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Original Article

Dentistry Section

Immunohistochemical Analysis of Ki-67 Expression in Odontogenic Keratocyst, Follicular Ameloblastoma, Well Differentiated Squamous Cell Carcinoma and Normal Oral Mucosa: A Cross-sectional Study

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ABSTRACT

Introduction: Odontogenic Keratocyst (OKC) is a developmental odontogenic cyst whereas ameloblastoma is a benign odontogenic epithelial tumour, and squamous cell carcinoma is a malignant epithelial neoplasm. Although OKC is classified as a cyst, its high proliferative potential and aggressive behaviour often lead to uncertainty regarding its neoplastic nature. Cellular proliferation can be assessed using Immunohistochemical (IHC) markers, among which Ki-67 is considered reliable as it is expressed in all active phases of the cell cycle (G1, S, G2, and M), making it an accurate indicator of proliferative activity.

Aim: To compare the Ki-67 Labelling Index (LI) of OKC, Follicular ameloblastoma, Well-Differentiated Oral Squamous Cell Carcinoma (WDOSCC) and normal oral mucosa.

Materials and Methods: The present cross-sectional study was conducted in Department of Oral Pathology, Pondicherry, Mahatma Gandhi Institute of Dental Science from June 2022 till June 2024 for a period of two years. The Study included histopathologically diagnosed, paraffin-embedded archival tissue blocks of OKC, Follicular Ameloblastoma, WDOSCC, and Normal Oral Mucosa, along with Fresh Biopsy Specimens of OKC, Follicular Ameloblastoma, WDOSCC, and Normal Oral Mucosa. A total of 48 Cases were included, comprising 12 Cases each of OKC without Inflammation (Group A), Follicular Ameloblastoma (Group B), WDOSCC (Group C), and Normal Oral Mucosa (Group D). Study was carried out using three microns paraffin embedded formalin fixed tissue sections which were stained immunohistochemically with Ki-67 antibody and its Labelling Index (LI) was evaluated by manual counting of 10 camera-captured hotspot areas at X200 magnification on zig-zag pattern to avoid repetition. The results were later evaluated statistically by IBM SPSS Version 20.0. Mean and Standard deviation (SD) were used to summarise the data. A p-value of <0.05 was considered as statistically significant difference. Statistical tests employed are tests of normality, One-way Analysis of variance (ANOVA) and appropriate post-hoc tests were performed for pairwise comparisons between groups.

Results: All cases of WDOSCC and normal oral mucosa were Ki-67 positive, whereas in contrast, positive expression was observed in 10 (83.3%) cases of OKC and 5 (41.7%) cases of Follicular Ameloblastoma. The mean labelling index of OKC was 17.13±10.40, Ameloblastoma was 2.14±2.97, of OSCC was 35.19±15.41, and of Normal oral mucosa was 19.29±4.09. Mean labelling index of WDOSCC was the highest followed by normal oral mucosa and OKC and the lowest in follicular ameloblastoma.

Conclusion: The study findings highlight distinct differences in cellular proliferation among oral lesions, supporting the aggressive nature of WDOSCC and the comparatively lower proliferative potential of follicular ameloblastoma. OKC and normal oral mucosa had almost similar Ki-67 LI.

Keywords: Biomarkers, Cell Proliferation, Labelling index, Odontogenic tumours, Tissue sections

INTRODUCTION

Odontogenic Keratocyst (OKC) is a developmental odontogenic cyst, Follicular Ameloblastoma is a benign odontogenic epithelial tumour, and Oral Squamous Cell Carcinoma (OSCC) is a malignant neoplasm arising from dysplastic oral epithelium [1-3]. Oral mucous membrane and odontogenic epithelium originate from the oral ectoderm [4]. The oral mucous membrane is the shared progenitor for OKC, ameloblastoma, and squamous cell carcinoma. However, OKCs and ameloblastomas are uniquely characterised by their additional origin in odontogenic epithelial tissue [5,6]. Though OKC is a cyst, there is always a dilemma whether it is a tumour because of its high proliferative nature and local aggressive behaviour [1]. Ameloblastoma is a benign tumour but locally infiltrative in nature [2]. Follicular ameloblastoma is the most common histopathological type of ameloblastoma among other types, i.e., plexiform, acanthomatous, granular, desmoplastic, and basal cell types [7]. Cells of normal appearing oral mucosa are regularly replaced by cell division in 2-3 weeks, beginning with the stratum basali, which is primarily made up of mitotic cells that proliferate before differentiating and migrating [8].

