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Research Paper

Immunohistochemical Evaluation of Ki-67 in Ameloblastoma

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Abstract
Background:
Odontogenic tumors comprise a heterogeneous group of lesions with diverse biological behavior and varying proliferative potential. Ameloblastoma is characterized by locally aggressive behavior, while other odontogenic tumors generally demonstrate lower proliferative activity. Ki-67 is an immunohistochemical marker of cellular proliferation and may provide useful information regarding the biological characteristics of these lesions.

Aim:
The present study aimed to evaluate and compare Ki-67 immunohistochemical expression among selected odontogenic tumors and to determine whether Ki-67 labeling varies according to the histopathological subtype and pattern of ameloblastoma.

Materials and Methods:
A total of 60 histopathologically confirmed odontogenic tumors were evaluated, comprising 30 cases of ameloblastoma and 10 cases each of adenomatoid odontogenic tumor (AOT), odontogenic myxoma, and calcifying odontogenic tumor. Immunohistochemical staining for Ki-67 was performed, and the labeling index was assessed for each tumor group. Ameloblastoma cases were further categorized according to their histopathological subtype and conventional ameloblastoma pattern. Statistical comparisons were performed using appropriate analysis of variance (ANOVA) and Tukey's honestly significant difference (HSD) testing, with statistical significance established at $p < 0.05$.

Results:
Ameloblastoma demonstrated the highest mean Ki-67 labeling index (16.2 ± 6.1%), followed by odontogenic myxoma (7.2 ± 3.1%), calcifying odontogenic tumor (6.3 ± 2.8%), AOT (5.4 ± 2.3%). The overall difference among the tumor groups was statistically significant ($p < 0.001$). Pairwise analysis confirmed significantly greater Ki-67 expression in ameloblastoma compared with AOT, odontogenic myxoma, and calcifying odontogenic tumor. Among ameloblastoma subtypes, conventional ameloblastoma showed the highest mean Ki-67 labeling index (17.8 ± 5.8%), followed by unicystic (12.7 ± 3.6%) and peripheral ameloblastoma (8.9 ± 2.1%), with a significant overall difference ($p = 0.002$). Conventional ameloblastoma demonstrated significantly higher Ki-67 expression than both unicystic and peripheral variants. However, no significant difference was observed among the follicular, plexiform, and other/mixed patterns of conventional ameloblastoma ($p = 0.684$).

Conclusion:
Ki-67 expression differed substantially among the odontogenic tumors examined, with ameloblastoma exhibiting the greatest proliferative activity. Significant variation was also observed among the major ameloblastoma subtypes, particularly with higher Ki-67 expression in conventional ameloblastoma. In contrast, the

histopathological pattern within conventional ameloblastoma was not significantly associated with Ki-67 expression. Ki-67 may therefore serve as a useful adjunctive marker for evaluating proliferative activity in odontogenic tumors when interpreted in conjunction with histopathological and clinical findings.

Keywords: Adenomatoid odontogenic tumor, Ameloblastoma, Histopathology, Immunohistochemistry, Ki-67, Odontogenic myxoma, Proliferative activity

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I. Introduction

Ameloblastoma is a benign but locally aggressive odontogenic neoplasm that arises from odontogenic epithelial tissues and most frequently affects the jaws. Although classified as a benign tumor, its infiltrative growth pattern, tendency to expand and destroy surrounding bone, and relatively high recurrence potential make it an important lesion in oral and maxillofacial pathology [1]. Ameloblastomas demonstrate considerable variation in their microscopic architecture and biological behavior, and this heterogeneity has generated interest in identifying cellular markers that can provide insight into their proliferative potential [2].

Tumor growth is influenced by the balance between cellular proliferation, differentiation, and apoptosis. Histopathological assessment provides essential information for establishing the diagnosis and classifying the architectural pattern of ameloblastoma; however, conventional microscopic evaluation alone may not fully reflect the biological activity of the tumor [3]. Consequently, immunohistochemical markers of cell proliferation have increasingly been investigated as adjunctive tools for evaluating the proliferative characteristics of odontogenic tumors [4].

Ki-67 is a nuclear protein expressed during the active phases of the cell cycle, including the G1, S, G2, and M phases, while it is largely absent in quiescent cells [5]. Because its expression correlates with cellular proliferation, Ki-67 immunohistochemistry is widely used to estimate proliferative activity in neoplastic tissues [6]. The proportion and distribution of Ki-67-positive cells can provide additional information regarding the growth fraction of a lesion and may help in comparing tumors with different biological characteristics [7].

