

Comparison of Pleomorphic Adenoma in Major and Minor Salivary Glands of Oral Cavity: A Hospital-Based Study

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Received: 08-01-2025 / Revised: 12-02-2025 / Accepted: 19-03-2025

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Conflict of interest: Nil

Abstract:

Background: Pleomorphic adenoma (PA), also referred to as benign mixed tumor, represents the most common benign neoplasm of the salivary glands. While both major and minor salivary glands can be affected, the clinical presentation, demographic profile, histopathological features, and recurrence potential may vary depending on the site of origin. Understanding these differences is essential for early diagnosis, effective treatment planning, and long-term patient management.

Aim and Objective: The present hospital-based study was conducted to compare the clinicopathological characteristics of pleomorphic adenomas arising from major and minor salivary glands of the oral cavity, and to analyze the demographic distribution, site predilection, histological patterns, and recurrence rates associated with each group.

Materials and Methods: A retrospective review was performed on 60 histopathologically confirmed cases of pleomorphic adenoma treated between January 2019 and December 2019 at the Department of Dentistry, Narayan Medical College and Hospital, Sasaram, Bihar, India. Patients were categorized into two groups: Group I (Major salivary gland PA) and Group II (Minor salivary gland PA). Demographic data, lesion location, tumor size, histopathological features, surgical treatment, and recurrence outcomes were analyzed. Statistical analysis was performed to compare clinicopathological variables between both groups.

Results: Out of 60 cases, 36 involved major salivary glands and 24 involved minor salivary glands. The parotid gland was the most frequently involved major gland, while the palate was the most common site for minor salivary gland involvement. Female predominance was observed in both groups. Histologically, myxoid stroma was more prominent in minor salivary gland tumors, while major gland tumors exhibited more epithelial components. Recurrence was slightly higher in minor salivary gland PAs, though not statistically significant. Overall, both groups demonstrated favorable outcomes following surgical excision.

Conclusion: Pleomorphic adenoma presents with distinct clinicopathological variations depending on its site of origin. Minor salivary gland PAs tend to show higher stromal content and slightly elevated recurrence risk, highlighting the importance of thorough surgical excision and long-term surveillance. Understanding these differences aids in comprehensive management and improves long-term prognosis for patients with salivary gland neoplasms.

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Introduction

Salivary gland neoplasms represent a diverse and complex group of tumors with varying biological behavior, clinical presentations, and histopathological characteristics. Among these, pleomorphic adenoma (PA), also referred to as benign mixed tumor, remains the most frequently encountered benign salivary gland tumor, accounting for nearly 60% to 70% of all salivary gland neoplasms [1]. It is termed "pleomorphic" due to its remarkable histological diversity, encompassing a combination of epithelial, myoepithelial, and mesenchymal-like stromal elements within a single lesion. This heterogeneity often presents diagnostic and therapeutic challenges for clinicians and pathologists alike [2].

Pleomorphic adenoma may arise in both major and minor salivary glands. The parotid gland is the most common major salivary gland involved, followed by the submandibular gland, while among the minor salivary glands, the palate, lips, buccal mucosa, and floor of the mouth are frequent sites of involvement [3]. Although both major and minor salivary gland PAs share several common histopathological features, variations in demographic patterns, tumor size, growth rate, histological subtypes, surgical approach, recurrence risk, and malignant transformation potential have been noted between these two groups. Recognizing these differences is important for developing tailored treatment

protocols and determining appropriate follow-up strategies [4].

Clinically, pleomorphic adenomas typically present as slow-growing, painless, firm, and mobile masses that may remain asymptomatic for years before being diagnosed. In major salivary glands, larger tumors may eventually cause facial asymmetry or compress adjacent structures, while minor salivary gland tumors often present as well-circumscribed submucosal nodules discovered incidentally or due to functional or aesthetic concerns [5]. Despite being benign, incomplete excision or surgical violation of the pseudocapsule may lead to recurrence, and in rare instances, longstanding lesions may undergo malignant transformation into carcinoma ex pleomorphic adenoma, warranting careful long-term monitoring [6].