Cellular proliferation is assessed by various methods. One of the methods used is detection and assessment of expression of proliferative markers using IHC technique. Among all proliferative markers, Ki-67 protein is a well established one that is present during all the active phases of cell cycle (G1, G2, M and S phase). It is not detected during DNA repair activities and is consistently lacking in quiescent cells (G0 phase). Hence, it is a more accurate IHC marker for determining the proliferative activity [8]. The novelty of the present study is to assess the of Ki-67 proliferation of OKC, Follicular ameloblastoma, well differentiated squamous cell carcinoma keeping normal oral mucosa as baseline for comparison as clinical assessment and H&E staining alone cannot predict the future outcome of these lesions. By calculating the Ki-67 nuclear staining, it was tried to predict whether OKC, a questionable cyst or tumour, is proliferating like a benign odontogenic tumour or a well-differentiated surface epithelial malignant tumour, so that prompt

treatment modalities could be planned accordingly. In a similar way, the odontogenic tumour ameloblastoma, though benign, has the infiltrative ability to involve the underlying bone and is compared with well-differentiated carcinoma and the aggressive cyst, OKC. On baseline comparison, normal oral mucosa was used. By analysing the Ki-67 labelling index, the early treatment plan for these slowly growing lesions could be assessed.

The aim of the study was to analyse and compare the Ki-67 labelling index in odontogenic keratocyst (OKC), follicular ameloblastoma, well-differentiated oral squamous cell carcinoma (WDOSCC), and normal oral mucosa using immunohistochemistry. The objectives were to prepare histological sections from confirmed cases of OKC, follicular ameloblastoma, WDOSCC, and normal oral mucosa, and to evaluate them using Ki-67 as a nuclear proliferative marker. Immunohistochemical staining was performed to visualise and quantitatively analyse the expression pattern and Ki-67 labelling index in these tissue types. A comparative analysis was carried out to characterise the biological behaviour of these lesions in relation to normal oral mucosa based on their Ki-67 labelling index.

Alternate hypothesis: There is a significant difference in the Ki-67 expression between OKC, follicular ameloblastoma, well differentiated squamous cell carcinoma and normal oral mucosa.

Null hypothesis: There is no significant difference in the Ki-67 expression between OKC, follicular ameloblastoma, well-differentiated squamous cell carcinoma and normal oral mucosa

MATERIALS AND METHODS

This cross-sectional study was conducted in Department of Oral Pathology, Mahatma Gandhi Institute of Dental Sciences, Pondicherry. After obtaining ethical clearance (MGPGIDS/IEC/2022/MDS/ No.005/436), the study was conducted from June 2022 till 2024 June for a period of two years.

The primary inclusion criteria were archived, histopathologically diagnosed paraffin-embedded tissue blocks of odontogenic keratocyst (OKC), well-differentiated oral squamous cell carcinoma (WDOSCC), follicular ameloblastoma, and normal oral mucosa from the previous five years, as well as fresh biopsy specimens of OKC without inflammation (Group A), follicular ameloblastoma (Group B), WDOSCC (Group C), and normal oral mucosa (Group D). Twelve cases were included in each group, giving a total of 48 cases in the study. Normal oral mucosa is utilised as a fundamental control in Ki-67 assessment to establish a standardised baseline for healthy cellular turnover within the oral epithelium.

