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Clinicopathological Profile of Salivary Gland Tumors in a Tertiary Care Setting in Odisha: A Retrospective Analysis

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Abstract

Background: Salivary gland neoplasms, characterized by significant histological heterogeneity and originating from any major (parotid, submandibular, sublingual) or minor salivary gland within the oral cavity and upper aerodigestive tract, were the subject of this retrospective study. The objective was to delineate the clinicopathological features of these tumors within a patient cohort from a tertiary care teaching hospital in coastal Odisha. ***Material and Methods:*** This study employed a retrospective, descriptive, cross-sectional design (2022-2024) to examine surgically diagnosed salivary gland tumors (SGTs), with subsequent collection of relevant clinicopathological information. ***Results:*** In this retrospective study of 150 diagnosed salivary gland tumors (SGTs), representing 1.31% of total diagnoses, a predominance of benign lesions (67.33%) was observed. The patient cohort exhibited a near-equal sex distribution, with a mean age of 55.5 years. The parotid gland was the most frequent site of tumor occurrence, followed by the palate and submandibular gland. Pleomorphic adenoma and mucoepidermoid carcinoma were the most commonly identified benign and malignant histotypes, respectively. Subsequent re-evaluation using updated WHO criteria resulted in the reclassification of 4.0% of cases. ***Conclusions:*** The clinicopathological characteristics of salivary gland tumors observed in this cohort aligned with findings reported in international literature, demonstrating a lack of sex-based predilection. While morphological evaluation remains paramount for initial diagnosis, immunohistochemical analysis is crucial for definitive diagnosis, particularly in diagnostically challenging cases.

Keywords: ***Salivary gland tumors, epidemiology, head and neck pathology.***

Introduction

Salivary gland tumors (SGTs) exhibit significant histological diversity, with the World Health Organization (WHO) recently updating its classification to include novel benign (e.g., sclerosing polycystic adenoma, keratocystoma) and malignant (e.g., microsecretory adenocarcinoma, sclerosing microcystic adenocarcinoma) entities [2]. Despite this heterogeneity, SGTs constitute a relatively small proportion (3-6%) of head and neck neoplasms, with a global incidence ranging from 0.4 to 13.5 per 100,000 individuals annually [2-5]. Given their varied biological behaviors, comprehensive clinicopathological characterization and accurate incidence data are crucial for optimal management and prognostic assessment [1,3,4].

While India, with its substantial population, lacks comprehensive epidemiological data on SGTs, particularly in the Eastern Region, this study aims to address this gap, focusing specifically on the state of Odisha. This research represents the second regional investigation of SGTs in Odisha [3]. Recognizing the reported variations in SGT incidence and clinicopathological profiles across different geographic regions [1,3,4,8,10-15], local data acquisition is essential for understanding population-specific characteristics [6]. This study, therefore, retrospectively analyzes the clinicopathological features of SGTs diagnosed in a tertiary care hospital, allowing for comparisons with existing epidemiological data from diverse populations. The goal is to contribute to improved diagnostic accuracy, tailored treatment strategies, and enhanced cancer prevention efforts within this specific demographic.

Material and Methods

A retrospective review of archival specimens from two tertiary care hospital AHPGIC, Cuttack and Shri Jagannath Medical College and Hospital, Puri was conducted, encompassing all salivary gland tumor (SGT) cases diagnosed between January 2022 and December 2024. Five-micrometer hematoxylin and eosin (H&E) stained sections were prepared and subjected to independent histological re-evaluation by participating oral pathologists. Tumor classification, adhering to the 2022 World Health Organization (WHO) Classification of Head and Neck Tumors, was performed to categorize lesions as benign or malignant. Discrepancies in diagnostic interpretations were resolved through consensus discussions. Clinical and demographic data, including patient age, sex, anatomical tumor location, and initial histopathological diagnosis, were extracted from patient records. Immunohistochemical and histochemical analyses were performed

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adjunctively when H&E staining was inconclusive for definitive diagnosis.

