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Risk Factor Trends among Oral Squamous Cell Carcinoma Patients in North Jordan: A Pilot Study

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ABSTRACT

Objectives: The aim of this study was to investigate the prevalence and patterns of oral squamous cell carcinoma (OSCC)-associated risk factors and patient characteristics in a sample of Jordanian population for further consideration of the results in oral cancer preventive programs.

Materials and Methods: The archives of Pathology Department at King Abdullah University Hospital were searched in the period from 2003 to 2023 for patients diagnosed with OSCC. The recorded data included demographics, tumor-related information and risk factors. Data was analyzed using (IBM SPSS Statistics 27.0.1).

Results: 168 cases out of which 54 had a full history of risk factors were identified. Age average was 63.5 years. Male: female ratio was 1.7:1. Lateral border of the tongue and lower lip were the most frequent locations. Lower lip was the most common site among outdoor workers.

OSCC risk factor analysis revealed low socio-economic status (SES) in 64.8%, smoking in 55.6%, positive family history of other malignancies in 51.9% who all were in the 40s of age, urban area residence in 50%, outdoor working in 38.9%, graduate degree holders in 29.6%, and office workers in 27.8%.

Smoking prevalence was 90% in males, 76.2% in outdoor workers, 60.7% in OSCC patients with positive family history of other malignancy, 63.3% in low-SES patients, 56.7% in urban residents, 53.3% in office workers, and 50% in graduate degree holders. OSCC female patients were non-smokers with a percentage of 85% and were non-employed with a percentage of 75%.

Conclusions: Low-SES patients, smokers, patients with positive family history of malignancy, urban residents, outdoor workers, graduate degree holders, and office workers are recommended to be targeted in oral cancer preventive programs. Smoking is still the most prevalent OSCC risk factor in our sample. Smoking cessation clinics will be of utmost importance. Wide-scale national studies of OSCC different risk factors with focus on smoking different modalities would be of high significance.

Keywords: Oral cancer, Risk factors, Smoking, Socio-economic status, OSCC.

1. Introduction

Oral cancer, a common human malignancy, refers to a sub-group of head and neck neoplasms affecting various parts of the oral cavity, including the lips, tongue, salivary glands, gingiva, floor of the mouth, oral mucosal surface, and palate (1). Oral squamous cell carcinoma (OSCC) is the most common malignant tumor affecting the oral cavity and compromising over 90% of all oral tumors (2), with an increase in mortality rate of 0.4% per year from 2010 to 2019 (3). According to the Global Cancer Observatory (GCO), the annual incidence of OSCC has increased to 377,713 cases in

2020 (1), compared to 274,300 cases in 2002 (4). In Jordan, the number of all new cancer cases was 12,328 in 2022 (5), and oral cancer accounts for 0.84% of this total number, ranking 20th among the most common cancers affecting Jordanians (5). Additionally, according to the GCO, oral cancer led to 48 deaths in 2022, making it the 22nd most killing cancer among Jordanian (5).

Several studies have shown that different risk factors are associated with OSCC (6-8). Among these, tobacco smoking and alcohol drinking behaviors, both separately and in combination, are major OSCC risk factors being associated with 64% of OSCC cases. This association is much less evident in women and young patients (9). The peak incidence occurred after the fifth decade of life (10); however, linear increases in age-standardized rates have been observed, with the greatest increase observed among individuals aged 20-34 years (11).

Occupational hazards are suspected to play a role in the occurrence of oral cavity cancer. Occupations with increased risk include butchers, machinists, leather workers, textile industry workers, and sugar cane producers (12). Moreover, socio-economic status (SES) is potentially a major factor in the etiology of oral cancer (10). The incidence and mortality of oral cancer are higher in low-developed countries (13). A cohort study illustrated that men with a low individual SES and those living in highly deprived municipalities have an elevated risk of head and neck cancer mortality (14). Dietary (15) and other lifestyle factors, such as physical activity (2) and oral hygiene (16), are currently considered relatively minor risk factors (2,16,17).

