Immunohistochemical Expression Of Survivin In Different Grades Of Oral Squamous Cell Carcinoma.

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Abstract:
Introduction: The survivin protein, called baculoviral inhibitor of apoptosis repeat-containing 5 or BIRC5 is expressed highly in most human tumours and fetal tissue, but is completely absent in terminally differentiated cells. However, its expression increases in oral squamous cell carcinoma.

Aim & objective: Evaluation of expression of Survivin in different grades of oral squamous cell carcinoma.

Materials & Methods: Biopsied tissue of 43 confirmed cases of Oral squamous cell carcinoma was taken and immunohistochemical expression of Survivin was seen in them.

Results: Between cases and control, the presence of survivin in OSCC was found to be statistically significant (p<0.001). Also, significantly high survivin expression was seen in PDSCC, compared to WDSCC & MDSCC (p < 0.01).

Conclusion: There is an increase in the level of survivin expression in the tissue of the patients with OSCC.

Keywords: IHC, Oral cancer, OSCC, Oral Squamous cell carcinoma, Survivin.

I. Introduction
Oral squamous cell carcinoma (OSCC) is the most common head and neck cancer and shows poor prognosis, the 5-year survival rate of OSCC being 35–50% despite recent advances in radiation therapy, improvement in surgical techniques, and the advent of aggressive chemotherapy protocols.¹ One of the primary reasons for the poor prognosis in OSCC is the lack of significant and unique molecular tumor markers to assess risk and prognosis. Identification of better prognostic factors is necessary to assist clinicians in more accurate lesional staging and prediction of prognosis.

Considerable interest has focused on the identification of regulators of programmed cell death, or apoptosis, which may influence the cell death/cell viability balance in cancer. In particular, deregulation of apoptosis resulting in aberrantly reduced cell death is thought to participate in cancer by facilitating the insurgence of additional transforming mutations.² Survivin, also called baculoviral inhibitor of apoptosis repeat-containing 5 or BIRC5, is a protein in humans encoded by the BIRC5 gene. It is a member of the inhibitor of apoptosis (IAP) family. The role of survivin protein is to inhibit caspase activation, thereby leading to negative regulation of apoptosis or programmed cell death. Survivin expression is also highly regulated by the cell cycle and is only expressed in the G2-M phase. It is known that survivin localizes to the mitotic spindle by interaction with tubulin during mitosis and may play a contributing role in regulating mitosis. The survivin protein is expressed highly in most human tumours and fetal tissue, but is completely absent in terminally differentiated cells.³ Survivin exhibits low or undetectable expression levels in most non-proliferating adult tissues, but is broadly expressed in a wide variety of cancers⁴, suggesting it has been implicated in both control of cell survival and regulation of mitosis in tumor cells.⁵

II. Material And Methods

A. Inclusion criteria:
1) Participants with primary OSCC
2) Not undergone any treatment in recent past.

B. Exclusion criteria:
1) OSCC with any other systemic disorders.
2) Participants not willing to participate.
An incisional biopsy was taken from the suspected cases of oral squamous cell carcinoma, processed using routine automatic tissue processor and blocks were prepared. 4 sections, 3-4 µ each were obtained from each block. 2 of them were stained with H&E and histopathologically diagnosed. Subsequent to their confirmation of being oral squamous cell carcinoma, they were graded according to Bryne’s grading system by 2 observers. Another 2 sections were stained for survivin expression performing IHC. Tissue sections of normal oral epithelium were taken as positive control.

### III. Interpretation Of IHC

The results of the immunohistochemical staining were evaluated separately by two observers blind to the histological grades. Survivin expression was evaluated by Lu et al, 1998 scoring method. A mean percentage of positive tumor cells was determined by the examination of 300 cells in at least five areas at 400x magnification. Cells were assigned to one of the five following categories:

- a) 0 - <5%
- b) 1 - 5-25%
- c) 2 - 26-50%
- d) 3 - 51-75%
- e) 4 - >75%

The results obtained were then tabulated & statistical analysis was carried out.

### IV. Statistical Method

The results obtained were analysed using various statistically tests. One way ANNOVA test, Student T test, Spearman Rank Correlation test were performed.

#### Results:

This study was carried out on 43 patients from out patient department of K.M. Shah Dental College and Hospital. The age of the patients in the present study ranged from 20-90 years with most patients in the age range of 30-70 years.

Of the 43 patients, 33(76.7%) were males and 10(23.2%) were females. Of the 33 males, 15(45.45%) were in the age group 46-60 while 10(80%) of females were in the age range 40-60.