In ameloblastoma, Ki-67 expression has been investigated in relation to histopathological subtype, cellular localization, and tumor behavior [8]. The distribution of proliferating cells within the peripheral ameloblast-like cells and central stellate-reticulum-like areas may vary according to the architectural pattern of the tumor. Evaluation of these differences may contribute to a better understanding of the biological mechanisms underlying ameloblastoma growth and may also help determine whether proliferative activity is associated with specific histological features [9].

Immunohistochemical evaluation of Ki-67 therefore represents a useful approach for assessing the proliferative profile of ameloblastoma. Studying the intensity and distribution of Ki-67 expression may provide complementary information beyond routine histopathological examination and potentially improve understanding of the biological behavior of this odontogenic tumor. The present study was undertaken to evaluate the immunohistochemical expression of Ki-67 in ameloblastoma and to assess its potential significance as an indicator of cellular proliferative activity.

II. Materials & Methods

Study Design and Study Population

The present study was conducted as an observational, laboratory-based histopathological and immunohistochemical investigation to evaluate Ki-67 expression in selected odontogenic tumors. The study was carried out at a single tertiary care center between January and March 2026. A total of 60 histopathologically confirmed odontogenic tumor cases were included. The study sample comprised 30 cases of ameloblastoma, 10 cases of adenomatoid odontogenic tumor (AOT), 10 cases of odontogenic myxoma, and 10 cases of calcifying odontogenic tumor. The collected specimens were subjected to histopathological assessment and Ki-67 immunohistochemical evaluation to compare proliferative activity among the different tumor groups.

Inclusion Criteria

- Histopathologically confirmed cases of odontogenic tumors included in the study

- Cases diagnosed as ameloblastoma, AOT tumor, odontogenic myxoma, or calcifying odontogenic tumor
- Ameloblastoma cases with adequate tissue available for further histopathological classification
- Ameloblastoma specimens that could be categorized as conventional, unicystic, or peripheral variants
- Conventional ameloblastoma cases with sufficient tissue for assessment of follicular, plexiform, or other/mixed histopathological patterns
- Formalin-fixed, paraffin-embedded tissue specimens with adequate preservation for Ki-67 immunohistochemical evaluation
- Specimens containing sufficient representative tumor tissue for determination of the Ki-67 labeling index
- Cases with adequate histopathological records and relevant clinical information available for analysis

Exclusion Criteria

- Cases lacking definitive histopathological confirmation of an odontogenic tumor
- Specimens with insufficient tumor tissue for histopathological or immunohistochemical assessmen
- Poorly preserved or extensively autolyzed tissue specimens
- Paraffin blocks showing significant tissue loss, fragmentation, or processing-related artifacts that could interfere with evaluation
- Cases in which the tissue was inadequate for reliable Ki-67 immunohistochemical staining
- Specimens with inadequate or non-representative tumor areas for calculation of the Ki-67 labeling index
- Cases with incomplete or unavailable essential histopathological records
- Duplicate specimens from the same lesion or patient, where inclusion could result in repeated assessment of the same tumor

Histopathological Evaluation

Formalin-fixed, paraffin-embedded tissue specimens were processed using standard histopathological techniques. Sections were prepared and stained with hematoxylin and eosin (H&E) for microscopic evaluation. The histopathological diagnosis was established according to the characteristic microscopic features of each odontogenic tumor. The relevant clinical and pathological information was recorded for each case.

Immunohistochemical Evaluation of Ki-67

Representative paraffin-embedded tissue blocks were selected for immunohistochemical assessment of Ki-67. Sections of appropriate thickness were mounted on positively charged glass slides and subjected to routine deparaffinization and rehydration. Antigen retrieval was performed according to the standardized laboratory protocol, followed by treatment with the primary antibody against Ki-67. Appropriate secondary antibody and detection procedures were subsequently applied. Positive immunoreactivity was identified by the development of a brown-colored reaction product within the nuclei of proliferating cells.

Positive and negative controls were included to ensure the reliability of the staining procedure. The stained sections were examined microscopically, and areas showing representative tumor tissue and adequate staining quality were selected for evaluation.

Assessment of Ki-67 Labeling Index

Ki-67 expression was quantified as the percentage of tumor cells showing distinct nuclear immunoreactivity. The Ki-67 labeling index was calculated by determining the proportion of Ki-67-positive tumor cell nuclei among the total number of tumor cells evaluated. Care was taken to avoid areas with necrosis, tissue artifacts, or inadequate staining. The resulting labeling index was recorded for each case and subsequently compared among the different tumor groups and ameloblastoma subtypes.