Statistical analysis was performed using SPSS version 20.0. Continuous variables were summarized as mean, median, and standard deviation. Categorical variables were presented as frequencies and percentages. The association between tumor biological behavior (benign vs. malignant) and clinicodemographic characteristics was assessed using Pearson's chi-square test or Fisher's exact test, with statistical significance defined as a p-value of ≤ 0.05 and a 95% confidence interval.

Results

A retrospective analysis of 150 cases (1.31%) diagnosed as salivary gland tumors (SGTs). Among these, 101 (67.33%) were benign and 49 (32.66%) were malignant, yielding a benign-to-malignant ratio of 2:1. The cohort comprised seven benign and ten malignant histological subtypes (**Table 1**).

The age distribution of SGTs demonstrated a bimodal peak in the fourth and seventh decades, with a mean age of 57.5 years (range: 20-95 years) (**Table 2**). The majority of tumors originated in the major salivary glands (n = 83, 55.33%), with the parotid gland being the most frequently affected site (n = 71, 47.33%), followed by the palate (n = 39, 26%), submandibular gland (n = 13, 8.66%), and buccal mucosa (n = 11, 7.33%). Four cases (2.66%) had unspecified anatomical locations. No tumors were identified in the sublingual gland. Both benign and malignant tumors exhibited a predilection for the parotid gland.

Among benign SGTs, pleomorphic adenoma (PA) was the most prevalent (n = 71, 70.29%), followed by Warthin's tumor (n = 15, 14.85%) and canalicular adenoma (n = 5, 4.95%) (**Table 1**). These benign tumors were predominantly diagnosed in patients within the fourth to seventh decades of life, although the age range extended to 20 years.

Table 1: Histologic and sex distribution of 174 salivary gland tumors.

Histologic types		n= 150	% a	% b	Male		Female	
					N	%	n	%
Benign tumors	Pleomorphic adenoma	71	47.33	70.29	28	18.66	43	28.66
	Warthin's Tumor	15	10	14.85	11	7.33	4	2.66
	Canalicular adenoma	5	3.33	4.95	4	2.66	1	0.66
	Myoepithelioma	4	2.66	3.96	2	1.33	2	1.33
	Cystadenoma	2	1.33	1.98	1	0.66	1	0.66
	Basal cell adenoma	2	1.33	1.98	1	0.66	1	0.66
	Oncocytoma	2	1.33	1.98	1	0.66	1	0.66
	Total	101	67.31	100	48	32	53	35.33
Malignant tumors	Mucoepidermoid carcinoma	16	10.66	32.65	7	4.66	9	6
	Adenoidcystic carcinoma	9	6	18.36	5	3.33	4	2.66
	Polymorphous adenocarcinoma	7	4.66	14.28	3	2	4	2.66
	Adenocarcinoma NOS	4	2.66	8.16	2	1.33	2	1.33
	Acinic cell carcinoma	4	2.66	8.16	3	2	1	0.66
	EMC	3	2	6.12	3	2	0	0.0
	Salivary duct carcinoma	2	1.33	4.08	1	0.66	1	0.66
	CXPA	2	1.33	4.08	0	0.0	2	1.33
	Squamous cell carcinoma	1	0.66	2.04	1	0.66	0	0.0
	Secretory carcinoma	1	0.66	2.04	1	0.66	0	0.0
	Total	49	32.62	100	26	17.33	23	15.33

[a] Percent concerning the total number of cases. [b] Percent concerning the group (benign or malignant); EMC. Epithelial myoepithelial carcinoma; CXPA. Carcinoma ex pleomorphic adenoma.

Most cases occurred in the parotid gland (n = 48, 32%) and female patients (n = 53; 35.33%), with afemale: male ratio of 1.1:1 (53 female and 48 male). Regarding the malignancies, mucoepidermoid carcinoma (MEC) was the most frequent malignant tumor (n= 16, 32.65%), followed by adenoid cystic carcinoma (ACC) (n = 9, 18.36%), and polymorphous adenocarcinoma (n = 7, 14.28%) (**Table 1**). The patient's ages ranged from 20 to 95 years, with a mean age of 57.5 years (**Table 2**).

Table 2: Age group distribution (decade of life) of 174 salivary gland tumor.

