RESEARCH ARTICLE

THE RELATIONSHIP BETWEEN THE USE OF SMOKELESS TOBACCO AND ORAL SQUAMOUS CELL CARCINOMA

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Abstract

Smokeless tobacco (ST) is a tobacco product that is used by means other than smoking. Evidence was available that ST products is a known risk factor for oral precancerous and cancers for long, with greater risk for oral cancer than others. The prospective, descriptive study has carried out to evaluate the relationship between the use of smokeless tobacco and oral cancer.

Biopsy samples have collected from 60 patients, whose have attended to Al-Gamhouria Teaching Hospital and histo-pathological private labs in Aden using a questionnaire during the period of 12 months. The sections from paraffin-embedded tissue specimens were stained with hematoxylin and eosin (H & E). A section containing the full thickness of the tumors have used for histopathological grading.

The prevalence of oral squamous cell carcinoma (OSCC) lesions showed different grade of differentiation among 60 studied patients cases, the Well differentiation squamous cell carcinoma (WDSCC) was the highest percentage (70%). No significant difference noticed in well-differentiated SCCs (WDSCC) between men (36.7%) and women (33.3 %; P < 0.05). The moderate differentiation SCC (MDSCC), and the poor differentiation SCC (PDSCC) represented (20% & 10%) respectively. According to the age of patients, WDSCC, MDSCC and PDSCC highest percentage age group was (51-60) years. Male were predominant in both genders, male to female ratio 1.2: 1. Anatomical sites of all OSCC lesions had analyzed and revealed that tongue was the most prevalent site (33.3%), followed by the buccal mucosa, (23.3%), floor of mouth (16.7%), lip (13.3%), Gingiva (8.3%), and the least prevalent site was the hard palate represented (5%) of all cases., the chief etiological factor which we observed, was tobacco, in the form of smoking tobacco used by 75% of the patients followed by smokeless tobacco product users, in form of shamma chewers, (61.7%), and in form of Hot sachet (58.3%), and Zarda users represented 51.7% of cases.

Our results indicate that the occurrence of OSCC among studied cases showed different grade of differentiation, age and gender have some relation with the presence of OSCC. and it is high association with risk habits of tobacco use in different forms particularly smokeless tobacco.

Keywords: Squamous cell carcinoma, Histopathological grades, Oral cancer, Tobacco.

Introduction:

Oral cancer is the 6th most common type of human cancer worldwide and about 90% of the oral cancer is oral squamous cell carcinoma [1, 2]. The incidence of oral squamous cell carcinoma (OSCC) increases with age, most commonly occur in patients middle aged or older >40 years, the increase rate in elderly adults because usually it takes many years to develop. Although recently an alarming rise in incidence among younger people is being documented worldwide, this rising is related to that nowadays most young patients were exposed to traditional popular and culturally accepted risk factors like tobacco-chewing habits, tobacco smoking and drinking alcohol. [3] The most common sites for OSCC are the tongue, buccal mucosa, gingiva and floor of the mouth [2]. OSCC is associated with

exposures to risk factors such as tobacco, betel nut, areca nut, alcohol, human papilloma virus, and additional conditions such as chronic inflammation, genetic alterations [2, 4, 5, 6]. OSCCs are classified microscopically into well differentiated or moderately and poorly differentiated carcinomas, based on the differentiation of neoplastic cells [7], the degree of cell differentiation is one of the most widely used criteria to predict prognosis of the disease [8]. Well-differentiated OSCCs generally show a tendency to metastasize into regional lymph nodes after invading connective, muscle or bone tissue. The poorly differentiated OSCCs are biologically more aggressive, with a tendency to progress to regional metastases at an early stage of the disease, and with a greater risk of developing distant metastases [9].

The grading systems provide valuable diagnostic and predictive information of OSCC. The prevalence rates of oral cancer were counted in about of 1.97/ 100,000 individuals in Arab countries, whose used tobacco and alcohol [3]. On other hand the smokeless tobacco products are typically chewed, dipped, sucked by place either in the buccal mucosa, labial mucosa or under the tongue, and then suck (dipped) or chew it on a timely basis. Or applied as a paste to the gingiva. ST known through different names such as: shammah (ordinary traditional ST), Hot (filter tobacco pouch ready to use sachet), Zarda (quid with smokeless tobacco), and others like toombak or neshoog, these are very popular in Yemen, Southern Saudi Arabia and Sudan [10, 11, 12, 13]. The ST products are major risk factors of oral cancer, where shammah is strongly associated with oral potentially malignant and oral malignant lesions [14, 15, 16]. This study aims to evaluate the relationship between the use of smokeless tobacco and oral cancer.

