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Clinicopathological Study of Salivary Gland Tumors in Tertiary Care Teaching Hospital

Priyank Kumar Chauhan[1], S S Bist[2]*, Lovneesh Kumar[3], Anuradha Kusum[4]

[1]*L D Bhatt Sub. Distt Hospital, Kashipur, (US Nagar)*

[2,3]*Department of Otorhinolaryngology, Himalayan Institute of Medical Sciences, Swami Rama Himalayan University, Swami Ram Nagar, Jollygrant, Dehradun (Uttarakhand) -248016*

[4]*Department of Pathology, Himalayan Institute of Medical Sciences, Swami Rama Himalayan University, Swami Ram Nagar, Jollygrant, Dehradun (Uttarakhand) – 248016.*

**Corresponding author's: S. S. Bist*

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Abstract

Background: *Salivary gland tumors are rare and their annual incidence is less than 1/100,000 and they represent less than 5% of head and neck tumors. About 80% of salivary gland tumors are located in the parotid glands, 10% in the submandibular glands and the remaining being distributed between the sublingual and minor salivary glands. Aims and objectives of the study were to know the epidemiology of cases of salivary gland tumors and to study the clinicopathological profile of salivary gland tumors.* ***Materials and Methods:*** *A total of 56 cases of age more than10 years and having swelling in head and neck region, were included. Laboratory investigations in the form of Fine needle aspiration cytology (FNAC) and histopathological examination (HPE) were done. Relevant radiological investigations were done to find out the site of swelling and its extension.* ***Result:*** *In our study, the most commonly involved salivary gland was parotid gland (46 cases; 82.1%), followed by minor salivary gland (6 cases; 10.6%). The least number of cases were of submandibular gland (4 cases; 7.1%). Fine needle aspiration cytology was done in all cases out of which, benign lesions were present in 35 (62.5%) cases and 7 (12.5%) cases had malignant lesions. Fine needle aspiration cytology was inconclusive in 14 (25%) cases. Histopathological examination was done in all cases out of which, benign lesions were present in 38 (67.9%) cases and 18 (32.1%) cases had malignant lesions.* ***Conclusion:*** *The most common benign tumor was pleomorphic adenoma followed by Warthin's tumor. The most common malignant tumor was mucoepidermoid carcinoma followed adenoid cystic carcinoma. Statistically significant association was found between fine needle aspiration cytology and histopathological examination, which led to the conclusion that HPE is necessary for the confirmation of the diagnosis so that further management can be carried out accordingly.*

Keywords: *Benign tumors, Epidemiology, Malignant tumors, Salivary gland tumors.*

1. Introduction

One among the few bodily parts that can experience a wide variety of tumors as well as disorders resembling malignancies is the salivary glands. These tumors are quite uncommon, which complicates both the identification and management. Salivary gland tumors (SGTs) account for less than 5% of the tumors found in the neck and head are extremely uncommon, with an annual incidence of less than 1/100,000 people worldwide, without any discernible regional variation. These tumors exhibit a remarkable variation in morphology across various tumor types as well as even within a single tumor mass. Furthermore, dedifferentiation, hybrid tumors, especially the tendency for some benign lesions to develop into malignancy might complicate the interpretation of histopathology (1).

About 80% of salivary gland tumors are located in the parotid glands, 10% in the submandibular glands and the remaining being distributed between the sublingual and countless minor salivary glands1. Major salivary gland tumors are mostly benign in nature whereas that of minor salivary glands are usually malignant (2). The gender distribution for the salivary gland cancer is almost equal

and majority of the cases are seen in the sixth decade (3).
Benign tumors of the salivary glands occur in the age group of 30 – 70 years. The peak incidence for malignant tumors is 6th and 7th decades. Malignant tumors are more frequent in women than men (4,5).

Salivary gland tumors have a high incidence in the Eskimos and atomic bomb survivors of Japan (6). The tumors of parotid and submandibular gland are insidious in onset, progress slowly in due course of time and do not show any other symptoms as such. Discomfort is caused by obstructing salivary flow, which is rarely caused by a few tumors. Pain is an uncommon feature but if present, usually heralds malignant change. Presence of malignant change may lead to facial weakness or palsy. These are very slow growing tumors and the symptoms may take time to seek attention of the case (7).