Histological types		Age range	Age groups							Total	
			10-19	20-29	30-39	40-49	50-59	60-69	>70	NS	n
Benign tumors	Pleomorphic adenoma	13-85	2	3	7	22	17	12	7	1	71
	Warthin'sTumor	37-90	0	0	0	3	2	7	3	0	15
	Canalicular adenoma	55-75	0	0	0	0	1	1	3	0	5
	Myoepithelioma	28-61	0	0	1	1	2	0	0	0	4
	Cystadenoma	45-62	0	0	0	1	1	0	0	0	2
	Basal cell adenoma	42-57	0	0	0	0	1	1	0	0	2
	Oncocytoma	61-65	0	0	0	0	0	2	0	0	2
	Total	13-90	2	3	8	27	24	23	13	1	101
Malignant tumors	Mucoepidermoid carcinoma	11-98	0	2	2	4	6	0	2	0	16
	Adenoidcystic carcinoma	25-78	0	0	2	1	2	3	2	0	9
	Polymorphous adenocarcinoma	32-65	0	0	0	1	1	1	0	0	7
	Adenocarcinoma NOS	38-70	0	0	0	1	0	1	1	0	4

	Acinic cell carcinoma	27-55	0	0	1	0	1	2	0	0	4
	EMC	20-60	0	0	1	0	0	1	0	0	3
	Salivary duct carcinoma	52-58	0	0	0	0	0	2	0	0	2
	CXPA	47-67	0	0	0	0	1	0	0	0	2
	Squamouscellcarcinoma	65-83	0	0	0	0	0	0	1	0	1
	Secretorycarcinoma	58	0	0	0	0	0	1	0	0	1
	Total	13-98	0	2	6	7	12	11	7	0	49

NS. Not specified; EMC. Epithelial-myoepithelial carcinoma; CXPA. Carcinoma expleomorphic adenoma

The parotid gland was the predominant anatomical site for salivary gland tumors in this cohort (n=30, 52.6%), followed by minor salivary glands of the palate (n=20, 40.81%). Histochemical analysis, employing Periodic Acid-Schiff (PAS), mucicarmine, and alcian blue staining to characterize mucinous components, was utilized in 18 cases (12%) to refine diagnoses. Immunohistochemical (IHC) analysis was performed in 8 cases (5.33%), with 5 cases focused on determining the proliferative index and 3 cases aimed at facilitating definitive cell and structural identification.

A retrospective review of morphology and immunohistochemical profiles led to the revision of diagnoses in 4.0% (n=6) of salivary gland tumors, adhering to the 2022 WHO Classification of Head and Neck Tumors. Specifically, two cases initially categorized as pleomorphic adenomas were reclassified as carcinoma ex-pleomorphic adenomas. Among malignant tumors, four adenocarcinomas not otherwise specified were re-categorized: two as polymorphous adenocarcinomas, one as mucoepidermoid carcinoma, and one as secretory carcinoma. One polymorphous adenocarcinoma demonstrated features consistent with cribriform adenocarcinoma of minor salivary glands, a recognized variant. However, in accordance with current WHO guidelines, it was retained as polymorphous adenocarcinoma. There is no significant association between the biologic behavioral (malignant versus benign tumors) and clinical and demographic characteristics ($P > 0.05$)

Discussion

Numerous studies over recent decades have documented the global prevalence of salivary gland tumors (SGTs) [1,3-14,16-19]. However, significant variations in reported frequencies are attributable to differences in referral patterns and the nature of diagnostic services utilized (e.g., private vs. public, hospital-based) [1]. In this study, SGTs constituted approximately 0.6% of all diagnosed lesions within the referred service. This finding aligns with the wide range of SGT prevalence reported in other pathology services, spanning from 0.08% [12] to 19.6% [13].

Published literature suggests a slight female predilection for salivary gland tumors (SGTs) overall [2]. However, sex-specific incidence varies significantly across distinct histological subtypes [1,3,4]. In the present study, a balanced male-to-female ratio (1:1) was observed for both benign and malignant SGTs, a finding corroborated by other studies [3,5,6,30], albeit less frequently reported. Conversely, several reports, including those from Brazil, indicate a male preponderance for malignant SGTs [3,4,11]. These discrepancies highlight the potential influence of tumor subtype, geographical location, and population demographics on the observed sex distribution of SGTs.

