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The intricate histopathological spectrum of salivary gland neoplasms in a tertiary care center in Vindhya region (Rewa, Satna, Sidhi, Maihar, Singrauli, Sahdol and Panna Districts of Madhya Pradesh, India)

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ABSTRACT

Background: Salivary gland tumors (SGTs) globally account for <2% of all tumors, with an annual incidence ranging from 0.4 to 13.5/100,000 persons. However, there is a notable dearth of information on SGTs in India, prompting this study to explore the histological spectrum in the Vindhya region. **Aims and Objectives:** The primary goal is to determine the epidemiological patterns of distinct SGTs in the Vidhya Region through a meticulous examination of histological characteristics. Comparative analysis with existing literature aims to enhance insights into these rare tumors. **Materials and Methods:** Ninety-one SGT biopsies from Shyam Shah Medical College underwent comprehensive scrutiny over a five-year period. Patient-specific data, including age, sex, and location, were collected. The histopathological examination involved formalin fixation, paraffin sections, and staining, with the occasional use of specialized stains for comprehensive categorization based on microscopic examination. **Results:** Out of 91 cases, 39.56% were malignant, and 60.44% were benign. The parotid gland exhibited the highest incidence, with pleomorphic adenoma (PA) as the most common benign tumor. Notably, in our study, adenoid cystic carcinoma surpassed mucoepidermoid carcinoma as the most frequent malignant tumor. **Conclusion:** This study provides valuable insights into the patterns of occurrence of SGTs in the Vindhya region, highlighting the significance of further research in this underexplored field. Notably, PA, mucoepidermoid carcinoma, and adenoid cystic carcinoma are prominently reported, with a notable male predominance.

Key words: Salivary gland tumors; Pleomorphic adenoma; Warthin's tumor; Benign salivary gland tumors; Malignant salivary gland tumors

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INTRODUCTION

Salivary gland tumors (SGTs) are relatively uncommon, accounting for approximately <2% of all tumors in humans and 3–10% of all head-and-neck neoplasms.[1,2] The global annual incidence of these tumors ranges from 0.4 to 13.5 cases/100,000 individuals.[3-5] The majority of SGTs, around 65–80%, are located in the parotid gland, while 10–15% are found in the submandibular gland and the remainder in minor salivary glands.[6] Among these, roughly 80% of parotid tumors and 50% of submandibular tumors are of a benign nature, while 50% of minor SGT and 70–90% of sublingual tumors are malignant.[7]

SGTs can affect individuals of all age groups, with the highest incidence of benign tumors occurring in the third and fourth decades of life and malignant tumors being more common in the fourth and fifth decades.[8] These

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tumors exhibit a wide range of morphological diversity, both between different tumor types and sometimes within the same tumor mass. Furthermore, the presence of hybrid tumors, dedifferentiation, and the potential for certain benign tumors to progress into malignancy can pose challenges for histopathological interpretation.[9]

In India, the overall incidence of SGTs is documented through the cancer registry established by the Indian Council of Medical Research.[10] However, it is worth noting that these registries cover limited geographic areas and populations, potentially not being fully representative of the entire Indian population. In addition, there is a scarcity of published literature regarding SGTs in the Indian population.[11]

The goal of this study was to determine the epidemiological pattern of distinct SGTs in the Vidhya Region of Madhya Pradesh by examining their histological characteristics. We also compared our results to information from other sources.

Aims and objectives

Aims

1. To analyze the epidemiological pattern of salivary gland tumors (SGTs) in the Vidhya Region of Madhya Pradesh, India, over a five-year period.
2. To investigate the histological characteristics of distinct SGTs in the specified region.
3. To compare the findings of the study with existing information from other sources to identify similarities and differences in the epidemiology of SGTs.

Objectives

1. To assess the age and sex distribution of individuals diagnosed with benign and malignant SGTs.
2. To identify the specific salivary glands most commonly affected by benign and malignant tumors.
3. To categorize the types of benign and malignant SGTs based on histological characteristics.
4. To compare the results of the study with available literature on SGTs in India and globally, highlighting any regional variations.

MATERIALS AND METHODS

This retrospective study examines all SGT biopsies performed at Shyam Shah Medical College in Rewa, Madhya Pradesh, India, over a 5-year period (2019–2023). The hospital is the primary tertiary health-care facility for the district as well as six more surrounding districts with histopathological services. Age, sex, and location-specific biodata were acquired from laboratory records based on data from histopathology request forms. All samples were fixed in 10% formalin before being divided into sections with paraffin and stained with hematoxylin and eosin. On occasion, specialized stains were used (for mucin, for example). The authors went over each slide and categorized them.