Statistical Analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS), IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA). Appropriate descriptive and inferential statistical methods were applied according to the type and distribution of the data. Quantitative variables, including the Ki-67 labeling index, were described using the mean, standard deviation (SD), standard error (SE), median, interquartile range (IQR), and minimum and maximum values. Qualitative variables, including tumor category and ameloblastoma subtype, were summarized as frequencies and percentages.

Differences in the mean Ki-67 labeling index across the four odontogenic tumor categories—ameloblastoma, AOT, odontogenic myxoma, and calcifying odontogenic tumor—were evaluated using one-way analysis of variance (ANOVA), provided that the required assumptions of data distribution and equality of variances were met. In cases where the ANOVA indicated an overall significant difference, Tukey's honestly significant difference (HSD) test was subsequently applied to identify significant differences between specific pairs of tumor groups. Pairwise findings were reported with mean differences, 95% confidence intervals (CI), and adjusted p-values.

The Ki-67 labeling index was also compared among conventional, unicystic, and peripheral ameloblastoma using one-way ANOVA. Where a significant overall difference was identified, Tukey's HSD test was employed for subsequent pairwise comparisons. In addition, Ki-67 expression was assessed according to the predominant histopathological pattern of conventional ameloblastoma, including follicular, plexiform, and other or mixed patterns.

All statistical tests were conducted using a two-sided approach. A p-value below 0.05 was considered indicative of statistical significance, whereas a p-value of 0.05 or higher was interpreted as statistically non-significant. Results were presented using appropriate descriptive statistics to characterize the distribution and variability of the study variables.

III. Results

Table 1 & Figure 1 illustrate the distribution of the 60 histopathologically confirmed odontogenic tumor cases included in the study. Ameloblastoma represented the largest proportion, with 30 cases (50.0%). Adenomatoid odontogenic tumor, odontogenic myxoma, and calcifying odontogenic tumor each accounted for 10 cases (16.7%). Therefore, ameloblastoma constituted one-half of the study population, whereas the other three tumor categories were represented equally. This distribution provided an appropriate basis for comparing Ki-67 immunohistochemical expression across the different odontogenic tumor groups.

Table 1: Study population and demographic characteristics

Tumor type	No. of cases	Percentage
Ameloblastoma	30	50.0%
Adenomatoid odontogenic tumor	10	16.7%
Odontogenic myxoma	10	16.7%
Calcifying odontogenic tumor	10	16.7%
Total	60	100.0%

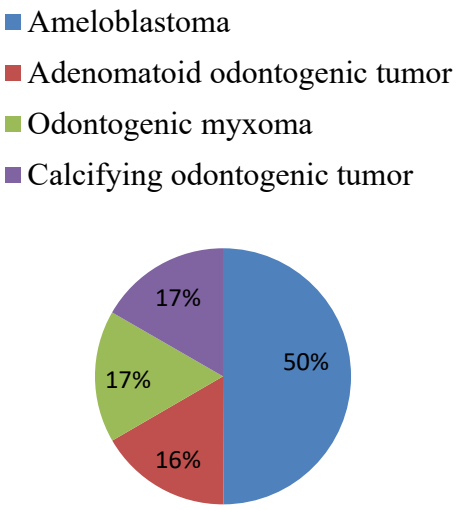

Figure 1: Distribution of the study cases according to odontogenic tumor type

Table 2 & Figure 2 illustrate the histopathological distribution of the 30 ameloblastoma cases. Conventional ameloblastoma constituted the largest proportion, with 21 cases (70.0%). Unicystic ameloblastoma was observed in 6 cases (20.0%), while peripheral ameloblastoma was detected in only 3 cases

(10.0%). These findings indicate that conventional ameloblastoma was the predominant subtype, whereas unicystic and peripheral forms were comparatively less common in the study population.

