



## STUDY OF EXPRESSION OF KI67 AS A MARKER FOR SEVERITY OF ORAL DYSPLASIA AND ORAL SQUAMOUS CELL CARCINOMA

### Pathology

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### ABSTRACT

**Background & objectives:** Oral epithelium shows transition from normal to various grades of dysplasia to Oral Squamous cell carcinoma by increased cellular proliferation. Ki67, a nuclear membrane protein, is an excellent marker of cellular proliferation. The labeling index and pattern of expression of Ki67 can be used to evaluate the grading of such lesion.

**Methods:** 15 dysplastic lesions were divided into low risk group (mild dysplasia) and High risk group (moderate and severe dysplasia). 20 cases of oral squamous cell carcinoma are divided into WDSCC (10), MDSCC (5), and PDSCC (5)

**Results:** All the cases showed Ki67 positivity. Most of low dysplastic cases showed only basal and parabasal positivity. And most of high dysplastic lesions and OSCC showed all layer positivity.

**Interpretation & Conclusions:** Expression of Ki67 provides objective criteria for determining the severity of dysplasia and grades of OSCC and thus can be used as an objective marker to evaluate the grading of such lesion.

### KEYWORDS

suprabasal, dysplasia, squamous, carcinoma, ki67, labelling index, oral epithelium

### INTRODUCTION

Oral squamous cell carcinoma is one of the most common cancers of head and neck region. Transition of normal oral epithelium to various degrees of dysplasia and to malignancy is featured by increased cell proliferation<sup>1</sup>. Ki67 is a nuclear membrane protein which is present in G1,S,G2 phase but absent in G0 phase. Therefore it is an excellent marker of cell proliferation<sup>2</sup>. The fraction of Ki67 positive cells i.e. Labeling index (Li) is correlated with the clinical course of the disease<sup>3</sup>. Here we are presenting expression of Ki67 in oral dysplastic lesions and OSCC.

### MATERIAL & METHODS

We have taken 15 cases of oral dysplastic lesions and 20 cases of OSCC. 15 dysplastic lesions were divided into low risk group (mild dysplasia) and High risk group (moderate and severe dysplasia), according to binary system of grading. 20 cases of oral squamous cell carcinoma are divided into WDSCC (10), MDSCC (5), PDSCC (5) according to Broders grading.

Nuclei positive just above basement membrane- parabasal layer (nuclei positive within two layers above basement membrane and next to basal layer) and suprabasal layer is above parabasal layer.

Standard procedures were followed while doing used IHC on the cases. Ki67 analysis was done on parameters such as distribution of expression in all layer, intensity of staining and the labelling index (LI).<sup>4,5</sup> The labeling index or percentage of positive cells is calculated by dividing the number of positive cells by total number of cell counted.<sup>6</sup> Only nuclear staining of epithelial cells was observed. Nuclei with clear brown color regardless of staining intensity regarded as positive. The area with maximum number of positive cell was considered in each section.

This study has been approved by the Institutional Ethics Committee of Gauhati Medical College and Hospital.

### RESULTS

(i) Ki67 positively stained in all of the cases

- (ii) Mean labeling index of PDSCC>MDSCC>WDSCC and OSCC>Dysplastic lesion.
- (iii) Most of low risk dysplastic cases showed basal and parabasal layer positivity.
- (iv) High risk dysplastic lesion and OSCC showed mostly suprabasal and all layer positivity,

All PDSCC = All Layer positive.

4/5 MDSCC = All layer positive., 1/5 = Suprabasal

7/10 WDSCC = Suprabasal

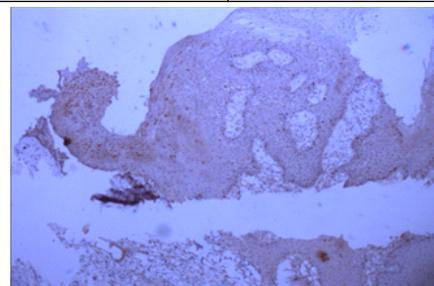
3/10 WDSCC = All layer

**Table 1: For mean labelling index of dysplastic and malignant lesions**

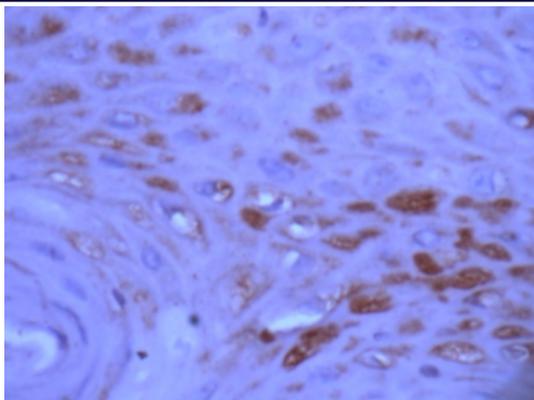
	MEAN LABELLING INDEX (%)	SD(±)
Dysplastic	33.2	4.76
Malignant	52.166	18.42

