ORIGINAL RESEARCH

An Institution based Epidemiological and Clinicopathological study of Intraoral Minor Salivary Gland Neoplasms: A Report of 36 Cases

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Abstract

Background: Minor salivary gland neoplasms (MSGNs) are infrequent intraoral tumors constituting only 10-15% of head and neck neoplasms. They demonstrate a wide diversity in biologic behavior. Literatures on their epidemiological trends, clinical presentation, and histopathological spectrum remains limited due to their rarity.

Aim: This study aims to add valuable input to the clinicopathological and histological profile of MSGNs for early diagnoses, prognostic evaluation and better management.

Methods and Material: A total of 36 cases of MSGNs were recorded in this institution over a period of 5 years, between 2020'May to 2025'May. Major salivary gland tumors and inflammatory lesions of the glands were excluded. Statistical evaluation was done using IBM SPSS (version 27.0), Software. Association was tested using inferential statistics, primarily the Fischer test, with P≤0.05 being statistically significant.

Results: Among the 36 study subjects, benign and malignant lesions were more common in the 40–49 year age group (73%) and 30–39 year group (56%), respectively. The benign lesions showed equal male-female predilections. The malignant lesions showed a higher proportion in males (45%) as compared to the females (31%). The preferential locations for benign and malignant MSGNs were the soft palate (57%), and the retromolar trigone area (13%) respectively. Pleomorphic adenoma was the most common benign lesion (38.89%), while the low-grade mucoepidermoid carcinoma (19.44%) was leading the malignant subtype.

Conclusions: Compiling the overall data, pleomorphic adenoma was the most common benign lesion (38.89%), while the low-grade mucoepidermoid carcinoma (19.44%) was leading the malignant subtype.

Keywords- Minor salivary gland neoplasm, Mucoepidermoid Carcinoma, Palate, Pleomorphic adenoma, Retromolar trigone.

Introduction

Minor salivary gland neoplasm (MSGNs) are uncommon entities, representing 10–15% of all salivary gland neoplasms and less than 1% of all tumors.[1-6] They most frequently arise in the palate (50%), lips (15%), buccal mucosa (12%), tongue (5%), and floor of the mouth (5%).[7] Despite their rarity, MSGNs are highly diverse and nearly 50% are malignant, particularly those in the floor of the mouth, retromolar trigone, tongue, and lower lip.[1] In contrast, tumors of upper-lip region are largely benign. Benign MSGNs, are largely present in the fourth decade of life, and grow slowly over 3–6 years. In contrast, malignant lesions tend to peak in the fifth decade, grow rapidly within a year, and often ulcerate.[1,8-11] Clinical signs suggestive of malignancy include pain, fixation, surface ulcerations, and lymphadenopathy. Recurrence is strongly linked to incomplete excision, occurring in 5–30% of cases. Approximately 6% of benign and 65% of malignant MSGNs relapse, reflecting their myriad biological behavior and initial treatment inadequacy.[9,12-15] With this background, this study aims to evaluate the epidemiological and clinicopathological characteristics of intraoral MSGNs to add further valuable inputs.

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Conflict of Interest: None

Materials and Methods

Study Design and Sample Collection:

This study was designed as an institution based observational study. All histopathologically confirmed intraoral

MSGNs diagnosed between May 2020 and May 2025 (n=36) were recorded. The relevant demographic, clinico-radiological, and histopathologic data were obtained from the institutional departmental records. Sample selection was based on defined inclusion and exclusion criterias.

Inclusion Criteria:

Histopathologically confirmed intraoral MSGNs, either benign or malignant, with adequate clinical and demographic data, were selected.

Exclusion Criteria:

Major salivary gland tumors, cases with incomplete clinical or histopathological documentation or non-neoplastic inflammatory conditions of minor salivary glands, were excluded. Neoplasms arising from ectopic minor salivary tissue or from odontogenic cystic linings were also excluded.

Statistical Analysis:

The collected data were analyzed using IBM SPSS Software Statistics Version 27.0. Normality was assessed using the Shapiro–Wilk test and visual inspection (histograms, Q–Q plots, box plots), which confirmed skewness in all quantitative variables.

