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Assessment of Apoptotic Index in Various Grades of Oral Epithelial Dysplasia

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ABSTRACT:
Background: Oral Squamous Cell Carcinoma (OSCC) spreads locally and metastasizes in the different routes of lymph nodes. This chronic disease is a public health problem both in developing as well as developed countries. The present study was conducted to assess apoptotic index in various grades of oral epithelial dysplasia.
Materials & Methods: 60 histopathologically diagnosed cases of hyperkeratosis with varying degree of dysplasia and different grades of oral squamous cell carcinomas of both genders were included. The apoptotic cells ratio was evaluated as: Apoptotic Index (AI) = Total no. of apoptotic cells/ Total no. of cells in 10 HPF.
Results: The mean dysplasia in normal cells was 0.0014, mild dysplasia was 0.003, moderate dysplasia was 0.005, severe dysplasia was 0.013 and no dysplasia was 0.002. The mean difference of different grades in normal cells was 0.014, in well differentiated SCC was 0.018, in moderately differentiated SCC was 0.016 and in poorly differentiated SCC was 0.002. The difference was significant ($P< 0.05$).
Conclusion: Authors found the clinical significance of apoptosis in assessing disease progression in oral potentially malignant disorders.
Key words: Apoptosis, potentially malignant disorder, Dysplasia

INTRODUCTION

Oral Squamous Cell Carcinoma (OSCC) spreads locally and metastasizes in the different routes of lymph nodes. This chronic disease is a public health problem both in developing as well as developed countries.[1] The burden of Oral squamous cell carcinoma is great because of the associated high cost of treatment, permanent impairment and high mortality. The prevalence of oral squamous cell carcinoma is high in Asian countries especially Southeast Asia.[2]

Oral squamous cell carcinomas (OSCC) are amongst the most aggressive of tumors. The 5-year survival rate reported for some parts of the oral cavity is as low as 9%, largely due to late-stage diagnosis of the tumor. In the case of early detection and treatment of OSCC, the survival rate significantly increases from 66% to 85%. It has been previously reported that the diagnosis and management at the "precancerous" stage would further improve survival rates. OSCC is commonly preceded by a range of tissue and cellular alterations consistent with carcinoma, termed oral epithelial dysplasia (OED).[3] These changes often manifest in a clinical mucosal lesion. Dysplasia, being a histopathological finding, is characterized by loss of polarity of basal cells, basilar hyperplasia, increased nuclear-cytoplasmic ratio, drop-shaped rete ridges, abnormal mitotic figures, bizarre mitoses, hyperchromatic nucleus, loss of cohesion, cellular and nuclear pleomorphism and nuclear hyperchromatism, and so on.[4]

An inefficient apoptotic mechanism can promote cancer development, both by allowing accumulation of dividing cells and by obstructing removal of genetic variants with enhanced

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malignant potential.[5] The present study was conducted to assess apoptotic index in various grades of oral epithelial dysplasia.

MATERIALS & METHODS

The present study was conducted among 60 histopathologically diagnosed cases of hyperkeratosis with varying degree of dysplasia and different grades of oral squamous cell carcinomas of both genders. Enrolment was done after obtaining written consent from all subjects.

Data such as name, age, gender etc. was recorded. Apoptotic cells were morphologically identified as shrunken cells with compact, segregated and sharply delineated mass of chromatin with a deeply eosinophilic cytoplasm. Cells showing fragmented nuclei were also included in the counting. For calculating apoptotic index, 5 high power fields were analysed per case and in each case field apoptotic cell/bodies were counted against total number of tumor cells. The apoptotic cells ratio was evaluated as: Apoptotic Index (AI) =Total no. of apoptotic cells/ Total no. of cells in 10 HPF. Results thus obtained were analyzed statistically where p value less than 0.05 was considered significant.

RESULTS

Table I Distribution of hyperkeratosis & Apoptosis index (AI)

Groups	Apoptosis index (AI) (Mean)	P value
Normal cells	0.0014	0.001
Mild dysplasia	0.003	
Moderate dysplasia	0.005	
Severe dysplasia	0.013	
No dysplasia	0.002	

Table I, graph I shows that mean dysplasia in normal cells was 0.0014, mild dysplasia was 0.003, moderate dysplasia was 0.005, severe dysplasia was 0.013 and no dysplasia was 0.002. The difference was significant (P< 0.05).