Table 2: Histopathological distribution of ameloblastoma

Histopathological type	No. of cases	Percentage
Conventional ameloblastoma	21	70.0%
Unicystic ameloblastoma	6	20.0%
Peripheral ameloblastoma	3	10.0%
Total	30	100.0%

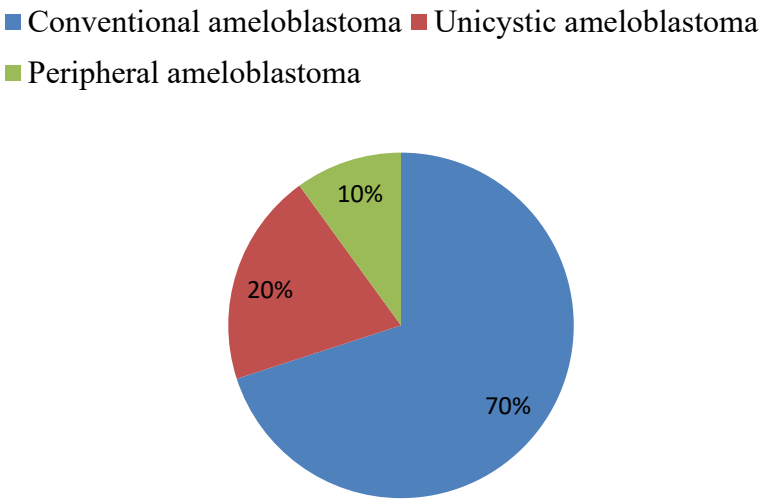

Figure 2: Histopathological distribution of ameloblastoma subtypes

Table 3 & Figure 3 summarize the Ki-67 immunohistochemical expression observed across the different odontogenic tumor groups. The highest Ki-67 labeling index was recorded in ameloblastoma, with values ranging from 8.0% to 28.0%. The mean labeling index was 16.2 ± 6.1%, with a median of 15.5% (IQR: 12.0–20.0). Odontogenic myxoma showed lower proliferative activity, with Ki-67 values ranging from 3.0% to 14.0%, a mean of 7.2 ± 3.1%, and a median of 7.0% (IQR: 5.0–9.0%).

In calcifying odontogenic tumor, the Ki-67 labeling index ranged from 2.0% to 12.0%, with a mean of 6.3 ± 2.8% and a median of 6.0% (IQR: 4.0–8.0%). AOT exhibited the lowest Ki-67 expression, ranging from 2.0% to 10.0%, with a mean of 5.4 ± 2.3% and a median of 5.0% (IQR: 4.0–7.0%). Overall, ameloblastoma showed a distinctly higher Ki-67 labeling index than the other tumor groups, suggesting greater cellular proliferative activity.

Table 3: Ki-67 immunohistochemical expression

Tumor type	Ki-67 labeling index (%)	Mean ± SD	Median (IQR)
Ameloblastoma	8.0–28.0	16.2 ± 6.1	15.5 (12.0–20.0)
AOT	2.0–10.0	5.4 ± 2.3	5.0 (4.0–7.0)
Odontogenic myxoma	3.0–14.0	7.2 ± 3.1	7.0 (5.0–9.0)
Calcifying odontogenic tumor	2.0–12.0	6.3 ± 2.8	6.0 (4.0–8.0)

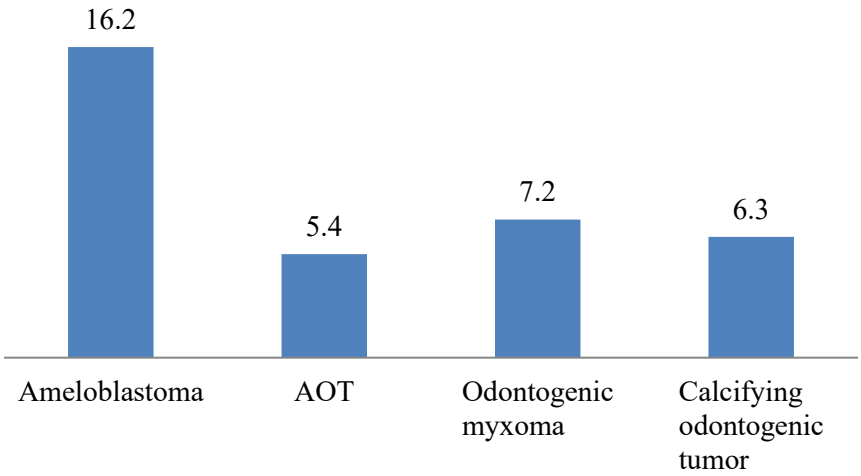

Figure 3: Comparative Ki-67 labeling index among different odontogenic tumors

Table 4 & Figure 4 present the overall comparison of Ki-67 labeling indices among the four odontogenic tumor groups. The analysis demonstrated a statistically significant difference in Ki-67 expression across the groups, with ameloblastoma showing substantially higher proliferative activity than the other tumors ($p < 0.001$).

