



Original Research Article

Analysis of Cytology, Mechanism, Biosynthesis, Growth and Redevelopment of Salivary Gland and their Tumors

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Abstract

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The salivary glands make saliva and empty it into your mouth through openings called ducts. Saliva helps with swallowing and chewing. It also can help prevent infections from developing in your mouth or throat. There are two sorts of salivary glands: the main salivary glands. Salivary glands are essential structures within the mouth. Spread of diseases, like cancer, autoimmune diseases, infections and physical traumas, can alter the functionality of those glands, greatly impacting the standard of lifetime of patients. Exocrine gland branching morphogenesis involves coordinated cell growth, proliferation, differentiation, migration, apoptosis, and interaction of epithelial, mesenchymal, endothelial, and neuronal cells in this article we'll discuss about anatomical, Cytology, Mechanism, Biosynthesis, growth and redevelopment of exocrine gland and histopathology of exocrine gland tumor. To determine the analysis of cytology, mechanism, Biosynthesis and redevelopment of salivary glands and histology of salivary gland tumors. Descriptive cross-sectional study. Basic Medical Sciences Department, Khost Shiekhzayed University, Khost Southeastern Afghanistan from January 2018 to March 2020. A descriptive Prospective cross sectional study done in Anatomy Department was carried out from January 2018 to March 2020 by accessing the subjects having Salivary gland evaluation done and filling the designed proforma. This research involved accessing the salivary gland in subjects's visiting in the Khost Shiekh Zayed University Khost Afghanistan. All the patients having age 16 years to 80 years irrespective of their sex, suffering from some Salivary gland problem were included in the study while those who presented for follow-up, Immune-compromised patients, getting anti-cancer treatment were excluded from the study. The data was analyzed by SPSS version 23. Distribution of Salivary gland tumors in gender indicated that the Significant salivary gland tumors were found in females (52.9%) while 12 males reported salivary gland tumors. Out of 29, (15.8%) males reported pleomorphic Adenoma, while (24.2%) females had pleomorphic adenoma. This was followed by Pleomorphous low grade carcinoma, (5.2%) respondents in males and EX Pleomorphic adenoma (3.4%) in females and EX Pleomorphic adenoma, (4.5%) males and (5.8%) females. Salivary glands, therefore, represent a major player in the maintenance of oral homeostasis and their study might shed light in more general disorders such as cancer, inflammation and healing upon mechanical traumas. Overall, their accessibility and heterogeneous histology provide an ideal structure to improve our understanding of tissue remodeling and interaction between cells and surrounding microenvironment. Data of 29 Subjects of Salivary Gland Tumors were documented, of which 39 (69.16%) cases were classified as Malignant tumors and 61 (22.39%) cases as Benign tumors. Female TO male ratio (F/M) and the mean age of Respondent were 2:3.5 and 46 years, correspondingly. Pleomorphic adenoma (61.82%) and adenoid cystic carcinoma (39.17%) were the most common benign and malignant neoplasms. Although the exocrine gland tumors encountered were similar in most of their characteristics to those reported in asia and other countries, some differences like frequency, age and gender prevalence were revealed. Exocrine gland represent a serious player within the maintenance of oral homeostasis and their study might shed light in additional general disorders like cancer, inflammation and healing upon mechanical traumas. Overall, their accessibility and heterogeneous histology provide a perfect structure to enhance our understanding of tissue remodeling and interaction between cells and surrounding microenvironment. Additionally to studies on the molecular control of the exocrine function, salivary glands are often used as a platform to research the physiology of epithelium, the dynamic of the somatic cell niche and basic developmental processes. Thus, future studies on salivary glands could be impactful to a spread of subjects and application in biomedicine.

Keywords: Salivary gland-resident stem cells, oral epithelium, salivary glands and tumors.

INTRODUCTION

Salivary gland branching morphogenesis involves coordinated cell growth, proliferation, differentiation, migration, apoptosis, and interaction of epithelial, mesenchymal, endothelial, and neuronal cells (Subhashraj, 2008). The sublingual salivary gland (SL) secretes mucous, a viscous solution rich in mucins. The submaxillary gland (SMG) consists by a mixed population of acini with a mucous and serous function. These three major salivary glands account for quite 90% of salivary secretion. Minor salivary glands are distributed throughout the mouth, specifically within the labial and lingual mucosa, also as palate and floor of the mouth (Nadershah and Salama, 2012).