According to the institutional records, a total of 600 biopsy cases with a clinical suspicion of cyst, tumour, or carcinoma were reported over a period of five years. Of these, 84 cases were histopathologically confirmed as odontogenic keratocyst (OKC), follicular ameloblastoma, or squamous cell carcinoma, giving a prevalence of 14%, which was calculated using the following formula:

$$\text{Prevalence} = \frac{\text{no. of old + new biopsy confirmed cases x 100}}{\text{No of total biopsy cases suspecting tumour/cyst/SCC}}$$

The following formula was used for sample size calculation [9]:

$$n = \frac{p(100-p)Z^2}{E^2}$$

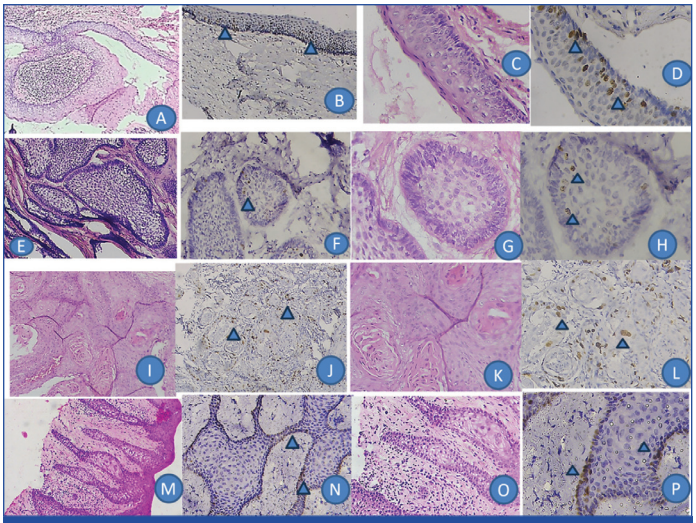
Where, 'n' is the sample size required, 'p' is the percentage occurrence of a state or condition (proportion or prevalence), 'E' is the maximum percentage error allowed, and 'Z' is the value corresponding to required confidence level. The prevalence of well differentiated OSCC, OKC, and ameloblastoma was reported to be 14% at the institution where the present study was conducted. With a 95% of confidence level and 10% maximum error, the minimum required sample size for the present study was calculated to be 47. Thus, a total of 48 specimens were included.

The study procedure was carried out using three microns of paraffin embedded formalin fixed tissue sections. Deparaffinisation of sections was performed using two changes of xylene for 30 minutes. Hydration of tissue sections was carried out in descending grades of ethanol, each for five minutes, followed by the antigen retrieval procedure. Later, the tissue sections were placed in stainless steel slide holding truff and kept in a small stainless steel container filled with antigen retrieval buffer solution (TRIS EDTA pH 8.8 to 9.2). Sections were fully immersed in the solution. Antigen retrieval was done using pressure cooker method. Antigen retrieval solution in the pressure cooker was preheated till vapour came using induction stove at 140°C. Tissue section containing container was placed in the pressure cooker, and the lid was closed. Heating was performed at 120°C until three whistles were released. Cooling was allowed to reach room temperature and then lid was opened. Sections were kept in deionised water for two changes, for two minutes each. Sections were kept in Tris wash buffer in two changes, for three minutes each. Peroxidase blocking was done for 12 minutes. Sections were immersed in wash buffer, two changes for three minutes. Sections were incubated with Ki-67 primary antibody (Pathnsitu) at room temperature in a humidifying chamber for one hour. A black paper was placed at the bottom of the humidifying chamber for better visualisation of the sections. The sections were then immersed in wash buffer in two changes, for three minutes each, followed by incubation with target binder (Pathnsitu) for 12 minutes. After incubation, the sections were immersed in wash buffer in two changes, for three minutes each, and subsequently incubated with biotinylated secondary antibody (Pathnsitu) at room temperature in a humidifying chamber for 12 minutes. The sections were again immersed in wash buffer in two changes, for three minutes each, followed by incubation with peroxidase-labelled streptavidin. Finally, the sections were immersed in distilled water in two changes, for two minutes each. Sections were incubated in freshly prepared 3,3′-diaminobenzidine (DAB) chromogen for five minutes. Sections were immersed in distilled water for two minutes in two changes. Counterstained with Mayer's haematoxylin for one minute. Bluing of sections was carried out for five minutes.