Descriptive statistics were presented as frequencies and percentages for categorical variables, and as mean ± SD or median (IQR) with minimum–maximum values and 95% confidence intervals for quantitative variables.

Fisher's exact test was used to evaluate associations between categorical variables. Welch's t-test was applied to compare lesion area and duration across histopathological diagnoses. The P value of ≤ 0.05 was considered statistically significant.

Ethical Consideration:

The study was approved by Institutional Ethics Committee approval no. RADCH/EC/048/2025.

Results

Demographic Profile:

A total of 36 intraoral MSGNs were analyzed. The mean age of the patients was 43.72 years, with a median age of 40 years and a range of 11–75 years. The age distribution showed clustering in the 40–49-year group. The distribution pattern has been shown using a bar graph. (graph 1)

Of the total cohort, benign neoplasms constituted 22 cases (61%), while 14 cases (39%) were malignant.

The overall data shows, 20 (56%) were male and 16 (44%) were female patients. The distribution of benign (55% in males; 69% in females) and malignant lesions (45% in males; 31% in females) showed no significant sex-based differences (P = 0.50).

Clinical Characteristics:

On summarization of the various clinical aspects, of MSGNs showed a wide range of findings.

Considering the size of the lesion, the mean lesional area was slightly higher in malignant cases (2.68 ± 1.54 cm^2) as compared to the benign lesions (2.29 ± 1.30 cm^2); although this difference did not reach statistical significance ($t = -0.78$, $P = 0.443$).

Considering the mean duration of symptoms, both benign and malignant categories includes long-standing cases. So, no significant conclusion can be drawn on the growth patterns as both benign and malignant groups showed overlapping histories of lesional duration.

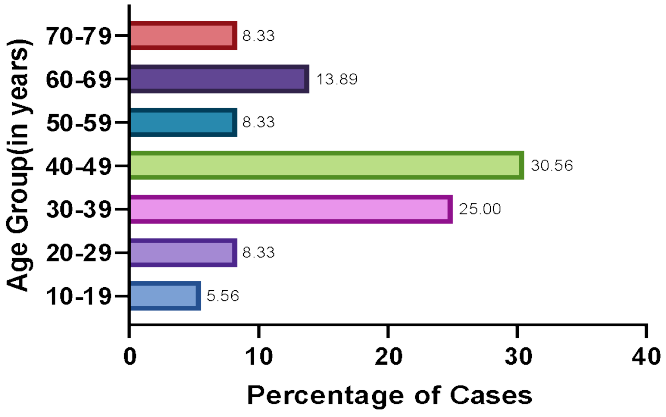
Site Distribution:

The most frequently involved anatomical site was the soft palate accounting for 17 of 22 benign cases (57%) and 5 of 14 malignant cases (22%), followed by the buccal mucosa in 5 of 22 benign cases (17%) and 5 of 14 malignant cases (22%). Involvement of the vestibular mucosa was seen in 4 of 22 benign cases (13%) and 5 of 14 malignant cases (22%). The distribution of the study subjects according to the anatomical sites has been shown in graph-2. Other less common sites included the lower lip (1/22; 3% benign; 0/14; 0% malignant), tongue (0/22; 0% benign; 1/14; 4% malignant), and maxillary tuberosity (1/22; 3% benign; 0/14; 0% malignant). Retromolar trigone involvement showed predilection for malignant cases (3 of 14; 13%). Strikingly no benign lesion was received involving this site in our study. A significant association was observed between lesion site and histopathological diagnoses (P = 0.044). Post-hoc analysis indicated that benign lesions were significantly more common in soft palate region, whereas the retromolar trigone demonstrated a clear predilection for malignant lesions. (Table 1)

Findings related to surface ulceration, pain, and growth pattern showed no significant association with histopathological diagnosis (all P > 0.05). Surface ulceration was present in 4 of 22 benign cases (18%) and 4 of 14 malignant cases (29%), without a much difference between the groups (P = 0.683). Pain was reported in 3 out of 22 benign lesions (14%) and 1 out of 14 malignant lesions (7%).