Materials and Methods

The prospective, descriptive study was carried out on randomly selected oral squamous cell carcinoma (OSCC), untreated histopathologically diagnosed, whose attending at Al-Gamhouria Teaching Hospital and histo-pathological private labs (Modern Histopathology Laboratory) in Aden using a questionnaire during the period from March 2020 till March 2021. The questionnaire was self-administered and was distributed to 60 targeted patients in this study. Incisional or excisional biopsy was done by the maxillofacial surgeons after obtaining the lesions samples, biopsy material was immediately fixed with formalin 10%, paraffin-embedded tissue specimens from 60 cases of OSCC were stained with hematoxylin and eosin (H & E). A section containing the full thickness of the tumors were used for histopathological grading. SPSS version 22.0 Statistical Software has used for analysis. The variables data were analyzed using Chi square, Mann Whitney and Fisher exact tests. The significant level was set at P≤ 0.05.

Results

Total selected 60 individuals for the study are oral squamous cell Carcinoma untreated patients and have been diagnosed in Histopathology laboratory Aden/ Yemen, for the period from March 2020 till March 2021. All studied oral squamous cell carcinoma (OSCC) lesions have shown different grade of differentiation according to histopathological diagnosis they have broken-down into three categories Well, Moderate, Poor differentiation. The Well differentiation squamous cell carcinoma (WDSCC) was the highest percentage (70%), followed by moderate differentiation SCC (MDSCC), which has represented less than quarter (20%) and the poor differentiation SCC (PDSCC) represented (10%), (table1)

Table 1: Distribution of oral squamous cell carcinoma (SCC) patients according to Grades of differentiation

Ca-differentiation	№	%
Well differentiation	42	70
Moderate differentiation	12	20
Poor differentiation	6	10
Total	**60**	**100**

Table (2) shows that, WDSCC lesions are more frequent than other lesions where cancer represented (33.3% and 36.7%) in both female and male of the population respectively. The Moderate differentiation lesions were presented 8.3% in female and 11.7% in male, whereas the Poor differentiation lesions were 3.3% in female and 6.7% in male. The difference between percentages of the three grade of differentiation in according to patients sex was statistically insignificant (p= 0.779).

Table 2: Histopathological Diagnosis according to sex of patient

Sex of patient	OSCC Grade of differentiation						Total	
	WDSCC (n=42)		MDSCC (n= 12)		PDSCC (n= 6)			
	№	%	№	%	№	%	№	%
Female	20	33.3	5	8.3	2	3.3	27	45.0
Male	22	36.7	7	11.7	4	6.7	33	55.0
Total	**42**	**70**	**12**	**20**	**6**	**10**	**60**	**100**

Table (3) displays that the number of patients show different percentage in different age groups. The mean age for all 60 patients was (54.57± 13.05) years, the highest percentage in age group (51-60) 35.0%, followed by (41-50) 28.3%, then (> 60) years 25%. In WDSCC the mean age was (55.55 ± 13.75) years, it had highest percentage 21.7% in age group (51-60) years followed by age group (41-50) and (>60years) represented (20% each). In MDSCC and PDSCC highest percentage in age group (51-60) years. The mean age in MDSCC was (54.17 ±11.77) and in PDSCC was (48.57±10.09) years. The percentage of most cancer increased with increasing

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age and There was no significant relationship between the age of patients and type of lesions (p: 0.916).

Table 3: Histopathological Diagnosis in relation to age group (years)

| Age group (years) | OSCC Grade of differentiation | | | | | | Total | |
| | WDSCC (n=42) | | MDSCC (n= 12) | | PDSCC (n= 6) | | | |
	№	%	№	%	№	%	№	%
21 – 30	2	3.3	0	0	0	0	2	3.3
31 – 40	3	5	1	1.7	1	1.7	5	8.3
41 – 50	12	20	4	6.7	1	1.7	17	28.3
51 – 60	13	21.7	5	8.3	3	5	21	35.0
> 60	12	20	2	3.3	1	1.7	15	25
Total	42	70	12	20	6	10	60	100
Mean age ± S.D.	55.55 ± 13.750		54.17 ± 11.777		48.50± 10.095		54.57± 13.053	

Anatomical sites of all OSCC lesions were analyzed and revealed that the tongue was the most prevalent site (33.3%), followed by the buccal mucosa, (23.3%), floor of mouth (16.7%), lip (13.3%), Gingiva (8.3%), and the least prevalent site was the hard palate, that was represented (5%) of all cases.

