

# Clinical and Histopathological Characteristics of Salivary Gland Tumours: A Cross-sectional Study

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## ABSTRACT

**Introduction:** Regional record is a useful strategy for the analysis of the clinicohistopathological presentation of Salivary Gland Tumours (SGTs) in a specific population by which appropriate management can be established.

**Aim:** To investigate the clinicohistopathological presentation of SGTs in a tertiary care cancer centre, Odisha, India.

**Materials and Methods:** This single centre hospital based cross-sectional study was carried in Acharya Harihar Post-Graduate Institute of Cancer, Cuttack, Odisha, India. Five years (from January 2015 to December 2019) clinical and histopathological data of SGTs were retrieved from hospital record section. The data collection and analysis was done from January 2019 to December 2020. The SGTs cases were classified under the histological criteria suggested by the World Health Organisation (WHO) in 2017. Count data were expressed as percentages and differences between the groups were compared using the Chi-square test. The results were analysed using Statistical Package for the Social Sciences (SPSS) computer software version 17.0.

**Results:** A total of 319 neoplastic SGTs were included out of which malignant tumours were comprised of 144 (45.14%). Mucoepidermoid Carcinoma (MEC) was the most common malignant type while Pleomorphic Adenomas (PA) was reported as the most common benign type. The mean±SD age of the patients with benign and malignant tumour was 41.94±13.94 years and 46.09±13.33 years, respectively. The percentage of malignant neoplasms in the minor salivary gland was higher (37/60, 61.66%) than benign tumours. while in major salivary glands, it was found (107/259, 41.31%). In major salivary gland, greater involvement of the parotid gland was observed. The mean tumour size of the major SGT was 3.34±1.09 cm whereas the mean tumour size of the minor salivary gland was 2.35±1.26 cm.

**Conclusion:** The PA and MEC were the most common benign and malignant types respectively. The knowledge regarding histopathological presentation of SGTs in present study would help to pathologist and surgeons for more accurate diagnosis and further management. As, the preoperative diagnosis of SGTs is very challenging, further study in this regard is needed.

**Keywords:** Mucoepidermoid carcinoma, Parotid gland, Pleomorphic adenoma

## INTRODUCTION

The Salivary Gland Tumours (SGTs) represent about 6% of head and neck neoplasms and about 0.5% of all malignancies in humans. Mortality depends on the stage and type of the lesion; however, the five years survival rate is estimated to be 72% [1]. SGTs are of particular interest to both histopathologists and surgeons because of their heterogeneous histological and biological characteristics and the difficulties involved in management [2]. Treatment of this tumour is based on the histological diagnosis. So, correct histological diagnosis is obligatory. Accurate histological diagnosis is dependent on clearly defining the histological cell type and morphological patterns, which is the basis of the 2017 WHO classification of SGTs [3].

Although many retrospective studies regarding the incidence of SGTs have been reported, the epidemiological studies from various parts of the globe revealed, geographical location and ethnic groups influence the incidence and clinicopathological characteristics of SGTs. So, regional records are a useful strategy for the analysis of the distribution and particular features of SGTs in a specific population by which appropriate management can be established [4]. In India, there is a paucity of published literature on the regional variation of incidence and clinicopathological characteristics of SGTs [5].

The study objective was to see the regional prevalence of benign and malignant SGTs and their clinicohistopathological presentation. The knowledge regarding the clinicohistopathological factors would

not only be helpful for preoperative presumptive diagnosis but also for further appropriate clinical management and prognosis.

## MATERIALS AND METHODS

This single centre hospital based cross-sectional study was carried in Acharya Harihar Post-Graduate Institute of Cancer, Cuttack, Odisha. Five years (from January 2015 to December 2019) clinical and histopathological data of SGTs were retrieved from hospital record section. The data collection and analysis was done from January 2019 to December 2020. Histopathological diagnosis and classification of included SGTs were done according to WHO; 2017 guidelines [3]. Institutional ethics committee approval was obtained.

**Inclusion criteria:** Out of the total enrolled cases, only those patients who have presented tumour like lesions in the head and neck region and subsequently diagnosed with neoplastic SGT by histopathology were included.