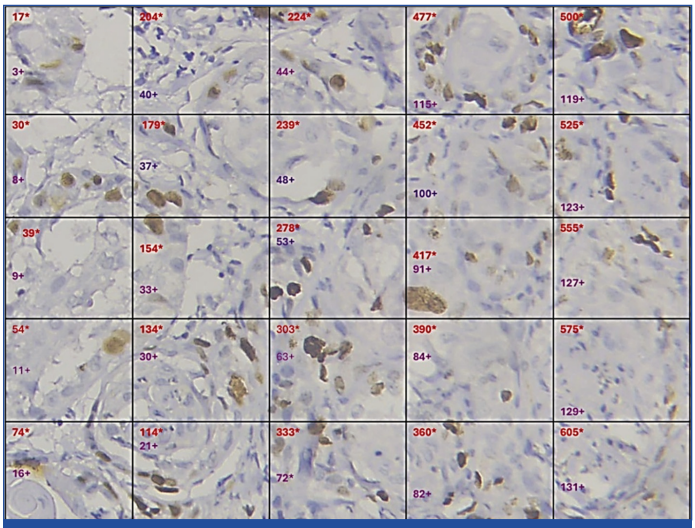
For IHC procedures, positively charged slides (Pathnsitu) were used, and for Haematoxylin and Eosin (H&E) staining, egg albumin-coated slides were used. Basically each group has total of 24 slides, 12 for H&E staining and 12 for IHC staining.

The stained sections mounted on glass slides were examined under a binocular light microscope. Brown coloured-stained nuclei were considered positive for Ki-67 [Table/Fig-1].

Per high-power field, Ki-67 positive cells were counted among the total number of cells in the epithelial lining of OKC, follicles of Follicular ameloblastoma, epithelial islands in WDOSCC, and stratified squamous epithelium of normal mucosa. In this study, an intraexaminer pathologist examined the IHC stained slides twice at different time intervals thoroughly and selected 10 hotspot areas. The 'hotspot areas' refers to the selection area of brown stained cells with a high proliferative activity of more positive area. Manual Counting was performed on Camera-Captured 10 hotspot areas under X200 magnification, whereas in each field of stained section, counting was done manually in a zig-zag manner starting from the top left-hand corner, going downwards untill the end of that field section, then turning towards the right-hand side and proceeding to the topmost area, ending at bottom right end side of that field. This approach was followed to avoid repetition during counting, and the results were evaluated statistically [Table/Fig-2]. The labelling index was calculated as the number of Ki-67 positive cells x 100 divided by the total number of cells in each field. The mean labelling index was calculated for 10 fields, and the average mean was considered as the mean labelling index for that case group. For 12 cases, an average mean was obtained for each case group, and the mean difference was also calculated by subtracting the values between the two different groups.



[Table/Fig-1]: Representative photomicrographs showing: A) OKC (H&E: x10); B) Ki-67 stained OKC (IHC; x10); C) OKC (H&E : x40); D) Ki-67 stained OKC (IHC; x40); E) follicular ameloblastoma (H&E: x10); F) Ki-67 stained follicular ameloblastoma (IHC: x10); G) follicular ameloblastoma (H&E; x40); H) Ki-67 stained follicular ameloblastoma (IHC; x40); I) WDOSCC (H&E; x10); J) Ki-67 stained WDOSCC (IHC; x10); K) WDOSCC (H&E; x40); L) Ki-67 nuclear stained area of WDOSCC (IHC; x40); M) lining area of normal oral mucosa (H&E; x10); N) Ki-67 stained normal oral mucosa (IHC; x10); O) normal oral mucosa (H&E; x40); P) Ki-67 stained normal oral mucosa (IHC; x40) represents area of Ki-67 positive cells region.



[Table/Fig-2]: Representative photomicrographs (X400) showing maximum positive Ki-67 cells in WDOSCC among the 4 groups. Coloured red number on top left-side of each grid 5x5 represents the total epithelial cells present and coloured violet number below it represents the positive stained cells which is later calculated by formula of total positive x 100 divided by total epithelial cells present.