All anatomical sites affected had observed in all grades of OSCC except hard palate noted only in WOSCC cases (p: 0.98) in table (4).

Table 4: Histopathological Diagnosis in relation to anatomical Site of lesion

| Site of lesion | WDSCC | | MDSCC | | PDSCC | | Total | |
	№	%	№	%	№	%	№	%
Tongue	13	21.7	5	8.3	2	3.3	20	33.3
Inner Cheek /Buccal mucosa	10	16.7	3	5	1	1.7	14	23.3
Floor of mouth	8	13.3	1	1.7	1	1.7	10	16.7
Lip	5	8.3	2	3.3	1	1.7	8	13.3
Gingiva	3	5	1	1.7	1	1.7	5	8.3
Hard Palate	3	5	0	0	0	0	3	5
Total	42	70	12	20	6	10	60	100

All studied 60 sample diagnosed with OSCC were practicing oral habits some with more than one in the same time.

Table (5) shows that (75%) of the screened patients were tobacco smokers represented (75%) of patients, followed by Qat and shamma chewers, both equally represented (61.7%) of total number of patients, next smokeless tobacco users represent nearly half of cases, the Hot sachet (*filter tobacco pouch ready to use sachet*) and Zarda users (*smokeless tobacco with Betel quid)* represent (58.3%, 51.7%) of cases respectively, the lower risk was noticed in Tambol users (*betel quid with no tobacco*) (28.3%) of cases and Alcohol drinkers represent in (8.3%) of total cases only. No significant association

obtained between the risk habits studied and OSCC patients, except Hot sachet (filter tobacco pouch ready to use sachet) users and Tambol users which both statistically significant (p≤0.05).

Table 5: Histopathological Diagnosis in relation to habits

| Risk factors (Oral habits) | WDSCC (n= 42) | | MDSCC (n= 12) | | PDSCC (n= 6) | | Total | | P value |
	№	%	№	%	№	%	№	%	
Smoking	31	45	10	18.3	4	6.7	45	75	0.705
Shamma ordinary smokeless tobacco	26	43.3	7	11.7	4	6.7	37	61.7	0.941
Qat chewing	25	41.7	7	11.7	5	8.3	37	61.7	0.514
Hot smokeless tobacco sachet	25	41.7	4	6.7	6	10	35	58.3	0.025
Zarda; Tambol betelquid – with tobacco	21	35	7	11.7	3	5	31	51.7	0.875
Betel nut- fufel	17	28.3	1	1.7	1	3.3	20	33.3	0.144
Tambol betelquid –no- tobacco	16	26.7	1	1.7	0	0	17	28.3	0.035
Alcohol	2	3.3	3	5	0	0	5	8.3	0.060

Table (6) shows that patients with smoking habit noticed in both sex the male smokers were more represent (55.5%) then female (44,4%). Related to the way of tobacco consumption; this table shows that Cigarette smoking was the highest among all, and noticed in (44,4%) of all habits in both sex. Cigarette smokers male were more (80%) and female only (20%) of all, on the contrary of that Shisha smoker female were more (75%) while in male 25%.

Table 6: Histopathological Diagnosis in relation to type of smoking

| Smoking | Female | | Male | | Total | |
	№	%	№	%	№	%
Cigarette	4	20	16	80	20	44.4
Shisha (water pipe)	12	75	4	25	16	35.5
Both (Cigarette+ Shisha)	4	44.4	5	55.6	9	20
Total	20	44.4	25	55.6	45	100

* * Percentages calculated in relation to the total of the column, while other to row p=0.012

Discussion

Oral cancer is characterized by high prevalence, mortality, and low survival rates [17]. In the current study, the researcher has evaluated the histopathological parameters of oral squamous cell carcinoma according to age, sex and their social habits of patients diagnosed at a governorate and private histopathology laboratory in Aden city, Yemen.

Although the etiology of oral cancer is certainly multifactorial, the social habits such as, qat chewing, tobacco use (smoking, smokeless "Shamma, Hot", betal nut, quid:"Zarda, tambol") are very widespread in Yemen at different age groups for both gender. Tobacco chiefly used in form of smoking either cigarettes, cigars, pipe or shisha, or in form of quid or in form of smokeless tobacco. All are acknowledged risk factors for oral cancer. The World Health Organization on its website affirms that the heavy use of tobacco is one of the main contributing factors towards the growing incidence of oral cancer.