Consistent with the majority of existing literature on salivary gland tumors (SGTs), this study observed a significantly higher prevalence of benign neoplasms (67.31%) compared to malignant lesions (32.62%). However, a subset of studies, particularly those conducted in African and Asian populations reported a contrasting trend of increased malignancy. This discrepancy may be attributable to referral bias, as tertiary centers in Africa, from which many of these reports originate, likely receive a disproportionate number of complex, malignant cases.

Salivary gland tumors (SGTs) demonstrate a wide age distribution, observed across all age demographics. In this cohort, the patient age range extended from 10 to 98 years, with a mean age of 54 years. A significant proportion (70%) of patients was within the fourth to seventh decades, consistent with prior research. Notably, the mean age of patients with malignant SGTs was comparable to that of patients with benign SGTs, a finding corroborated by other studies.

Pleomorphic adenoma (PA) demonstrated the highest prevalence among benign salivary gland tumors in this cohort, representing 70.29% of cases, with Warthin's tumor (14.85%) and canalicular adenoma (4.95%) occurring less frequently. This finding aligns with established literature indicating PA as the predominant benign neoplasm across salivary gland sites. However, variations in the second most common tumor type exist, with some studies reporting myoepithelioma or basal cell adenoma, highlighting potential regional or population-specific differences. Nonetheless, PA, Warthin's tumor, basal cell adenoma, and myoepithelioma are consistently observed as the most prevalent benign salivary gland tumors.

In this cohort of malignant salivary gland tumors, mucoepidermoid carcinoma (MEC) exhibited the highest incidence (32.68%), followed by adenoid cystic carcinoma (ACC) at 18.36% and polymorphous adenocarcinoma at 14.28%. This observation aligns with the prevailing literature citing MEC as the most frequent malignant subtype, although a subset of studies reports ACC predominance [3,4,7-9,11,14]. Polymorphous adenocarcinoma was also observed among the three most common malignancies, consistent with less frequent prior reports [5,6,10]. Rare malignant histotypes, including secretory carcinoma, squamous cell carcinoma, salivary duct carcinoma, and carcinoma ex pleomorphic adenoma, were identified, consistent with their low reported prevalence [1,3,4,8,12].

The observed discrepancies in tumor frequency reported across various studies can be attributed to several factors, including the inherent complexity of tumor definitions, the substantial morphological heterogeneity of these neoplasms, variations in classification systems, the relatively low prevalence of these tumors, and differences in pathologist experience and familiarity [1,3,4]. Furthermore, inter-observer variability in morphological assessment is a well-documented phenomenon [19]. To mitigate these potential sources of bias, this study conducted a retrospective re-evaluation of all tumor diagnoses according to the 2017 World Health Organization classification [2]. This process resulted in the reclassification of 4.0% of cases, based on both morphological and immunohistochemical findings, including the revision of two pleomorphic adenomas to carcinoma ex pleomorphic adenomas.

Histopathological evaluation of carcinoma ex pleomorphic adenomas (CXPAs) typically reveals a discernible transition from benign pleomorphic adenoma (PA) to carcinoma. However, this transition may be obscured, particularly in limited incisional biopsies, leading to potential misdiagnosis as PA. Immunohistochemical (IHC) analysis has demonstrated increased expression of Ki-67, HER2/neu, p53, androgen receptor, and BCL-2 in CXPAs compared to PAs. Furthermore, combined assessment of fatty acid synthase and Ki-67 expression aids in identifying malignant components within CXPAs. Consequently, meticulous examination of PAs for atypical histological features, notably

necrosis and prominent hyalinization, is crucial due to their association with malignant transformation.

In this study, observed increases in mitotic activity, cellular pleomorphism, prominent hyalinization, and necrosis in PAs raised suspicion for carcinomatous transformation. Suspected cases underwent IHC for Ki-67, p53, and HER2/neu, revealing a high proliferative index and intense diffuse labeling for HER2/neu and p53. These findings underscore the importance of rigorous morphological analysis and adjunctive IHC in suspected cases to accurately identify the carcinomatous component and ensure correct diagnosis.

