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Study of the relationship between expression of Retinoic acid receptor: Beta by IHC in different grade of oral squamous cell carcinoma

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Abstract
In India Oral squamous cell carcinoma is the most common type of oral cancer (90%). The most common site of oral cancer is buccal mucosa. It has been observed that Vitamin A deficiency is associated with Squamous metaplasia in mucosa of upper aerodigestive tract. Present study intends to observe the estimate of Retinoic acid receptor-Beta expression in different grades of oral squamous cell carcinoma. Retinoic acid receptor-Beta expression is corelated with the grade of the tumor statistically.
Material and Methods: Study was conducted over a period of 2 year (Sep 2015-Sep 2017) on the specimen sent to pathology department of government medical college and hospital. It was studied histologically to assess the grade and then immunohistochemistry for RAR ß was performed.
Result: Study showed that 59.53% of cases belong to grade I followed by grade II (35.71) and grade III(4.76%).59.53% cases were positive for RAR ß and 40.47% cases were negative. There was significant association between grade of differentiation and status of RAR ß of the patients (p=0.0091). Proportion negativity of RAR ß increased with the increase in grade of differentiation**.**
Conclusion: A significant correlation was seen between the loss of RAR ß expression and advanced histopathological grade tumors of oral squamous cell carcinoma.

Keywords: Beta, IHC, Retinoic acid receptor

Introduction
Oral and Oropharyngeal carcinomas are the sixth most common cancer in the world. In India, Oral cancer is one of the most top three types of cancers. The Oropharyngeal region consist the following anatomical areas: Lip, floor of mouth, oral tongue, buccal mucosa, gingiva, retromolar trigone, hard palate, base of tongue, tonsillar area, soft palate and pharyngeal wall. The risk factors for the oral squamous cell carcinoma include the use of tobacco in any form (cigarette, bidi, gutkha, khaini etc.), betel nut chewing, chronic alcoholism and Human Papilloma Virus. Other risk factor include poor oral hygiene, poor diet and nutrition, radiation and genetic factor. Retinoids have protective role in physiological and pathological function of human body like immunomodulator, tumor suppressive activity, apoptosis and anti-proliferative activities. In oral squamous cell carcinoma, it has been studied that expression of Retinoic acid receptor - Beta is either absent or down regulated on. 13 cis retinoic acid restores the expression of Retinoic Acid Receptor - Beta mRNA and also prevents the development of oral squamous cell carcinoma. Carcinogenesis of Oral Squamous cell carcinoma is suppressed by retinoids dependent signaling pathway indicating that Vitamin A deficiency is related with development of oral squamous cell carcinoma. Retinoids are natural and synthetic vitamin A metabolites and analogues. Itinhibit the proliferation of several types of tumour cells, such as head and neck squamous cell carcinoma (SCC), oesophageal cancer, lung cancer, prostate cancer, and cervical cancer. The retinoids action are mediated by both nuclear retinoid receptors (RARs and RXRs) and cytoplasmic retinoic acid binding proteins (CRABP1 and CRABP2). It has been used as a chemopreventive or chemotherapeutic agent for patients with many solid tumours, and some successful results from the clinical trials has been reported.

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Material and methods
The hospital based prospective observational study was carried out at the Department of Pathology of government medical college. The study was conducted on surgically resected tumor samples from patients with oral squamous cell carcinoma on histopathological examination. Immunohistochemistry for *RAR ß* was done.

Result

Table 1: Distribution of grade of differentiation of the patients

Grade	Number	%
Grade-I	25	59.53%
Grade-II	15	35.71%
Grade-III	2	4.76%
Total	42	100.0%

59.53% of the cases were with Grade-I which was significantly higher (Z=3.25; p<0.0001).

Table 2: Distribution of status of RAR ß of the patients

RAR ß	Number	%
Positive	25	59.53%
Negative	17	40.47%
Total	42	100.0%

Test of proportion showed that proportion of positive cases (59.53%) was significantly higher. (Z= 2.54; p=0.0107).