Saliva is an important fluid for mouth maintenance and functionality. Digestive enzymes within saliva initiate the digestion process, and at an equivalent time, saliva acts as a lubricant of solid nutrition, thus helping its passage through the esophagus. By moisturizing the tongue and other tissues of the mouth, saliva has an important role in speech and taste sensitivity (Goh et al., 2016). It also balances the pH of the mouth, thus protecting the soft oral tissues and teeth from an extended exposure to an acidic environment. Saliva contains several signalling molecules, like EGF, FGF, NGF and TGF- α , that are essential for the regeneration of oral and oesophageal mucosa. Finally, the antibacterial and antifungal components of the saliva, like lysozymes, immunoglobulins and lactoferrin, inhibit the progression of bacterial infection and cavity (Agha-Hosseini and Moosavi, 2013). Structures secreting fluid to facilitate feeding emerge progressively throughout evolution and may be found in very simple organisms (e.g. *Caenorabditis elegans*) and more complex species (e.g., *Drosophila*, placental mammals). In humans, major and minor salivary glands produce and secrete digestive fluids or protein-rich fluids. The three pairs of major salivary glands (i.e., parotid, submandibular and sublingual glands) are liable for the assembly and secretion of saliva within the mouth, whose moisturizing effect preserves oral hygiene and allows taste, speech and mastication (Barbe, 2017).

Physiological functions and therefore the histological appearance of salivary glands are rather conserved between species and individuals, but clear distinctions exist in terms of anatomical position and volume (i.e., the PG is that the largest of the salivary glands in humans, while the SMG is that the largest in mice). In humans, 20% of people possess an adjunct PG, equipped with its own blood supply, and a secondary excretory duct independent from the most body of the gland (Woo et al., 2014). The salivary glands are a crucial set of exocrine glands that functions to supply, modify and secrete saliva into the mouth. They glands are divided into two main types: the main paired salivary glands, which incorporates the parotid, submandibular and sublingual

glands, and therefore the minor salivary glands, which line the mucosa of the upper aero digestive tract and therefore the overwhelming entirety of the mouth (Moghe et al., 2012).

Human salivary glands produce anywhere from 0.5 to 1.5 L of saliva daily, which has many various functions within the mouth. This includes lubrication of food to support mastication and swallowing, lubrication of the buccal mucosa to facilitate proper speech and provision of an aqueous medium, which is important to experience taste (Andrade et al., 2016). It also facilitates digestion of triglycerides and starches via the secretion of lipases and amylases, respectively, and plays a protective role against infections via its many protective organic constituents (Garatea-Crelgo et al., 1993). These include the secretory piece, a glycoprotein that forms a mesh with immunoglobulin A (IgA) to defend against viruses and bacteria, lysozymes that cause bacterial agglutination, autolysin to degrade bacterial cell walls and lactoferrin to sequester iron, a component vital to bacterial growth. Additionally, saliva contains ionic compounds, like bicarbonate, (Li et al., 2007) which buffer acids produced by bacteria and protects the mouth and esophagus from digestive juice. As a result, saliva plays a particularly important role in protecting the mouth from chronic buccal mucosal infections and cavity (Ricour et al., 2016).

Salivary gland biogenesis is characterized by branching morphogenesis of epithelium, which is closely associated with the developing vasculature and nerves to form a branched glandular structure of ducts with terminal buds that become acini by around 14 weeks (Davis et al., 1956). The neural crest-derived mesenchyme provides growth factors and other important molecular cues for epithelial branching morphogenesis. By 13–16 weeks in humans, the SMG appears well differentiated, with desmosome and microvillus projections from cells adjacent to the lumens (Proctor and Carpenter, 2014). The basal lamina surrounds the epithelium, with a few elongated cells that appear similar to myoepithelial cells. The striated and intercalated ducts can be recognized as early as 16 weeks, with the acinar cells beginning to predominate the tissue by 20–24 weeks. In humans, the salivary glands continue to develop up to 28 weeks, at which stage secretory products can be seen in acini. At birth the glands are functional to secrete saliva (Pathology and Genetics Head and Neck Tumours, 2005). In humans there are genetic diseases affecting salivary glands that inform us about salivary gland biogenesis. Similar gene mutations have been generated in mice to learn more about the genetic and cellular mechanisms of gland development. For example, patients with hypohidrotic ectodermal dysplasia present clinically with defects in the teeth, hair, sweat glands and salivary glands. Hypohidrotic ectodermal dysplasia is caused by mutations in ectodysplasin-A, its receptor