To evaluate these lesions “fine needle aspiration cytology” has emerged as a useful and recognized procedure to make the diagnosis. Histopathology is the gold standard as it avoids diagnostic pitfalls of FNAC (8).

The parotid gland is easily accessible for palpation; it is often possible to characterize the lesion by fine-needle aspiration cytology, which has a sensitivity of 80% and a 97% specificity (9).

2. Materials and Methods

This observational cross-sectional study was conducted in tertiary care teaching hospital in the department of Otorhinolaryngology, Swami Rama Himalayan University, Dehradun, Uttarakhand. A total of 56 cases of age >10 years and having swelling in head and neck region, later diagnosed as salivary gland tumor on FNAC and HPE were included from IPD after obtaining a written informed consent.

Inclusion criteria:
The research included all individuals with salivary gland enlargements, swelling regardless of minor or major cases.

Exclusion criteria:
Cases who were diagnosed as non- neoplastic / infective lesion on cytology and HPE were not included in the study.

Methodology

All cases were subjected to detailed clinical history and examination. Laboratory investigations in the form of FNAC and HPE were done. After fixing in 10% formalin, all of the specimens were transformed into slices encased in paraffin and stained with eosin and hematoxylin. On rare occasions, specific stains (such as those for mucin) were used. The authors examined each slide and categorized it using the WHO's 2005 histological classification system for cancers.
Relevant radiological investigations (MRI/USG/CT scan) were done to find out the site of swelling and extension.

Ethical Statement

The Ethical Clearance Committee provided ethical clearance prior to the start of the study. The Swami Rama Himalayan University's research and ethics council gave its approval to this study. From case document records, demographic information, the diagnosis, and intra-operative results were gathered. Operative notes and histology reports contained the histopathological results.

Statistical Analysis:

MS Excel 2010 was used to input the gathered data. Version 22 of the IBM Statistical Package for the Social Sciences (SPSS) was utilized for various types of statistical analyses. Consequently, only one sample from the Kolmogorov-Smirnov test was used to ascertain whether or not the data sets deviated from a normal distribution. When analyzing normally distributed data, parametric tests were used; when analyzing non-normally distributed data, non-parametric tests were used. Regarding the quantitative variables, descriptive statistics were computed.

Frequencies and percentages were computed for both category and qualitative data. To make the findings easier to grasp, a graphical depiction of the variables was provided, and chi-square tests were used to examine categorical data. A p-value of <0.05 was deemed statistically significant, but a p-value of >0.05 was deemed insignificant.

3. Results

The mean age of cases was 42.91 years ranging from 11 to 82 years of age (Figure 1). The maximum

numbers of cases in present study were found in an age range of 31-40 years (21.4%). Male to female ratio was of 1.4:1. In the present study, the most common presenting symptom was pre-auricular swelling in 23 (41.1%) followed by infra-auricular swelling in 22 (35.7%) cases.