**Exclusion criteria:** The synchronous cases, non neoplastic salivary gland lesions, metastatic cases, sick patients, and patients having incomplete data were excluded from this study.

From included cases, the data such as age, sex, anatomical site, tumour size, and histopathological characteristics (tumour type, grade, Perineural Invasion (PNI), Lymphovascular Space Invasion (LVS), lymph node status) were obtained from the medical record.

## STATISTICAL ANALYSIS

Measurement data were expressed as the mean±standard deviation. Count data were expressed as percentages and differences between the groups were compared using the  $\chi^2$  test. A p-value of <0.05 was

defined as statistically significant. The results were analysed using SPSS computer software version 17.0.

## RESULTS

A total of 349 SGT cases were included during this study period. Histological diagnosis included 30 (8.59%) cases of non neoplastic lesions and 319 (91.4%) cases of the neoplastic tumour. The clinicopathological characteristics of neoplastic tumours were evaluated in this study. Among neoplastic tumours, benign and malignant tumours were comprised of 175 (54.85%) and 144 (45.14%) respectively. The distribution of benign and malignant SGTs is shown in [Table/Fig-1].

In this study, 153 (47.96%) of affected patients were male and 166 (52.03%) were female. In benign cases, males were slightly predominated over female 94 (53.71%) whereas in malignant cases, females were comprised of 89 (59.02%). This difference was found statistically significant (p-value=0.023).

The age of patients in this study was between 3 and 85 years. The majority of tumours 146 (41.83%) were observed in age between 31 to 50 years. The mean±SD age of the patients with benign tumours was 41.94±13.94 years and it was 46.09±13.33 years in malignant tumours [Table/Fig-1]. This difference was found statistically significant (p-value=0.0073).

Diagnosis	Total No. (%)	Total Mean age±SD (Range years)	Male (N=153) Mean age±SD (Range years)	Female (N=166) Mean age±SD (Range years)
<b>Benign types</b>				
Warthin tumour	11 (6.28%)	58.63±16.76 (26-85)	58.63±16.76 (26-85)	-
Pleomorphic adenoma	155 (88.57%)	39.80±12.80 (13-75)	39.53±12.61 (11-74)	40.09±12.9 (13-75)
Basal cell adenoma	5 (2.85%)	65.75±9.25 (48-75)	65.75±9.25 (48-75)	75
Monomorphic adenoma	1 (0.57%)	34	-	34
Oncocytoma	2 (1.14%)	49.71±17.67 (68)	49.71±17.67 (68)	-
Myoepithelioma	1 (0.57%)	52	-	52
Total benign types	175	41.94±13.94 (13-85)	42.73±14.62 (11-85)	41.02±13.03 (13-75)
<b>Malignant types</b>				
Mucoepidermoid carcinoma	64 (44.44%)	39.44±12.82 (3-70)	42.29±14.78 (3-70)	37.30±11.01 (13-68)
Acinic cell carcinoma	14 (9.72%)	48.78±15.04 (12-75)	43.4±0.96 (41-44)	51.77±19.80 (12-75)
Adenoid cystic carcinoma	38 (26.38%)	48.37±11.50 (22-72)	49.25±12 (36-72)	47.96±11.49 (22-65)
Adenocarcinoma NOS type	12 (8.33%)	55	-	55
Salivary duct carcinoma	6 (4.16%)	64.66±5.33 (59-74)	64.66±5.33 (59-74)	-
Squamous cell carcinoma	7 (4.86%)	52±13.33 (40-72)	72±0 (72)	42±2 (40-44)
Ex-pleomorphic adenoma	2 (1.38%)	56±16 (40-72)	40±0 (40)	72±0 (72)
Basal cell carcinoma	1 (0.69%)	38	-	38
Total malignant types	144	46.09±13.33 (3-75)	44.33±13.13 (3-74)	44.52±13.37 (12-75)

**[Table/Fig-1]:** Mean age±SD (range) and sex wise distribution of benign and malignant Salivary Gland Tumours (SGT).

Forty-three cases (12.32%) were below 18 years of age out of which 29 (67.448%) cases were found to be neoplastic SGTs.

