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A Study on p53 Expression Patterns and Patients Features: Descriptive Study

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Abstract

Introduction: Among the most widely studied tumour suppressor gene are RB & p53 which express PRB retinoblastoma protein & p53 protein respectively. These proteins control cell cycle and are involved in the inhibition of cell proliferation. Mutation of these proteins produce uncontrolled cell proliferation. *Methodology:* The detailed history including the duration, site, onset, progression, personal habits and duration of those habits like smoking, beetle quid chewing were noted. The clinical diagnosis was recorded. *Results:* In our study, the most common location was tongue 48% followed by the BUCCAL mucosa of 34% and the least common was the floor of the mouth 6%. It was observed that 59% of the cases in the age group 50-60 year showed suprabasal p53 positivity. *Conclusion:* No significant association observed between P53 and age,smoking and tobacco use.

Keywords: Oral Lesions; P53; Tobacco.

Introduction

Oral cancers are one of the 10 leading cancers in the world. However in India it is the one of the most common cancer and constitutes a major public health problem [1].

The suffering , disfigurement and death associated with oral cancer is definitely avoidable due to surgical accessibility , etiological factors and the precedence of precancerous lesions provides an excellent opportunity for early detection and control.

Oral cancers is the 6th most common in the world [2]. Of all the oropharyngeal malignancies reported & registered to SEER{surveillance, Epidemiology and research program of national cancer institute of U.S public health services} in U.S.A from 1973-1987 more than 95% were squamous cell carcinoma [3].

Among the most widely studied tumour suppressor gene are Rb & p53 which express pRb retinoblastoma protein & p53 protein respectively. These proteins control cell cycle and are involved in the inhibition of cell proliferation. Mutation of these proteins produce uncontrolled cell proliferation.

The p53 protein was first identified in 1979 as transformation related protein [p3]. p53 is the most commonly mutated gene in human cancer. The p53 acts as transcription factor for cell cycle inhibitors such as p21 a and cycle prevent cell from going beyond G1 phase of cell cycle, permitting DNA repair.

If repair is not possible, p53 induces apoptosis of these cells to avoid transmission of potentially carcinogenic information.

The p53 gene is inactivated in approximately half of the head and neck cancers. Aberrant expression of p53 has been reported in mild dysplasia by some authors [4].

Over expression of p53 and gene mutation have also been detected in oral epithelial dysplasia [OED] adjacent to OSCC.

The association of p53 gene mutation with OSCC were studied by several authors.

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Methodology

All the patients referred to the department of pathology with oral lesions for histopathological examination from the department of surgery and ENT were included in our study. The detailed history including the duration, site, onset, progression, personal habits and duration of those habits like smoking, beetle quid chewing were noted. The clinical diagnosis was recorded.

Inclusion Criteria

Histopathologically diagnosed benign lesions, premalignant lesions & SCC were included in the study which consist of 33 cases of oral squamous *cell carcinaoma.* (of which14 were well differentiated, 14 moderately differentiated and 02 poorly differentiated) and 03 were verrucous carcinoma. 11 premalignant lesions and 08 were benign lesions of the oral cavity. These cases were subjected to routine H&E staining and p53 immunohistochemical staining.

Exclusion Criteria

- Mechanical, thermal injury.
- Drug indused oral ulcers.
- Vitamin B12 deficient oral ulcers and other patches.
- Iron deficiency anemia caused lesion/ ulcers.

Compiling the clinical history and diagnosis we got different types or oral growth in our department i.e Exophytic, endophytic, leukoplakic, erythroplakic and erythroluekoplakic.

Histopathological examinations were done from tissue samples obtained by excisional, incisional and punch biopsy. Histopathological sections were routinely stained with haematoxylin an eosin [H&E] and also p53 was done on same specimens.

Results

As depicted in the table 67% of the non abusers showed suprabasal p53 positivity as against 67 % of chronic abusers.

The above histogram shows that of the total 52 patients, 19 were chronic abusers, 15 were non abusers and in 09 cases showed no history.

In 13/20(65%) cases of chronic smokers suprabasal p53 positivity was seen compared to 52.2% in non smokers.