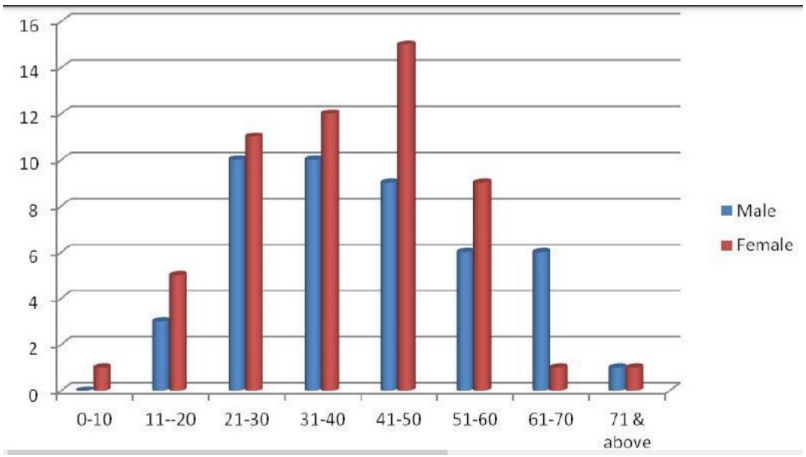


Figure 1: Distribution of sex and age of the SGT patients

In our study, the most common site of swelling for salivary gland tumor was parotid gland (PG) with 46 cases (82.1%), followed by minor salivary gland with 6 (10.6%) cases. The least number of cases were of submandibular gland, i.e., 4 (7.1%) cases. It was observed that the sub sites of parotid glands were equally involved. In 23 (50%) cases, main gland of parotid gland was involved and in remaining 23 (50%) cases, the tail of parotid gland was involved. In the minor salivary gland tumor, in 2 (33.3%) cases hard palate was involved, 3 (50%) cases, Sino-nasal mucosa was involved and in 1 (16.6%) case, buccal mucosa was involved.

In the submandibular gland, 3 (75%) cases, superficial part of submandibular gland was involved and 1 (25%) case; deep part of submandibular gland was involved (see Table 1 and Figure 2 - Figure 4).

Table 1: Distribution of cases on the basis of involvement of salivary gland tumors and subsites distribution (n=56)

Salivary glands	Number of cases (%)	Subsites distribution
Parotid glands	46(82.1%)	a- Main gland - 23(50%) b-Tail of parotid - 23(50%)
Minor salivary glands	6(10.6%)	a- Hard palate - 2(33.3%) b- Sinonasal mucosa - 3(50%) c- Buccal mucosa - 1(16.6%)
Submandibular glands	4(7.1%)	a- Superficial part - 3(75%) b- Deep part - 1(25%)
Total	**56(100%)**	**56(100%)**

a) b)

Figure 2: a) Showing left parotid main gland swelling and b) showing right parotid gland tail of swelling.