The mean age of male and female in benign tumour was found to be 42.73±14.62 and 41.02±13.03 (p-value=0.4224) while in malignant cases, the mean age of male and female was 48.33±13.13 and 44.52±13.37 years respectively (p-value=0.0924).

The percentage of malignant neoplasms in the minor salivary gland was (37/60, 61.66%) while in major salivary glands, it was found (107/259, 41.31%). On the other hand, maximum numbers (152/259, 58.68%) of benign tumours were observed in the major salivary gland with greater involvement of the parotid gland (119/152, 78.28%). The difference was found statistically significant (p-value=0.004307).

The sex difference between major and minor SGTs was not found statistically significant (p-value=0.9649).

The distribution frequencies of 319 salivary gland neoplasms according to the location are shown in [Table/Fig-2].

Tumour types	Total (N) M:F	Parotid (N) M:F	SMG (N) M:F	SLG (N) M:F	Palate (N) M:F	BM (N) M:F	Lip (N) M:F	Tongue (N) M:F
<b>Benign types</b>								
Warthin tumour	11, 11:0	11, 11:0	-	-	-	-	-	-
Pleomorphic adenoma	155, 79:76	104, 51:53	30, 14:16	1, 0:1	11, 7:4	5, 3:2	4, 4:0	-
Basal cell adenoma	5, 4:1	1, 0:1	2, 2:0	-	2, 2:0	-	-	-
Monomorphic adenoma	1, 0:1	1, 0:1	-	-	-	-	-	-
Oncocytoma	2, 2:0	2, 2:0	-	-	-	-	-	-
Myoepithelioma	1, 0:1	-	-	-	-	-	1, 0:1	-
Total benign	175, 94:81	119, 64:55	32, 16:16	1, 0:1	13, 9:4	5, 3:2	5, 4:1	-
<b>Malignant types</b>								
Mucoepidermoid carcinoma	64, 28:36	48, 21:27	6, 2:4	-	7, 3:4	3, 2:1	-	-
Acinic cell carcinoma	14, 5:9	14, 5:9	-	-	-	-	-	-
Adenoid cystic carcinoma	38, 12:26	9, 2:7	8, 3:5	1, 0:1	9, 1:8	5, 3:2	2, 1:1	4, 2:2
Adenocarcinoma NOS type	12, 2:10	7, 2:5	1, 0:1	-	3, 0:3	1, 0:1	-	-
Salivary duct carcinoma	6, 6:0	4, 4:0	1, 1:0	-	-	-	1, 1:0	-
Squamous cell carcinoma	7, 5:2	5, 5:0	1, 0:1	-	1, 0:1	-	-	-
Ex-Pleomorphic adenoma	2, 1:1	1, 0:1	1, 1:0	-	-	-	-	-
Basal cell carcinoma	1, 0:1	-	-	-	1, 0:1	-	-	-
Total malignant	144, 59:85	88, 39:49	18, 7:11	1, 0:1	21, 4:17	9, 5:4	3, 2:1	4, 2:2

**[Table/Fig-2]:** The distribution frequencies of 319 salivary gland neoplasms according to the location.

SMG: Sub mandibular gland; SLG: Sublingual gland; BM: Buccal mucosa, M: Male; F: Female; N: Numbers

Average size of benign and malignant tumours was 3.27±1.03 and 3.06±1.29 cm, respectively. No statistically significant difference was found. Mean tumour size of major SGT was 3.34±1.09 with range 0.4-9 cm whereas mean tumour size of minor salivary gland was 2.35±1.26 cm, with range 0.3-6 cm. This difference was found statistically significant [Table/Fig-3].

The presence of regional metastasis was only observed in six malignant major SGTs.

In this study, the researchers attempted to compare and analyse the results of clinical (preoperative diagnosis) and histopathological diagnosis. The result is shown in [Table/Fig-4].

