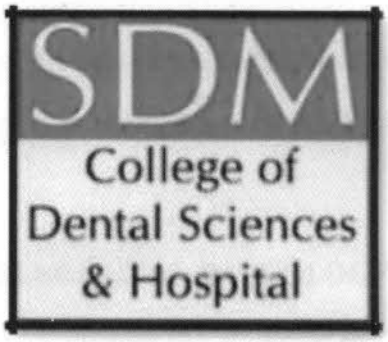
"IMMUNOHISTOCHEMICAL ANALYSIS OF CELL-CYCLE ASSOCIATED PROTEINS Mcm-2 AND Ki-67 IN ORAL VERRUCOUS LESIONS AND ORAL SQUAMOUS CELL CARCINOMA: A COMPARATIVE STUDY"



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ABSTRACT

Background: Oral potentially malignant lesions (PML) and malignant lesions (ML) of the verrucous type have been considered as a histologically diverse and diagnostically difficult group of lesions.[1] Various studies have been put forward to differentiate between PML and ML. Many immunohistochemical markers of various groups have been used for tumor prognostication in oral verrucous lesions including PML and ML. Mcm-2 is a biomarker belonging to Mcm family of proteins which has rarely been used in oral potentially malignant and malignant lesions of the verrucous type. It is expressed throughout the whole cell cycle including G0 and G1 phase. This characteristic cell cycle event is not found in other proliferative markers like Geminin, AgNOR, Ki-67and PCNA.

Aims and Objectives: The objective of this study is to assess the expression of Mcm-2 in Normal Oral Mucosa (NM), Verrucous Hyperplasia (VH), Verrucous Carcinoma (VC), Verrucous Squamous Cell Carcinoma (VSCC) and Oral Squamous Cell Carcinoma (OSCC) and compare it with the clinicopathological characteristics. This study alsoaims to assess the overall survival and disease free survival in VSCC and conventional OSCC and compare with the Mcm-2 and Ki-67 nuclear expression.

Materials and Methods: A total of 90 cases, including buffered formalin fixed, paraffin embedded tissues (FFPE) of previously histopathologically diagnosed cases of NM, VH with/without dysplasia, VC, VSCC and OSCC, were retrieved from the Department of Oral and Maxillofacial Pathology, SDM College of Dental Sciences and Hospital, Dharwad. Quantitative analysis was done by evaluating the percentage of positive tumor cells (nLI) among a minimum of 500 tumor cells. The semi-quantitative analysis was carried out by dividing the epithelium level-wise and evaluating the percentage of positive cells in each level in Groups B, C and D. The

obtained results were subjected for statistical evaluation using Independent T-test, Spearman's rho analysis, Cox-regression model and Kaplan-Meier Survival analysis.

Results: The average nLI of Mcm-2 and Ki-67expression in NM was 49.08% and 19.05% respectively. Mcm-2 overexpression was seen in all the cases of VH with Dysplasia, VC, VSCC, and conventional OSCC. There was a significant progressive increase in nuclear Labelling Indices (nLI) of Mcm-2 and Ki-67 from NM (49.08%), VC (60.45%), VH with Dysplasia (64.10%), and OSCC (89.22%). Increase nuclear expression of Mcm-2 in several clinico-pathologic parameters and other histological prognosticators like Broder's grading, POI, DOI, PVI, PNI, ECS was noted, although no statistical significance was noted. There was a difference in the level-wise expression pattern of Mcm-2 and Ki-67 in verrucous group of lesions (Group B, C and D). The 3 year OS and DFS was reduced in conventional OSCC (75% and 64.3%) as compared to VSCC (90% and 70%).

Conclusion: The present study was the first initiative with Mcm-2 and Ki-67 to differentiate between oral verrucous lesions and OSCC. Mcm-2 can be used to differentiate among the diverse group of oral potentially malignant and malignant verrucous lesions. Moreover, Mcm-2 is a pan-cell cycle marker which overcomes the shortcomings of conventional proliferation markers like Ki-67.

Mcm2 as a proliferation marker may be superior to Ki67 because it indicates licensed capacity.

Key words: Mcm-2, Ki-67, hyperplasia, dysplasia, carcinoma.