

DIFFERENT HISTOPATHOLOGICAL GRADES OF ORAL SQUAMOUS CELL CARCINOMA IN PATIENTS WITH HISTORY OF SNUFF DIPPING

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ABSTRACT

Objective: To determine the frequency of different histopathological grades of squamous cell carcinoma in patients with history of snuff dipping.

Material and Methods: This descriptive cross sectional study was conducted at Department of Oral and Maxillofacial Surgery Khyber College of Dentistry. A total of 157 patients were observed using 27.5% proportion of grade 2 of oral squamous cell carcinoma on histopathology among snuff dippers, 95% confidence interval and 7% margin of error under World Health Organization sample size calculations. Study duration was six months in which consecutive (non probability) sampling technique was used for sample collection.

Results: In this study mean age of the patients was 62 years with $SD \pm 3.71$. Eighty three percent patients were male and 17% patients were female. Forty two percent patients had snuff dipping from 20-30 years and 58% patients had snuff dipping from 31-40 years. Sixty six percent patients had grade 1 oral squamous cell carcinoma, 30% patients had grade 2 oral squamous cell carcinoma and 4% patients had grade 3 oral squamous cell carcinoma.

Conclusions: Our study concluded that well differentiated Oral squamous cell carcinoma (G1) is the most common grade of the tumour in those patients with positive history of snuff dipping. Grading of this tumour favours good prognosis if the lesion is diagnosed at an early stage. Snuff dipping is the most common form of smokeless tobacco use in this part of the world. Snuff dipping is a strong risk factor in the aetiology of oral squamous cell carcinoma.

Key words: Histopathological grades, Squamous cell carcinoma, Snuff dipping.

INTRODUCTION

Oral cancer is the third most common malignancy in the developing countries and the eighth most common in developed countries¹. About 90% of malignant neoplasms in the oral cavity are Squamous Cell Carcinomas². Oral squamous cell carcinoma remains one of the most debilitating and disfiguring of all malignancies and is the fourth leading cause of cancer death in men³. The most common affected sites are the tongue, lower lip and floor of the mouth⁴.

Etiology of squamous cell carcinoma is multi-factorial⁵. Alcohol and tobacco use are the two

most widely implicated etiological factors⁶. About 30 brands of snuff available in Pakistan were tested for carcinogens such as cadmium, arsenic, lead, nitrite, nitrate and nicotine. All these carcinogens were found to be well above the allowable limits making it a health hazard for the consumers⁷.

The etiological role of snuff in oral squamous cell carcinoma is well established. The use of snuff over the years resulted in carcinoma of the buccal sulcus mucosa directly adjacent to the site where it was habitually placed. The most common site has been reported to be lower left gingivolabial sulcus which is the also the most favorite site for the habitual placement of niswar⁸.

Histopathological Grading plays an important role in treatment planning of squamous cell carci-

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noma. Histological differentiation of tumor cells is a prognostic indicator and is associated with treatment outcome³. In high grade squamous cell carcinoma mortality was found to be 2.35 times more than in low grade squamous cell carcinoma⁹. Poor histological differentiation of oral squamous cell carcinoma is related to positive nodal status, extracapsular spread, perineural invasion of primary tumors and the probability of developing neck recurrence and distant metastasis after treatment¹⁰. There are several histopathological grading systems of squamous cell carcinoma, however Border,s System is most widely used. This System is quantitative and is based on the degree to which the tumor cells resemble the cells of origin¹¹.

The incidence rate of squamous cell carcinoma in Pakistan has been reported to be 4.1 per 100000/year for males and 4 per 100000/year for females¹². The most common histopathological grade in snuff dippers is grade 1 (66.55%), followed by grade 2 (27.5%) and grade 3 (5%)¹³. One study conducted in Khyber Pakhtukhwa showed that 84 % of patients suffering from squamous cell carcinoma were chronically addicted to snuff⁸.

The current study is designed to determine the frequency of different histopathological grades of squamous cell carcinoma among its newly diagnosed patients and having history of snuff dipping.

METHODS AND MATERIALS

This descriptive cross-sectional study was carried out in the Department of Oral and Maxillofacial Surgery Khyber College of Dentistry.

A total of 157 patients were recruited using 27.5% proportion of grade 2 of oral squamous cell carcinoma on histopathology among snuff dippers, 95% confidence interval and 7% margin of error under WHO sample size calculations.

All newly diagnosed patients of squamous cell carcinoma having history of snuff dipping age group above 25 years and either gender were included while those with no history of snuff dipping and positive history of any treatment received were excluded from the study.

Approval of institutional ethical committee was taken. The purpose, procedure, risk and benefits was

explained to them and informed consent was taken from them to participate in the study and assured of confidentiality of all data.