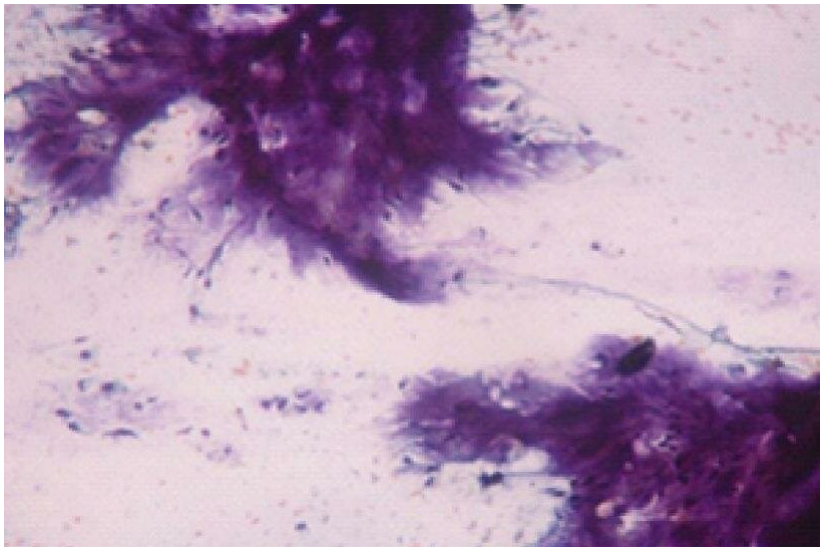
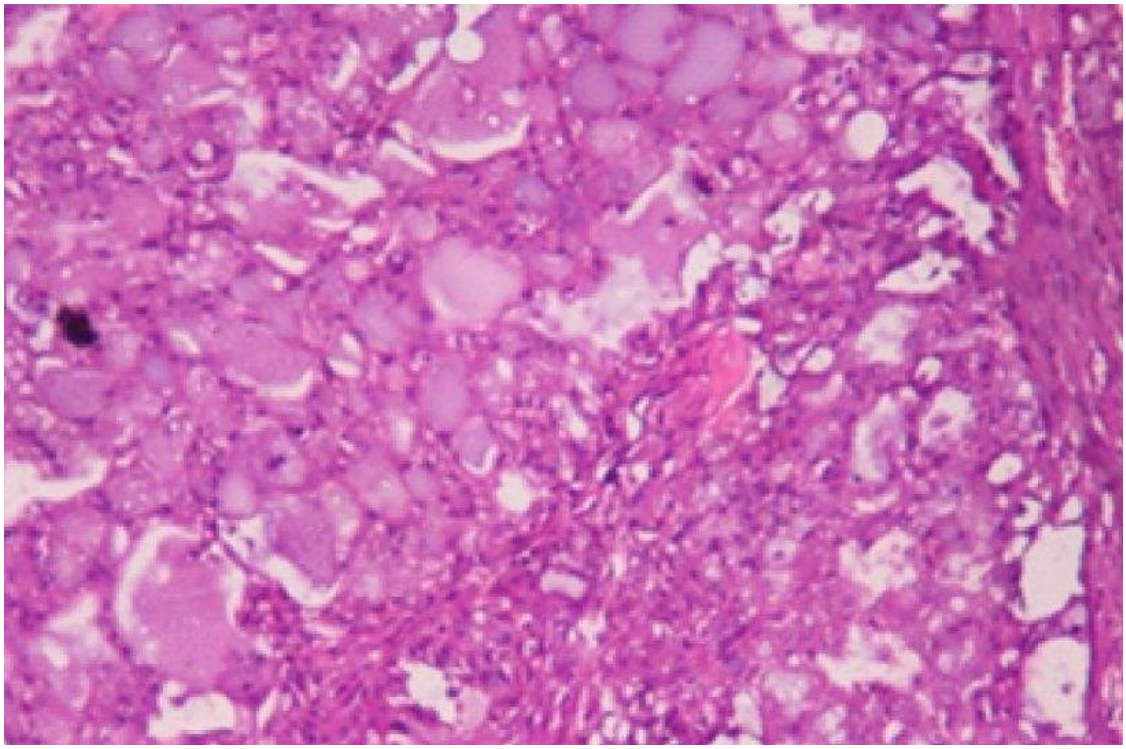
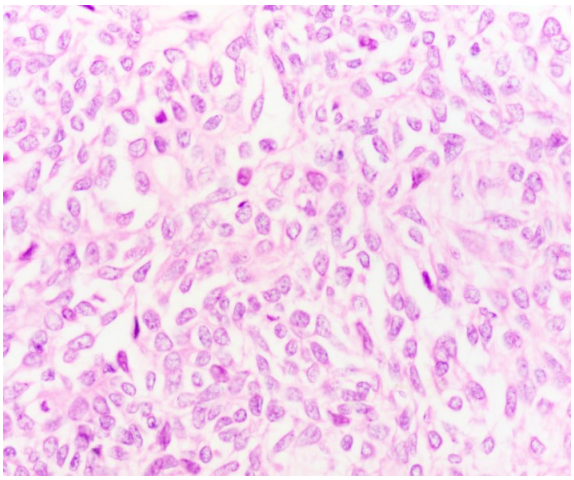


Figure 3: Smear (cytology) taken from the parotid gland



a)



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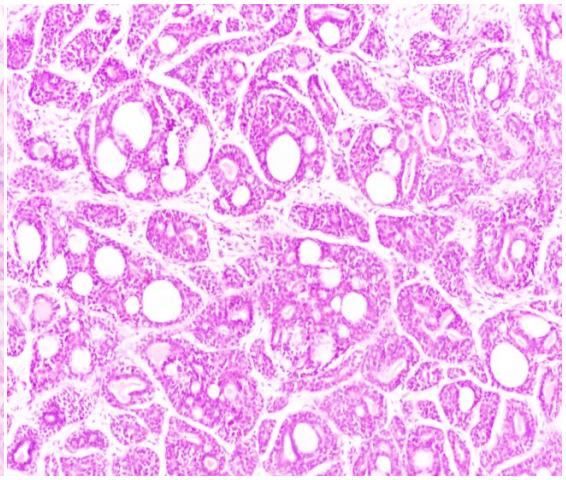

c)

