

Survivin Expression in Patients with OPMD and OSCC - A Potential Independent Prognostic Marker for Risk Stratification

Sandeep Singh Sihmar¹, Karthikeyan Ramalingam², Shalini Rathi³, Monika Solkhe¹, Sathya Sethuraman⁴

ABSTRACT

Background: Survivin is a recently discovered protein belonging to the inhibitor of the apoptosis gene family. Survivin is also upregulated in a variety of human cancers and its expression in tumors is associated with a more aggressive phenotype, shorter survival times, and a decreased response to chemotherapy.

Aim and Objective: The present research aims to identify changes in the expression of survivin in normal mucosa (NM), oral potentially malignant disorders (OPMD) and oral squamous cell carcinoma (OSCC).

Materials and Methods: Paraffin-embedded blocks of histologically diagnosed cases of NM, OPMD and OSCC were retrieved from the department archives. A total of 70 samples including 10 NM, 30 OPMD, and 30 OSCC cases were included in the study. Immunohistochemical staining of Survivin expression was done using an IHC kit from Biogenex, CA. The slides were graded for color and positivity. The results were tabulated and statistically analyzed with SPSS v21.0 (IBM, Armonk, USA) by Tukey HSD Posthoc test.

Results: The mean score in the control group was 1.55 with a standard deviation of 1.36. The mean score in the OPMD group was 1.78 with a standard deviation of 1.32. The mean score observed in the OSCC group was 2.08 with a standard deviation of 1.32. We performed the Tukey HSD posthoc test and evaluated the difference between the NM and OPMD was 0.2300 and the p-value was 0.8806, which did not achieve statistical significance. The difference between NM and OSCC was 0.5500, and the p-value was 0.2169, which was not significant. The difference between the OPMD and OSCC groups was 0.3000 and the p-value was 0.6437 which was not significant.

Conclusion: Survivin is site-specific and dependent on differentiation. Its expression was noted in the basal and parabasal region of normal mucosa, salivary tissue, OPMD and OSCC. There was a progressive increase in the Survivin expression from the normal mucosa to OPMD to OSCC but our values did not reach statistical significance.

Keywords: Oral Potentially malignant disorders, OPMD, Oral Squamous Cell Carcinoma, OSCC, Normal Mucosa, Immunohistochemistry, Survivin, Prognosis, Risk stratification,

INTRODUCTION

Survivin is an inhibitor of the apoptosis gene family that regulates mitosis. It has limited expression in adult tissues but is abundantly noted during embryogenesis and malignancies. In adults, it is expressed in Thymus, Bone marrow stem cells, and basal cells of epithelium.¹ The gene encoding Survivin was cloned by Ambrosini et al in 1997 and is located on chromosome 11E2. Survivin is essential for the execution of mitosis and cell division. Regulation of cell division is recognized as a prominent function of Survivin. Cell cycle-dependent synthesis, expression, and degradation of Survivin with Aurora Kinase B activity are noted in normal cells.^{2,3}

The Survivin gene has multiple isoforms including Survivin, Survivin-2B, Survivin-Ex-3, Survivin-3B, and Survivin-2-alpha.² Studies have revealed that 2B has pro-apoptotic action and EX3 has anti-apoptotic nature.³

Survivin isoforms are highly expressed in malignancies. Survivin has a dual function both a role in cell death regulation and mitotic progression. Survivin-2B is found in the cytoplasm and Survivin-Ex-3 is found predominantly in

¹Department of Oral Pathology and Microbiology, Surendera Dental College and Research Institute, Sriganganagar, Rajasthan, India; ²Department of Oral Pathology and Microbiology, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai, India; ³Department of Oral Medicine and Radiology, Surendera Dental College and Research Institute, Sriganganagar, Rajasthan, India; ⁴Department of Physiology, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai, India.