Inclusion criteria

All epithelial origins, major and minor SGTs.

Exclusion criteria

1. All inflammatory and cystic lesions of the salivary glands
2. All mesenchymal-origin SGTs
3. Metastasis in the salivary glands.

RESULTS

A total of 91 cases of SGT that was reported during the past 5 years were evaluated for the study, and 36 (39.56%) cases were found to be malignant while 55 (60.44%) cases were found to be benign. The age of the patients ranged from 13 to 76 years of age, with the mean age being 53.2 years of age. The age and sex distribution of benign and malignant tumors is shown in Tables 1 and 2.

The parotid glands had the highest percentage of tumors, either benign or malignant (Table 3), with 39.56% (benign) and 62.73% (malignant) of the 91 instances. This represents 67.03% of the overall number of tumors. A minimal quantity of instances was seen in the minor salivary glands.

Table 4 displays the distribution of benign salivary gland tumors. Pleomorphic adenoma (PA) was the most prevalent histologic form of benign salivary gland tumor, followed

Table 1: Distribution according to age and sex

Malignant salivary gland tumors			
Age (in years)	**Male**	**Female**	**Total**
11–20	0	0	0
21–30	1	0	1
31–40	3	2	5
41–50	6	3	9
51–60	10	5	15
61–70	2	1	3
71–80	2	1	3
			36

Table 2: Distribution according to age and sex

Benign salivary gland tumors			
Age (in years)	**Male**	**Female**	**Total**
11–20	1	0	1
21–30	2	0	2
31–40	8	5	13
41–50	16	6	22
51–60	4	2	6
61–70	6	4	10
71–80	1	0	1
			55

Table 3: Distribution according to salivary glands

Glands	Malignant	%age	Benign	%age	Total	%age
Parotid	23	34.33	44	65.67	67	73.63
Submandibular	12	57.14	9	42.86	21	23.08
Minor salivary glands	1	33.33	2	66.67	3	3.30
Total	36	39.56	55	60.44	91	

Table 4: Distribution of benign tumors in salivary glands

Tumor	Parotid	%age	Submandibular	%age	Minor salivary gland	%age	Total
Pleomorphic adenoma	25	69.44	9	25.00	2	5.56	36
Warthin's tumor	14	100.00	0	0.00	0	0	14
Oncocytoma	2	100.00	0	0.00	0	0	2
Basal cell adenoma	2	100.00	0	0.00	0	0	2
Schwannoma	1	100.00	0	0.00	0	0	1
						Total	55

Table 5: Distribution of malignant tumors in salivary glands

Glands	Parotid	%age	Submandibular	%age	Minor salivary gland	%age	Total
Mucoepidermoid carcinoma	4	50.00	4	50.00	0	0.00	8
Adenoid cystic carcinoma	7	43.75	8	50.00	1	6.25	16
Acinic cell carcinoma	3	100.00	0	0.00	0	0.00	3
Adenocarcinoma NOS	2	100.00	0	0.00	0	0.00	2
Carcinoma ex pleomorphic adenoma	2	100.00	0	0.00	0	0.00	2
Unclassified malignant tumor	1	100.00	0	0.00	0	0.00	1
Squamous cell carcinoma	1	100.00	0	0.00	0	0.00	1
Basal cell carcinoma	1	100.00	0	0.00	0	0.00	1
Polymorphous low-grade adenocarcinoma	1	100.00	0	0.00	0	0.00	1
Metastatic undifferentiated carcinoma	1	100.00	0	0.00	0	0.00	1
						Total	36

by Warthin's tumor. Table 5 displays the distribution of malignant tumors in the salivary glands. The most frequent type of malignant salivary gland tumor was adenoid-cystic carcinoma (44.4%). The most typical location for adenoid cystic carcinoma occurrences was the parotid. The parotid gland and submandibular gland were the next most frequent sites of acinic cell carcinoma incidence. The parotid gland was the sole organ affected in every instance of cancer ex PA, basal cell carcinoma, adenocarcinoma, squamous cell carcinoma, and metastatic undifferentiated carcinoma.