Histopathological Distribution:

Benign lesions occurred most frequently among individuals aged 40–49 years, whereas malignant lesions were more common in the 30–39year and 50–59 age year groups. Predominantly the most common benign lesion was pleomorphic adenoma (38.89), whereas the most common malignant lesion was mucoepidermoid carcinoma (19.44%) followed by adenocarcinoma (8.33%). Distribution of study subjects according to the histopathological diagnoses has been shown using a bar graph (graph-3).



Graph 1: Distribution of study subjects according to Age

Table 1. Association between categorical clinical characteristics and histopathological diagnosis in salivary gland lesions:

Outcome Variables	Category	Benign (n = 22)	Malignant (n = 14)	Overall (N = 36)	P value[a]
Site[†]	Soft palate	17 (57%)[a]	5 (22%)[b]	22(42%)	0.044*
	Buccal mucosa	5 (17%)	5 (22%)	10(19%)	
	Tuberosity	1 (3%)	0 (0%)	1(2%)	
	Retromolar trigone	0 (0%)[a]	3 (13%)[b]	3(6%)	
	Lower lip	1 (3%)	0 (0%)	1(2%)	
	Tongue	0 (0%)	1 (4%)	1(2%)	
	Vestibular mucosa	4 (13%)	5 (22%)	9(17%)	
	Others	2 (7%)	4 (17%)	6(11%)	
Surface ulceration	No	18 (82%)	10 (71%)	28 (78%)	0.683 (NS)
	Yes	4 (18%)	4 (29%)	8 (22%)	
Pain	Absent	19 (86%)	13 (93%)	32 (89%)	>0.99 (NS)
	Present	3 (14%)	1 (7%)	4 (11%)	
Growth pattern	Gradual	20 (91%)	13 (93%)	33 (92%)	>0.99 (NS)
	Slow	2 (9%)	1 (7%)	3 (8%)	
Perineural Invasion	Absent	22 (100%)	14 (100%)	36(100%)	>0.99 (NS)
Radiologic features	Nothing significant	22 (100%)	14 (100%)	36(100%)	>0.99 (NS)

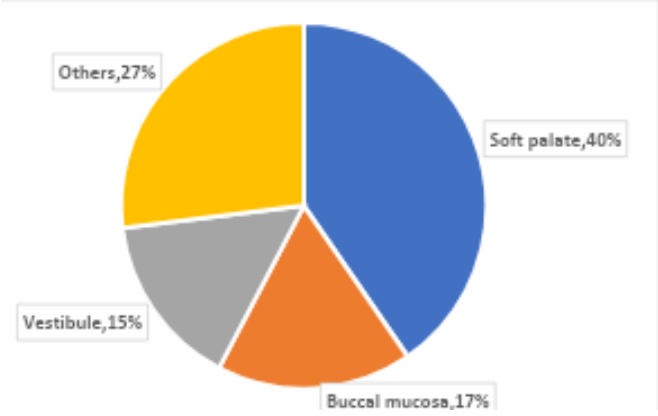
n: number of subjects per HPE diagnosis; *N*: Total Sample size

a-analyzed by the Fisher's test

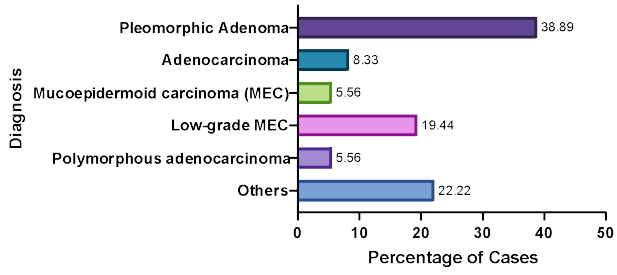
NS:not significant(P>0.05),*: Significant at P≤0.05

†:Multiple subjects had lesions occurring at more than one site

#: responses were significantly different from the rest of the responses



Graph 2: Pie Chart showing the distribution of subjects according to the anatomical sites of the lesions.