Figure 4: a) and b) Haematoxyline and eosin stain on histological Section shows Pleomorphic Adenoma (400x) and c) showing adenoid cystic carcinoma (100X)

FNAC was done in all cases out of which, benign lesions were present in 35 (62.5%) cases and 7 (12.5%) cases had malignant lesions. There were inconclusive FNAC in 14 (25%) cases. According to Chi square test, p value was 0.107, which was insignificant. Histopathological examination was done in all cases out of which, benign lesions were present in 38 (67.9%) cases and 18 (32.1%) cases had malignant lesions. According to Chi square test, p-value was 0.036, which was significant (Table-2).

Table 2: Association of salivary gland tumors on the basis of FNAC and HPE (n=56)

Tumor Type	FNAC No of cases (%)	HPE No of cases (%)
Benign	35(62.5%)	38(67.8%)
Malignant	7(12.5%)	18(32.1%)
Inconclusive result	14(25%)	-

Total	56(100%)	56(100%)

Out of 56 cases, 38 (67.9%) cases had benign neoplasm and 18 (32.1%) cases had malignant neoplasm. Out of 38 (67.9%) who had benign neoplasm, 28 (50%) cases had pleomorphic adenoma, 9 (16.1%) cases had Warthin's tumor and only 1 (1.8%) case had benign intraductal papilloma. Out of 18 (32.1%) who had malignant disease, 11 (19.6%) cases had mucoepidermoid carcinoma, 3 (5.4%) cases had adenoid cystic carcinoma, and 1 (1.8%) case each had acinic cell carcinoma, Carcinoma Ex pleomorphic adenoma, squamous cell carcinoma and lymphoepithelial carcinoma. According to chi square test, p value was 0.072, which was insignificant. (Table 3 and Figure 5).

Table 3: Association of salivary gland tumors according to gender (histological findings) (n=56)

Histopathological examination				**Total**
Histopathological Diagnosis		**Gender**		
		Male	**Female**	
Pleomorphic Adenoma	Benign 38(67.9%)	16 (48.5%)	12 (52.2%)	28 (50%)
Warthin's Tumor		9(27.3%)	0(0%)	9(16.1%)
Benign Intraductal papilloma		1(3%)	0(0%)	1(1.8%)
Mucoepidermoid Carcinoma	Malignant 18(32.1%)	4(12.1%)	7(30.4%)	11(19.6%)
Adenoid Cystic Carcinoma		1(3%)	2(8.7%)	3(5.4%)
Acinic cell Carcinoma		1(3%)	0(0%)	1(1.8%)
Ca Ex Pleomorphic Adenoma		1(3%)	0(0%)	1(1.8%)
Squamous Cell Carcinoma		0(0%)	1(4.3%)	1(1.8%)
Lymphoepithelial carcinoma		0(0%)	1(4.3%)	1(1.8%)
Total	56(100%)	33(100%)	23(100%)	56(100%)