Corresponding Author: Karthikeyan Ramalingam, Department of Oral Pathology, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai, India, E-mail: karthikeyanr.sdc@saveetha.com

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the nucleus. The presence of the Ex3 variant has been associated with unfavorable clinical outcomes and prognosis.³

The overexpression of Survivin has been associated with the inhibition of cell-initiated apoptosis via the extrinsic and intrinsic pathways. Depletion of Survivin in human cells induces defects in apoptosis and multiple defects in cell division.⁴

The cyclin-dependent kinase (p34cdc2-cyclin B1) phosphorylates Survivin and colocalizes with it on the mitotic apparatus. Elevation in p34cdc2 kinase induced by the spindle checkpoint activation leads to enhanced Survivin expression. The non-phosphorylatable Survivin produced by a mutation of Thr34-Ala is more rapidly cleared than wild-type Survivin by the ubiquitin-proteasome pathway. These findings indicate that the phosphorylation of Thr34 is critical for the anti-apoptotic role of Survivin.¹

The mechanism behind the differential expression of Survivin in neoplastic tissues versus normal terminally differentiated adult tissues is largely unknown. The regulation of Survivin is also being investigated in non-neoplastic cell lines. Regulation of Survivin expression by various cytokines and growth factors likely plays an important role in neoplasia.¹ Overexpression of survivin in various carcinomas has been correlated with increased invasion, poorer prognosis, and chemo-resistance. Targeted therapy against Survivin can suppress tumor growth and also reduce endothelial cell proliferation around tumors.^{3,4}

Oral squamous cell carcinoma (OSCC) has a very high incidence among the Indian population. Similarly, oral potentially malignant disorders (OPMD) show a higher risk for conversion into malignancy. Low patient awareness, lack of clinical expertise, and improper referral often end with a delay in the presentation or reporting of OSCC/OPMD. This causes increased morbidity and mortality.⁵⁻¹⁰

Xie et al⁵ have proposed that Survivin is a potential prognostic marker for OSCC. We have observed an increased expression of Survivin in OSCC and in dysplasia. But, further studies with larger samples, well-designed inclusion criteria, and clinical follow-up data are needed to confirm our findings. Survivin expression can play a key role in the future in defining the clinical behavior and management of OSCC. It could be used as a diagnostic/therapeutic target in the development of malignant tumors. The limitations of their meta-analysis were that they included studies published only in English and potentially relevant studies may be present in other languages. The tendency to publish only positive findings over negative results could introduce bias. The biostatistical methods to extract data were not similar to multiple studies and many studies did not differentiate between nuclear and cytoplasmic staining.

Early detection of genetic changes by immunohistochemical or advanced methodologies can help in improving prognosis. Hence, our study attempted to analyze the Survivin expression in normal oral mucosa, OPMD, and OSCC along with its comparison to understand its value as a prognostic marker.

This study attempts to study the differential expression of Survivin protein in potentially malignant disorders such as

Leukoplakia, OSMF, OLP and OSCC for its significance in the progress and evolution of oral neoplasia and its possibility for permitting initial diagnosis and in serving in the choice of the suitable action.

MATERIALS AND METHODS

Source of Data

Reported cases of OPMD and OSCC from the Department of Oral and Maxillofacial Pathology and Oral Microbiology, Surendera Dental College and Research Institute, Sriganganagar, Rajasthan, India. Histopathologically diagnosed cases of potentially malignant disorders and oral squamous cell carcinoma and tissues with adequate size (minimum of 5mm) were chosen for the study. Potentially malignant disorders of sites other than the oral cavity proper like the oropharynx, maxillary sinus, etc., Carcinomas of sites other than the oral cavity proper like the oropharynx, maxillary sinus, etc. were excluded.

The present study involved the collection of OPMD and OSCC Formaline Fixed Paraffin Embedded (FFPE) blocks from the department archives. Once the FFPE blocks with adequate tissue were segregated, Immunohistochemical (IHC) staining of Survivin was performed for the samples. IHC stained slides were evaluated for staining, data was tabulated and statistical analysis was performed.

A total of 70 samples including 10 normal oral mucosae, 30 OPMD, and 30 OSCC were included in the study. This procedure was cleared by the Institutional Ethical Committee vide letter - SDCRI/IEC/2015/007.

Hematoxylin and Eosin stained slides were evaluated and reconfirmed for the histopathological diagnosis of OPMD and OSCC as per previous reports.

Then, the tissue blocks were utilized for immunohistochemical staining of Survivin using the Polymer IHC Detection Kit (Biogenex; CA, USA) using EZ Retriever system V.2.1, (Biogenex; USA). 3 μ sections were made with a Yorco YSI-062 Fully automatic rotary microtome and staining was performed as per manufacturer instructions.

