STUDY OF IMMUNOHISTOCHEMICAL EXPRESSION OF Ki-67 IN SQUAMOUS CELL CARCINOMA OF CERVIX

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ABSTRACT

BACKGROUND
Cervical cancer is the second most common cancer cause of death among women in developing countries. Recently parameters of cell proliferation have emerged as important tools in the evaluation of dysplastic and neoplastic lesions of the cervix.

The aim of this study was to study the immunohistochemical expression of Ki-67 in squamous cell carcinoma of the cervix.

MATERIALS AND METHODS
63 cases of histologically proven squamous cell carcinoma (SCC) of the cervix were included in the study. Ki-67 immunostaining was done and labelling index was calculated. ANOVA test was applied to see correlation of Ki-67 expression with different grades of squamous cell carcinoma.

RESULTS
The Ki-67 labelling index was maximum in poorly differentiated SCC and minimum in well-differentiated SCC and p value amongst these groups was found to be statistically significant.

CONCLUSION
Ki-67 labelling index has a positive association with histological grading in squamous cell carcinoma of cervix.

KEYWORDS
Ki-67, Squamous Cell Carcinoma of Cervix.

peroxide. To visualise the end product haematoxylin was used as a counter stain.

Ki-67 labelling index was calculated by the number of positive cells per 200 cervical epithelial cells under ×400 magnification. Positive nuclei were expressed as the percentage of total nuclei counted. Modified Broder’s grading system was used for grading squamous cell carcinomas. Carcinomas were divided into three grades: well-differentiated squamous cell carcinoma (WDSCC), moderately differentiated squamous cell carcinoma (MDSCC) and poorly differentiated squamous cell carcinoma (PDSCC). WDSCC showed abundant intercellular bridging, cytoplasmic keratinisation and keratin pearls, nuclear pleomorphism was minimal and mitotic figures were <2/hpf. In MDSCC individual cell keratinisation, moderate nuclear pleomorphism and mitotic figures up to 4/hpf were present. In PDSCC immature tumour cells with scant cytoplasm, marked nuclear pleomorphism, and mitotic figures, >4/hpf were present.

All the data was entered in database file and analysis was done using SPSS 20 version. ANOVA test was applied to see correlation of Ki-67 expression with different grades of SCC. P value less than 0.05 was considered as significant.

RESULTS
The mean Ki-67 Index % observed was 54.0 ± 2.64 for those diagnosed as well-differentiated squamous cell carcinoma (SCC-WD), 63.0±4.17 for patients diagnosed as moderately differentiated squamous cell carcinoma (SCC-MD), and 85.5±9.3 for patients diagnosed for poorly differentiated squamous cell carcinoma (SCC-PD), and the difference in the Ki-67 Index among different forms of squamous cell carcinoma was highly statistically significant P<0.001 (Table 1).

Increase in Ki-67 expression was seen with the increasing grade of SCC. All 5 patients of SCC-PD were highly proliferative with an expression of Ki-67 in 70% or more of the cells. Among the SCC-MD lesions, 34/49 (69.4%) expressed Ki-67 in 30 to <70% of the cells and 9 out of 49 (18.4%) cases showed Ki-67 expression in 70% and more than of the cells. In SCC-WD lesions, mostly 5 patients out of 9 (55.5%) had expression of Ki-67 in 30 to <70% of the cells.

DISCUSSION
In the present study, total number of cases was 63. Among them, most (77.7%) were diagnosed as Moderately Differentiated Squamous Cell Carcinoma (SCC-MD) followed by 14.2% cases of Well-Differentiated Squamous Cell

![Figure 1. Photomicrograph of SCC-WD Showing Ki-67 Positivity (IHC Ki-67, 40X)](image1)

![Figure 2. Photomicrograph of SCC-MD Showing Ki-67 Positivity (IHC Ki-67, 40X)](image2)

![Figure 3. Photomicrograph of SCC-PD Showing Ki-67 Positivity (IHC Ki-67, 40X)](image3)
Carcinoma (SCC-WD) and 7.9% cases of Poorly Differentiated Squamous Cell Carcinoma (SCC-PD) respectively. Similar results were found by Hemlata Panwar et al. where out of the 78 cases of biopsy-proven invasive carcinoma, 54 cases had moderately differentiated squamous cell carcinoma, followed by 10 cases of well-differentiated SCC and 5 cases of poorly differentiated SCC.

Our cases showed an increase in the Ki-67 expression in relation to increase in the grade of the lesion. The mean Ki-67 Index % observed was 54.0 ± 2.64 for patients diagnosed as Well Differentiated Squamous Cell Carcinoma (SCC-WD), 63.0 ± 4.17 for patients diagnosed as Moderately Differentiated Squamous Cell Carcinoma (SCC-MD), and 85.5 ± 9.3 for patients diagnosed as Poorly Differentiated Squamous Cell Carcinoma (SCC-PD), and the difference was highly significant statistically (P<0.001). Similar result was found by Gupta K et al in their study which reported the mean LI in WD SCC was 55.33 ± 7.79; in MDSCC was 43.97 ± 3.152 and in PDSCC was 80 ± 5. The study conducted by Pahuja et al showed an increase in LI from WDSCC to PDSCC with maximum mean value in PDSCC similar to the present study. The study conducted by Nam et al. also showed an increase in LI from WD SCC to PD SCC.

Mehrotra A et al reported Ki-67 labelling index (LI) increased from dysplasia to carcinoma group. Statistical analysis showed that Ki-67 LI was significantly higher in diseased group as compared to normal group (P<0.001). Carreras R et al. reported increase in the Ki-67 expression in relation to increases in the severity of the lesions which is similar to our study.

In SCC-WD lesions, 5 patients out of 9 (55.5%) had expression of Ki-67 in 60 to <70% of the cells; 4/9 (44.4%) had expression of Ki-67 in 10 to <30% of the cells. None of the cells showed expression of 0 to <10% and in between to 70 to 100%. Among the SCC-MD lesions, 34/49 (69.4%) showed expression of Ki-67 in 30 to <70% of the cells, 9 out of 49 (18.4%) cases showed Ki-67 expression in 70% and more than of the cells and 6 out of 49 (12.24%) cases showed Ki-67 expression in 10 to <30%. None of the cases showed Ki-67 expression in 0 to <10%. All 5 patients of SCC-PD were highly proliferative with an expression of Ki-67 in 70% or more of the cells. None of the cases showed Ki-67 expression in 0 to <10%, 10 to <30% and 30 to <70% category (Table 2). Reuschenbach M et al. found the proportion of lesions with Ki-67 expression in 70% or more of the cells was somewhat higher in the carcinomas (21/46, 45.7%) than in the CIN3/carcinoma in situ (CIS) group of cases.

CONCLUSION
We conclude that MIB-1 staining shows an increasing trend in the Ki-67 labelling index with increasing grades of SCC.

REFERENCES