A thorough history was taken so as to confirm the use of snuff dipping. Clinical examination of soft tissues, bone and lymph nodes was carried out to determine the site, size and clinical picture. Incisional biopsy was taken to confirm the diagnosis of squamous cell carcinoma. Grading of the tumor was done according to Border,s System¹⁴. To maintain uniformity of procedures and techniques used for grading of squamous cell carcinoma one reference laboratory and one histopathologist (with minimum 5 years experience) was used. All information was gathered by myself and was checked by a senior consultant who was a fellow of College of Physicians and Surgeons Pakistan and was recorded on a proforma. Exclusion criteria was strictly followed to control confounders and bias in the study results.

Data so collected was analyzed by SPSS version 17. Descriptive statistics was done to compute the mean \pm standard deviation for numerical variables like age and duration of snuff dipping. Frequencies and percentages were calculated for categorical variable like Histopathological grades and gender. For gender male to female ratio was calculated. All results were presented as tables and graphs. Histopathological grades were stratified among age, gender and duration of snuff dipping to see the effect modifications.

RESULTS

Out of total of 157 patients the age distribution was such that majority of the patients were in 51-70 (70%) followed by age group 41-50 (30%). Mean age was 62 years with SD \pm 3.71. Detail is given in Table-1. Gender distribution among 157 patients was analyzed as 130(83%) patients were male and 27(17%) patients were female.

Duration of snuff dipping among 157 patients was such that most of the patients (58%) used snuff form 31-40 years. Mean duration of snuff dipping was 32 years with SD \pm 2.88. Detail is given in Table-2.

Histopathological grades of oral squamous cell carcinoma among 157 patients was analyzed as 104(66%) patients had grade 1 oral squamous cell car-

cinoma, 47(30%) patients had grade 2 oral squamous cell carcinoma and 6(4%) patients had grade 3 oral squamous cell carcinoma. Detail is given in Table-3. The degree of differentiation was such that majority of the lesions were well differentiated (66 %) followed by moderately differentiated (30%). Figure-1.

Table No-1: Age Distribution

Age	n	%
41-50 years	47	30
51-60 years	55	35
61-70 years	55	35
Total	157	100

Mean age was 62 years with SD ± 3.71

Table - 2: Duration of Snuff Dipping

Snuff Dipping	n	%
20-30 years	66	42
31-40 years	91	58
Total	157	100

Mean age was 32 years with SD ± 2.88

Table No - 3: Histopathological grades

Histopathological Grade	n	%
Grade 1	104	66
Grade 2	47	30
Grade 3	6	4
Grade 4	0	0
Total	157	100

Mean age was 62 years with SD ± 3.71

Table No - 4: Stratification of histopathological grades with age

Histopathological Grade	41-50 years	51-60 years	61-70 years	Total
Grade 1	37	32	35	104
Grade 2	10	20	17	47
Grade 3		3	3	6
Grade 4				0
Total	47	55	55	157

Chi square test was applied in which P value was 0.003

Table No - 5: Stratification of histopathological grades with gender

Histopathological Grade	Male	Female	Total
Grade 1	95	9	104
Grade 2	31	16	47
Grade 3	4	2	6
Grade 4	0	0	0
Total	130	27	157

Chi square test was applied in which P value was 0.003

Table No - 6: Stratification of histopathological grades with duration of snuff dipping

Histopathological Grade	20-30 years	31-40 years	Total
Grade 1	44	60	104
Grade 2	19	28	47
Grade 3	3	3	6
Grade 4			0
Total	66	91	157

Chi square test was applied in which P value was 0.003

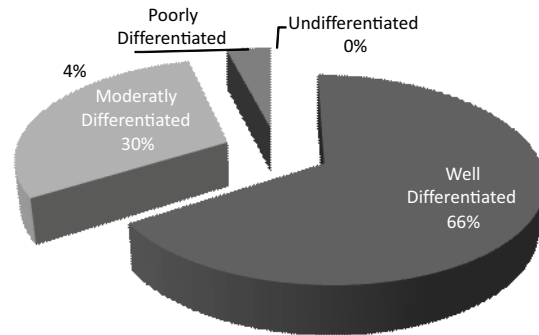


Fig-1. Distribution of histopathological grades

Stratification of histopathological grades of oral squamous cell carcinoma with age, gender and duration of snuff dipping is given in Table 4 - 6.

DISCUSSION

Tobacco in its various forms has been used for centuries. In Pakistan, tobacco is used in both smoked as well as in smokeless form. Smoking cigarette is common throughout the country. Pan a type of smokeless tobacco is popular in Karachi and some cities of Punjab. Snuff which is powdered tobacco mixed with ash or lime and some flavoring or chemical agents, is placed between the gums and upper or lower lip. This type of smokeless tobacco is popular in Balochistan and North West Frontier Province (NWFP), (KPK)^{15,16}.