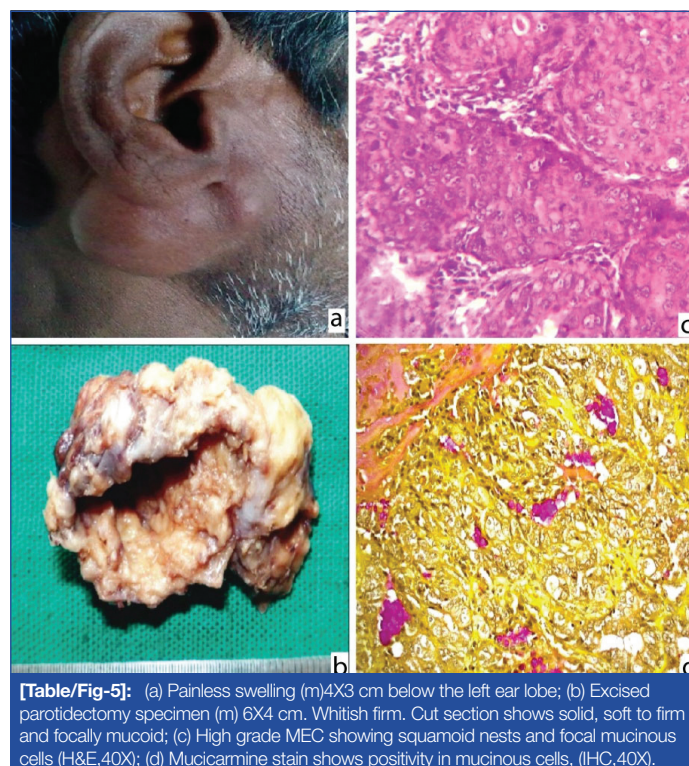
The PA was comprised of the maximum numbers among benign tumours whereas MECs were the highest among malignant tumours. The clinical features and histopathological presentation of benign and malignant SGTs are presented in [Table/Fig-5a-d, 6a-d].

Tumour type vs tumour size	Total Mean±SD Range (cm)	Parotid Mean±SD Range (cm)	SMG Mean±SD Range (cm)	SLG Mean±SD Range (cm)	Palate Mean±SD Range (cm)	BM Mean±SD Range (cm)	Lip Mean±SD Range (cm)	Tongue Mean±SD Range (cm)
<b>Benign tumour types</b>	3.27±1.03 (0.4-9)	3.36±1.04 (0.4-9)	3.25±0.95 (1.5-6)	-	-	3.9±0.13 (3.7-4)	2±1 (1-3)	-
Warthin tumour	3.7±1.32 (2-9)	3.7±1.32 (2-9)	-	-	-	-	-	-
Pleomorphic adenoma	3.31±1.01 (0.4-8)	3.38±1.01 (0.4-8)	3.31±0.95 (1.5-6)	-	3.02±1.18 (0.8-5)	3.9±0.13 (3.7-4)	2±1 (1-3)	-
Basal cell adenoma	1.8±0.75 (1.2-3.3)	-	2.4±0.9 (1.5-3.3)	-	1.2	-	-	-
Monomorphic adenoma	1.5	1.5	-	-	-	-	-	-
Oncocytoma	1.8	1.8	-	-	-	-	-	-
Myoepithelioma	1	-	-	-	-	-	1	-
<b>Malignant types</b>	3.06±1.29 (0.3-8)	3.55±1.13 (0.7-8)	2.59±1.17 (0.8-5)	0.4	2.07±1.18 (0.3-6)	1.97±0.8 (1-4)	1.13±0.8 (0.5-2.8)	3.42±0.67 (2.4-4)
Malignant Mucoepidermoid carcinoma	3.01±1.17 (0.5-6.5)	3.51±1.006 (0.8-6.5)	2.1±0.73 (1-2.8)	-	1.37±0.57 (0.7-2)	1.2	-	-
Acinic cell carcinoma	4.3±1.68 (1.5-8)	4.3±1.68 (1.5-8)	-	-	-	-	-	-
Adenoid cystic carcinoma	2.82±1.1 (0.4-6)	2.88±0.71 (1-4.5)	2.93±1.31 (0.8-5)	0.4	3.16±1.25 (2-6)	2.76±1.008 (1-4)	1.8±1 (0.8-2.8)	2.87±1.12 (1.6-4)
Adenocarcinoma NOS type	2.45±1.3 (0.3-4.6)	3.55±0.62 (2.4-4.6)	1.6	-	0.63±0.22 (0.3-0.9)	1	-	-
Salivary duct carcinoma	3.2±1.03 (1-5)	3.55±0.55 (2.5-4.2)	5	-	-	-	1	-
Squamous cell carcinoma	1.82±1.04 (0.7-3.9)	2.2±1.16 (0.7-3.9)	1	-	0.8	-	-	-
Ex-Pleomorphic adenoma	2.75±0.75 (2-3.5)	3.5	2	-	-	-	-	-
Basal cell carcinoma	1	-	-	-	1	-	-	-