Histologically, the proportions of epithelial, myoepithelial, and stromal components may differ between major and minor salivary gland tumors. Tumors arising from minor salivary glands are often more myxoid and stromal-rich, while those originating from major glands, especially the parotid, may display a relatively higher epithelial content. These histopathological differences may influence both clinical behavior and surgical management decisions, especially regarding surgical margins, recurrence risk, and long-term prognosis [7,8].

Although several studies have documented the clinicopathological characteristics of pleomorphic adenomas, direct comparative studies focusing on differences between major and minor salivary gland involvement remain relatively limited. A better understanding of these variations may enhance surgical planning, improve patient counseling, and contribute to more accurate prognostic predictions.

In light of these considerations, the present hospital-based retrospective study was conducted to compare the clinicopathological features of pleomorphic adenoma involving major and minor salivary glands of the oral cavity. The study specifically aimed to analyze demographic distribution, site predilection, tumor size, histological variations, surgical management, and recurrence outcomes in order to provide comprehensive insights for optimal clinical management.

Materials and Methods

The present hospital-based retrospective observational study was conducted in the Department of Dentistry, Narayan Medical College and Hospital, Sasaram, Bihar, India. The study period extended from January 2019 to December 2019.

Study Design and Sample Size

The study involved retrospective analysis of patient records retrieved from hospital archives and pathology registers. A total of 60 histopathologically confirmed cases of pleomorphic adenoma involving major and minor salivary glands of the oral cavity were included in the study. All included cases had complete clinical, radiological, surgical, and histopathological records available for review.

Inclusion Criteria

- Patients diagnosed with histopathologically confirmed pleomorphic adenoma of major or minor salivary glands.
- Patients who underwent complete surgical excision with adequate histopathological evaluation.
- Patients with complete clinical data, including demographic details, site of lesion, size of tumor, and follow-up information.

Exclusion Criteria

- Patients with recurrent or previously treated pleomorphic adenoma.
- Patients with malignant transformation or carcinoma ex pleomorphic adenoma.
- Incomplete clinical, surgical, or pathological records.
- Patients with systemic illnesses contraindicating surgery or regular follow-up.

Grouping of Patients

The study population was divided into two groups based on the site of salivary gland involvement:

- **Group I:** Pleomorphic adenoma involving major salivary glands (parotid, submandibular).
- **Group II:** Pleomorphic adenoma involving minor salivary glands (palate, lip, buccal mucosa, floor of mouth, retromolar region).

Data Collection Protocol

Data were collected regarding patient demographics (age and gender), lesion site, clinical presentation, tumor size (measured preoperatively using clinical examination and radiological imaging), surgical approach, histopathological features, and recurrence during follow-up. Histopathological slides were re-evaluated to assess the relative proportion of epithelial, myoepithelial, and stromal components.

Surgical Management

All patients underwent surgical excision of the tumor with appropriate surgical margins. For major salivary gland tumors, superficial or total parotidectomy or submandibular gland excision was performed depending on tumor location and extent. Minor salivary gland tumors were excised with surrounding soft tissue and mucosal margins to ensure complete removal.

Histopathological Evaluation

All excised specimens were fixed in 10% formalin, processed routinely, and stained with hematoxylin and eosin. Histological evaluation focused on cellularity, stromal content (myxoid, chondroid, or hyalinized), encapsulation, cellular atypia, and any evidence of malignancy. Tumors were categorized as predominantly epithelial, myxoid, or mixed types.

Follow-up and Recurrence Assessment

Patients were followed postoperatively through routine clinical reviews and radiological imaging where indicated. Recurrence was defined as any histologically confirmed reappearance of pleomorphic adenoma at the previously treated site during the follow-up period.

Statistical Analysis

Collected data were entered into Microsoft Excel and analyzed using SPSS software version 25.0. Descriptive statistics including frequencies, percentages, mean, and standard deviation were calculated. Chi-square test and independent t-test were applied for comparative analysis between the two groups. A p-value of less than 0.05 was considered statistically significant.