The aim of this study was to look into the patterns and prevalence of various risk factors in a sample of patients diagnosed with OSCC in northern Jordan, with the goal of identifying high-risk patient groups to target them in oral cancer prevention programs.

2. Materials and Methods

The archives of the Pathology Department at King Abdullah University Hospital, Irbid, Jordan. were searched over a period from 2003 to 2023 for biopsies diagnosed as squamous cell carcinoma in any anatomic locations extending from the lips to the anterior pillars of the fauces. Oropharynx, tonsils, and the major salivary glands were excluded, but jawbones were included in the studied sites. Upon obtaining ethical approval, patients' data was extracted from electronic records anonymously with no personal identifying information.

168 cases were identified initially; however, some phone numbers were inactive or not reachable, so the required data was collected for 54 patients; 34 males and 20 females.

The recorded data included demographics, risk factors and tumor related information. This data included age, gender, educational level, occupation, place of residence, type of smoking (cigarettes, nargileh or e-cigarettes, chewing, betel quid, others), alcohol consumption, medical history, oral hygiene and dental prostheses.

Disease related information included: tumor site, histologic grade, family history of other tumors, treatment modality, and patient's current disease state. The patients were classified according to their SES into two categories: high-SES patients and low-SES patients. Using Boroffka and Olatawura system (17) of 1977, six sub-groups were identified: Group 1 consisted of professionals with a college degree (e.g. doctors, lawyers, teachers, high governmental officials). Group 2 consisted of professionals without a college degree (teachers, large-scale farmers, higher clerical officers, entrepreneurs, armed force officers). Group 3 comprised (clerks, drivers, mechanics, butchers, policemen, soldiers of low rank, small scale entrepreneurs). Group 4 included (domestic servants, cooks, palm wine tappers, goldsmiths, small-scale farmers). Group 5 was made up of unskilled laborers and petty traders. Group 6 comprised (unemployed, retired, students, housewives, apprentices). Groups 1 and 2 were considered high-SES patients, while groups from 3 to 6 were considered low-SES groups.

All statistical analyses and significant results were calculated using (IBM SPSS Statistics 27.0.1), including descriptive analysis and Pearson chi-square test, with a significance level of $P<0.05$. Pearson chi-square test was employed to assess the association between categorical variables, such as the relationship between risk factors (e.g. smoking, occupation, socio-economic status) and the occurrence of OSCC. This test was chosen, because it is specifically designed to evaluate the significance of associations among categorical variables, making it suitable for analyzing the prevalence of risk factors across different patient groups.

3. Results

Over a 20-year period (2003-2023), 168 patients

were diagnosed with OSCC at King Abdullah University Hospital. Of these, 59.4% (100/168) were over 60 years old, while 40.6% (68/168) were under 60 years old. The male-to-female ratio was 1.75:1 with 107 (63.7%) male patients and 61 (36.3%) female patients. 90% of the patients were Jordanians, while the rest of them were Syrian refugees and of other nationalities.

The anatomic distribution of OSCC subjects is presented in Table 1. The most frequently affected sites were; the lateral border of the tongue (50/168, 29.8%), and the lower lip (48/168, 28.5%) (Table 1). The lateral tongue was the most common site overall and specifically in females, accounting for 33.3% of the females' cases; on the other hand, the most common site in males was the lower lip, accounting for 30.3% of all males' cases. However, these inferences were not statistically significant ($\chi 2$, P > 0.05).

The most frequent histopathologic grade of OSCC was well differentiated (44%, 74/168) followed by moderately differentiated (38.7%, 68/168), and then by poorly differentiated (17.2%, 29/168) OSCC.