EDAR or EDARRAD, an intracellular signaling molecule (Pathology and Genetics Head and Neck Tumours, 2005). These genes make proteins that function together during gland development and are critical for signaling between the salivary epithelium and mesenchyme. Importantly, genetic manipulation of the mouse genome enables the development of models to study the molecular mechanisms of hypohidrotic ectodermal dysplasia. Mice lacking EDAR have SMG aplasia or hypoplasia, which is caused by reduced SMG epithelial cell proliferation, lumen formation and histodifferentiation (Tobias and Hochhauser, 2015). Other examples of genetic mutations in humans that cause problems with salivary biogenesis include patients with mutations in genes that affect fibroblast growth factor (FGF) signaling. Patients with a mutation or deletion of FGF10 have a syndrome called aplasia of lacrimal and salivary glands (OMIM180920). The cytokeratins have been used extensively to study stem/progenitor cells in many epithelial organs. Basal cells expressing K5 and K14 (K5+K14+) label a population of stem/progenitor cells across different tissues, such as prostate, mammary gland and skin (DeVita et al., 2019). However in the salivary gland it appears these cytokeratins may label distinct progenitor cell populations. K5+ cells, which are mainly in the ductal structures, were shown to be a progenitor population in SMGs by genetic lineage tracing. However, a significant finding was that the neuronal niche, i.e. the submandibular parasympathetic ganglion, which is present during SMG biogenesis, plays a critical role in the maintenance of these K5+ progenitors. Parasympathetic innervation and signaling via muscarinic receptors in the salivary epithelium, in combination with epithelial growth factor receptor signaling, maintained the K5+ cells during development and was critical for salivary gland biogenesis (Beermann, 1962). More recently, a separate population of K14+ cells was shown to contain multipotent progenitors in SMGs. The K14+ progenitors increase in cell number in response to Fgfr2b and Kit signaling and are located in the salivary gland end buds during biogenesis. Furthermore, epithelial Kit+ cells in the end buds produce neurotrophic factors, such as neurturin (NrtN), which promote parasympathetic nerve survival and axon extension (Berendes, 1965). Salivary gland tumors (SGTs) are rare and their annual incidence is <1/100,000 inhabitants, without noticeable geographical gap, and they represent <5% of head and neck tumors (Bodenstein, 1943). These tumors 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.

MATERIAL AND METHODS

A descriptive Prospective cross sectional study done in Anatomy Department was carried out from January 2018 to March 2020 by accessing the subjects having Salivary gland evaluation done and filling the designed proforma. This research involved accessing the salivary gland in subjects's visiting in the khost Shiekh Zayed University Khost Afghanistan. All the patients having age 16 years to 80 years irrespective of their sex, suffering from some Salivary gland problem were included in the study while those who presented for follow-up, Immune-compromised patients, getting anti-cancer treatment were excluded from the study. This is a 2-year retrospective study of Tumors of salivary gland biopsies received at this teaching hospital. All specimens were fixed in 8% formalin, then processed into paraffin-embedded sections and stained with hematoxylin and eosin. All the slides were reviewed by the authors and classified according to the World Health Organization histological typing of tumors. The data was analyzed by SPSS version 23.

RESULTS

Among 29 respondent the 12 (41.3%) were Male and 17 (58.9%) were Female as shown in Table 1.

Out of the total study population, the level of education ranged from Masters to Matric (Grade 10) as shown in Figure 1. According to this 23 (6.4%) had Master qualification, 87 (24.3%) were Bachelors, 179 (50.0%) were Intermediate (grade 12) and 69 (19.3%) were Matric (grade 10). Figure 2 shows the gender distribution and percentage of respondent.

Table 2 shows the distribution of salivary gland tumors in respondents and significant PA salivary gland tumors observed in female.

Description

Distribution of Salivary gland tumors in gender indicated that the highest salivary gland tumors were found in females (52.9%) while 12 males reported salivary gland tumors. Out of 29, (15.8%) males reported pleomorphic Adenoma, while (24.2%) females had pleomorphic adenoma. This was followed by Pleomorphous low grade carcinoma, (5.2%) respondents in males and EX Pleomorphic adenoma (3.4%) in females and EX Pleomorphic adenoma, (4.5%) males and (5.8%) females.(Figure 3)

Distribution of Salivary gland tumors in gender

Table 1. Gender distribution among respondents.