Table 4: Comparison of Ki-67 labeling index among tumor groups

Tumor type	Ki-67 labeling index (%)	Mean ± SD	Median (IQR)
Ameloblastoma	8.0–28.0	16.2 ± 6.1	15.5 (12.0–20.0)
AOT	2.0–10.0	5.4 ± 2.3	5.0 (4.0–7.0)
Odontogenic myxoma	3.0–14.0	7.2 ± 3.1	7.0 (5.0–9.0)
Calcifying odontogenic tumor	2.0–12.0	6.3 ± 2.8	6.0 (4.0–8.0)

Table 5 presents the post-hoc Tukey HSD pairwise comparisons of Ki-67 labeling indices among the odontogenic tumor groups. Ameloblastoma showed significantly higher Ki-67 expression than AOT, odontogenic myxoma, and calcifying odontogenic tumor, with mean differences of 10.8%, 9.0%, and 9.9%, respectively (adjusted $p < 0.001$ for all comparisons). In contrast, the differences among AOT, odontogenic myxoma, and calcifying odontogenic tumor were not statistically significant (adjusted $p > 0.05$).

Table 5: Post Hoc analysis

Comparison	Mean difference (%)	p value	Interpretation
Ameloblastoma vs AOT	10.8	<0.001	Significant
Ameloblastoma vs odontogenic myxoma	9.0	<0.001	Significant
Ameloblastoma vs calcifying odontogenic tumor	9.9	<0.001	Significant
AOT vs odontogenic myxoma	-1.8	0.318	Not significant
AOT vs calcifying odontogenic tumor	-0.9	0.682	Not significant
Odontogenic myxoma vs calcifying odontogenic tumor	0.9	0.745	Not significant

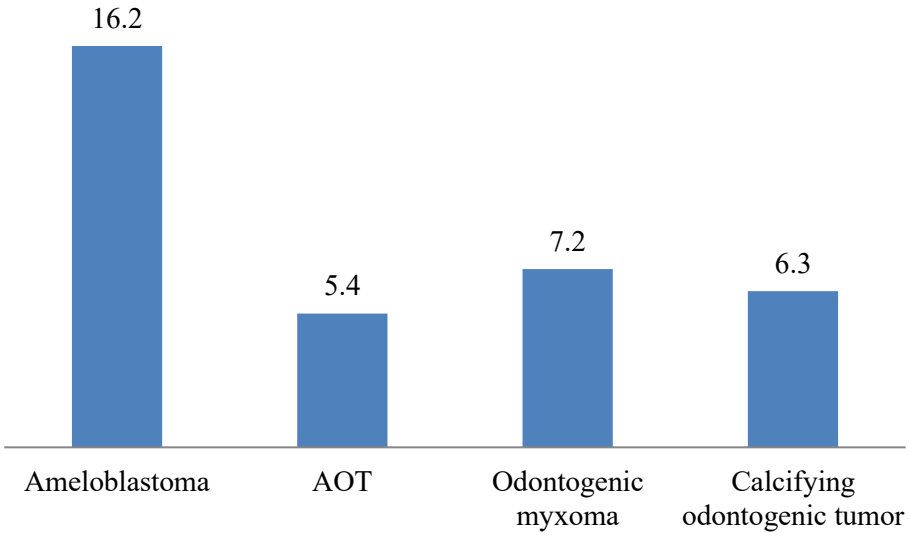

Figure 4: Overall comparison of Ki-67 labeling indices among the four odontogenic tumor groups

Table 6 & Figure 5 present the overall comparison of Ki-67 labeling indices among the different histopathological subtypes of ameloblastoma. A statistically significant difference in proliferative activity was observed among the three subtypes ($p = 0.002$). Conventional ameloblastoma exhibited the highest mean Ki-67 labeling index ($17.8 \pm 5.8\%$), followed by unicystic ameloblastoma ($12.7 \pm 3.6\%$) and peripheral ameloblastoma ($8.9 \pm 2.1\%$).