Table 1: Site distribution of OSCC among the subjects

Site	Frequency	Percent (%)
Tongue/lateral	50	29.8
Hard palate	3	1.8
Floor of the mouth	3	1.8
Lower lip	48	28.6
Tongue/ventral	7	4.2
Buccal mucosa	16	9.5
Mandible bone	11	6.5
Maxilla bone	6	3.6
Upper lip	9	5.4
Gingiva	8	4.8
Tongue/dorsal	7	4.2

Among patients with follow-up data, the mortality rate in at least 5-year follow-up was (22.2%), which was higher in females (7 out of 20 cases) compared to 14.7% of males (5 out of 34 cases) At the time of diagnosis, one patient (1.9%) reported to have distant metastasize, while 26 cases (48.1%) reported to be tumor free. The treatment modalities of the study sample showed that surgery was the most common single treatment modality for about 61% of the cases, followed by combined treatment modalities in 33.3%, while 3 cases (5.6%) were treated with non-surgical methods.

Records of the OSCC risk factors (Table 2) considered in this study were available for 54 cases (34 males and 20 females) which were included for further statistical analysis and correlations**.** Urban residence was the most common (50%) residence type, followed by sub-urban residence (31.5%), while rural residence was the least frequent among OSCC patients (18.5%).

The most common educational level of OSCC patients in our sample of recorded data was the non-educated (31.5%: 58.8% males and 41.2% females), followed by school degree (primary to high school) (38.9%: 66.7% males and 33.3% females). Holders of graduate or post-graduate degrees were the least prevalent (29.6%: 62.5% males and 37.5% females). Occupational distribution showed that 38.9% were outdoor workers, 33.3% were unemployed and 27.8% were office workers, Outdoor workers were predominantly male patients (95.2%), with only one female patient who reported to be an outdoor worker. Socio-economic status (SES) revealed that 64.8% of the patients were ranked in the low-SES group, while 35.2% were in the high-SES group. 44.1% males were in the high-SES rank compared to only 20% of females.

A statistically significant relationship ($\chi 2$, P<0.001) between gender and occupation was noted, illustrating that 75% of the females who developed OSCC were unemployed. Correlating occupation with the grade of OSCC showed that 14.3% of the outdoor patients developed poorly differentiated OSCC, scoring 75% of all poorly differentiated OSCC cases recorded in this study.

Out of the OSCC cases that have complete records, 55.6% were smokers and 44.4% were non-smokers. Among patients with smoking history, males were found to be the majority (90%). Most of the smokers (60%) were from the heavy smoking group (more than 40 packs per year), while 17.6% were moderate smokers (20-40 P/Y) and 29.4% were light smokers (less than 20 P/Y). But, no significant relationship was found between the amount of smoking and prognosis or the histological grade of OSCC. Four cases reported using waterpipes, in addition to their conventional cigarette smoking, while only one case reported using vape, and no cases reported using either E-cigarettes (I-COS) or smokeless tobacco. Alcohol consumption was reported in only 4 cases and all of them were smokers.

Correlating smoking as a risk factor of OSCC with place of residence revealed that smoking decreases as residency moves from urban to sub-urban to rural areas

(56.7%, 23.3% and 20% respectively). A significant relationship between smoking and occupation was identified ($\chi 2$, P <0.027). Smoking prevalence was the highest among outdoor workers (76.2%), followed by office workers (53.3%), and then by unemployed patients (33.3%).

A family history of malignant tumors in either first- or second-degree relatives was present in about a half of the OSCC cases (51.9%).

Inadequate oral hygiene practice was statistically significantly correlated with poorly differentiated grade of OSCC ($\chi 2$, P <0.008). Inadequate oral hygiene, presented as brushing less than once daily to never, was evident among 77.8% of OSCC patients.