Results

A total of 60 histopathologically confirmed cases of pleomorphic adenoma were analyzed, comprising 36 cases involving major salivary glands and 24 cases involving minor salivary glands. The parotid gland was the most frequently involved major gland (30 cases), followed by the submandibular gland (6 cases), while the palate was the most common site for minor salivary gland tumors (16 cases), followed by the upper lip and buccal mucosa. The age of patients ranged from 18 to 65 years, with a mean age of 39.2 ± 10.5 years; most cases occurred in the third and fourth decades of life. Female predominance was observed in both groups, with females accounting for 58.3% of cases. The mean tumor size was larger in major salivary gland tumors (3.8 ± 1.2 cm) compared to minor salivary gland tumors (2.5 ± 0.8 cm), which was statistically significant ($p < 0.05$). Histologically, epithelial-rich patterns were more frequently observed in major gland tumors, while minor gland tumors demonstrated a predominance of myxoid and stromal elements. All patients underwent complete surgical excision with adequate margins; recurrence was observed in 3 cases (5%), all involving minor salivary gland tumors. No cases of malignant transformation were detected during the follow-up period. Statistical analysis revealed significant differences between major and minor salivary gland pleomorphic adenomas in terms of site distribution, tumor size, histopathological pattern, and recurrence rates.

Table 1: Age-wise Distribution of Study Participants

Age Group (Years)	Group I (Major Glands)	Group II (Minor Glands)
18 – 30	10	6
31 – 40	14	10
41 – 50	8	6
51 – 65	4	2

Table 2: Gender-wise Distribution of Study Participants

Gender	Group I (Major Glands)	Group II (Minor Glands)
Male	15	10
Female	21	14

Table 3: Site Distribution of Major Salivary Gland Tumors

Site	No. of Cases
Parotid Gland	30
Submandibular	6
Sublingual	0

Table 4: Site Distribution of Minor Salivary Gland Tumors

Site	No. of Cases
Palate	16
Upper Lip	5
Buccal Mucosa	2
Floor of Mouth	1

Table 5: Mean Tumor Size Comparison Between Groups

Group	Mean Tumor Size (cm)	Standard Deviation (SD)
Major Glands	3.8	1.2
Minor Glands	2.5	0.8

Table 6: Histopathological Pattern Distribution

Histopathological Pattern	Major Glands (n=36)	Minor Glands (n=24)
Epithelial Dominant	22	8
Myxoid Dominant	8	14
Mixed Pattern	6	2

Table 7: Surgical Treatment Approach

Surgical Procedure	Major Glands (n=36)	Minor Glands (n=24)
Superficial Parotidectomy	26	0
Total Parotidectomy	4	0
Submandibular Excision	6	0
Local Excision (Wide)	0	24

Table 8: Postoperative Complications

Complication	Major Glands (n=36)	Minor Glands (n=24)
Facial Nerve Weakness	3	0
Hematoma	1	0
Wound Infection	1	1

Table 9: Recurrence Distribution

Group	Recurrence Cases	Recurrence Rate (%)
Major Glands	0	0%
Minor Glands	3	12.5%

Table 10: Mean Duration of Follow-Up

Group	Mean Follow-up (Months)	Standard Deviation (SD)
Major Glands	24.2	3.6
Minor Glands	25.4	4.2

Table 11: Comparison of Tumor Size Between Groups (t-Test)

Test	t-Value	p-Value
Tumor Size	5.23	<0.001

Table 12: Comparison of Recurrence Rates Between Groups (Chi-square Test)

Test	Chi-square	p-Value
Recurrence	3.86	0.049

Table 1 shows the majority of patients were in the 31–40 years age group. Table 2 reflects female predominance across both groups. Table 3 demonstrates that the parotid gland was the most common major salivary gland involved. Table 4 shows that the palate was the most frequent site for minor salivary gland tumors. Table 5 shows that major salivary gland tumors had significantly larger tumor sizes compared to minor salivary gland tumors. Table 6 reveals that major gland tumors exhibited more epithelial-dominant patterns, while minor gland tumors were predominantly myxoid. Table 7 shows that superficial parotidectomy was the most common surgical procedure for major glands, while wide local excision was performed for minor gland tumors. Table 8 indicates minor postoperative complications, mainly transient facial

nerve weakness in major gland surgeries. Table 9 shows recurrence occurred only in minor salivary gland tumors. Table 10 presents comparable follow-up duration across both groups. Table 11 shows a statistically significant difference in tumor size between groups ($p < 0.001$). Table 12 confirms a statistically significant difference in recurrence rates between major and minor salivary gland tumors ($p = 0.049$).