Graph I Distribution of hyperkeratosis

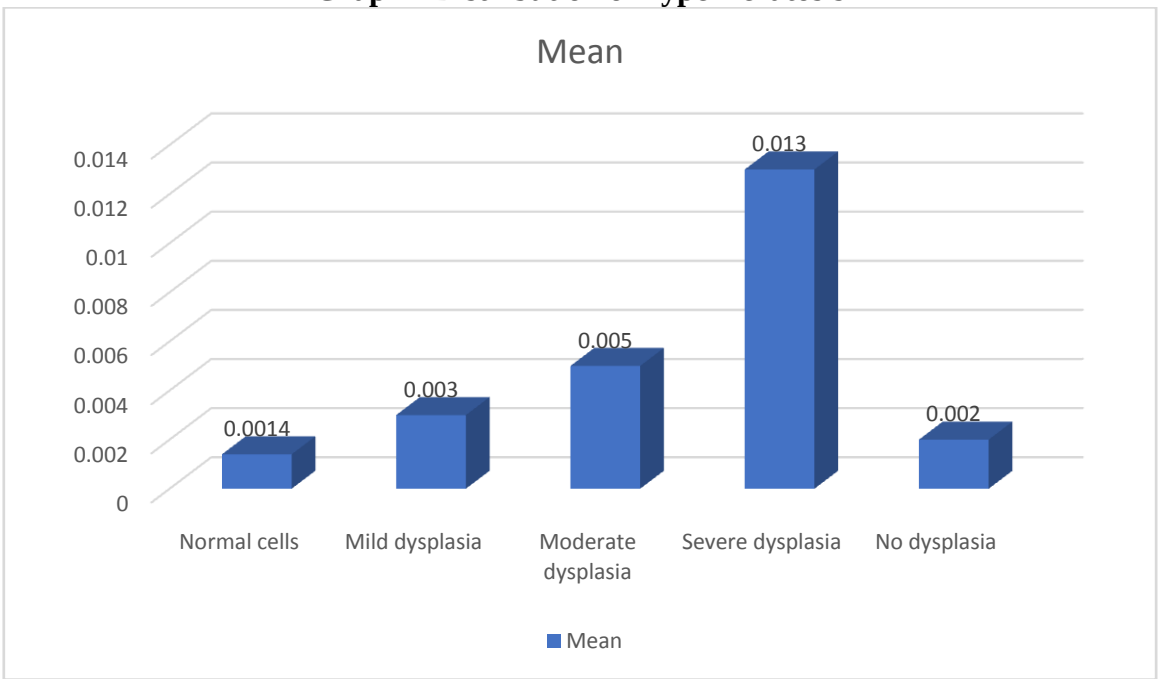

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Table II Mean difference of different grades of oral squamous cell carcinoma

Groups	Apoptosis index (AI) (Mean)	P value
Normal cells	0.014	0.001
Well differentiated SCC	0.018	
Moderately differentiated SCC	0.016	
Poorly differentiated SCC	0.002	

Table II shows that mean difference of different grades in normal cells was 0.014, in well differentiated SCC was 0.018, in moderately differentiated SCC was 0.016 and in poorly differentiated SCC was 0.002. The difference was significant (P< 0.05).

DISCUSSION

Many countries report the tongue as the most frequently affected site. Prognostic evaluation for oral squamous cell carcinoma (OSCC) is mainly based on clinical TNM classification, but this staging system is not sufficient for optimal prognostication and must be supplemented by other reliable methods.[6] The biological activity of OSCC is evaluated and descriptively categorized as highly, moderately and poorly differentiated. Broder primarily developed this quantitative grading of cancer in 1920.[7] Recent clinical advances have shown that 10 to 20% epithelial dysplastic lesions may lead to squamous cell carcinoma. The most accepted classification developed by the World Health Organization divides OED into mild, moderate, severe dysplasia, and carcinoma in situ. Of them, the risk of severe dysplasia to transform into carcinoma is as high as 43%.[8] The present study was conducted to assess apoptotic index in various grades of oral epithelial dysplasia.

In present study, mean dysplasia in normal cells was 0.0014, mild dysplasia was 0.003, moderate dysplasia was 0.005, severe dysplasia was 0.013 and no dysplasia was 0.002. Pwar et al[9] constituted 30 cases, previously diagnosed with various grades of oral epithelial dysplasia (OED). AI was calculated as the number of apoptotic bodies/cells expressed as a percentage of the total number of cells counted in each case. A statistically significant difference was observed between mild dysplasia and severe dysplasia where P = 0.002. The mean AI was increased progressively with increasing grades of OED.

We observed that mean difference of different grades in normal cells was 0.014, in well differentiated SCC was 0.018, in moderately differentiated SCC was 0.016 and in poorly differentiated SCC was 0.002. Roy et al[10] compared the Apoptotic Index in Hyperkeratosis with varying degree of dysplasia and varying grades of oral squamous cell carcinoma with that of normal tissue sections. Apoptotic Index increased with increasing degrees of dysplasia compared with that of normal healthy tissue. On the contrary, Apoptotic Index increased in well differentiated squamous cell carcinoma and was least in poorly differentiated squamous cell carcinoma which was even less than normal healthy tissue specimen. Thus, they concluded that apoptotic count significantly increases in cases of dysplasia and squamous cell carcinoma when compared to normal mucosa.

Singh et al[11] showed the impact of the apoptotic index (AI), MI, and turnover index (TI) to access the behavior of the lesion. A total of 68 histologically proven cases of premalignant and malignant squamous cell carcinoma were analyzed over a period of 1 year. Biopsy specimen with hematoxylin and eosin-stained sections was evaluated and correlated with different grade of the oral lesion with AI, MI, and TI. Statistical analysis in premalignant between mild, moderate, and severe dysplasia shows no significant difference, whereas premalignant and malignant show a significant difference.

OSCC is commonly preceded by a range of tissue and cellular alterations including OED. It has been suggested that alterations in apoptosis accompany the onset of invasion in OPMD.

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Apoptosis is an ordered and orchestrated cellular process that occurs in physiological and pathological conditions.[12] A large number of stimuli can induce apoptosis in a cell. Multiple signaling pathways lead to activation of the apoptosis depending on the triggering factor and the cell type. Apoptosis prevents the development of aneuploidy and other genetic aberrations that are associated with the development and progression of OPMD.[13] At certain stages during the development of a tumor, the equilibrium between the cell proliferation and its apoptosis is interrupted, resulting in dysregulation of cell proliferation. Thus, a dysfunction in the apoptotic system can lead to a wide variety of diseases including oral cancers.[14]

CONCLUSION

Authors found the clinical significance of apoptosis in assessing disease progression in oral potentially malignant disorders.

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