DISCUSSION

Out of 91 individuals, 36 malignant and 55 benign salivary gland tumors were analyzed in this study. This is consistent with the majority of research that indicates benign tumors outnumber malignant ones.[12-15] However, some studies do show more prevalence of malignant tumor that may be because they are specialized cancer care hospitals.[16]

SGTs were discovered in patients with modest overall male preponderance in this 5-year investigation, with ages ranging from 13 to 76 (mean: 53.2 years). This conclusion is consistent with previous studies.[5,17,18] Fewer studies, meanwhile, have indicated a greater preference for women in SGTs.[18,19] While malignant neoplasms were more prevalent in the sixth and seventh decades, benign neoplasms were more common in the fifth decade. In all salivary glands examined in this study, benign tumors were more prevalent than malignant ones. In addition, in line with the majority of published findings, the data demonstrated that patients with malignant SGTs were older than those with benign tumors.[15,19,20]

The submandibular gland, the minor salivary gland on the palate and floor of the mouth, and the parotid gland were the most often found sites of SGTs.

According to the results of the current investigation, PA and adenoid cystic carcinoma were the most frequent benign and malignant tumors of the parotid gland and submandibular gland. Warthin's tumor was exclusively found in the parotid gland. On the other hand, only the parotid gland was associated with other benign tumors. There was just one occurrence of a malignant tumor, namely adenoid cystic carcinoma in the palate, and only one benign tumor, PA, occurred in small salivary glands.

With 65.45% of benign SGTs, PA was the most prevalent SGT. Every epidemiological study conducted on SGTs

has revealed a clear 42–80% PA prevalence.[18,21,22] Two distinct histological features (Figure 1) are visible: Mesenchymal and epithelial differentiation. The well-formed ductal structures made up of outer myoepithelial and inner epithelial cells, together with their associated spindle, squamous, basaloid, cuboidal, oncocytoid, mucous, sebaceous, round, polygonal, or clear cell characteristics, comprise the epithelial component. Four instances had squamous differentiation with keratin pearls (positive CK19), while one tumor had a predominance of adipose tissue. While the mesenchymal component was composed of myxoid, hyaline, cartilaginous, or osseous differentiation, the cytologic characteristics of the epithelial cells were bland. Cellular variants with a predominance of epithelial components and myxoid types with myxochondromatous mesenchymal elements are examples of variations. Fibrous capsule thickness varied; in tumors that are mostly myxoid, it is frequently absent. While non-contributory, special stains and immunohistochemistry (IHC) provide positive results for carcinoembryonic antigen (CEA), secretory component, gross cystic disease fluid protein-15, interleukin-6, and steroid C-21 hydroxylase. Clonal chromosomal rearrangements are observed in cytogenetic analyses for 8q12 (usually found in younger individuals) and 12q13–15.

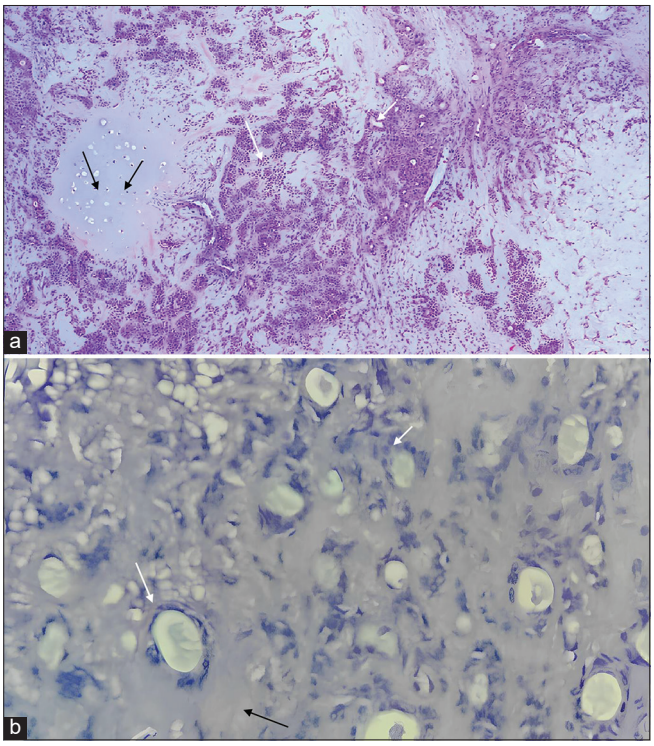

Figure 1: H and E-stained sections (a ×10 magnification, b ×40 magnification) revealed well circumscribed tumor tissue showing bimodal population of epithelial (white arrow) and stromal component (black arrow). Epithelial element consists of tubules and ducts lined by inner layer of epithelial cells and outer layer of myoepithelial cells in myxoid stroma (F/S/O PA)

Two examples of differential diagnosis (DD) include carcinoma ex PA and PLGA.[9]