Above histogram shows that out of 52 patients, 13

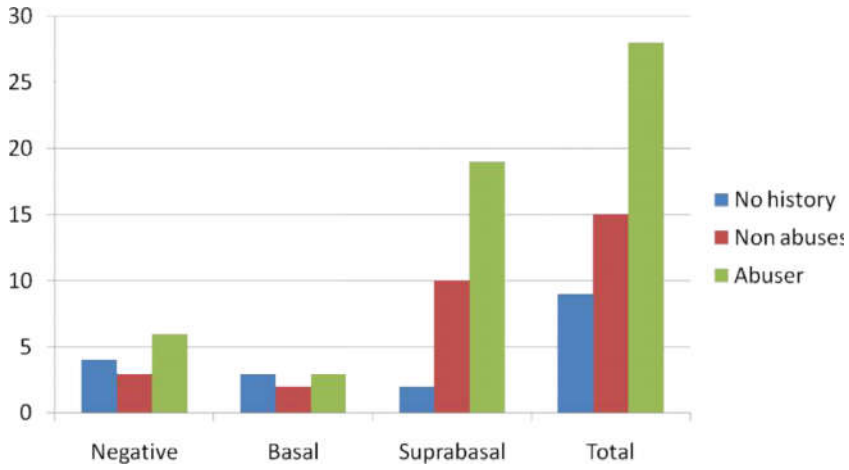

Fig. 1: Staining pattern in relation to betel quid/ tobacco use

Table 1: Staining pattern in relation to betel quid/ tobacco use **(p=0.181)**

	P53			Total No
	Negative	Basal	Supra Basal	
No History	04	03	02	09
	44%	33%	22%	
Non Abuser	03	02	10	15
	20%	13%	67%	
Chronic Abuser	06	03	19	28
	20%	11%	67%	

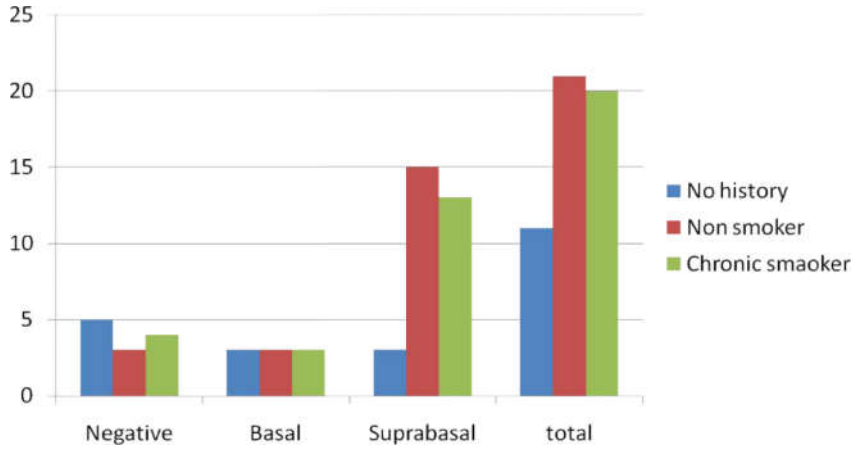

Fig. 2: Staining pattern in relation to smoking

Table 2: Staining pattern in relation to Smoking (p=0.165)

	P53			
	Negative	**Basal**	**Suprabasal**	**Total No**
No History	05	03	03	11
	46%	27%	27%	
Non Smoker	03	07	11	21
	14%	33%	52%	
Chronic Smoker	04	03	13	20
	20%	15%	65%	

were chronic smokers, 21 were non smokers and in 11 No history was available.

In our study, the most common location was tongue 48% followed by the buccal mucosa of 34% and the least common was the floor of the mouth 6%.

In our study, the commonest location was tongue and the least common was the floor of mouth.

Table 3: Staining pattern According to location (p=0.616)

	Negative	**Basal**	**Suprabasal**	**Total No**
Buccal Mucosa	03	05	10	18
	17%	28%	55%	
Tounge	08	04	13	25
	32%	16%	52%	
Floor Of Mouth	00	01	02	03
		33%	67%	
Palate	02	00	04	06
	33%		67%	