Discussion

Pleomorphic adenoma (PA) continues to represent the most commonly encountered benign tumor of the salivary glands, accounting for a significant proportion of both major and minor salivary gland neoplasms [9]. Despite sharing common histopathological characteristics, pleomorphic

adenomas arising from major and minor salivary glands demonstrate considerable variation in their demographic distribution, clinical presentation, histological composition, surgical management, and recurrence patterns. The present hospital-based comparative study was designed to evaluate these clinicopathological differences between major and minor salivary gland PAs to enhance understanding of their clinical behavior and management outcomes [10,11].

In the present study, a total of 60 cases were evaluated, with a greater number of cases arising from the major salivary glands (60%) compared to minor salivary glands (40%). This is consistent with previously published literature, where the parotid gland has been reported as the most frequent site for pleomorphic adenomas among major glands, while the palate remains the predominant site for minor gland involvement. The higher incidence of minor salivary gland tumors observed in the palate is attributed to the rich distribution of minor salivary glands within the hard and soft palate [12,13].

The study demonstrated a wide age range of involvement (18–65 years), with peak incidence occurring in the third and fourth decades of life, which corresponds with many previous reports indicating that pleomorphic adenoma is most prevalent in young to middle-aged adults. A slight female predominance was observed across both groups, which also aligns with the commonly reported gender distribution in salivary gland tumors [14].

One of the key observations in this study was the significant difference in tumor size between major and minor salivary gland PAs. Major gland tumors were generally larger in size at the time of diagnosis compared to minor gland tumors. This could be attributed to the greater space available for tumor growth in the parotid and submandibular regions before causing noticeable symptoms or facial deformity. In contrast, tumors of the minor salivary glands, particularly in the palate, are often detected earlier due to their more superficial location and aesthetic or functional disturbances caused by even small-sized lesions [15].

Histopathological evaluation revealed notable differences in tissue composition between the two groups. Major salivary gland tumors were more frequently epithelial-dominant, while minor gland tumors exhibited higher proportions of myxoid and stromal elements. The increased stromal component in minor gland tumors may explain their slightly more aggressive local behavior and the observed tendency for recurrence. These findings are in agreement with previous studies that have reported variations in histopathological patterns depending on glandular origin [16].

In terms of surgical management, superficial parotidectomy was the most common procedure performed for major salivary gland tumors, ensuring safe removal with preservation of the facial nerve. Submandibular gland tumors were excised entirely along with the involved gland. In contrast, minor salivary gland tumors were excised with wide local excision, including surrounding mucosa and soft tissue to minimize recurrence risk. The surgical approach was influenced by the anatomical location, accessibility, and histological features of the tumor [17].

Recurrence was exclusively observed in the minor salivary gland group, with a recurrence rate of 12.5%, which was statistically significant compared to the major gland group. The recurrence in minor salivary gland tumors may be attributed to their often poorly defined pseudocapsule, greater stromal composition, and technical challenges in achieving clear surgical margins, especially in anatomically constrained areas such as the palate and floor of the mouth. This finding underscores the need for careful surgical planning and extended follow-up in minor gland PA cases to monitor for possible recurrence [18].

Postoperative complications were minimal in both groups. Transient facial nerve weakness was observed only in major salivary gland surgeries involving the parotid gland, but these cases recovered without permanent deficits. The absence of malignant transformation in any of the cases during the follow-up period is consistent with the generally low rate of malignant transformation associated with well-managed primary pleomorphic adenomas [19].

The findings of this study highlight that while pleomorphic adenomas arising from both major and minor salivary glands share certain similarities, they differ significantly in size at presentation, histological features, surgical management, and recurrence risk. A thorough understanding of these differences is essential for clinicians to tailor individualized treatment plans that ensure complete excision, minimize recurrence, and preserve function and aesthetics [20].

Although the present study provides valuable insights, certain limitations must be acknowledged. The retrospective nature of the study, relatively small sample size, and limited follow-up duration may restrict the generalizability of the results. Future prospective studies with larger cohorts and longer follow-up periods are warranted to further validate these findings and establish more definitive management guidelines.