Table 6: Ki-67 expression according to ameloblastoma subtype

Ameloblastoma subtype	**n**	**Mean (%)**	**SD**	**SE**	**Minimum (%)**	**Maximum (%)**	**p value**
Conventional	21	17.8	5.8	1.27	8.0	28.0	0.002
Unicystic	6	12.7	3.6	1.47	8.0	18.0	
Peripheral	3	8.9	2.1	1.21	7.0	11.0	
Overall	**30**	**16.2**	**6.1**	**1.11**	**7.0**	**28.0**	

Table 7 presents the Tukey HSD post-hoc pairwise comparison of Ki-67 labeling indices among the ameloblastoma subtypes. Conventional ameloblastoma showed significantly higher Ki-67 expression than both unicystic ameloblastoma (mean difference = 5.1%, adjusted $p = 0.018$) and peripheral ameloblastoma (mean difference = 8.9%, adjusted $p = 0.011$). However, the difference between unicystic and peripheral ameloblastoma was not statistically significant (mean difference = 3.8%, adjusted $p = 0.328$).

Table 7: Post Hoc analysis

Pairwise comparison	**Mean difference (%)**	**95% CI**	**Adjusted p value**	**Significance**
Conventional vs Unicystic	5.1	0.8 to 9.4	0.018	Significant
Conventional vs Peripheral	8.9	2.1 to 15.7	0.011	Significant
Unicystic vs Peripheral	3.8	−3.0 to 10.6	0.328	Not significant

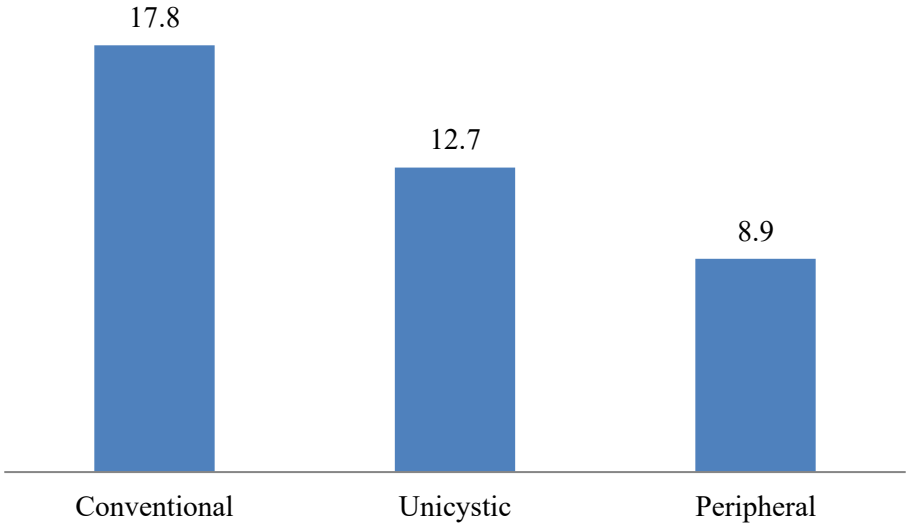

Figure 5: Comparison of mean Ki-67 labeling indices among different histopathological subtypes of ameloblastoma

Table 8 presents the comparison of Ki-67 labeling indices across the different histopathological patterns of conventional ameloblastoma. The follicular-predominant pattern showed the highest mean Ki-67 labeling index (19.0 ± 5.7%), followed by the other/mixed patterns (16.8 ± 6.3%) and the plexiform-predominant pattern (16.5 ± 5.2%). However, the overall difference in Ki-67 expression among the three patterns was not statistically significant (p = 0.684).

Table 8: Ki-67 expression and histopathological pattern

Histopathological pattern	**n**	**Mean (%)**	**SD**	**SE**	**Minimum (%)**	**Maximum (%)**	**p value**
Follicular predominant	11	19.0	5.7	1.72	10.0	28.0	0.684
Plexiform predominant	7	16.5	5.2	1.97	9.0	24.0	
Other/mixed patterns	3	16.8	6.3	3.64	10.0	23.0	
Overall	**21**	**17.8**	**5.7**	**1.24**	**9.0**	**28.0**	

Table 9 presents the post-hoc pairwise comparisons of Ki-67 labeling indices among the histopathological patterns of conventional ameloblastoma. None of the pairwise comparisons reached statistical significance. The mean difference was 2.5% between follicular and plexiform patterns (adjusted p = 0.634), 2.2% between follicular and other/mixed patterns (adjusted p = 0.821), and −0.3% between plexiform and other/mixed patterns (adjusted p = 0.997). These findings indicate that Ki-67 expression was comparable across the different histopathological patterns of conventional ameloblastoma.