Gender	Frequency	Percent	Valid Percent	Cumulative Percent
Male	12	41.3	41.3	41.1
Female	17	58.6	58.6	100.0
Total	29	100.0	100.0	

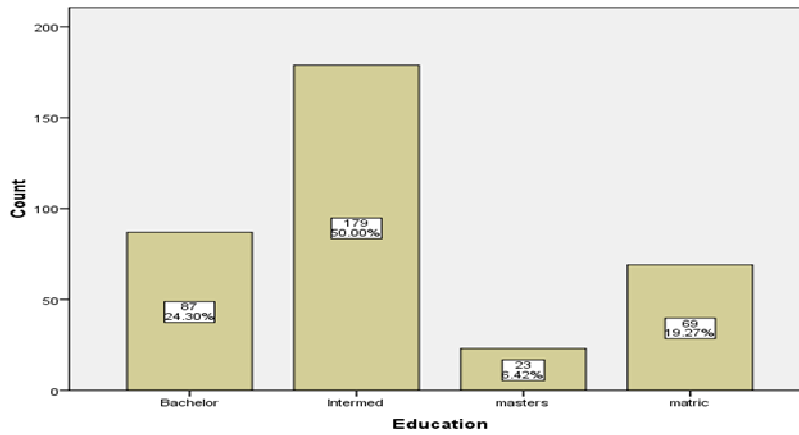
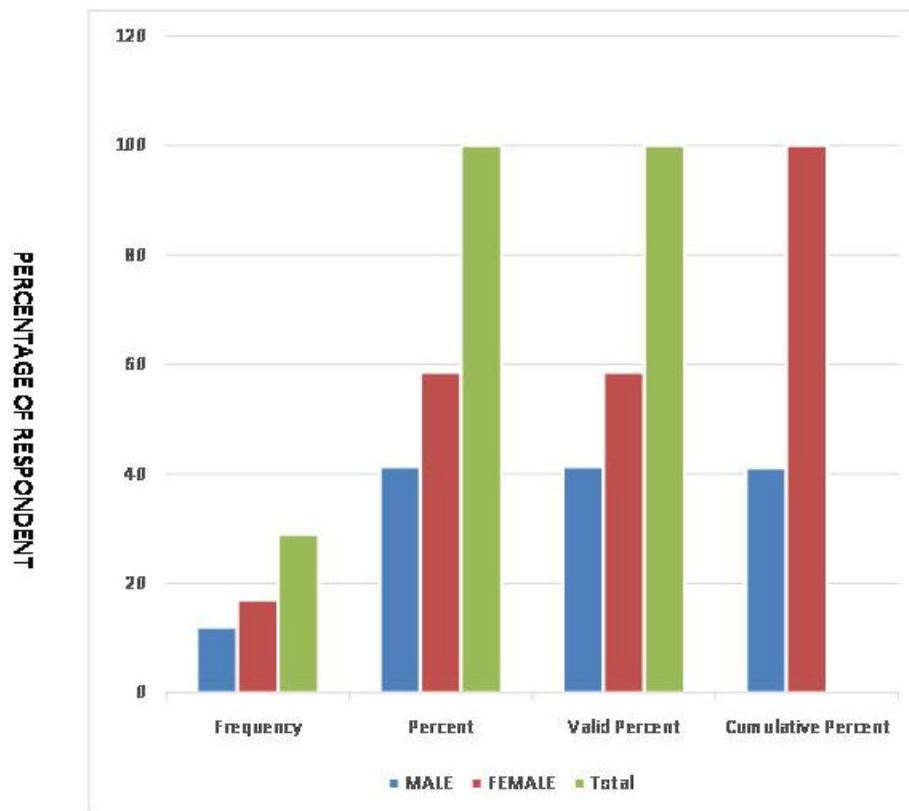


Figure 1. Education of Respondents



Gender Distribution

Figure 2. Percentage of Respondent.

Table 2. Distribution of salivary gland tumors in respondents.