STATISTICAL ANALYSIS

The collected data was analysed using both descriptive and inferential statistics. Mean and SD were used to summarise the data. Statistical analysis was done by IBM SPSS (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp). A p-value of <0.05 was considered statistically significant. Statistical tests employed were tests of normality, one-way ANOVA and if appropriately required pair wise tests were used.

RESULTS

The mean age of patients with OKC in this study was 24±10.76 years, with a range of 10-50 years; Follicular ameloblastoma was 35.67±14.92 years, with a range of 15-70 years; OSCC was 54.17±9.38 years, with a range of 39-71 years; and normal oral mucosa was 25.25±2.8 years, with a range of 21-30 years [Table/Fig-3].Among OKC and normal oral mucosa cases, seven were male and five were female. Among follicular ameloblastoma and WDOSCC cases, nine were male and three were females [Table/Fig-3]. Out of the 48 cases in this study, all cases of well-differentiated OSCC and normal oral mucosa were Ki-67 positive, whereas Ki-67 positivity was observed in 83.3% of OKC cases and 41.7% of follicular ameloblastoma cases [Table/Fig-3].

Ki-67 positive cells were seen in the basal and suprabasal layers of the epithelial lining, with more suprabasal cells observed in OKC, peripheral ameloblast-like cells, and a few stellate reticulum-like cells of follicular ameloblastoma, peripheral cells and a few cells above them in the epithelial island of WDOSCC; and basal cells of the stratified squamous epithelium of normal oral mucosa. The mean Ki-67 labelling index of WDOSCC was the highest, followed by normal oral mucosa and OKC, and was lowest in follicular ameloblastoma [Table/Fig-3].

A one-way ANOVA (analysis of variance) test was employed to assess the intergroup comparison of Ki 67 expression, showing a significant difference with a p-value < 0.001 [Table/Fig-4].

Hence, the pair wise analysis was carried out to find the multiple comparison between groups, which showed that there were significant differences in the Ki-67 labelling index values between Groups A, B, C, and D. Group-C showed higher labelling index value than groups A, B and D. However, there was no significant difference in Ki-67 expression between Group A and Group D, indicating that both groups showed similar Ki-67 expression levels. Group-B showed lower labelling index value compared to the rest of the groups i.e., Group-A, Group-C and Group-D are with a statistically significant difference (p-value 0.002, <0.000 and <0.000), respectively [Table/Fig-5].

DISCUSSION

Cellular proliferation assessing methods used earlier included mitotic figure count, AgNOR count, and S phase labelling with thymidine and BrdUrd. Recent methods for assessing proliferation include immunohistochemistry, in situ hybridisation, and flow cytometry. Immunohistochemistry is quicker, easier to use, and comparatively less expensive than other techniques. It also preserves cellular and tissue structures better. Therefore, IHC techniques are better than alternative methods [8].

There are many IHC proliferative markers, e.g., PCNA, Ki-67, mitosin, MCM complex, geminin, cyclin D1, and topoisomerase II. "Proliferative markers" (PM) are proteins that precisely indicate actively growing and dividing cells. For this kind of marker two requirements have been postulated (van Dierendonck et al., 1989):

	Sum of squares	Degrees of freedom (DF)	Mean square	F	p-value
Between groups	6574.652	3	2191.551	23.614	<0.001
Within groups	4083.597	44	92.809		

[Table/Fig-4]: Intergroup comparison of Ki-67 expression of study participants. One-way ANOVA is used. Values presented as mean±SD, p<0.001 considered statistically significant

Groups	Age (Mean±SD)	Gender n (%)		Positive cases	Negative case	Mean Ki-67 (Mean±SD)
		Male	Female			
Group-A (OKC)	24±10.76	7 (58.3%)	5(41.7%)	10 (83.33%)	2 (16.67%)	17.13±10.40
Group-B (Follicular ameloblastoma)	35.67±14.92	9 (75%)	3 (25%)	5 (41.67%)	7 (58.33%)	2.14±2.97
Group-C (WDOSCC	54.17±9.38	9 (75%)	3 (25%)	12 (100%)	0	35.19±15.41
Group-D (normal oral mucosa)	25.25±2.8	7 (58.3%)	5(41.7%)	12 (100%)	0	19.29±4.09

[Table/Fig-3]: Distribution of study participants according to age, gender, immunohistochemical reactivity, and mean Ki-67 labeling index.