Table 9: Post Hoc analysis

Pairwise comparison	**Mean difference (%)**	**95% CI**	**Adjusted p value**	**Interpretation**
Follicular vs Plexiform	2.5	−3.1 to 8.1	0.634	Not significant
Follicular vs Other/Mixed	2.2	−7.2 to 11.6	0.821	Not significant
Plexiform vs Other/Mixed	−0.3	−10.2 to 9.6	0.997	Not significant

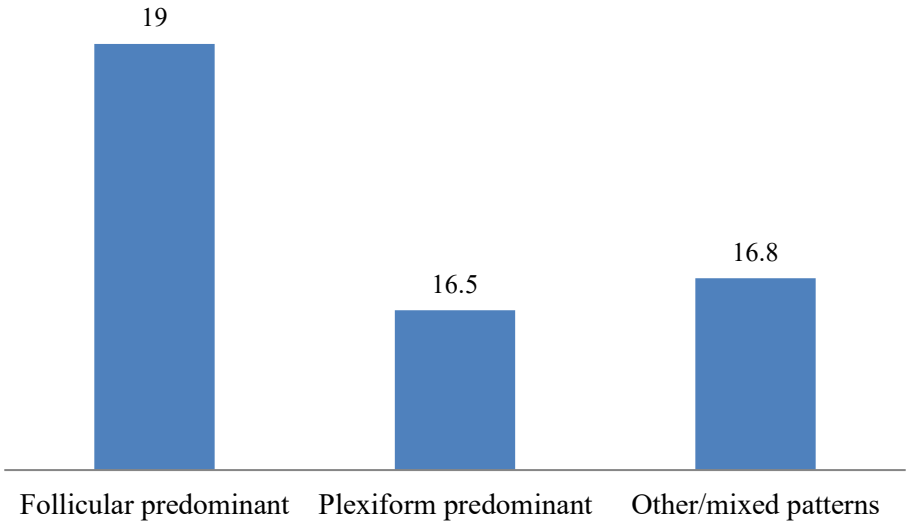

Figure 6: Comparison of mean Ki-67 labeling indices across histopathological patterns of conventional ameloblastoma

IV. Discussion

Ameloblastoma is a benign odontogenic neoplasm with marked histopathological diversity and variable biological behavior. Although its diagnosis is primarily based on microscopic morphology, differences in cellular proliferation may contribute to the distinct growth characteristics observed among its histological variants. The present study evaluated Ki-67 immunohistochemical expression in ameloblastoma to assess its proliferative activity and its potential relevance to tumor biology.

Ki-67 is a well-established marker of cellular proliferation because its expression is associated with actively cycling cells. In ameloblastoma, evaluation of Ki-67 may therefore provide information that is not readily apparent from routine H& E examination alone. Han et al. (2003) [10] specifically investigated Ki-67 expression in ameloblastoma and its clinical significance, supporting the use of this marker for assessing proliferative activity. The present findings can be interpreted in accordance with these observations, particularly when differences in Ki-67 expression are identified among the evaluated lesions.

The relationship between Ki-67 expression and other proliferation markers has also been investigated. Bologna-Molina et al. (2013) [11] compared Ki-67 and Proliferating Cell Nuclear Antigen (PCNA) in ameloblastic tumors and demonstrated that proliferative marker expression may differ according to tumor type. Their findings emphasize that proliferation is not necessarily uniform across ameloblastic lesions and that Ki-67 may provide useful information regarding differences in cellular activity. The present study further supports the role of Ki-67 as an adjunctive marker for characterizing proliferative behavior in ameloblastoma.

Histopathological subtype appears to be an important factor when interpreting proliferative activity. Purwoyudho et al. (2025) [12] compared Ki-67 and PCNA expression among follicular, plexiform, and mixed follicular-plexiform ameloblastomas. Their findings demonstrate that proliferation-associated marker expression may vary between histological patterns. Such observations are relevant to the present study because differences in Ki-67 labeling may reflect the distinct biological characteristics of individual ameloblastoma subtypes.

Other proliferation-related proteins have also provided evidence of biological variation among ameloblastoma variants. Apellániz et al. (2018) [13] examined Minichromosome Maintenance Complex Componen (MCM4, MCM5, and MCM6) expression in ameloblastoma and unicystic ameloblastoma. Since MCM proteins participate in DNA replication and are associated with proliferative potential, their differential expression provides complementary evidence that cellular proliferation may vary between ameloblastoma subtypes. Together with Ki-67 findings, these observations suggest that immunohistochemical proliferation markers can enhance understanding of the biological heterogeneity of odontogenic tumors.