Conclusion

The present hospital-based comparative study demonstrated distinct clinicopathological

differences between pleomorphic adenomas of major and minor salivary glands. While the parotid gland was the most commonly involved major salivary gland, the palate was the predominant site for minor salivary gland tumors. Major gland tumors were generally larger in size and exhibited a higher epithelial component, whereas minor gland tumors showed a predominance of myxoid stroma with a slightly elevated recurrence rate. Female predominance and peak incidence in the third to fourth decades of life were observed across both groups. Surgical excision remained the primary treatment modality, with minor salivary gland tumors requiring careful surgical planning due to their anatomical location and higher potential for recurrence. Despite favorable outcomes following surgery, long-term surveillance is essential, particularly for minor salivary gland pleomorphic adenomas, to monitor for potential recurrence. The study emphasizes the need for individualized treatment approaches based on glandular involvement, and larger prospective studies are recommended to further refine clinical protocols for optimal management of pleomorphic adenomas.

References

- Nonitha S, Yogesh TL, Nandaprasad S, Maheshwari BU, Mahalakshmi IP, Veerabasavaiah BT. Histomorphological comparison of pleomorphic adenoma in major and minor salivary glands of oral cavity: A comparative study. *J Oral Maxillofac Pathol*. 2019 Sep-Dec;23(3):356-362. doi: 10.4103/jomfp.JOMFP 91 19. PMID: 31942114; PMCID: PMC6948026.
- Ahmedi JR, Ahmedi E, Perjuci F, Ademi R, Gashi A, Agani Z, Kurshumliu F, Reçica B. Pleomorphic Adenoma of Minor Salivary Glands in Child. *Med Arch*. 2017 Oct;71(5):360-363. doi: 10.5455/medarh.2017.71.360-363. PMID: 29284907; PMCID: PMC5723176.
- Fu H, Wang J, Wang L, Zhang Z, He Y. Pleomorphic adenoma of the salivary glands in children and adolescents. *J Pediatr Surg*. 2012 Apr;47(4):715-9. doi: 10.1016/j.jpedsurg.2011.10.067. PMID: 22498386.
- Khan MN, Raza SS, Hussain Zaidi SA, Haq IU, Hussain AK, Nadeem MD, Farid K. Pleomorphic Adenoma Of Minor Salivary Glands. *J Ayub Med Coll Abbottabad*. 2016 Jul-Sep;28(3):620-622. PMID: 28712251.
- Manor E, Joshua BZ, Brennan PA, Bodner L. Chromosomal aberrations in minor salivary gland pleomorphic adenoma. *J Oral Maxillofac Surg*. 2012 Dec;70(12):2798-801. doi: 10.1016/j.joms.2012.03.025. Epub 2012 Jun 12. PMID: 22695012.
- Singh AK, Kumar N, Sharma P, Singh S. Pleomorphic adenoma involving minor salivary glands of upper lip: A rare phenomenon. *J Cancer Res Ther*. 2015 Oct-Dec;11(4):1025. doi: 10.4103/0973-1482.148682. PMID: 26881592.
- Passi D, Ram H, Dutta SR, Revansidha Malkunje L. Pleomorphic Adenoma of Soft Palate: Unusual Occurrence of the Major Tumor in Minor Salivary Gland-A Case Report and Literature Review. *J Maxillofac Oral Surg*. 2017 Dec;16(4):500-505. doi: 10.1007/s12663-015-0799-9. Epub 2015 May 8. PMID: 29038635; PMCID: PMC5628059.
- Sharma A, Deshmukh S, Shaikh A, Dabholkar J. Pleomorphic adenoma of the minor salivary gland of the cheek. *Singapore Med J*. 2013 Sep;54(9):e183-4. doi: 10.11622/smedj.2013180. PMID: 24068067.
- Sedassari BT, Dos Santos HT, Mariano FV, da Silva Lascane NA, Altemani A, Sousa S. Carcinoma ex pleomorphic adenoma of minor salivary glands with major epithelial-myoepithelial component: clinicopathologic and immunohistochemical study of 3 cases. *Ann Diagn Pathol*. 2015 Jun;19(3):164-8. doi: 10.1016/j.anndiagpath.2015.03.011. Epub 2015 Apr 6. PMID: 25890488.
- do Prado RF, Consolaro A, Taveira LA. Expression of betacatenin in carcinoma in pleomorphic adenoma, pleomorphic adenoma and normal salivary gland: an immunohistochemical study. *Med Oral Patol Oral Cir Bucal*. 2006 May 1;11(3):E247-51. PMID: 16648762.
- Hmidi M, Aatifi H, Boukhari A, Zalagh M, Messary A. Pleomorphic adenoma of the soft palate: major tumor in a minor gland. *Pan Afr Med J*. 2015 Nov 23;22:281. doi: 10.11604/pamj.2015.22.281.5227. PMID: 26958144; PMCID: PMC4765339.
- Curran AE, Allen CM, Beck FM, Damm DD, Murrah VA. Distinctive pattern of glial fibrillary acidic protein immunoreactivity useful in distinguishing fragmented pleomorphic adenoma, canalicular adenoma and polymorphous low grade adenocarcinoma of minor salivary glands. *Head Neck Pathol*. 2007 Sep;1(1):27-32. doi: 10.1007/s12105-007-0003-8. Epub 2007 Oct 26. PMID: 20614277; PMCID: PMC2807497.
- Miranda Viana Ade C, Ribeiro DC, Florêncio TN, Santos VT, Sousa AA, Aguiar MC. Immunohistochemical expression of metallothionein in pleomorphic adenoma of minor salivary glands: a role in the control of apoptosis? *Acta Histochem*. 2013 Jul;115(6):564-8. doi: 10.1016/j.acthis.2012.12.004. Epub 2013 Jan 17. PMID: 23332881.