In this study, the chief etiological factor which the researcher has observed is tobacco with 75% of the patients using in the form smoking. Shamma chewers, (61.7%), the Hot sachet (smokeless tobacco users) (58.3%), and Zarda users (quid with smokeless tobacco) represent 51.7% of cases. The OSCC lesions has shown different grade of differentiation in studied cases, well differentiation squamous cell carcinoma (WDSCC) is the highest percentage (70%), than other two. These results are similar to previous studies that they have been suggested well differentiated SCC (WDSCC) as the most common type followed by moderate differentiated SCC (MDSCC) and poorly differentiated SCC (PDSCC) [18, 19, 20, 21].

The researcher has observed the Grades of differentiation is high in male compared to female, WDSCC lesions has represented (36.7%) in male and (33.3%) in female. Another two grades also have shown increased percentage in male than female, probably the men were more exposed to risk factors [22].

The age (*51-60*) years has shown a highest percentage 21.7% of WDSCC followed by, 8.3% of MDSCC and 5% of PDSCC respectively. The comparison of OSCC between young and old groups according to the three grading systems have shown no statistically significant difference. In contrast to the current study, some studies showed statistically significant difference between younger and older patients [1]. Another study found a correlation between the occurrence of oral cancer and age, with 60% of cases diagnosed after the age of 50 years [23]. In the USA, the average age at diagnosis of oral cancer is 62 years, and two-thirds of individuals with this disease are over the age of 55 [24].

In the present study the most location of OSCC is the tongue (33.3%), has followed by the buccal mucosa (23.3%), floor of mouth (16.7%), lip (13.3%), Gingiva (8.3%), and the least prevalent site is the hard palate, that has represented (5%) of all cases. Some studies suggested that the most common site of OSCC was the tongue according to other studies in UK, Sri Lanka and Iran [2, 20, 24, 25]

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مقالة بحثية

العلاقة بين استخدام التبغ الذي لا يدخن وسرطان خلايا الحرشفية للفم

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المُلخّص

يعد التبغ عامل خطر رئيسي لسرطان الفم والعديد من السرطانات الأخرى. أجريت هذه الدراسة الوصفية المحتملة لتقييم تأثير عادات استخدم مضغ التبغ على الفم. جمعت عينات (الخزعة) من 60 مريض المرتادين مستشفى الجمهورية التعليمي والمختبرات الخاصة بعلم الانسجة المرضية خلال فترة عامين. المقاطع النسيجية من العينات المطمورة بالبارافين تم صبغها بالهيماتوكسيلين ويوزين (H&E) لتعيين درجة الانسجة المرضية .

أظهرت النتائج انتشار سرطان الخلايا الحرشفية للفم (OSCC) عند درجات مختلفة من التمايز بين 60 حاله مرضيه تمت دراستها حيث شكلت الخلايا الحرشفية السرطانية جيد التمايز (WDSCC) اعلى نسبة 70%.

لم يلاحظ أي فرق كبير في الخلايا السرطانية المتمايزة جيداً (WDSCC) بين الرجال (36.7%) والنساء (33.3%). التمايز المعتدل (MDSCC) والتمايز الضعيف PDSSC شكل حوالي (20%، 10%) على التوالي. وفقاً لأعمار المرضى فان اعلى نسبة المئوية للتمايز الجيد، المعتدل والضعيف لوحظت عند عمر 51-60 عام، وكانت سائدة في الذكور عند كلا الجنسين، بنسبة 2:1:1 للذكور مقارنة بالاناث . تم تحليل المناطق التشريحية لجميع حالات OSCC وتبين ان اللسان المنطقة الأكثر انتشارا بمعدل (33.3 %) يليه الغشاء المخاطي للشدق (23.3%)، قاع الفم (16.7%)، الشفه (13.3%)، اللثة (8.3 %)، و المنطقة الاقل انتشارا هو سقف الحنك بمعدل (5%) من جميع الحالات. لاحظنا ان المسبب الرئيسي هو تعاطي 75% من المرضى للتبغ بصورة (smokeless tobacco) عن طريق مضغ الشمه التقليدي عند نسبة (61.7%)، اكياس الحوت (Hot sachet) عند نسبة (58.3%) والزرده عند نسبة (51.7%) من الحالات المدروسة.

نستنتج من ذلك ان سرطان الخلايا الحرشفية للفم (OSCC) أظهر درجات مختلفة من التمايز. العمر والجنس لهما علاقة بظهور هذه الحالات التي ترتبط ارتباطًا وثيقًا بالعادات الخطرة لتناول التبغ بأشكال مختلفة وخاصة التبغ غير المُدخّن (smokeless tobacco).

الكلمات المفتاحية:خلايا السرطان الحرشفية، درجات الانسجة المرضية، سرطان الفم، التبغ.