The stained slides were analyzed using a 5MP Digital camera attached to a Labomed Research Microscope (LX-400), a Desktop or a Laptop computer, PIXELPRO software (LABOMED Inc, USA), and DIGIMIZER image analysis software (Medcalc Software BVBA, Belgium)

Survivin showed both nuclear and cytoplasmic positivity with brown staining due to DAB chromogen. The number of positive cells counted in 50 cells of each field under high power magnification was assessed by two observers. The scoring was as follows: (-) no color, (+) Yellow, (++) Light brown, and (+++) Dark brown. Cases were assigned to one of the following categories: 0% positive cells (-), 10% positive cells (+), 10-25% positive cells (++) , 26-50% positive cells (+++) or more than 50% positive cells (++++). The fields containing Artefactual changes and areas of stromal positivity for Survivin were not taken into account.

RESULTS

Our study comprised 70 samples that included 10 cases of normal mucosa which was obtained from patients who



had undergone routine oral surgical procedures like reactive gingival lesions, third molar impactions etc. We also used 30 samples of OPMD including 10 cases of Mild epithelial dysplasia and 20 cases with moderate dysplasia. We also used 30 cases of Oral Squamous Cell Carcinoma (OSCC) which was 25 cases of well-differentiated OSCC, 3 cases of moderately differentiated OSCC and 2 cases of poorly differentiated OSCC.

The H & E stained slides from FFPE of NM, OSCC and

OPMD groups were re-evaluated before IHC staining. (Figure 1)

Fig.2: shows photomicrographs of immunohistochemical staining. A - Normal mucosa, B - Within sheets of malignant epithelial cells in oral squamous cell carcinoma, C - within islands of malignant epithelial cells in oral squamous cell carcinoma, D - within islands of malignant epithelial cells in

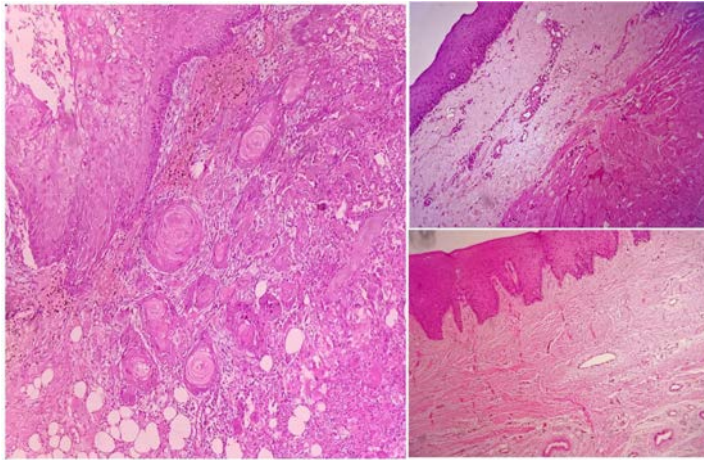


Fig. 1: showing photomicrographs of well differentiated squamous cell carcinoma (Left), Oral submucous fibrosis (Right top) and Normal mucosa (Right lower) [10x, H&E]

Immunohistochemical staining was performed for Survivin and graded by two independent oral pathologists. (Figure 2)

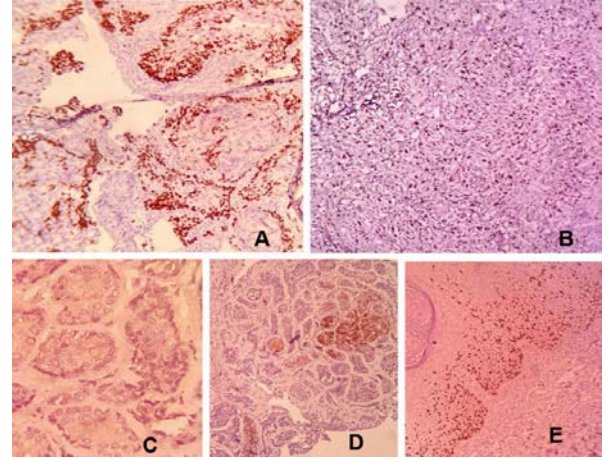


Fig.2: shows photomicrographs of immunohistochemical staining. A - Normal mucosa, B - within sheets of malignant epithelial cells in oral squamous cell carcinoma, C - within islands of malignant epithelial cells in oral squamous cell carcinoma, D - within islands of malignant epithelial cells in oral squamous cell carcinoma, E - within dysplastic epithelium [10x, Survivin]