Chi-square test, p-value=0.072

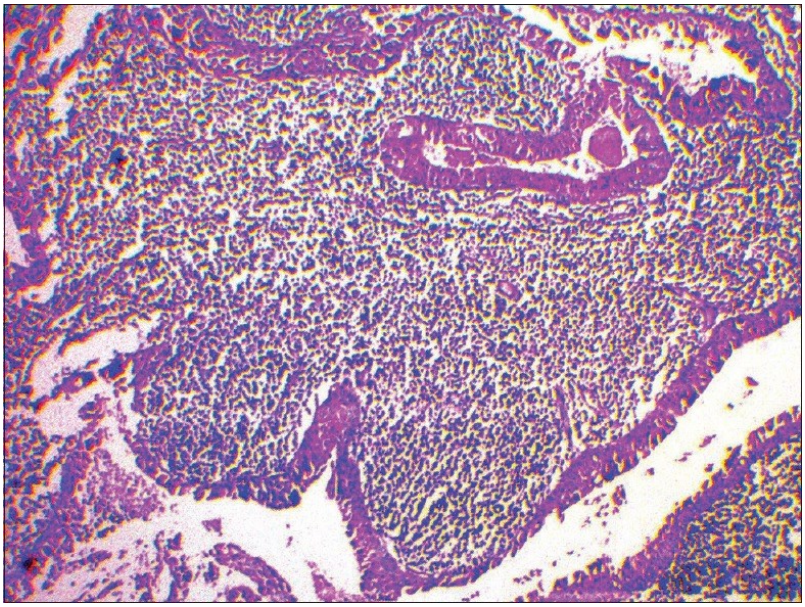

Figure 5: Warthin's tumor characterized by cuboidal and columnar oncocytic cells in a lymphoid stroma surrounding cystic cavities (6).

Out of 28 (50%) cases of pleomorphic adenoma, HPE results of 21 (60%) cases were consistent with FNAC report while in 7 (33.3%) cases, the result was inconsistent. Out of 9 (16.1%) cases of Warthin's tumor, HPE results of 8 (22.9%) cases were consistent with FNAC report while the result of 1 (4.8%) case was inconsistent.

HPE results of 3 (5.4%) cases of adenoid cystic carcinoma were consistent with FNAC report whereas HPE results of cases of acinic cell carcinoma, benign intraductal papilloma, Carcinoma Ex-pleomorphic adenoma, Squamous cell carcinoma, Lymphoepithelial carcinoma were inconsistent with FNAC reports. According to Chi square test, p value was 0.009, which was significant. (Table-4).

Table 4: Cytopathological association between histopathology and FNAC (n=56)

Histopathological diagnosis		**FNAC diagnosis**	
	No. of cases	Consistent	Inconsistent
Pleomorphic Adenoma	28(50%)	21(60%)	7(33.3%)
Warthin's Tumour	9(16.1%)	8(22.9%)	1(4.8%)
Adenoid Cystic Carcinoma	3(5.4%)	3(8.6%)	0(0%)
Acinic cell Carcinoma	1(1.8%)	0(0%)	1(4.8%)
Mucoepidermoid Carcinoma	11(19.6%)	3(8.6%)	8(38.1%)
Benign Intraductal papilloma	1(1.8%)	0(0%)	1(4.8%)
Ca Ex Pleomorphic Adenoma	1(1.8%)	0(0%)	1(4.8%)
Squamous Cell Carcinoma	1(1.8%)	0(0%)	1(4.8%)
Lymphoepithelial Carcinoma	1(1.8%)	0(0%)	1(4.8%)
Total	56(100%)	35(100%)	21(100%)

FNAC-based diagnoses were compared with diagnoses from histological examination of specimens. Considering the result of malignancy on FNAC, there were 7 true positive cases for malignancy, 11 false negative cases of malignancy, 38 true negative cases of malignancy and there were no false positive cases.

According to present study, the sensitivity of FNAC was 38.89%, specificity was 100%, positive predicted value was 100%, negative predicted value was 77.55% and accuracy was 80.36%.

4. Discussion

In the present study, the average age of cases was 42.91 years, ranging from 11-82 years of age, youngest being 11 years and eldest being 88 years. The maximum number of cases in the current study was from age group of 31-40 years (21.4%). The study done by Bobati et al., described similar age range (18-68 years). The mean age for malignant tumors was 45 years while it was 35 years for benign tumors (10).

The most common salivary gland involved in the present study was parotid 82.1%, followed by submandibular gland 7.1%, minor salivary glands of nose and paranasal sinus 7.1% and lastly oral cavity 3.5%. Similar study was done by Rajat et al., where 41.9% had tumor in parotid gland, 37.8 % had in submandibular gland, 14.9% in minor salivary gland and 5.4% had in sublingual gland (11). Also, Nanda et al., studied that in 51.1% cases parotid gland was involved, submandibular gland was involved in 37% cases, and sublingual gland and minor salivary glands were involved in 4.7% and 7% of case respectively (12).