All the 43 cases were confirmed histopathologically & graded into well differentiated squamous cell carcinoma(WDSCC), moderately differentiated squamous cell carcinoma (MDSCC) and poorly differentiated squamous cell carcinoma (PDSCC). Out of 43 patients with OSCC, 22(51.1%) cases were well differentiated, 16(37.2%) moderately differentiated OSCC, and 5(11.6%) cases showed poorly differentiated OSCC.

Of the 22 cases of WDSCC, 11 (50%) showed negative expression, 9(40.9%) showed mild expression & 2(9%) showed moderate expression. In case of MDSCC, 10(62.5 %) out of 16 showed negative response while the rest 6(37.5%) showed a score of 1. 4(80%) out of 5 of patients with PDSCC had IHC score 1 and 1 (20%) showed score 3. Between cases and control, the presence of survivin in OSCC was found to be statistically significant (p<0.001). This is also depicted in Table 1 % bar diagram in Graph 1. The IHC expression is shown in Photomicrograph 1, Photomicrograph 2, Photomicrograph 3.

<table>
<thead>
<tr>
<th>S.NO.</th>
<th>GRADE OF OSCC</th>
<th>IHC SCORING*</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>WDSCC</td>
<td>0 1 2 3 4</td>
<td>22</td>
</tr>
<tr>
<td>2</td>
<td>MDSCC</td>
<td>11 9 2 0 0</td>
<td>16</td>
</tr>
<tr>
<td>3</td>
<td>PDSCC</td>
<td>0 4 0 1 0</td>
<td>5</td>
</tr>
<tr>
<td>TOTAL</td>
<td></td>
<td>21 19 2 1 0</td>
<td>43</td>
</tr>
</tbody>
</table>

Table 1: IHC Expression Scores Of Survivin In Different Grades Of OSCC

0- <5% 1 - 5-25% 2 - 26-50% 3 - 51-75% 4 - >75%

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Immunohistochemical expression of Survivin in different grades of oral squamous cell carcinoma.

Graph 1: Bar Diagram IHC Expression Scores Of Survivin In Different Grades Of OSCC

Photomicrograph 1 showing: Survivin staining in WDSCC (10 X)

Photomicrograph 2 showing: Survivin staining in MDSCC (10 X)
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V. Discussion

Apoptosis has become a basic tool in developing cancer research and establishing new cancer strategies. Considerable interest has recently focused on the identification of regulators of apoptosis, which may potentially influence the cell death/cell viability balance in cancer.\(^7\) In addition to pro- and antiapoptotic bcl-2 molecules, a second gene family of inhibitor of apoptosis (IAP) has been recently identified. IAP proteins target a downstream step in apoptosis by inhibiting the terminal effector caspase-3 and -7 and by interfering with processing/activation of the pinnacle caspase, caspase-9.\(^8\)

Survivin, an inhibitor of apoptosis protein (IAP), is abundantly expressed in most solid and haematological malignancies, but undetectable in normal adult tissues. Interference with survivin function induces pleiotropic cell-division defects and apoptosis, suggesting a potential role at the interface between cell division and apoptosis control.\(^9\)

The present study showed no statistically significant difference in the expressions of surviving IN OSCC between males and females. This is analogous with a study conducted by G. Pannone et al\(^10\) who concluded that analysis of expression levels of survivin compared to other clinical-pathological findings such as age, sex, did not reveal further statistically significant differences in this randomly chosen sampling of tumors. In the present study, the expression of survivin in OSCC was found to be statistically significant (p < 0.001) between cases and control. These results are in accordance with studies conducted by Jane et al,\(^11\) Muzio et al,\(^12\) & C. Tanaka et al\(^13\). Yong Hun Kim et al\(^7\) also concluded in their study that Survivin expression was detected in all (100%) OSCC cell lines at a varying level but not observed in normal gingival keratinocyte cells. Similar results where found by Su L et al\(^14\) in their study concluded that high survivin mRNA expression was correlated with poorer tumor differentiation (P < .05).

In the present study, significantly high survivin expression was seen in PDSCC, compared to WDSCC & MDSCC (p < 0.01). This is in contrast with a study conducted by Yong-Hun Kim\(^7\), who observed no correlation between survivin expression and differentiation of OSCCs. However, Su L et al\(^14\) in their study concluded that high survivin miRNA expression was correlated with poorer tumor differentiation (P < .05).

VI. Conclusion

In the present study the immunohistochemical expression of survivin levels in tissue of patients in different grades of OSCC was done. The conclusion derived from the results of this study is that there is an increase in the level of survivin expression in the tissue of the patients with OSCC compared to the controls. However, present data should be considered preliminary, and thus the use of Survivin as a single marker may be not sufficient for the early diagnosis of OSCC. Further investigations with larger samples and multiple biomarkers evaluation are required to clarify this issue.

References


DOI: 10.9790/0853-1607047579 www.iosrjournals.org 78 | Page
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