Groups		Mean difference	Std. error	p-value	95% Confidence interval	
					Lower bound	Upper bound
Group-C	Group-A	18.0641667	3.9329594	<0.001*	7.563143	28.5655191
	Group-B	33.0250000	3.9329594	<0.001*	22.975953	43.907380
	Group-D	15.9000000	3.9329594	0.001*	5.398976	26.401024
Group-D	Group-A	2.1641667	3.9329594	0.946	-8.336857	12.665191
	Group-B	17.1250000	3.9329594	<0.001*	6.623976	27.626024
Group-A	Group-B	14.9608333	3.9329594	0.002*	4.459809	25.461857

[Table/Fig-5]: Pair wise analysis of comparison between the groups.
Post-hoc analysis done, p<0.001 considered statistically significant

1) the antigen should be continuously present during the cell cycle of all cell types; and 2) the transition to any type of non-proliferative state from any phase of the cell cycle should be followed by a rapid disappearance of the antigen [10].

Among all these markers, Ki-67 protein fulfils these criteria, as it is present during all the active phases of the cell cycle, absent during DNA repair activity and is lacking in quiescent cells. Hence, it is a more accurate IHC marker for determining cell proliferative activity [10].

Gerdes J et al., first discovered Ki-67 as a monoclonal antigen recognised by the antibody in early 1980. This antibody was created by immunising animals with nuclei from the Hodgkin cancer cell line L428. The number of the original clone in the 96-well plate and the city of origin (Kiel) are combined to form the name Ki-67. Since the antigen had not yet been described, it was first known as the Ki-67 antigen. Once it was discovered to be a protein, it was named as Ki-67 protein. To avoid confusion, the name Ki-67 was retained [11].

In this study, The mean age of OKC (Group A) was similar to the study of Myoung H et al., [12]. The mean age of follicular ameloblastoma (Group B) was similar to that reported by Ragunathan YT et al., [13]. The mean age of WDOSCC (Group-C), was also similar to that reported by Bhurgri Y et al., in 2006 [14].

The mean Ki-67 LI of OKC (Group A) in this study was 17.13±10.40 which was similar to the findings of studies conducted by Modi TG et al., and Dandena VK et al., [8,15]. They reported the mean LI values of OKC were 12.76± 4.78 and 7.4±0.54, respectively. They reported mean Ki-67 LI values of 12.76±4.78 and 7.4±0.54, respectively. They also observed high Ki-67 positivity in 93% of cases. In contrast, low Ki-67 positivity (23%) was observed in the study by Hammad HM et al., [16]. Kaplan I et al., studied the proliferation rate of 45 OKC cases with and without inflammation using two proliferative markers, i.e., Ki-67 and PCNA [17]. The study mentioned that there was a focal increase in Ki-67 expression adjacent to moderate and severe inflammation, however it did not show a significant effect on the overall proliferation activity of OKC. To study the exact proliferation rate, all OKC cases without inflammation were selected, similar to the study conducted by Hammad HM et al., [16]. Modi TG et al., in 2018, studied the expression of Ki-67, among 45 cases of odontogenic cysts, included 15 cases each of OKC, Radicular Cyst (RC) and Dentigerous Cyst (DC) [8]. They observed Ki-67 positivity separately in basal and supra-basal layer of epithelial lining of all these cysts. RC and DC had higher labelling index in basal cells whereas OKC had higher labeling index in the suprabasal cells. In present study , the proliferation rate was counted in all layers of the epithelial lining of OKC, similar to the studies conducted by Kim DK et al. and Li TJ et al. [18,19].