FNAC was done in all cases in our study, out of which benign lesions were present in 62.5% cases and 12.5% cases had malignant lesions. There were inconclusive FNACs in 25% cases. According to Chi square test, p value was 0.107, which was insignificant. In a similar study by Upasana et al., the following lesions were recognized in FNAC where 63.3% cases belonged to Pleomorphic adenoma, chronic sialadenitis was present in 13.3% cases, Warthin's tumor was present in 3.3% cases, cystic lesions were seen in 4.2% cases (8), Mucoepidermoid carcinoma was observed in 5% cases, Acinic cell carcinoma was present in 2.5% cases, Carcinoma ex-pleomorphic adenoma was seen in 2.5% cases, metastatic deposits were observed in 1.6% cases, benign parotid tumor was present in 1.6% cases, Malignant tumor (non-specific) was seen in 1.6% cases and Neuroblastoma was present in only 0.83% case (13).

According to present study, FNAC had the sensitivity of 38.89%, specificity was 100%, positive predicted value was 100%, negative predicted value was 77.55% and accuracy was 80.36%. This was according to the study done by Upasana et al., who observed similar results with FNAC with the sensitivity, specificity, diagnostic accuracy, positive predictive value, and negative predictive value being 89.29%, 91.67%, 86.21%, 96.15% and 78.57% respectively (13). This draws our attention to the fact that FNAC is an important tool for diagnosing the salivary gland tumors.

Histopathological examination was carried out in every case out of which benign lesions were found in 67.9% cases and 32.1% cases had lesions which were malignant. The well-formed ductal structures made up of outer myoepithelial as well as inner epithelial cells, together with their associated oncocytoid, spindle, mucous, basaloid, squamous, sebaceous, cuboidal, round, polygonal, or clear cell characteristics, comprise the epithelial component. Chi square test was done in which, 0.036 was the p value which was significant.

In 62.5% cases histopathological results were consistent with the FNAC, while in 37.5% cases, HPE results were inconsistent with the FNAC. Statistically significant association was found between FNAC and HPE. This added weight to the statement that histopathological test is important for the confirmation of the diagnosis so that further management can be carried out accordingly.

Out of 67.9% cases who had benign neoplasm, 50% cases had pleomorphic adenoma, 16.1% cases had Warthin's tumor and 1.8% cases had benign intraductal papilloma. Out of 32.1% who had malignancy, 19.6% cases had mucoepidermoid carcinoma, 5.4% cases had adenoid cystic carcinoma and 1.8% cases each had acinic cell carcinoma, Carcinoma ex pleomorphic adenoma, squamous cell carcinoma and lymphoepithelial carcinoma.

Since there is 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 are published from India. As a result, prospective studies involving larger samples are necessary to more accurately identify the influencing factors. Our study was successful in establishing the clinicopathological profile of salivary gland tumors, in which parotid gland was the most commonly involved gland and Pleomorphic adenoma was the most common benign tumor while mucoepidermoid carcinoma was the most common malignant tumour. Our study displayed the importance of some relevant investigations such as FNAC,

MRI and also the histopathological test, which helped us in reaching a particular diagnosis of salivary gland tumor so that we could plan further management accordingly.

5. Conclusion

This study emphasizes how important it is to prepare for the patient's future care by using histopathological analysis of salivary gland tumors that exhibit various structural characteristics associated with benign and malignant salivary gland tumors. The most common site of predilection of salivary gland tumors was parotid and most common subsite was superficial lobe of parotid gland. The most common benign tumor was pleomorphic adenoma followed by Warthin's tumor. The most common malignant tumor was mucoepidermoid carcinoma followed adenoid cystic carcinoma. Out of 56 cases, in 35 cases, the HPE results were consistent with FNAC while in 21 cases, the HPE results were inconsistent. Statistically significant association was found between FNAC and HPE, which led to the conclusion that histopathological examination is necessary for the confirmation of the diagnosis so that further management can be carried out accordingly.

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