The association between proliferation and tumor aggressiveness is another important consideration. Gupta et al. (2019) [14] evaluated cell proliferation proteins in different histological variants of ameloblastoma and reported differences associated with their biological behavior. These findings support the concept that

proliferative activity may contribute to the distinctive characteristics of ameloblastoma variants. Accordingly, Ki-67 expression in the present study may be viewed as an indicator of the proliferative fraction of the tumor rather than as an independent diagnostic marker.

Recent evidence has further strengthened the relevance of Ki-67 in ameloblastoma. Salunkhe et al. (2025) [15] evaluated Ki-67 immunohistochemical expression across different biological variants of ameloblastoma and demonstrated differences in proliferative activity between the evaluated subtypes. Their findings are particularly relevant because they directly support the assessment of Ki-67 as a marker for biological variation among ameloblastoma variants. The results of the present study may therefore contribute to the growing evidence that differences in proliferative activity are associated with histological diversity in ameloblastoma.

Variation in Ki-67 findings between studies may be related to differences in sample size, histological composition, antibody clones, antigen-retrieval procedures, staining protocols, selection of microscopic fields, and scoring methods. Differences in the definition of a positive cell and the method used to calculate the labeling index may also influence reported values. Standardization of immunohistochemical techniques and scoring criteria is therefore important for reliable comparison between studies.

Although Ki-67 provides valuable information about proliferative activity, its interpretation should remain cautious. Increased Ki-67 expression may indicate a greater proportion of actively proliferating cells, but tumor behavior is influenced by several additional mechanisms, including differentiation, apoptosis, invasion, molecular alterations, and interactions with the tumor microenvironment. Therefore, Ki-67 should be considered a complementary biomarker rather than a sole predictor of aggressiveness or recurrence.

Overall, the present study supports the usefulness of Ki-67 immunohistochemistry for evaluating proliferative activity in ameloblastoma. The findings are consistent with the above-mentioned studies, which collectively indicate that proliferation-associated markers can help characterize biological differences among ameloblastoma variants. Further studies involving larger samples, standardized Ki-67 assessment, additional molecular markers, and long-term clinical follow-up are warranted to determine its precise prognostic significance.

V. Limitations

The present study has certain limitations that should be considered when interpreting the findings. First, the sample size was relatively small, particularly within the individual odontogenic tumor subgroups and ameloblastoma variants, which may have limited the statistical power to detect subtle differences in Ki-67 expression. Second, the study was conducted in a single institutional setting; therefore, the findings may not be directly generalizable to populations with different demographic or clinical characteristics.

The assessment of Ki-67 expression was based on immunohistochemical staining, which may be influenced by factors such as tissue fixation, staining procedures, antigen preservation, and the method used for determining the labeling index. Although standardized assessment criteria were applied, some degree of observer-related variation in identifying and counting positive cells cannot be completely excluded. In addition, the study evaluated Ki-67 as an indicator of cellular proliferative activity but did not investigate other molecular markers that could provide complementary information regarding the biological behavior of these tumors.

The cross-sectional nature of the study also prevented assessment of changes in Ki-67 expression over time or its direct relationship with clinical outcomes such as recurrence, treatment response, or long-term prognosis. Furthermore, the relatively small number of cases in some histopathological subgroups may have contributed to the absence of statistically significant differences despite numerical variations in Ki-67 labeling. Future multicenter studies involving larger cohorts, standardized digital image analysis, and longer clinical follow-up are warranted to validate these findings and clarify the prognostic significance of Ki-67 expression in odontogenic tumors.

VI. Conclusion

The present study demonstrated that Ki-67 immunohistochemical expression varies among odontogenic tumors and their histopathological subtypes. Ameloblastoma exhibited the highest Ki-67 labeling index, indicating greater proliferative activity compared with odontogenic myxoma, calcifying odontogenic tumor, and AOT. Within ameloblastoma, conventional ameloblastoma showed significantly higher Ki-67 expression than unicystic and peripheral variants, suggesting differences in proliferative potential among the major clinicopathological subtypes.

However, Ki-67 expression did not differ significantly among the follicular, plexiform, and other/mixed histopathological patterns of conventional ameloblastoma. These findings support the potential value of Ki-67 as an adjunctive marker for assessing proliferative activity in odontogenic tumors, particularly ameloblastoma. Nevertheless, Ki-67 expression should be interpreted alongside conventional histopathological findings and clinical characteristics rather than used as an independent indicator of tumor behavior. Larger, multicenter studies with standardized assessment methods and long-term follow-up are recommended to further establish the biological and prognostic significance of Ki-67 in odontogenic tumors.

Conflicts of Interest: Nil
Financial Support: None

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