Ki-67 positivity in follicular ameloblastoma (Group-B) was 41.7%, in the present study [Table/Fig-3]. In previous research, Li TJ et al., found 75% positivity [20], whereas Jaafari-Ashkavandi Z et al., found 100% Ki-67 positivity of all ameloblastoma case examined [2]. In the present study, follicular ameloblastoma (Group-B) showed around showed a Ki-67 negativity rate of approximately 58.33%. In previous studies, Li TJ et al., reported a 25% Ki-67 negativity rate, whereas Mithra S et al. reported a 100% negativity rate [20,21].

Among six histopathologically classified types of ameloblastoma, Piattelli A et al., and Hegab A et al., found the highest Ki-67 positivity in plexiform ameloblastoma, whereas Rizzardi C et al., found the highest Ki-67 positivity in granular cell ameloblastoma [22-24]. In this study, Ki-67 expression was evaluated in follicular ameloblastoma alone, without comparison of other ameloblastoma subtypes. In the present study, the mean LI of Ki-67 in follicular ameloblastoma (Group-B) was 2.14±2.97, which is comparable to the findings reported by Jaafari-Ashkavandi Z et al., Li TJ et al., Ong'uti MN et al., Razavi SM et al., and Sandra F et al., [2,20,25-27]. These studies reported mean LI values of 6±4.2, 4.1 (±1.6), 5.0 (±0.5), 4.31±6.27, and 3.7±2.3, respectively.

In the present study, all cases of WDOSCC (Group-C) were positive for Ki-67, similar to the findings reported by Birajdar SS et al., Dwivedi N et al., and Kurokawa H et al., [3,28,29]. In this study, the mean Ki-67 LI of WDOSCC (Group-C) was 35.19± 15.41, similar to the study done by Dwivedi N et al., and Kurokawa H et al., [28,29]. Mean LI values reported in their studies were 39.45±21.1 and 42.87±18, respectively. Studies conducted by Takkem A et al. and Tumuluri V et al., found lower mean LI values of 23.3and 15.49±8.06, respectively [30,31].

In the present study, all cases of normal oral mucosa (Group D) showed 100% Ki-67 positivity, similar to the findings reported by Montebugnoli L et al., Torres-Rendon A et al., and Beevi BH et al., [32-34]. Mean Ki-67 LI values in their study were 17.6% (±8.2%), 22.94 (±5.2), and 23.20 (±2.89), respectively. In the present study, the mean Ki-67 labeling index of normal oral mucosa was 19.29±4.09.

On comparison of the proliferative Ki-67 index of the OKC, follicular ameloblastoma, well-differentiated oral squamous cell carcinoma and normal oral mucosa, follicular ameloblastoma showed the least proliferative rate. OKC was found to proliferate at the same rate as normal oral mucosa.

This reduced basal Ki-67 expression in OKC compared to oral mucosa indicates that OKC grows through a distinct, ordered expansion of the entire epithelium rather than through only rapid basal cell division. Quantitative variations in the epithelium's proliferative activity in OKC are thought to indicate an innate growth potential that may contribute to the cell's development and biological behaviour, as well as aberrant cell cycle regulation. By various molecular discoveries, OKCs may be a low-grade neoplasm rather than a developing cyst due to their biologically aggressive behaviour and intrinsic growth potential of the epithelium.

Future investigations incorporating larger, multi-center cohorts, standardised IHC protocols, and correlation with clinical outcome. Molecular markers are recommended to further elucidate the prognostic significance of Ki-67 expression and to better define the biological behaviour of these lesions.

Limitation(s)

More number of cases could not be studied in all groups due to lack of availability of cases, OKC with inflammation interference, archived tissues greater than five years, decalcified tissues which reduces antigencity of the tissues this study has the inability to determine precise proliferative rates, likely due to the limited sample

size and inherent methodological constraints, warrants cautious interpretation of the results.

CONCLUSION(S)

The present study demonstrates distinct differences in Ki-67 expression among odontogenic and epithelial lesions, underscoring variability in their proliferative potential. OKC exhibited a significantly higher Ki-67 labelling index than follicular ameloblastoma, yet a lower proliferative activity when compared with OSCC.

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