Warthin's tumor (32.72%) was the second most frequent benign salivary gland tumor and was only observed in males. It was found only in parotid glands. The primary etiological cause of Warthin's tumor, which primarily affects older individuals and seldom occurs in those under thirty, with a peak incidence in the sixth decade of life, is smoking habits.[23] There might be ethnic, behavioral, regional, or other environmental variables influencing the variations in the results. Under a microscope (Figure 2), the cystic areas are filled with lymphoid stroma, and a small number of them display lymphoid follicles. Epithelial tall columnar (IHC-somatostatin) cells surrounding the cysts produce noticeable papillae. Other methods of diagnosis are not relevant.[9]

The current study's findings demonstrated that 42.85% of SGTs are malignant SGTs. The most frequent malignant SGT was adenoid cystic carcinoma (44.4%), which was followed by mucoepidermoid carcinoma (22.2%). Sando et al., and Subhashraj[21,22] discovered that the incidence of adenoid cystic cancer was 25% and 6.6%, respectively. Nonetheless, mucoepidermoid carcinoma was discovered by Kalburge et al., and Ochicha et al., to be the most common malignant tumor (58.53% and 5.12%), surpassing adenoid cystic carcinoma (33.33% and 1.28%).[18,24] The majority of

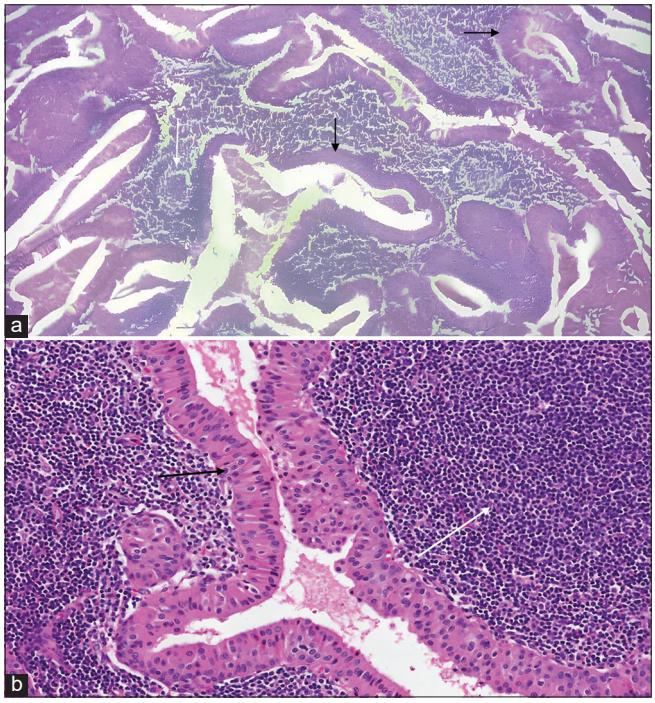

Figure 2: H and E-stained section (a ×10 magnification, b ×40 Magnification) showed a well-circumscribed tumor with a papillary architecture. The papillae are lined by bilayered oncocytic epithelial cells (black arrow) with a surrounding lymphoid stroma, containing germinal centers (white arrows) (F/S/O Warthin's tumor)

tumors include a combination of cytoarchitectural patterns. Conventionally, the histopathologic hallmarks of adenoid cystic carcinoma are cribriform (50%), tubular (20–30%), and solid patterns (10–15%). The stroma is collagenous, hyalinized, or eosinophilic. The propensity for perineural invasion, which was seen in more than 50% of the patients in the current investigation, is a diagnostic hallmark of this malignancy. PLGA, epithelial-myoepithelial carcinomas, and basaloid squamous cell carcinomas are DDs. Keratin, CEA, lysozyme, lactoferrin, S-100 protein, and CD117 are positive IHC markers.[9,25]

Based on microscopic analysis (Figure 3), mucoepidermoid carcinoma is made up of different ratios of mucous, epidermoid, and intermediate-type cells with cystic or papillary mucin-filled cystic lumens. The surrounding tissue frequently contains pools of extravasated mucin that strongly reacts with mucicarmine stain (IHC positive for simple mucin-type carbohydrate antigens, i.e., T, Tn, and syalosyl–Tn). Clear cells with clear cytoplasm, mostly glycogen and little mucus, may also be present in these carcinomas. Grade I, which is predominantly cystic, Grade II, which is cystic and cellular, and Grade III, which is predominant solid pattern, are the three grading systems used to describe this cancer. Cystometaplasia and sialometaplasia are examples of DDs.[9,25]