SR.#	Salivary Gland Tumors	Males (%)	Females (%)
1	PA	(15.8%)	(24.2%)
2	Warthins Tumors	(3.3%)	(1.7%)
4	BCA	(4.3%)	(2.9%)
5	SCHWANOMMA	(4.1%)	(5.6%)
6	PLGA	(5.2%)	(3.4%)
7	EX PA	(4.5%)	(5.8%)
8	ACCa	(3.2%)	(2.1%)
9	MECa	(2.4%)	(3.1%)
10	AdCC	(2.2%)	(2.5%)

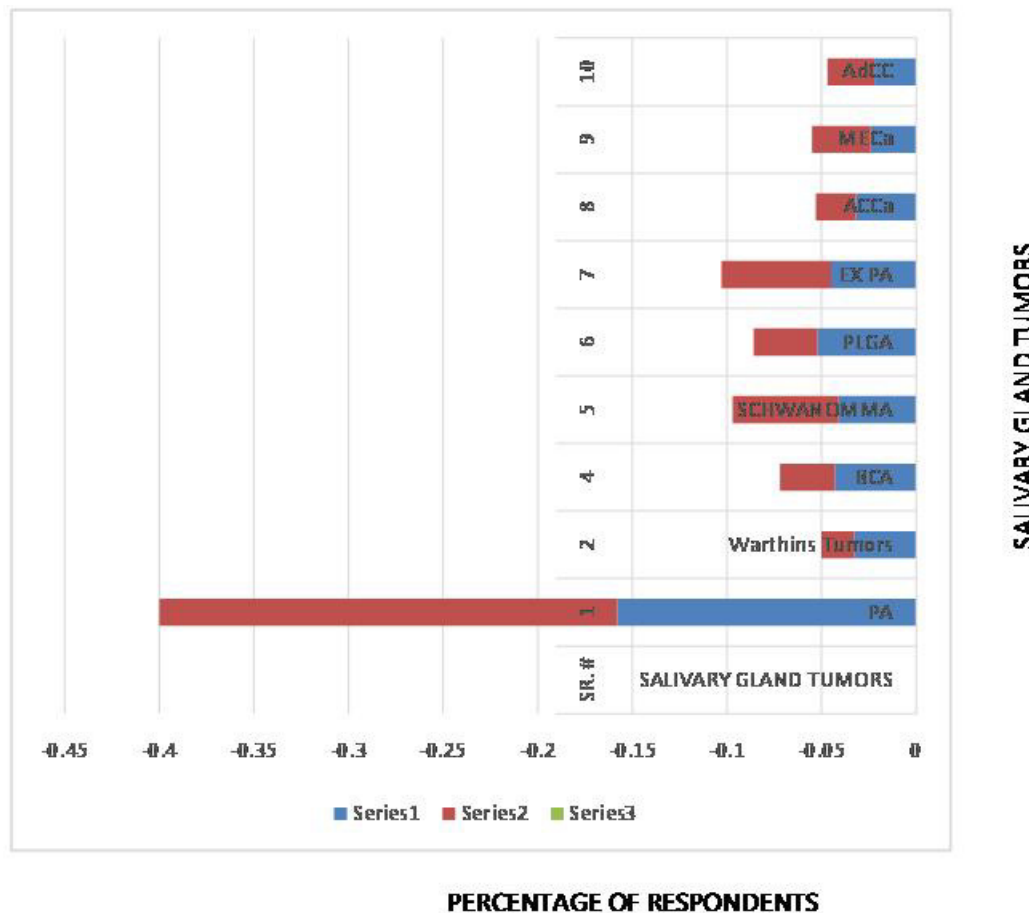


Figure 3. Distribution of Salivary gland tumors in respondents.

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A study result suggested that the incidence of benign neoplasms was more within the fifth decade whereas malignant neoplasms were seen more common in sixth and seventh decades. Within the present study, benign tumors were more common than malignant ones altogether the salivary glands.

CONCLUSION

Salivary glands, therefore, represent a major player in the maintenance of oral homeostasis and their study might shed light in more general disorders such as cancer, inflammation and healing upon mechanical traumas. Overall, their accessibility and heterogeneous histology provide an ideal structure to improve our understanding of tissue remodelling and interaction between cells and surrounding microenvironment. In addition to studies on the molecular control of the exocrine function, salivary glands can be used as a platform to investigate the physiology of epithelial tissue, the dynamic of the stem cell niche and basic developmental processes. Thus, future studies on salivary glands might be impactful to a variety of subjects and application in biomedicine.

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