Table 2: Risk factors associated with OSCC among north Jordan population

Risk factor		Frequency	Percent (%)
Gender	Male	34	68
	Female	20	32
Residency	Urban	27	50
	Suburban	17	31.5
	Rural	10	18.5
Education	Non-educated	17	31.5
	School Degree	21	38.9
	Higher education	16	29.6
Occupation	Non-worker	18	33.3
	Office worker	15	27.8
	Outdoor worker	21	38.9
Socio-economic status	High SES	19	35.2
	Low SES	35	64.8
Smoking	Smokers	30	55.6
	Non-smokers	24	44.4
Family history of malignancy	First-degree relative	20	37
	Second-degree relative	8	14.8
	No history	26	48.1

4. Discussion

OSCC is the 20th leading cause of death among Jordanians (5). Over the past two decades**,** the relative survival rates of cancer patients have increased significantly and steadily (18). Oral cancer survival rates could reach up to 80% (19). Target screening programs for high-risk groups of people have contributed to this improvement by reducing the rate of progression of premalignant conditions and enabling earlier detection of OSCC. Smoking habits, socio-economic and medical factors can all play a role in the development and progression of the disease. Targeting population groups at high risk to develop OSCC will enhance early detection and survival. Thus, our study aimed to shed light on the risk factors associated with OSCC in a sample of the Jordanian population, providing a baseline for larger studies at the institutional level (20).

Data collection of the considered risk factors was based on the availability of details in patients' electronic medical records. If details were missing, phone calls using the registered contact numbers were conducted to fill in the missing data.

The results of our study revealed that smoking, occupation, socio-economic status, and family history of cancer are the most associated risk factors with OSCC among the study sample. These findings could serve as

the foundation for an early detection program aimed at high-risk patients.

The prevalence of conventional smoking in our study showed a statistically significant relationship between gender and smoking cigarettes. Males were found to be the majority (90%) compared to females This finding highlights the need for targeted smoking cessation programs, especially for males. It has been previously published that 42% of the Jordanian population are smokers (different types of tobacco) with 66.1% of males and 17.4% of females smoking in 2019, which is known to be a strong risk factor of OSCC (20). Overall conventional cigarette smoking prevalence among Jordanians for the age group from 18 years to 69 years in 2019 was 33.4% for both genders (55.8% for males and 10.6% for females), while electronic cigarettes and other vaping devices comprised 9.6% for both sexes (15.9% for males and 2.6% for females) (21). In addition, it has been shown that males are more susceptible to head and neck cancers than females, regardless of whether they drink alcohol or smoke tobacco (22). It is highly recommended that longitudinal studies be carried out to monitor the effect of e-cigarettes, vape and other modalities of using tobacco on oral health and OSCC prevalence (23,24). Similarly, other countries have shown similar percentages of smoking among their OSCC patients, reaching 50% or more in Libya, Iraq, and Egypt (25). The WHO estimated that OSCC incidence will increase by 140.9% among males and by 150% among females in Jordan by 2045, which is dramatically higher than the worldwide estimation, which is 51.1% among males and 60.5% among females (23).

Although the prevalence rate of vaping and e-cigarettes is 9.4% of the population in Jordan (21), vaping was reported in only one case, where the patient used it for less than an hour a day for less than a year. Vaping and e-cigarettes are considered relatively new smoking modalities, thus they need more time to reliably observe their effects. Future studies could better explore the association of vaping with OSCC.

A significant relationship between smoking and occupation was identified. This indicates that occupation could be a relevant factor in smoking behavior. This effect was most pertinent with outdoor workers, as they made up 40% of the diagnosed OSCC cases. Smoking prevalence among this group was the highest, as 76.2% of outdoor workers were smokers. In addition, outdoor workers have a variety of other risk factors, such as chemicals and sun exposure, which may explain why lips are the most common affected site among this group. Lower-lip cancer accounted for 52.4% of the affected sites in outdoor workers. In other words, 64.4% of the lower-lip cancer cases were reported for outdoor workers, whether being smokers or non-smokers. Moreover, outdoor workers were often in the low-SES category, as 81% of the outdoor workers in our study were in the low-SES category. Although the sample size in the current study was limited, a significant association between occupation and alcohol consumption was identified. Alcohol consumers in our study (4 cases) were all outdoor workers as well. Preventive and educational programs about oral health awareness targeting this population group are necessary.