Table 1: Showing the grading of color and Survivin positivity among the Normal mucosa NM group

Grading system	First examiner		Second examiner	
	N	%	N	%
Survivin Color Grading				
No color=0	1	10	1	10
Yellow=1	0	0	0	0
Light Brown=2	7	70	5	50
Dark Brown=3	2	20	4	40
Chi-square	1			
p value	0.61			
Grading				
0 (0% +ve cells)	3	50	3	30
1 (10% +ve cells)	3	20	2	20
2 (10-25% +ve cells)	1	20	1	10
3 (26-50% +ve cells)	3	10	3	30
4 (>50 % +ve cells)	0	0	1	10
Chi square	0.53			
p value	0.97			

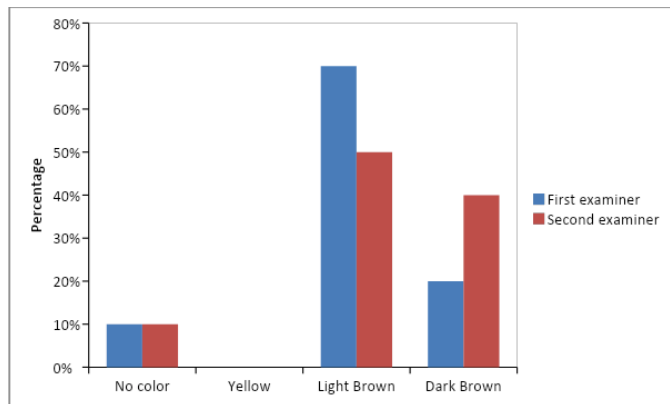
Table 2: Staining of Oral Potentially Malignant Disorders

Grading system	First examiner		Second examiner	
	N	%	N	%
Color Grading				
No color=0	1	3.03	3	9.09
Yellow=1	4	12.12	8	24.24
Light Brown=2	16	48.48	11	33.33
Dark Brown=3	12	36.36	11	33.33
Chi-square	3.3			
p value	0.35			
Grading				
0 (0% +ve cells)	8	24.24	6	18.18
1 (10% +ve cells)	9	27.27	10	30.3
2 (10-25% +ve cells)	8	24.24	5	15.15
3 (26-50% +ve cells)	6	18.18	7	21.21
4 (>50 % +ve cells)	2	6.06	5	15.15
Chi-square	2.39			
p value	0.66			



oral squamous cell carcinoma, E - within dyplastic epithelium [10x, Survivin]

Table 1 displays the distribution of cases, indicated by graded colors, as well as the percentage assessments provided by two oral pathologists within the control group. Additionally, it presents the grading of positive cells within this group. Notably, among 10 samples, both observers noted that one sample each (10%) did not exhibit any coloration. Furthermore, no samples displayed yellow coloration according to either observer. Analysis revealed that 7 samples (70%) and 5 samples (50%) exhibited light brown and dark brown colorations, respectively, with values of 2 (20%) and 4 (40%). Among the 10 samples, 3 (50%) and 3 (20%) scored (-), 3 (20%) and 2 (20%) scored (+), 1 (20%) and 1 (10%) scored (++) , and 3 (10%) and 3 (30%) scored (+++) according to both observers. Additionally,



Graph 1: Graded color along with the percentage of the control group as scored by two oral pathologists.

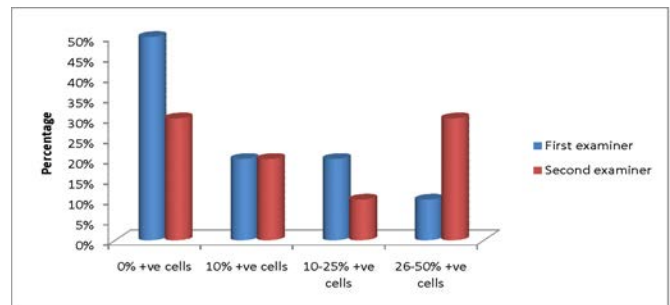
Table 3: Staining observed in Oral Squamous Cell Carcinoma (OSCC) group