**Table 2: Mean labeling Index of Malignant cases.**

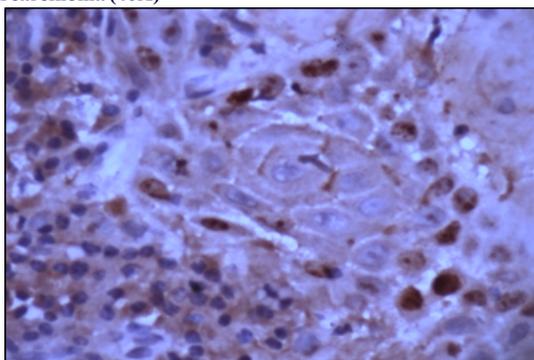
GRADING	Mean Labelling Index(LI) %
WDSCC (Ia)	42.52
MDSCC (Ib)	71.14
PDSCC (Ic)	91.0



**Figure 1: Ki67 positivity in well-differentiated Squamous cell carcinoma (6x)**



**Figure 2: Ki67 positivity in moderately differentiated squamous cell carcinoma (40X)**



**Figure 3: Suprabasal expression of ki67 in moderately differentiated squamous cell carcinoma (40x)**

#### DISCUSSION

The labeling index of Ki67 is increased according to severity and grades of dysplasia. Statistically significant difference of LI among dysplastic and OSCC is seen<sup>7</sup>. In low risk dysplasia maximum expression of Ki67 seen in basal and parabasal layer.

High risk dysplastic lesions and most of OSCC showed all layer or suprabasal expression.

Study done by Humayun S, Ram Prasad *et al*<sup>4</sup>(2011) found statistically significant difference of LI among normal, nondysplastic, premalignant and malignant lesions.

Study done by Nidhi Dwivedi *et al*<sup>5</sup>(2013) found significant difference of LI according to increased severity of dysplasia.

Study done by Sharmistha M *et al*<sup>6</sup>(2014), found significant difference towards high grades of tumour.

Study done by Smita Shrishai *et al*<sup>8</sup> (2014) found statistically significant difference among dysplastic premalignant lesion and oral squamous cell carcinoma.

Our study correlates with the above mentioned studies.

This pattern of expression and Labelling index of Ki67 provides an objective criteria for determining the severity of dysplasia and grades of OSCC. So can be used as an objective marker to evaluate the grading of such lesion. This may serve as an important tool for cancer prevention programme or prognostic marker for oral premalignant and malignant lesions.

#### CONCLUSION:

Thus from the above study we can conclude that labeling index of Ki67 and its expression can be taken as a prognostic marker and to assess the severity of the disease.

**Conflicts of Interest :** No conflict of interest

#### REFERENCES.

1. Dwivedi N, Chandra S, Kashyap B, Raj V, Agarwal A. Suprabasal expression of Ki-67 as

a marker for the severity of oral epithelial dysplasia and oral squamous cell carcinoma. Contemporary clinical dentistry. 2013 Jan;4(1):7.

2. Scholzen T, Gerdes J. The Ki-67 protein: from the known and the unknown. Journal of cellular physiology. 2000 Mar;182(3):311-22.
3. Gonzalez-Moles MA, Ruiz-Avila I, Rodriguez-Archilla A, Martinez-Lara I. Suprabasal expression of Ki-67 antigen as a marker for the presence and severity of oral epithelial dysplasia. Head & Neck: Journal for the Sciences and Specialties of the Head and Neck. 2000 Oct;22(7):658-61.
4. Humayun S, Prasad VR. Expression of p53 protein and ki-67 antigen in oral premalignant lesions and oral squamous cell carcinomas: an immunohistochemical study. National journal of maxillofacial surgery. 2011 Jan;2(1):38.
5. Dwivedi N, Chandra S, Kashyap B, Raj V, Agarwal A. Suprabasal expression of Ki-67 as a marker for the severity of oral epithelial dysplasia and oral squamous cell carcinoma. Contemporary clinical dentistry. 2013 Jan;4(1):7.
6. Patel SM, Patel KA, Patel PR, Gamit B, Hathila RN, Gupta S. Expression of p53 and Ki-67 in oral dysplasia and squamous cell carcinoma: An immunohistochemical study. Int J Med Sci Public Health. 2014 Oct 1;3:1201-4.
7. Macluskey M, Ogden GR, Green M, Chisholm DM, Schor SL, Schor AM. The association between epithelial proliferation and disease progression in the oral mucosa. Oral oncology. 1999 Jul 1;35(4):409-14.
8. Birajdar SS, Radhika MB, Paremala K, Sudhakara M, Soumya M, Gadivan M. Expression of Ki-67 in normal oral epithelium, leukoplakic oral epithelium and oral squamous cell carcinoma. Journal of oral and maxillofacial pathology: JOMFP. 2014 May;18(2):169