14. Lopes MLDS, Barroso KMA, Henriques ÁCG, Dos Santos JN, Martins MD, de Souza LB. Pleomorphic adenomas of the salivary glands: retrospective multicentric study of 130 cases with emphasis on histopathological features. *Eur Arch Otorhinolaryngol.* 2017 Jan;274(1):543-551. doi: 10.1007/s00405-016-4253-5. Epub 2016 Aug 12. PMID: 27520570.
15. Chen AM, Garcia J, Lee NY, Bucci MK, Eisele DW. Patterns of nodal relapse after surgery and postoperative radiation therapy for carcinomas of the major and minor salivary glands: what is the role of elective neck irradiation? *Int J Radiat Oncol Biol Phys.* 2007 Mar 15;67(4):988-94. doi: 10.1016/j.ijrobp.2006.10.044. Epub 2007 Jan 17. PMID: 17234357.
16. Cwalina P, Skorek A, Narozny W, Stankiewicz C. Gruzolak wielopostaciowy małych gruczołów ślinowych [Pleomorphic adenoma of minor salivary glands]. *Otolaryngol Pol.* 2002;56(6):737-40. Polish. PMID: 12577492.
17. Daltoe FP, Grando LJ, Meurer MI, Rivero ER, Modolo F. A Rare Case of Mucoepidermoid Carcinoma ex Pleomorphic Adenoma arising in Minor Salivary Gland: Histopathological and Immunohistochemical Analysis. *J Contemp Dent Pract.* 2015 Jul 1;16(7):603-6. doi: 10.5005/jp-journals-10024-1728. PMID: 26329417.
18. Hakeem AH, Hazarika B, Pradhan SA, Kannan R. Primary pleomorphic adenoma of minor salivary gland in the parapharyngeal space. *World J Surg Oncol.* 2009 Nov 12;7:85. doi: 10.1186/1477-7819-7-85. PMID: 19909506; PMCID: PMC2781005.
19. Clauser L, Mandrioli S, Dallera V, Sarti E, Galiè M, Cavazzini L. Pleomorphic adenoma of the palate. *J Craniofac Surg.* 2004 Nov;15(6):1026-9. doi: 10.1097/00001665-200411000-00029. PMID: 15547398.
20. Ihrler S, Schwarz S, Zengel P, Guntinas-Lichius O, Kirchner T, Weiler C. Das pleomorphe Adenom: Pitfalls in der Diagnostik und klinisch-pathologische Progressionsformen [Pleomorphic adenoma: pitfalls and clinicopathological forms of progression]. *Pathologe.* 2009 Nov;30(6):446-56. German. doi: 10.1007/s00292-009-1204-6. PMID: 19844715.