Grading system	First examiner		Second examiner	
	N	%	N	%
Color Grading				
No color=0	0	0	0	0
Yellow=1	2	6.67	2	6.67
Light Brown=2	11	36.67	11	36.67
Dark Brown=3	17	56.67	17	56.67
Chi-square	0			
p-value	1			
Grading				
0 (0% +ve cells)	3	10	4	13.33
1 (10% +ve cells)	9	30	8	26.67
2 (10-25% +ve cells)	7	23.33	4	13.33
3 (26-50% +ve cells)	8	26.67	6	20
4 (>50 % +ve cells)	3	10	8	26.67
Chi-square	3.57			
p value	0.47			

one observer noted a single sample (10%) scored (++++). (Graphs 1 and 2)

Table 2 shows the number of cases and graded color and positivity of cells along with the percentage that was given by two oral pathologists for the OPMD group. It was observed that out of 30 samples, n=1(3.03%) sample by 1st observer and n=3 (9.09%) sample by 2nd observer showed no color. It was observed that n=4(12.12%) and n=8(24.24%) samples were showing yellow color by both observers. It was observed that n=16(48.48%) for light brown, n=12 (36.36%) and n=11(33.33%) for dark brown by both observers respectively. Out of 30 samples n=8(24.24%) and n=6(18.18%) scored (-), n=9(27.27%) and n=10(30.3%) scored (+) respectively. Both observers scored(++) for n=8(24.24%) and n=5(15.15%) samples. n=6(18.18%) and n=7(21.21%) were scored (+++). (++++) was scored for n=2(6.06%) and n=5(15.15%) by both the observers. (Graph 3, 4)

Table 3 presents the distribution of cases, classified by graded color, and the corresponding percentages provided by two pathologists within the cancer group. Additionally, it details the grading of positive cells within this cohort. Notably, both observers noted coloration in all samples. Among the 30



Graph 2: Control group

Graph 2: Percentage of positive cells among the control group as scored by two pathologists.

Table 4: Mean grading scores

Groups	Mean±SD	Anova test	p-value
Control (Group 1)	1.55±1.36	0.74	0.48
Dysplasia (Group 2)	1.78±1.32		
OSCC (Group 3)	2.08±1.32		

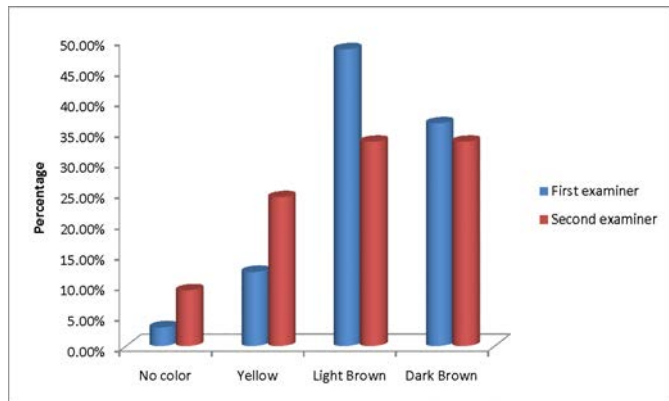
Tukey HSD posthoc Test.

Group 1 vs Group 2: Diff=0.2300, 95%CI=-0.9155 to 1.3755, p=0.8806

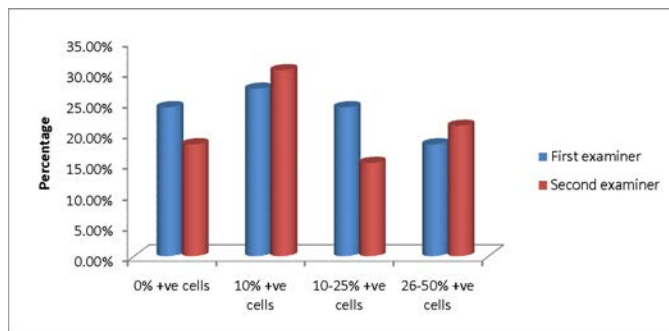
Group 1 vs Group 3: Diff=0.5300, 95%CI=-0.6287 to 1.6887, p=0.5202