Graph 3: Distribution of study subjects according to the histopathological diagnoses

Discussion:

Minor salivary gland neoplasms constitute a biologically diverse group of tumors, with considerable variability across populations and clinical profile.[1,2-7] The present study with analysis of 36 cases of MSGNs provides a valuable insight into the demographic, clinical, and histopathological characteristics of these heterogenous tumors. It further allows a comparison with established previous literatures, particularly the works of Jansisyanont et al. (2002) and Pons-Vicente et al. (2008).[1,8]

In this study, the overall mean patient age for MSGNs is 43.7 years, which is younger than the age profiles reported by Jansisyanont et al. and Pons-Vicente et al. Both the reference studies demonstrated peak incidence between the fifth and seventh decades. In our study, the mean age for benign tumors is 40-49 years and that for malignant tumors is 30-39 years.[1,8,16] The younger age predilection in this cohort may be hypothesized by population-based differences, earlier healthcare-seeking behavior and referral-related factors.

Considering the gender predilection, this study showed equal distribution of benign lesions in both the sexes. Malignant lesions showed a slightly higher proportion in males (56%) as compared to females (44%), which is in disagreement with the study done by Jansisyanont et al. and Pons-Vicente et al. Female-to-male ratios of 1.6:1 and 2:1 were observed respectively in their studies.[1,8,16] This suggest that sex predilection is influenced by population pool, referral patterns and intrinsic tumor biology. Further molecular studies are invited to justify bias related to gender predilections.

In the present study, most of the tumors are of benign category (61%). This is in sharp contrast to the studies of Dmitry Jose de Santana Sarmento (2016) and Sharma S et al (2024), where a preponderance of malignant tumors were noted by 76.3% and 72.27% respectively. This contrast can be attributed to the "harvesting effect" described in their paper, which stated, malignant cases were more often referred to a maxillofacial oncology unit, leading to an increased representation of such lesions.[1,3-7,17]

On the other hand, the 2008 Barcelona study documented 94.4% benign cases due to an opposite referral trend, where primary clinics handled the cases, among which mostly were benign lesions.[1,8]

Case distribution in our study therefore stands in between the two extremes. This reflects a balanced representation without significant referral bias, as all received cases are recorded in our institution only, which is a multidisciplinary unit.

While considering the anatomical predilection of MSGNs, the palate was the most common site of occurrence in this study, being consistent with global literatures. Benign lesions showed a broader distribution. The most frequently involved site being the soft palate (57%), is followed by buccal mucosa (17%), vestibular mucosa (13%) and lower lip (3%).[2,4,7,18] Malignant lesions involved the retromolar trigone and vestibular mucosa predominantly. The retromolar area was exclusively involved