**[Table/Fig-3]:** Mean tumour size±SD, range (cm) of major and minor Salivary Gland Tumours (SGT).  
SMG: Sub mandibular gland; SLG: Sublingual gland; BM: Buccal mucosa; SD: Standard deviation

Clinical diagnosis	No.	Histopathology diagnosis			Accuracy (%)
		Non neoplastic	Benign	Malignant	
<b>Parotid non neoplastic</b>	28	5	6	17	17.85%
Benign	157	1	110	46	70%
Malignant	28	-	3	25	89.28%
<b>SMG non neoplastic</b>	19	8	3	8	42.1%
Benign	36	1	29	6	80.55%
Malignant	4	-	-	4	100%
<b>SLG non neoplastic</b>	-	-	-	-	-
Benign	1	-	1	-	100%
Malignant	1	-	-	1	100%
<b>Palate non neoplastic</b>	7	-	1	6	0
Benign	21	-	12	9	57.14%
Malignant	6	-	-	6	100%
<b>BM non neoplastic</b>	4	-	3	1	0
Benign	9	-	2	7	22.2%
Malignant	1	-	-	1	100%
<b>Lip non neoplastic</b>	15	10	4	1	66.6%
Benign	5	4	1	-	20%
Malignant	2	-	-	2	100%
<b>Tongue non neoplastic</b>	-	-	-	-	-
Benign	3	1	-	2	0
Malignant	2	-	-	2	100%
<b>Total non neoplastic</b>	73	23	17	33	31.5%
Benign	232	7	155	70	66.81%
Malignant	44	-	3	41	93.18%

**[Table/Fig-4]:** Site wise distribution of preoperative diagnostic accuracy of Salivary Gland Tumours (SGT).  
SMG: Sub mandibular gland; SLG: Sublingual gland; BM: Buccal mucosa

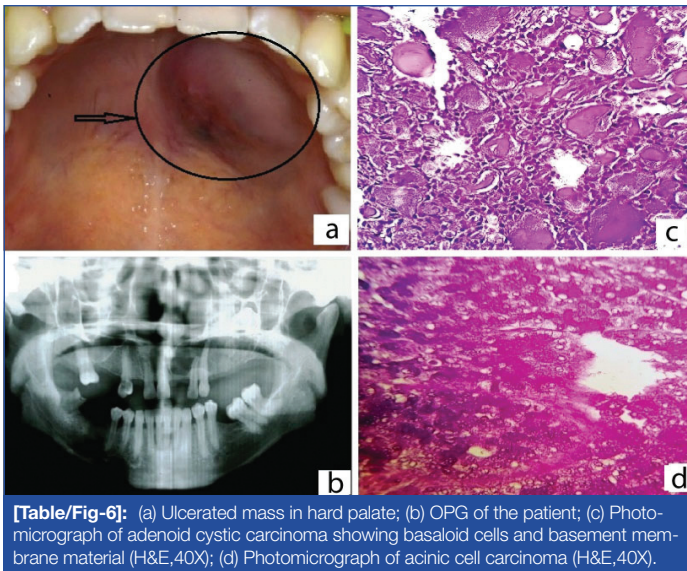


**[Table/Fig-5]:** (a) Painless swelling (m)4X3 cm below the left ear lobe; (b) Excised parotidectomy specimen (m) 6X4 cm. Whitish firm. Cut section shows solid, soft to firm and focally mucoid; (c) High grade MEC showing squamoid nests and focal mucinous cells (H&E,40X); (d) Mucicarmine stain shows positivity in mucinous cells. (IHC,40X).