Group 2 vs Group 3: Diff=0.3000, 95%CI=-0.5005 to 1.1005, p=0.6437

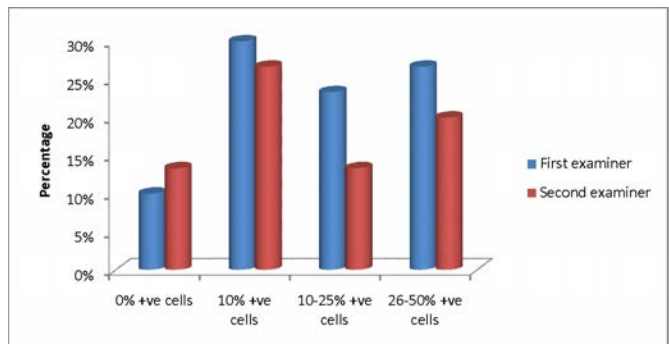
samples, none displayed an absence of color. According to the first observer, 2 samples (6.67%) and according to the second observer, 2 samples (6.67%) exhibited a yellow hue. Light brown coloration was observed in 11 samples (36.67%) by both observers, while dark brown coloration was observed in 17 samples (56.67%) by both observers. In terms of grading, both observers scored 3 samples (10%) and 4 samples (13.33%) as (-), and 9 samples (30%) and 8 samples (26.67%) as (+), respectively. Additionally, both observers assigned (++) to 7 samples (23.33%) and 4 samples (13.33%), and (+++) to 8 samples (26.67%) and 6 samples (20%), while 3 samples (10%) and 8 samples (26.67%) were scored as (+++). Graphs 5 and 6)



Graph 3: Color along with the percentage given as scored by two oral pathologists among the potentially malignant group.



Graph 4: Percentage of positive cells among the potentially malignant group as scored by the two pathologists.



Graph 6: Percentage of positive cells among the OSCC group as scored by two oral pathologists.

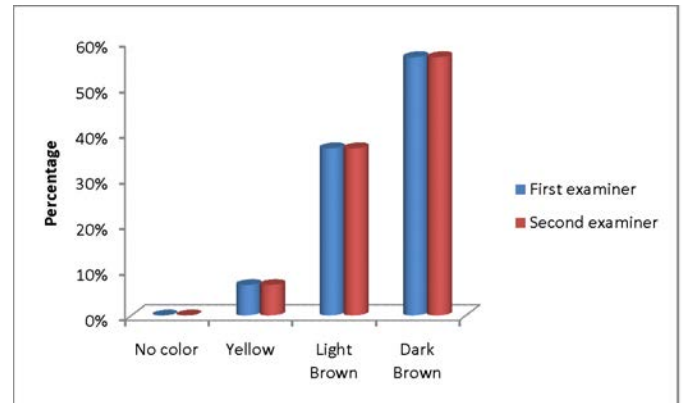
Table 4 shows the mean score and comparison between NM, OPMD and OSCC. The mean score in the NM group was 1.55 with a standard deviation of 1.36. The mean score in the OPMD group was 1.78 with a standard deviation of 1.32. The mean score observed in the OSCC group was 2.08 with a standard deviation of 1.32. (Graph 7)

We performed the Tukey HSD posthoc test and evaluated the differences between the three study groups. The NM and OPMD group was 0.2300 and the p-value was 0.8806, which did not achieve statistical significance. The difference between the NM and OSCC groups was 0.5500, p-value of 0.2169, which was not significant. The difference between the OPMD and OSCC groups was 0.3000 and the p-value was 0.6437 which was also not significant.

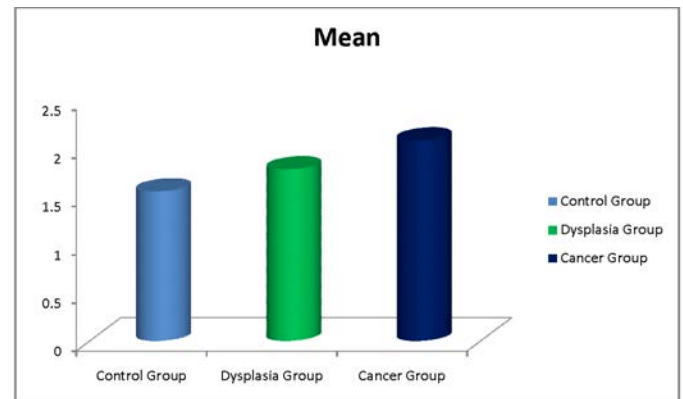
DISCUSSION

Survivin is a new member of the Inhibitors of Apoptosis (IAP) family that can directly block caspase-mediated cell death. It is a bifunctional protein that overwhelms apoptosis and controls cell division.^{2, 3, 6, 8, 10}

Its expression is at high levels in embryonic tissues but low or non-detectable levels in normal adults but abundant in malignancies. Survivin expression has been reported in



Graph 5: Immunohistochemical staining along with the percentage as scored by the two oral pathologists in the OSCC group.