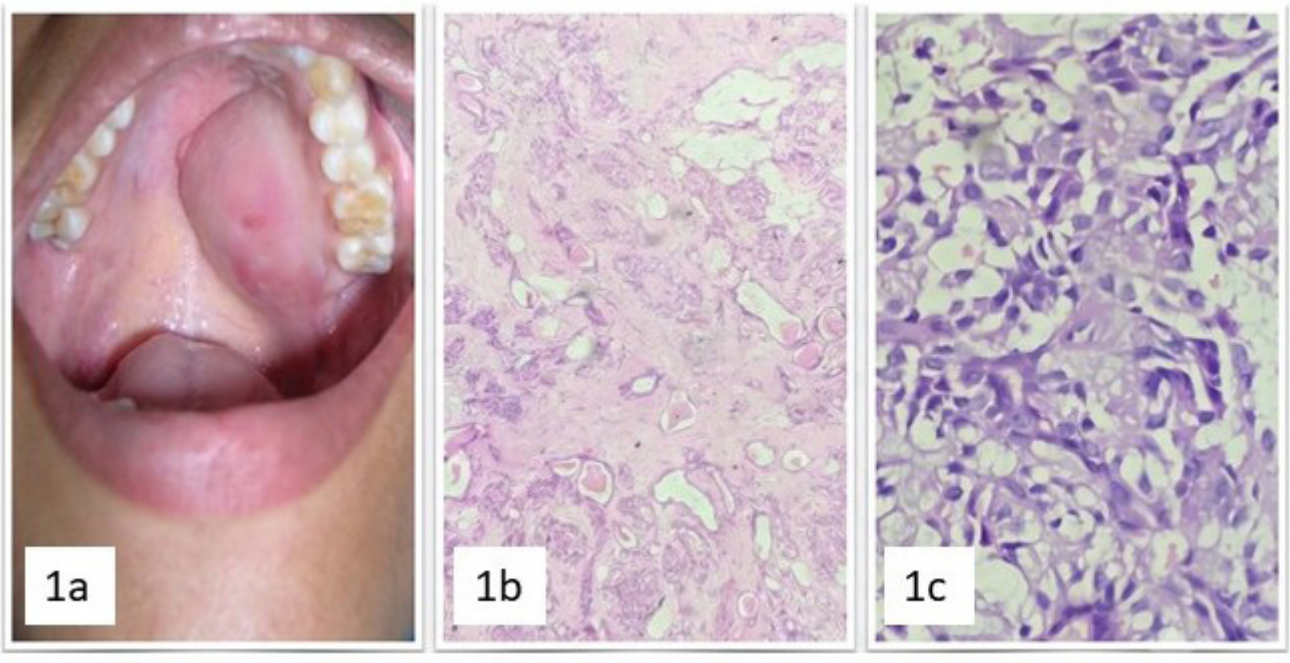


Fig. 1: 1a: A case of Pleomorphic adenoma showing intraoral presentation, as a smooth surfaced, firm, expansive growth involving left hard & soft palate region, with extension from 23 to 28 tooth region. **1b:** H&E (10X): tumor shows chondromyxoid stroma having glandular epithelial and ductal components with varying diameters of lumina. **1c:** H&E (40X): The lesion demonstrates predominantly plasmacytoid and spindle- shaped myoepithelial cells within a chondromyxoid stroma showing focal hyalinization. Ductal structures are present, accompanied by eosinophilic coagulum-like deposits. Focal adipocytic changes also noted.

by malignant cases (13%), which marks it as a significant finding. Jansisyanont et al. similarly reported 8.2% involvement of malignant tumors in the retromolar fossa.[1,2,4,11,15,17] This reinforces the concept that the retromolar lesions warrant high suspicion for malignant MSGNs. This further emphasizes the diagnostic challenges that may be faced in day-to-day clinical practices. Characteristically, the neoplastic lesions may be masked by or misinterpreted as inflammatory pathologies, like pericoronitis, leading to delayed and incorrect diagnoses. Histopathological evaluations following biopsy are of utmost necessities in such instances to rule out the possibility of malignant lesions.

The study by Pons-Vicente et al. also recognized the retromolar trigone as an important site for MSGNs, although with a mix of benign and malignant lesions.[1,2,4,8]

Our study shows a statistically significant association between lesional site and histopathological diagnoses (P = 0.044), highlighting the strong predilection of benign tumors for palate and malignant lesions for retromolar entities.

Considering the clinical presentation & in agreement with both the previous studies, most lesions in our study presented as painless, slowly growing masses. More than 90% of our cases showed gradual enlargement. Pain and ulceration were not strongly associated with malignancy—similar to the findings