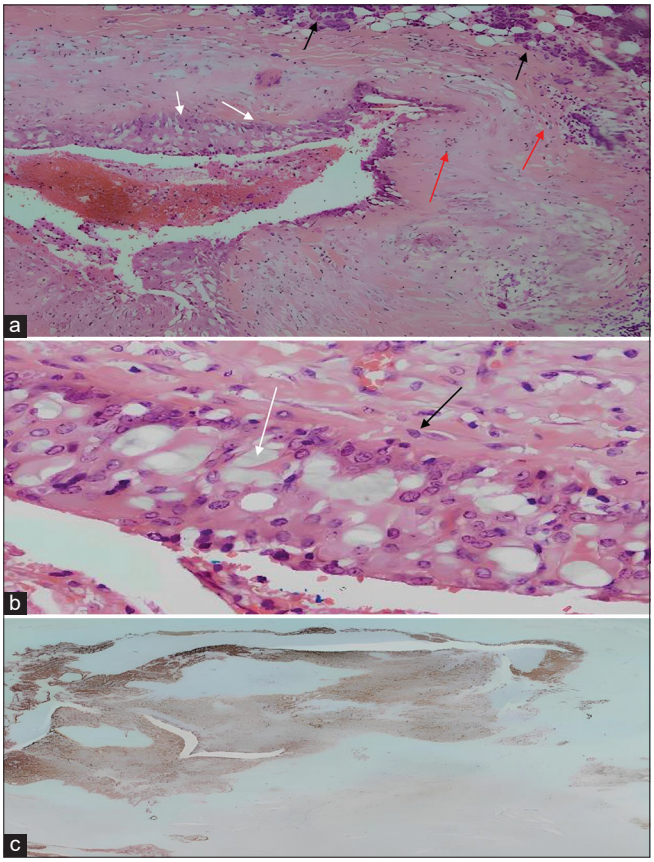

Figure 3: H and E-stained section (a ×10 magnification, b ×40 magnification) revealed predominantly malignant squamous cells (black arrows) along with mucin containing cells (mucous cells) (white arrows) and intermediate cells. Stroma shows chronic inflammatory infiltrates, blood vessels, and focal areas of necrosis (red arrows) (F/S/O mucoepidermoid carcinoma). (c) Cytokeratin stain showing MEC. The tumor cells showed positive immunostaining for p63, p40, pan-cytokeratin, and CK7 and negative for TTF-1, CK20, SOX 10, calponin, SMA, and napsin A

Cytogenetic balanced translocation involving C-kit expressions and 6q areas is seen in AdCCa, whereas translocation of (11; 19) in MECa results in the fusion gene transcript CTRC1/MAML2.[9,25]

Males had less incidences of acinic cell carcinoma and PLGA, whereas females were more likely to have ex-carcinoma PA, basal cell adenoma, and schwannoma. However, as there are no consistent statistics in the literature, these few reported occurrences have no bearing on the data that are given.

Limitations of the study

1. Single Institutional Experience: The study is based on data from Shyam Shah Medical College in Rewa, Madhya Pradesh, which may limit the generalizability of the findings to the broader population.
2. Retrospective Design: The study adopts a retrospective design, relying on historical data from the past five years. This may introduce selection bias and limit the ability to control variables.
3. Limited Geographic Scope: The study focuses on the Vidhya Region of Madhya Pradesh, and therefore, the findings may not be representative of the entire Indian population due to regional variations in demographics and environmental factors.
4. Small Sample Size: The study includes 91 cases of SGTs, which may be considered a relatively small sample size. Larger sample sizes could provide more robust insights into the epidemiology of SGTs.
5. Limited Follow-up Data: The retrospective nature of the study might restrict the availability of long-term follow-up data on patients, hindering the assessment of disease outcomes and progression.

CONCLUSION

Tumors of the salivary gland are uncommon. PA was the most common lesion, followed by mucoepidermoid carcinoma and adenoid cystic carcinoma. The most afflicted gender was male and the parotid gland. In the current study, 91 SGTs were analyzed in a single institutional experience. Our study's results regarding age, sex, site distribution, and pathologic characteristics agreed with those of other studies published in India and other regions of the world.

Despite the limited number of SGTs included in this study, the results should help us understand the illness better. Since there has been little data on head-and-neck tumors over the past two to three decades, only a small number of SGTs based on a notably large number of cases have been published in India. As a result, prospective studies involving larger samples are necessary to more accurately identify the factors that influence the disease.

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Authors Contribution:
S- Definition of intellectual content, literature survey, prepared first draft of manuscript, implementation of study protocol, data collection, data analysis, manuscript preparation, and submission of article; **PA-** Concept, design, clinical protocol, manuscript preparation, editing, and manuscript revision; **LT-** Design of study, statistical analysis, and interpretation; **SKS**- Review manuscript; **PSR**- Literature survey and preparation of figures; **SY-** Data collection, **DT –** Data collection, **PS**- Data collection.

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