Graph 7: Mean value of the score for Survivin expression between the study groups shows that NM (Light Blue) < OPMD (Green) < OSCC (Dark blue).



odontogenic tumors, oral sub-mucous fibrosis, different grades of oral squamous cell carcinoma and oral leukoplakia. Survivin expression has also been detected in salivary samples.¹³⁻²¹

Malignant transformation of oral epithelium is a complex process involving the interplay of multiple proteins and dysregulation of apoptosis. Survivin expression and its role in different cancers are not fully understood. It has been associated with higher tumor grade, increased recurrence, and resistance to treatment.^{2, 8, 16, 18}

Oral squamous cell carcinoma (OSCC) is among the five major cancers in India, representing 19% of the total count in males and 7% of cases in females. Approximately 90% of OSCC arises in the mucosal lining. It is strongly associated with extensive consumption of tobacco and its products. The risk of malignant transformation of OPMD varies between 1% to 18%. The expression and role of Survivin in OPMD and OSCC are still unclear. Survivin-2B and Survivin-Ex3 are proposed as specific markers for malignancy.^{20, 22, 23}

Xie et al performed a meta-analysis for the clinicopathological and prognostic significance of Survivin expression in OSCC patients. They reported that in 15 papers, a total of 1040 cases were detected for Survivin expression using immunohistochemistry (IHC) or reverse transcription polymerase chain reaction (RT-PCR). The fixed-effect model was therefore used to combine the pooled ORs and CIs, suggesting a significant relationship between Survivin expression and lymphatic metastasis (OR = 0.62, 95% CI = 0.44–0.88, $p < 0.05$) and clinical stage (OR = 0.63, 95% CI = 0.41–0.96, $p < 0.05$). It revealed a correlation between Survivin expression and lymph node metastasis, clinical stage and poor prognosis. However, no significant association was found between Survivin expression and grade of tumor differentiation, depth of invasion, age or gender. Subgroup analysis using stratified detection methods did not show any significant association between Survivin expression and clinicopathological variables of OSCC.^{8, 10}

This retrospective study was carried out in the Department of Oral & Maxillofacial Pathology and Oral Microbiology, Surendera Dental College and Research Institute, Sriganganagar, Rajasthan, India on Paraffin-embedded tissue blocks of histologically diagnosed cases. We analyzed 70 Formalin-fixed paraffin-embedded (FFPE) blocks from our archives and got the appropriate ethical clearance for the study. Muzio et al⁶ performed their study on 110 FFPE samples of OSCC and 7 samples of metastatic lesions of OSCC. Freier et al²² used 296 FFPE cases from the university archives. Negi A et al¹⁹ performed their study on 45 FFPE including 15 normal mucosae, 5 mild epithelial dysplasia, 9 moderate epithelial dysplasia, 1 severe epithelial dysplasia, 4 well-differentiated OSCC, 9 moderately-differentiated OSCC and 2 cases of poorly-differentiated OSCC. Jane C et al²⁰ analyzed 17 cases of Leukoplakia and 38 cases of OSCC including 13 well-differentiated OSCC, 14 moderately-differentiated OSCC, and 11 poorly-differentiated OSCC. Tanaka C et al⁵ used 71 OSCC specimens with the adequate histological material in their study. De Maria S et al²³ analyzed 22 OSCC specimens in their study. Kim YH et al¹⁰ used 38 patients with OSCC for their analysis.

Our study group included 10 cases of normal mucosa, 10 cases of Mild epithelial dysplasia, 20 cases with moderate epithelial dysplasia, 30 cases of Oral Squamous Cell Carcinoma (OSCC) with 25 well-differentiated, 3 moderately differentiated and 2 poorly differentiated types. Negi A et al¹⁹ studied 15 samples of normal mucosa, 15 samples of leukoplakia and 15 OSCC samples. The leukoplakia cases were histopathologically categorized as mild dysplasia (5 cases), moderate dysplasia (9 cases), and severe dysplasia (1 case). The cases of the OSCC group were histopathologically categorized as histopathologically categorized as well differentiated SCC (4 cases), moderately differentiated SCC (9 cases), and poorly differentiated SCC. Tanaka C et al⁵ studied 9 samples of the normal oral mucosa, 37 potentially malignant and 58 OSCC samples. Kim et al¹⁰ studied 38 OSCC samples. Jane et al²⁰ studied 38 OSCC and 17 leukoplakia samples. De Maria et al²³ studied on 77 OSCC samples. K Freier et al²² in 2006 studied on 296 OSCC samples. Khan KA et al²¹ used 40 patients of oral submucous fibrosis in their study.