## DISCUSSION

We observed dominance of neoplastic lesion, among which benign tumours were predominated. These findings were similar to the previous study reports from India as well as other parts of the globe [5-7].

On the other hand, Shukla NK et al., found more numbers of malignant tumours (77.5%) than benign tumours while Tilakarathne WM et al., reported an almost equal frequency of benign and malignant tumours [8,9].



**[Table/Fig-6]:** (a) Ulcerated mass in hard palate; (b) OPG of the patient; (c) Photomicrograph of adenoid cystic carcinoma showing basaloid cells and basement membrane material (H&E,40X); (d) Photomicrograph of acinic cell carcinoma (H&E,40X).

In previous studies, some have reported women predominance with an average of 55.4% while some other authors have reported men predominance [7]. It has also reported that, benign tumours are more common in women, while malignant tumours are more common in men [6,7].

According to a study report by Bobati SS et al., the mean age of malignant and benign tumours was found to be 45 and 35 years, respectively [5]. In this study, patients with malignant salivary gland neoplasms were older than patients with benign tumours. But in another study done by Jansisyant P et al., reported that patients affected by malignant tumours were on average 6 years younger than those affected by benign neoplastic tumours [10]. In the paediatric population (<18 years age), no significant sex difference was observed (male to female ratio 1:1.07) in this age group, and the mean age of paediatric patients was 15.1 years while in another study female predilection was observed (male to female ratio 1:1.25) with mean age 13.74 [11]. The most common benign tumour was PA, and the most common malignant tumour was MEC. The above findings were similar to the study report from India and other parts of the globe [11].

In this present study, a higher percentage of major SGTs as compared to minor SGTs were found which were similar to the previous study reports [5,6]. But in another study, there was a greater incidence of minor SGTs as compared to major SGTs [12]. Unlike other studies, parotid was found the most common among major salivary glands while the palate was found the most commonly affected site among minor salivary glands [5,13,14]. The percentage of malignant tumours was highest in minor salivary glands, which was consistent with the previous study report [15].

Unlike other studies, PA was found the most common benign SGT with male predilection in both major and minor salivary gland [5-7,16].

According to the literature review, it was found relatively rare in children and the majority of cases are occurring in the major salivary gland, especially parotid. It is rare in minor salivary glands and if it occurs, it involves the palatal gland (42.8–68.8%), followed by the upper lip (10.1%) and cheek (5.5%) [16]. The PAs of the minor salivary glands typically present as painless submucosal swellings with diameter range from 2-6 cm, but some tumours can be huge. They are usually encapsulated, solitary, well-defined, ovoid, or round masses [17].

In this study, the Warthin tumour was the second most common benign salivary gland neoplasm. Similar findings were observed by different investigators [5,6].

This tumour was found only in the male and occurred exclusively in the parotid gland which was consistent with the previous study

reports [5-8]. But in recent studies, the difference has been on the decline and reached up to 1:1 [18]. Warthin tumour has the highest incidence in the early '60s and occasionally occurs in young patients. In men, the peak incidence is in the 7<sup>th</sup> decade whereas it is the 6<sup>th</sup> decade in women.

It has also been described in other extremely uncommon sites, including sub maxillary or sublingual or minor salivary glands [18].

Malignant transformation and the incidence of recurrence after surgical treatment is extremely rare. Partial, subtotal, or total parotidectomy with preservation of the facial nerve is the best treatment of choice.

Basal Cell Adenoma (BCA) of the salivary gland is a rare neoplasm (1–2%) of all SGTs. According to the study report, the most frequent location of BCA is the parotid gland, followed by the upper lip, Buccal mucosa, lower lip, and palate. This tumour most frequently affects patients between their 5<sup>th</sup> and 7<sup>th</sup> decades and most often presents as a slow-growing, asymptomatic, freely movable mass, which is often observed in women above 50 years of age. In contrast to Pleomorphic adenoma, it tends to be multiple and its recurrence rate after surgical excision is high [19].

