to 5th decades for malignant tumors (but had a wide range of age 2nd to 6th decades). The mean age of patients with salivary gland lesions was 36.2 years. This finding was similar to works done in Cameroon (37.4 years) [30] and Ghana (37 years) [32], but contradicted to the result of Croatian study (57 years), which may be explained by their relatively longer life expectancy [28]. Salivary gland lesions were more common in females as compared to their male counterparts with an F:M ratio of 1.13:1. This result was in consensus with that of Uganda (1.3:1) [27]; however, there is a reversal of this in Trinidad and Tobago (1:1.2) [31] and Pakistan (1:1.2) [35]. Among all salivary gland lesions, pleomorphic adenoma was the single most common lesion with (33.1%) which was in parallel with most of the literatures like the Brazilian (91%) [33], Iranian (32.6%) [34], Pakistani (73.8%) [35] and Indian studies (36.4) [37]. The most common site of occurrence was the parotid glands (42.4%) followed by the palate (21.8%) and the submandibular glands (13.6%). This was also true for the study done in Croatia, parotids (65.3%) followed by the minor salivary glands (27.2%) and the submandibular glands (6.6%) in contrary to our study where the submandibular gland were the second most frequently affected anatomical location (25%) [42].

In our study, majority of the salivary gland lesions were neoplastic accounting for 56% of the cases which was comparable with a study done in Ajmer region, India (56.2%) [37]. But, this study is differing from a study done in Brazil in which the majority of the salivary gland lesions were non-neoplastic (88.5%) [29]. In this investigation, sialadenitis was the commonest non-neoplastic salivary gland lesion 77 (53.1%) which was comparative to a study done in India [39] and contradicted to Yemenis study (12.9%) [40]. Chronic non-specific sialadenitis was the commonest form of sialadenitis followed by chronic sialadenitis with sialolithiasis. The second most frequently reported non-neoplastic salivary gland lesion was sialadenosis (22.1%) followed by mucocele (13.1%) and benign cystic lesions (7.6%). Among the 107 major salivary glands, 67 (62.6%) occurred in the submandibular glands which was in accordance with that of the Yemenis study (89.3%) [40] and the WHO Classification of head and neck, 2017 edition. 37 (34.6%) cases of non-neoplastic lesions arose in the parotids. One case each originated from the sublingual glands, Stensen's duct and Wharton's duct. Of the 14 non-neoplastic lesions, 10 (71.4%) cases were originated from the lower lip. No neoplastic lesions were reported in the lower lip.

Pleomorphic adenoma was the most commonly encountered tumor of all salivary gland neoplasms with 99 cases (56.0%), which was similar to an Ethiopian study (58.5%) [42], followed by the mucoepidermoid carcinoma 23 (7.6%), adenoid cystic carcinoma 21 (6.9%) and 6 cases of acinic cell carcinoma (3.4%). PA was the most frequently encountered benign salivary gland tumor in our study with 99 (89.2%) cases followed by the myoepithelioma and basal cell adenoma with 3 cases (2.7%) each. This result was in accordance with that of the Ugandan study PA (73.8% of all benign tumors) followed by myoepithelioma (11.2%), and the basal cell

adenoma (6.2%) [27]. Regarding the location, 42 cases (37.8%) were located in the parotid followed by the palate 34 (30.6%) and the submandibular glands 19 cases (17.1%). This is comparable to an Ethiopian work, parotid (43.2%) followed by the minor salivary glands (31.9%) and the submandibular glands (25%) and a Brazilian study, parotid (14.1%, the minor salivary glands (12.3%) and the submandibular glands [36]. All of the 4 pleomorphic adenomas that occurred in lips involved the upper lip which was similar with that of the Croatian study [28]. No neoplastic lesion was diagnosed in the lower lip.

Mucoepidermoid carcinoma was the most frequent salivary gland cancer in our study with 23 cases (33.3%) followed by 21 cases of adenoid cystic carcinoma (30.4%) and 6 cases of acinic cell carcinoma (8.7%). This result was in agreement with a Pakistani study, MEC (6.4%) followed by adenoid cystic carcinoma (3.8%) and acinic cell carcinoma (2.6%) [35] and an Indian study, MEC (50%) followed by adenoid cystic carcinoma (21.4%). However, it was deviated from many literatures such as Uganda, 29% adenoid cystic carcinoma followed by 20.3% mucoepidermoid carcinoma [27], Cameroon 31% adenoid cystic carcinoma followed by 22.4% MEC and 19% adenocarcinoma, NOS [30] and Brazil, 25.5% adenocarcinoma followed by 18.6% adenoid cystic carcinoma and 18.6% MEC [33]. Anatomically, 33 (48.5%) of the cases originated from the parotid gland followed by the minor salivary glands 30 (44.1%) and 5 cases (7.4%). This result was in accordance with a study done in Santa Catarina, Brazil 53.5%, 32.6% and 7% of cancers occurred in the parotid, minor salivary glands and submandibular glands respectively [33]. This out puts were against the results of an Iranian study in which 73.9% of cancers arose from the palate followed by the 14.6% in the parotids [36]. No malignant tumor of the salivary glands was reported in the sublingual glands which was in conflict with a Brazilian study (3 cases of malignant salivary gland cancers occurred in the sublingual glands) [33]. The most common malignant salivary gland tumor in the minor salivary glands was the adenoid cystic carcinoma (44% of the cases occurred in the palate). This finding was in line with a study done in Croatia, 53.6% occurred in the palate [31].

7. Conclusion

This study revealed heterogeneous groups of non-neoplastic and neoplastic salivary gland lesions that show a striking range of morphological diversity between different tumor types and sometimes within an individual tumor mass that pose diagnostic difficulties. Pleomorphic adenoma was the commonest salivary gland lesion followed by chronic sialadenitis and mucoepidermoid carcinoma. About 3.2% of all salivary gland morphologies were normal glands. The mean age for malignant tumors was at least 5 years older (42.5 years) than their benign counterparts (36.9 years).
Majority of the salivary gland tumors originated in the major glands, especially in the parotids. The most frequently encountered malignant tumor in the minor salivary glands was the adenoid cystic carcinoma.

8. Limitations of the study

- The majority of patient's medical records in our department were incomplete and handled inappropriately. Therefore, the record archiving of the department needs to be improved.
- Most of the data sent to the department of Pathology are incomplete, especially radiology reports are missing. This would create a great problem in giving accurate histopathological diagnosis. Hence, it would be helpful to have interdepartmental communications between the clinicians, Radiologists and Pathologists to solve such problems.

9. Recommendation

- Few cases of carcinoma ex-pleomorphic adenoma were diagnosed without mentioning any specific histologic type of the malignant component. However, carcinoma ex PA should not be considered a standalone diagnosis, as the type and extent of the carcinoma component impact the clinical course, management and prognosis of patients.
- Pathology reports of the salivary gland tumors should be based on the current WHO Classification of tumors of the head and neck.
- In most of the hematolymphoid tumors diagnosed in the salivary glands were not having specific microscopic anatomy mentioned in our reports (i.e. whether the presence or absence of remnant normal salivary gland tissue).

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