**Table 3:** Distribution of grade of differentiation and status of RAR ß of the patients

Grade of differentiation	Status of RAR ß		Total
	Positive	**Negative**	
G1	19	6	25
Row %	76	24	100.0
Col %	82.61	31.58	59.52
G2	4	11	15
Row %	26.67	73.33	100.0
Col %	17.39	57.9	35.71
G3	0	2	2
Row %	0.0	100.0	100.0
Col %	0.0	10.53	4.76
Total	23	19	42
Row %	54.76	45.24	100.0
Col %	100.0	100.0	100.0

χ^2 =9.39; p=0.0091 S- Significant

Images
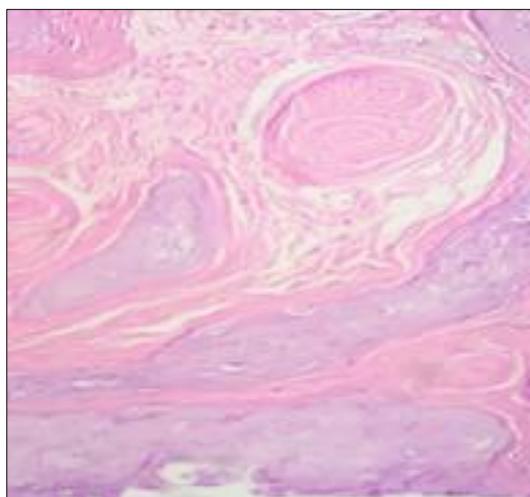
Fig 1: Image showing well differentiated squamous cell carcinoma
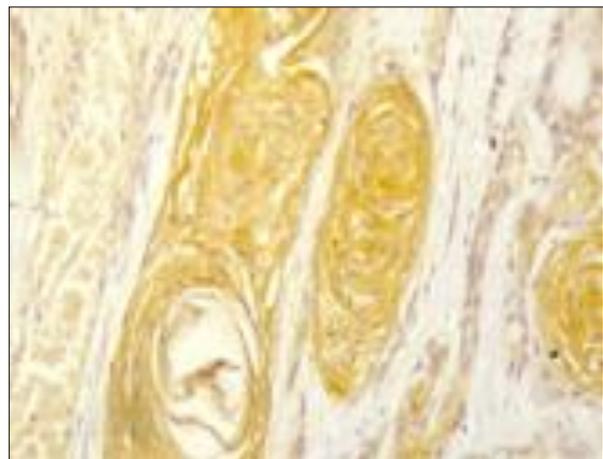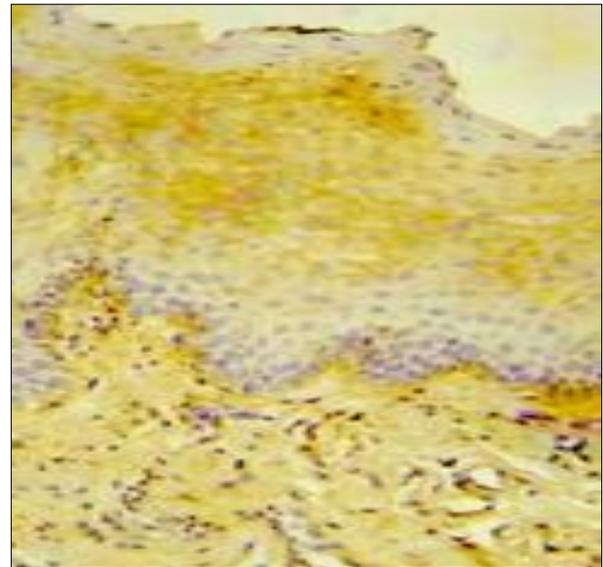
Fig 2: Image showing *RAR ß* immunohistochemistry strongly positive**.**

Discussion
The present study comprises of 42 patients with prospective observation Histopathological diagnosis and grading were done. Study showed that there was significant association between grade of differentiation and status of RAR ß of the patients (p=0.0091). Proportion negativity of RAR ß increased with the increase in grade of differentiation. Chakravarti N *et al*. (2001) [9] conducted a study to show there was no detectable Retinoic acid receptor-Beta immunoreactivity in 46/64 (75%) oral SCCs analyzed, 18/64 (25%) showed weak nuclear immunoreactivity for Retinoic acid receptor-Beta.our study also support the same finding.

Conclusion
We found that loss of *RAR ß* immunoreactivity is associated with advanced stage and hence poor outcome. So estimation of *RAR* ß can be helpful to assess the prognosis of oral squamous cell carcinoma.

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