Two cases initially classified as adenocarcinoma not otherwise specified (AcNOS) were re-evaluated and reclassified. One case was identified as cribriform adenocarcinoma of minor salivary gland origin (CAMSG), while the other was reclassified as secretory carcinoma (SC). Secretory carcinoma, initially described in 2010 as mammary analogue secretory carcinoma (MASC) and subsequently recognized by the World Health Organization (WHO), is distinguished from adenoid cystic carcinoma (AcCC) and AcNOS by its histological resemblance to mammary-secreting carcinoma and the presence of the specific ETV6-NTRK3 gene fusion resulting from the t(12;15)(p13;q25) translocation [2]. Although exhibiting an indolent clinical course similar to AcCC, SC demonstrates a higher propensity for cervical lymph node metastasis, with reported rates up to 25%. Cribriform adenocarcinoma of minor salivary gland origin (CAMSG), originally described as cribriform adenocarcinoma of the tongue (CAT), was later renamed to reflect its occurrence in various intraoral locations beyond the tongue [2,23,24,25].

Canalicular adenocarcinoma of salivary glands (CAMSG) is currently classified as a potential variant of polymorphous adenocarcinoma due to shared morphological features [23]. However, polymorphous adenocarcinomas exhibit greater histological diversity and characteristic nuclear "ground-glass" appearance. While both tumor types may demonstrate indolent clinical behavior, CAMSG presents a higher propensity for cervical lymph node metastasis. Despite regional aggressiveness, definitive survival rate differences remain inconclusive [23,25].

Molecular analysis reveals PRKD1-3 rearrangements, specifically ARID1A-PRKD1 and DDX3X-PRKD1 gene fusions, in approximately 80% of CAMSG cases, contrasting with less than 10% in polymorphous adenocarcinomas with classical morphology. Conversely, PRKD1 E710D mutations are predominantly observed in classical polymorphous adenocarcinomas, with only 10% incidence in CAMSG. The shared genetic family driving both tumor types supports their classification as a spectrum of variants, as reflected in the 2017 WHO classification [2,23,25-28].

The classification of salivary gland tumors (SGTs) remains dynamic, with ongoing refinements driven by advancements in immunohistochemistry and molecular analysis. Epidemiological studies are crucial for elucidating clinicopathological characteristics and informing classification updates [1,3,29].

In this study, the parotid gland was the most frequent site of SGTs (43.33%), followed by the minor salivary glands of the palate (26.0%), consistent with many reports. However, some studies demonstrate a higher prevalence in minor salivary glands of the palate. This discrepancy may reflect sampling bias, as hospital-based studies often report parotid gland predominance, while oral pathology service studies emphasize intraoral minor salivary gland involvement, likely due to the nature of specimens received. No sublingual gland tumors were observed, consistent with their reported low prevalence.

This study's findings are generally consistent with existing literature, although no significant age differences between benign and malignant SGTs were noted [3,5,9,12]. Given the diversity of SGTs, accurate diagnosis and timely intervention are essential for optimal patient outcomes.

Conclusion

The findings of this study are consistent with previously published investigations conducted in diverse geographic regions. Notably, contrary to some reports, no significant age disparity was observed between patients with benign and malignant salivary gland tumors. Despite their relative infrequency, the diverse histopathological spectrum of salivary gland tumors necessitates clinical awareness among physicians and dentists to facilitate timely diagnosis, optimize therapeutic interventions, and contribute to oncologic prevention strategies.

Declarations

Ethical Approval and Consent to participate

Not applicable as retrospective nature of study. Consent for publication: Not applicable as retrospective nature of study.

Availability of supporting data

Upon request to the corresponding author.

Competing Interests

Nil

Funding Statement

Nil

Authors contributions

All authors made substantial contributions to the reported work, including in the areas of conception, study design, execution, data collection, analysis, and interpretation. They participated in drafting, revising, and critically reviewing the article, gave final approval for the version to be published, agreed on the journal for submission, and accepted responsibility for all aspects of the work.

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