Our study comprised of Immunohistochemical expression of Survivin by using antibody from BioGenex; CA, USA for analysis similar to Negi et al¹⁹. Tanaka et al⁵, Muzio et al⁶, Kim et al¹⁰ used the DAKO kit, Jane et al²⁰ used the Santacruz Kit and Freier et al²² used the Novus Biological kit for analysis.

Survivin protein expression can be localized to the cytoplasm or nuclear compartments. Localization to the nucleus corresponds to unfavorable prognosis in many malignancies.²³ We observed nuclear and cytoplasmic expression of Survivin in our study samples. In the present study, the percentage of stained cells was estimated in 5 randomized microscopic fields by two oral pathologists and classified as (-): 0%, (+): <10%, (++) : 10-25%, (+++) : 26-50%, (++++): >50% positive cells. We also graded samples on the basis of color staining (No color=0, Yellow=1, Light Brown=2, and Dark Brown=3). Similar scoring methodology was performed by Negi et al¹⁹ and Jane et al.²⁰

Our results of Survivin expression among the study groups were tabulated and subjected to statistical analysis using SPSS v22.0 (SPSS Inc, Chicago, IL). We analyzed the Mean \pm SD and Tukey HSD posthoc test. The probability value of < 0.05 was considered to be significant. In the present study, we observed that Survivin expression had increased with the severity of dysplasia (Mild<Moderate)and was highest in OSCC. The mean score was 1.55 in NM, 1.78 in OPMD, and 2.08 in OSCC but did not achieve statistical significance.

The finding of Survivin expression in normal tissue is not completely surprising. Although most studies employing immunochemistry techniques reported no Survivin expression in the clinically normal mucosa, several studies employing this technique demonstrated Survivin expression in basal and parabasal cells of the oral mucosa. According to Lodi et al⁷, Survivin expression has been demonstrated in all samples of normal mucosa. 13 out of 15 samples were in the 'low expression' group and this result was probably due to the highly sensitive staining method and to the relatively high proliferation rate of the oral mucosa. Upregulation of Survivin in cancer specimens 80% in the 'high expression' group confirms the putative role that this protein plays in carcinogenesis processes.⁷



Jane et al²⁰ reported Survivin expression in the spinous layer and surface keratin of oral leukoplakia. They also observed weaker expression in Well-differentiated OSCC and Moderately differentiated OSCC. Moderate to Strong expression was observed in poorly differentiated OSCC. Muzio et al⁶, Negi et al¹⁹, and De Maria et al²³ also reported high expression within OSCC. It was similar to our findings.

The prognostic value of Survivin has been reported in breast cancer by Span et al²⁴, in colorectal cancer by Krieg et al²⁵ and in breast cancer by Martinez et al²⁶. Very few studies have been performed on OSCC and survivin expression.^{27, 28}

Limitations and Future Scope:

Our limitation could be that the samples were from the same geographical location. Further multi-center studies of larger sample size with clinical findings, follow-up details, and similar inclusion criteria have to be done to emphasize our findings and corroborate their clinical significance.

CONCLUSION

Oral cancer is linked with significant mortality and the physical impact of those who survive. Despite progress in therapy, the five-year survival percentage remains low. The detection of dependable biomarkers in OSCC will aid in precise categorization and forecasting.

In our study, we found that Survivin expression was localized and dependent on cellular differentiation. Its expression was noted in the basal and parabasal regions of normal mucosa, OPMD, and OSCC. There was a progressive increase in the Survivin expression from the normal mucosa to OPMD to OSCC but our values did not reach statistical significance.

Survivin expression and its variants in oral squamous cell carcinoma (OSCC) can aid as a predictive indicator for gauging tumor aggressiveness and evaluating the propensity of pre-malignant lesions to transform in patients. Clinical trials testing survivin-blocking mechanisms are underway and showing encouraging results.

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