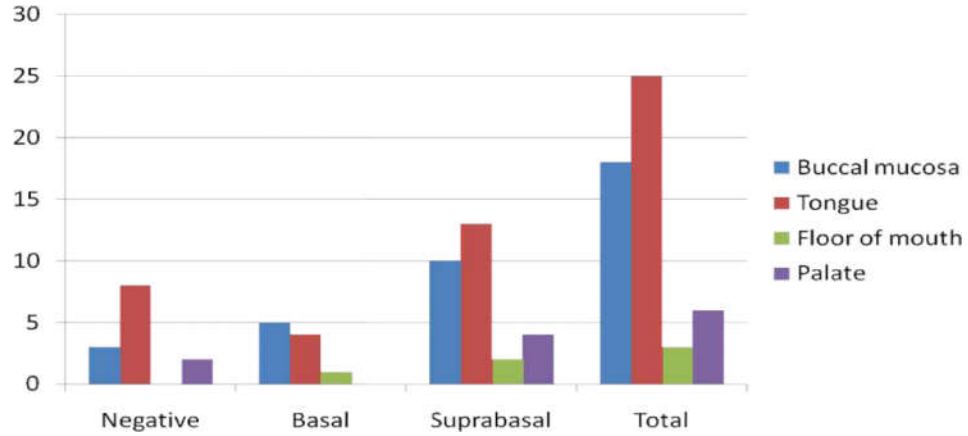

Fig. 3: Staining pattern According to location

Table 4: Staining pattern According to age group

Age Group	P53			Total No of Cases
	Negative	Basal	Suprabasal	
20-30	00	01	01	02
		50%	50%	
30-40	04	02	08	14
	29%	14%	57%	
40-50	02	02	06	10
	20%	20%	60%	
50-60	04	03	10	17
	24%	17%	59%	
60-70	01	00	02	03
	33.3%		66.6%	
70-80	02	00	04	06
	33.3%		66.6%	

Table 5: Staining pattern According to SEX

	P53			
	Negative	Basal	Suprabasal	Total No
Female	06	01	06	13
	46%	08%	46%	
Male	07	07	25	39
	18%	18%	64%	

It was observed that 59% of the cases in the age group 50-60 year showed suprabasal p53 positvity

As seen from the above table majority of cases in both gender showed suprabasal positivity 25%of females and 75% of males respectively with a 1:3 ratio.

Discussion

In many studies including oral lesions the reported incidence of p53 expression has varied from 11- 85% probably as a result of substantial difference in technique used as well asvaried oral habits practiced in different geographical regions and Races [5].

A high frequency of elevated levels of p53 protein in SCC of Head and neck has been reported [6].

In our study 26 cases out of 33 cases of oral SCC expressed p53 protein. Our results are similar ar reported by kaur et al [7].

Immunoexpression of p53 in oral SCC & dysplastic lesion in patients with habit of reverse smoking was studied by Alverez and found 74% p53 positive in dysplastic lesions. P53 positivity in reverse smokers and 78% in conventional smoker. This result confirms p53 in the premalignant lesion may be an early episode in the oral carcinogenesis.

An important finding in our work is strong p53 positivity is more i smokers (65%) 13/20 cases of chronic smokers this is consistent with Field et al [8] who analyzed the smoking history of 71 patients by logistic regression and found that smoking correlates with p53 over expression. Similarly increase p53 positive cells were detected in patients with both betel quid chewing and smoking habits [9].

P53 was found to be positive in 72.7% of cases of leukoplakia by a study done by priya Kumar et al, their study involved subjects indulging in various form of tobacco use as smokeless, smoking and combination of both they concluded, study of mutation status of p53 may be of more prognostic significance [10].

Another study results by Murthy et al suggest that the detection of p52 by IHC in biopsy of betel quid/ tobacco induced oral precancerous lesions , has no significant relationship to their likely malignant transformation. Based on these results they have reported to conclude that p53 protein detection may serve as an intermediate biomarker of cancer risk [11].

In our study suprabasal staining observed in 67% (n=19) cases of abusers is lesser than non abusers. History was not available in 9 cases in betelquid & tobacco users.

Our study is contradictory to the previous study of Murthy et al.

In our study the expression of p53 by immunohistochemical analysis in SCC was seen in 78.7% cases which comprises of 12 cases of well differentiated SCC,11 cases of Moderately differentiated SCC, 01 case of Poorly differentiated SCC.

An interesting observation was noted in the present study that highly differentiated tumour had a high p53 immunostaining while Poorly differentiated SCC showed significant weaker IHC expression of p53

compared with Well differentiated form. These results are consistentwith other studieswhich have demonstrated; statistically significant correlation was between histological grade and p53 expression. This might be interpreted as most of the mutation in Poorly differentiated OSCC is truncating mutations which may lead to less protein production and absence of its reactivity in the nucleus which inturn indicate the aggressive nature of the poorly differencing nature[12,13].

Conclusion

In the present study no statistically significant association was found between p53 expression pattern and various clinical parameters like age, sex, location, smoking and tobacco.

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