Niswar(snuff) is the most frequently used form of tobacco in the periphery of Peshawar and other regions of Khyber Pkhtunkhwa(KPK), i.e., 64.5% followed by chillum 17.5% (which is a form of smoked tobacco used by local people as an alternative to cigarette smoking). A study from Sharifullah shows that the habit of snuff dipping is more common in Afghanistan. In a study at Nangrahar University it was found that 80 percent of males and 20 percent of female were used to the habit. Whereas 18% of the University students were in the habit of using niswar¹⁷.

Snuff use has been recorded as a possible cause of oral SCC¹⁸⁻²¹. A study from Shahshows that Niswar is the most common form of smokeless tobacco, used in the periphery of Peshawar. The results of the study show that 64% of both sexes are used to snuff (Niswar) dipping¹⁸⁻²².

Our study shows that mean age of the patients was 62 years with SD \pm 3.71. This finding is consistent with the literature on squamous cell carcinoma as it has been mentioned in different studies that oral squamous cell carcinoma is a disease of middle and old age. Khan M. et al²³. in their study found the mean age to be 60 years with \pm 2.14. Similarly Pires²⁴ in their study, conducted on 346 patients, found the mean age to be 62.3 years.

In our study 83% of the patients were male while 17% were female. So far as the male to female ratio is concerned it is argued that due to the less exposure of women to harmful agents such as snuff, tobacco smoking and alcohol the male to female ratio is heavily tilted in favour of men²⁵. 75 similar results were reported by Khan²² wherein the male to female ratio was 85% male and 15 % females. Pires²⁴ found that 87 % patients were male while 13% patients were female.

Forty two percent patients had snuff dipping from 20-30 years and 58% patients had snuff dipping from 31-40 years. Various studies on this subject have concluded that a long period of exposure to snuff is required for squamous cell carcinoma to develop. Typically 20-50 years are required for malignant changes to appear in oral mucosa.¹⁷⁻¹⁹

Sixty six percent patients had grade 1 oral squamous cell carcinoma, 30% patients had grade 2 oral squamous cell carcinoma and 4% patients had grade 3 oral squamous cell carcinoma. Similar results were found in study conducted by Khan M et al²³ in which sixty eight percent patients had grade 1 oral squamous cell carcinoma, 28% patients had grade 2 oral squamous cell carcinoma while 5% patients had grade 3 oral squamous cell carcinoma.

Histologically Oral SCC presents itself as well differentiated, moderately differentiated and poorly differentiated tumour. This finding has got a great bearing on prognosis and 5 year survival because the prognosis for poorly differentiated tumours is poor as compared to well differentiated tumours. According to a study from John Isaacs²⁶ carried out on 27 oral SCC

patients at Liaquat University of Medical and Health Sciences (LUMHS) Jamshoro, 66% of the tumours were graded as G1 and 34% as G3, while none of the patient was graded as G2 i.e., moderately differentiated oral SCC. The result of our study shows that only 4% of the patients are graded as G3, and 30% as G2 contrary to John Isaac study. 66 % of patients were graded as G1. The important fact about John Isaac study is that it was conducted on patients without regard to etiological factors. Other studies²²⁻²⁴ reported the grading of squamous cell carcinoma to be 30.75% as well differentiated 45.5% moderately differentiated and 23.8% as poorly differentiated. Fang²⁷ conducted a study on 150 patients with history of betel quid chewing. They found the histological differentiation to be 36% well differentiated, 56% moderately differentiated and 8% poorly differentiated.

CONCLUSIONS

Our study concluded that well differentiated Oral SCC (G1) 66% is the most common grade of the tumour in those patients with positive history of snuff dipping. Grading of this tumour favours good prognosis if the lesion is diagnosed at an early stage. Snuff dipping is the most common form of smokeless tobacco use in this part of the world i.e., North West Frontier Province. Snuff dipping is a strong risk factor in the aetiology of oral SCC in area.

RECOMMENDATIONS

1. Our first recommendation is to discourage the use of snuff in the general population. Various methods can be used to achieve this goal. Awareness should be created among the general population through media campaign through the people who have the clout with the general population like Imams of mosques, local leaders and members of the civil society should be utilized to inform the public about the hazards of snuff use.
2. On the official level legislation should be enacted making the easy availability of snuff and other related products more difficult. Heavy taxes should be imposed on snuff making it more expensive thereby decreasing its use.
3. Another recommendation is to disseminate the findings of this study among the general dental as well as general medical practitioners urging them for timely referral of any suspected lesion so as

to make an early diagnosis and treatment which will result in better prognosis.

4. All quakes should be banned through proper legislation and administrative measures as most of the times these quakes are the first to receive these patients. Having no knowledge of malignant lesions they mismanage the patients resulting in late presentation and adversely affecting prognosis.

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