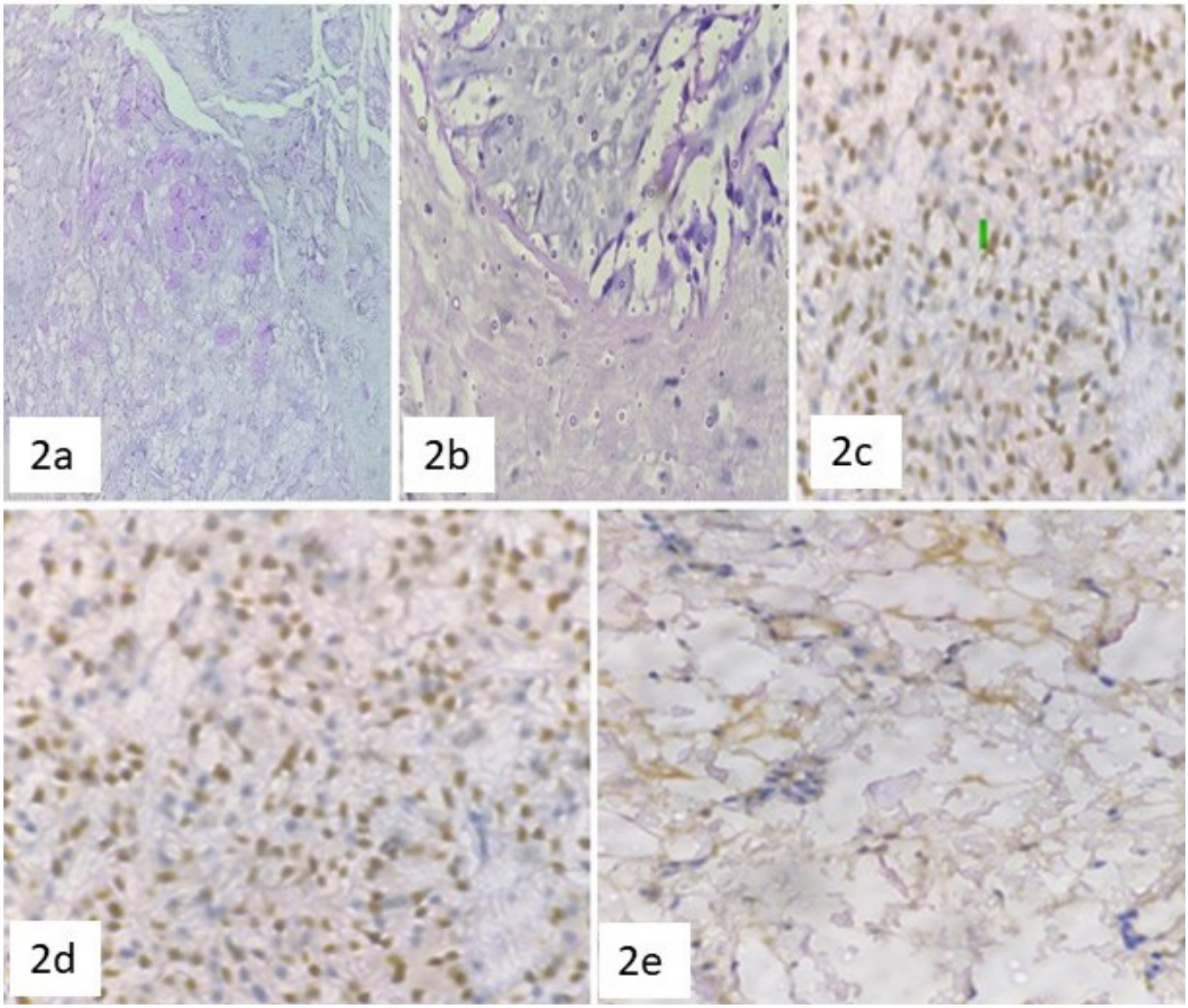


Fig 2: 2a & b Histopathologically (H&E- 10X & 40X), the tumor (SMEC) comprised epithelial nests with occasional central keratinization, peripheral atypical basaloid cells, and scattered mucin-containing cells within a prominently fibrosclerotic stroma. **2c:** IHC showing strong p40 nuclear positivity involving lesional epidermoid/tumor cells; **2d:** MUC5 is focally positive; **2e:** patchy Ki67 staining noted.

of Pons-Vicente et al. They recorded ulceration in only 16.7% of cases, including some benign tumors.[1,8,15,17] Our study exhibits an overall 18% benign cases and 29% malignant cases with surface ulcerations. By this, it can be hypothesized that, there is no definite association of factors, such as surface ulcerations, pain, or growth rate, to the of characterization of malignant lesions. It further reinforces the long-standing literary findings. So clinical features alone shouldn't be considered to differentiate benign and malignant MSGNs. The extremely low rate of symptomatic cases (with pain and ulceration) in our study further supports the literature that malignant MSGNs often mimic benign conditions clinically.