The MEC was the most common malignant SGT, which was similar to the results of other studies [5-7]. In contrast, to other studies, Adenoid Cystic Carcinoma (ACC) was found the most common malignant SGT [8,20].

In this study, the preferred localisation of MEC was the major salivary glands which were in agreement with the previous study findings [13,20]. But in another study, MEC cases were most commonly observed in the minor salivary glands [7].

AdCC occurred in equal frequencies in the major and minor glands. However, some studies have shown AdCC to be more common in the minor salivary glands (hard palate, followed by the base of the tongue where up to 96% of all tumours are malignant) than in the sub mandibular and parotid glands. AdCC located in the tongue occurs more frequently in female patients [7,21]. The most frequent clinical feature of AdCC affecting the major salivary gland is reported to be the presence of tumour-usually 2-4 cm at its greatest diameter and intra oral ACC seldom larger than 3 cm at its greatest diameter [22]. In this study, two patients were presented >3cm (4 cm in the tongue and 6 cm in the hard palate).

In relation to MEC and AdCC, the other published series have not been able to establish a gender predilection for either lesion [23]. But in this study, both tumour types were found female predominance.

Another uncommon epithelial malignant neoplasm of the salivary glands that mostly affects women is ACC. It arises most frequently in the parotid gland, other sites being the sub mandibular gland and minor salivary gland. It is the second most common SGT in children.

The ACC is seen most widely in the 4-6 decades of life affecting women than men in the ratio 3:2. The most common presentation is a well-defined painless solid mass [24]. Salivary duct carcinoma is a rare tumour that makes up 1-3% of all malignant SGTs. It occurs more commonly in the parotid gland than in the sub mandibular or minor salivary glands. It may develop from a pre-existing pleomorphic adenoma in some cases, but it can also occur de novo. Patients are typically elderly men, ranging in age from 55-61 years. It manifests as a rapidly expanding mass that grows rapidly, with the potential for early distant metastases, local recurrence, and a high mortality rate [25].

Carcinoma ex Pleomorphic adenoma (Ca.Ex-PA) is a carcinoma that develops from a benign pleomorphic adenoma that is either primary or recurrent. This tumour most commonly present a firm mass in the parotid gland and creates preoperative diagnostic difficulties. The macroscopic characteristics of this neoplasm are determined by the proportion of adenoma and carcinoma components [26].

The PSCC accounts for less than 1% of SGTs. The parotid gland accounts for about 80% of PSCC cases, while the submandibular gland accounts for 20% [27]. Patients with PSCC of the submandibular gland normally present with a heavy, sometimes fixed mass and a one-year or less background. PSCC occurs in the 6<sup>th</sup> to 8<sup>th</sup> decades. The male to female ratio is 2:1.

It has been observed that benign tumours tend to be insidious and slow-growing, whereas malignant lesions develop quickly (often in less than a year), stick to deep layers, and have an ulcerated or telangiectatic surface. The most telling sign of cancer is pain.

Moreover, benign tumours were found to be significantly smaller than malignant tumours and disease duration was significantly longer for benign tumours. Regional and distant metastasis is important clinical signs of malignancy, but in our study, none of the cases were presented distant metastasis while regional metastasis was rarely observed [28].

As the most common clinical presentation of both benign and malignant SGTs in this study was a symptom less mass or lump over the affected area. It is very difficult to distinguish the disease on the basis of clinical signs and symptoms. So appropriate surgical intervention should be recommended in patients with parotid tumours clinically suspected to be malignant, and all submandibular, sublingual, and minor SGTs.

### Limitation(s)

It was a single hospital-based study. Clinicopathological factors related to the prognosis of SGTs were not analysed.

### CONCLUSION(S)

The PA and MEC were the most common benign and malignant types respectively. The knowledge regarding histopathological presentation of SGTs in present study would help pathologist and surgeons for more accurate diagnosis and further management. Still, the preoperative diagnosis of SGTs is challenging. Further study in this regard would help to establish presumptive early diagnostic method.

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