Other interesting findings in our study shows that malignant lesions in this cohort had variable history of durations, though not statistically significant. Jansisyanont et al. observed that malignant tumors frequently demonstrated a rapid growth spurt, with 50.8% cases presenting significant increase in tumor size within one year.[1] In contrast, the benign tumors characteristically showed a slow, indolent course, enlarging gradually over periods, often exceeding a year. Our findings showed comparable duration ranges for both malignant and benign lesions. This suggests patients with delayed presentation of malignant cases with overlapping clinical behavior.[1,5,8,15,18]

Considering the histopathological diagnosis, and reflecting the reference studies our study emphasized pleomorphic adenoma as the dominant benign tumor and mucoepidermoid carcinoma as the most common malignancy. The significant involvement of the palate by benign cases (predominantly pleomorphic adenoma), in our study, also aligns well with both the reference works.[1,2,5,7,18] Genetic profiling shows, pleomorphic adenomas demonstrate recurrent chromosomal rearrangements involving the PLAG1 and HMGA2 genes. On the other hand, mucoepidermoid carcinoma is molecularly characterized by MAML2-associated gene fusions, particularly the CRTC1–MAML2 fusion.[2,16,19-24]

Histologically, pleomorphic adenoma showed epithelial (ductal) cells having varied arrangement patterns like ducts tubules, nests within a chondromyxoid stroma. Plasmacytoid and spindle-shaped myoepithelial cells were also visible. (Fig 1) Sclerosing mucoepidermoid carcinoma of the salivary gland (SMEC) is a rare subtype of mucoepidermoid carcinoma (MEC), initially described in 1987 by Chan and Saw.[25] In our study, we noted an instance of SMEC. Histopathologically, the tumor comprised epithelial nests with scattered mucin-containing cells in a predominant fibrosclerotic stroma. Immunohistochemically, the tumor cells showed positivity for CK7 and p40, with focal expression of MUC5. The p63 positivity highlighted the myoepithelial cells, while smooth muscle actin (SMA) demonstrated periductal positivity. The Ki-67 labeling index was low, ranging between 4–5%. (Fig 2)

Comment on perineural invasion cannot be done as it warrants close vigilance of the overall tumor mass after complete surgical removal. As most of the documented cases were incisional biopsy samples, conclusive decision cannot be done pertaining to perineural invasions.

Radiologic investigations in our study did not reveal significant diagnostic differences between benign and malignant lesions, a finding consistent with Pons-Vicente et al. Corroborating to their finding, it can be concluded that imaging is helpful for surgical planning and servs as an adjunct to diagnostic protocols[8,13].

The following comparative analysis of our study with that of the other studies, demonstrates, that, although geographical and institutional differences influence the proportions of benign and malignant MSGNs, the clinical ambiguity, overall palatal predilection as a favoured anatomical site, and histopathological diversity remain as universal features[3,9,13-14].

Comparative Overview:

Parameter	Present Study	Jansisyanont *et al.* (2002)	Pons-Vicente et al. (2008)
Sample size	36	80	18
Mean/median age	43.7 / 40	54–60	51.8
Sex predilection	Mild male	Female	Female
Benign: Malignant	61: 39	23: 76	94: 6
Palate involvement	High	High	Very high
Retromolar involvement	Malignant-specific	Mostly malignant	Mixed
Pain/ulceration	Not predictive	Not predictive	Not predictive
Perineural invasion	None	Present in ACC	Rare

Clinical Implications:

Biopsy remains indispensable for confirmatory diagnoses as clinical features alone are insufficient in distinguishing benign from malignant lesions.

Site-specific suspicion should guide for urgent intervention, especially for retromolar lesions.

Long-term follow-up is essential, as malignant transformation of benign lesions and recurrences are well-documented in the literature.

Early detection strategies may help reduce diagnostic delays, particularly pertaining to the younger age group in any population.

Limitations of the study:

The present study has certain limitations. As single-institution based setting, the study design may influence the observed clinicopathological distribution. The absence of uniform long-term follow-up and advanced molecular analysis, restricted the detailed evaluation of the tumor behavior and prognostic outcomes.

Conclusion

The findings of our study, are broadly consistent with established literatures. The factors like palatal predominance, overlapping clinical characteristics between benign and

malignant lesions, and the importance of histopathology for confirmatory diagnoses, mirror global evidences. Variations in parameters like age distribution and benign–malignant ratios, highlight the influence of referral patterns and geographical differences.

Overall, the findings underscore the critical importance of early histopathological confirmation, meticulous clinical assessment, and sustained long-term follow-up in the effective management of minor salivary gland neoplasms.

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