Office workers comprised 27.8% of the patients diagnosed with OSCC. Over a half (53.3%) of them were smokers. This may indicate that the office working environment may encourage smoking or may incorporate other hidden risk factors. Furthermore, 35.2% were ranked in the high-SES group, which implies that, although they are relatively educated and financially stable, they were affected with OSCC more than the unemployed who were in a lower-SES status (not statistically significant).

Unemployed OSCC patients accounted for the least frequent employment status (33.3%), and consisted of females with a percentage of 83.3%. The prevalence of smoking in this group was 33.3%, which was the lowest among all groups of employment. Since OSCC is multi-factorial, other risk factors could have contributed to the development of OSCC in these patients, such as variables related to low SES, as 100% of the unemployed patients were in the low-SES rank.

Another risk factor investigated was the family history of malignancy, where over a half of the cases reported having a family history of malignancy (51.9%), noting that 71.4% were first degree relatives and 28.6% were second degree relatives. This finding supports the genetics influence of cancer development. Positive family history of other malignancies has been previously linked to higher risk of developing oral cancer (24,26). A previous paper showed that having a family history of any type of cancer will increase the risk of developing oral cancer (27). Current results are in line with the published findings, where in the current study, 82.1% reported family malignancy but of non-head and neck

origin. A significant relationship between the type of cancer reported in the family and the histological grade of OSCC was identified, as all the cases reported having a family history of oral cancer that developed exclusively a well-differentiated OSCC. This can be attributed to early detection because of patients' experience and knowledge of the disease. It is worth mentioning that a significant association was found between patients with family history of oral malignancy and the age of diagnosis, as all were diagnosed in the age of 40-49 years. So, patients with family history of any cancer should be screened for oral cancer before the age of 40.

OSCC patients living in rural areas in our study showed to be least, which goes with the conclusion of a recent longitudinal study from the USA, that revealed that long-term survival rates for patients residing in rural locations were superior to those of their urban counterparts. Urban status remained a poor prognostic factor in patients with OSCC (28). National preventive programs and longitudinal studies are encouraged to consider this result.

Having graduate or post-graduate degrees did not lower the risk of getting oral cancer, where about 29.6% of the OSCC patients in our sample had graduate or post-graduate degrees. A pooled analysis from 24 case-control studies suggested that patients with at least a high-school degree are not at an increased risk for developing head and neck cancers (29), while another research found that patients with higher education were protective against all oral premalignant lesion outcomes (30), which does not apply to the patients in the current investigation. However, one third of these graduates/post-graduates were outdoor workers and 25% of them were unemployed. Multi-variate analysis of a larger sample is necessary to identify such correlations and conclude with a well-structured preventive program.

When considering residency, education and income, the socio-economic status revealed that 64.8% of the OSCC patients were in the low-SES category, which may increase the likelihood of being under more stressful conditions, consuming tobacco in different modalities, eating fewer vitamin-rich and anti-oxidant food such as fruits and vegetables, and having a lower Body Mass Index (BMI) (16). However, high SES did not immune patients from getting OSCC, as 35.2% of our sample were in the high-SES rank and about 42% of them were non-smokers. It can be inferred that other factors, such as genetic pre-disposition, high-risk viral infection, COVID-19 pandemic, or its vaccines could have possible roles in OSCC development.

Interesting relationship between oral hygiene and the grade of differentiation of OSCC illustrates that 100% of the patients with poorly differentiated OSCC reported not to brush their teeth at all, which may be an indicator of the role of microbiota in the oral cavity in the progression of the disease (31). Studies with larger sample sizes are encouraged.

A variation of age groups of patients with OSCC was noticed in the literature (32-34). The mean age in the current study was 63.5 years, which is higher than the mean age in a similar previous study in Jordan with 57.6 years (35) and in another study in a neighboring country with 46.93 years (33), though close to the worldwide mean age of 62 years (34). This may be due to the differences in the exposure to risk factors.

Male: female ratio identified in the present study was 1.75:1, which is comparable to a previous study in the early 2000s in Jordan, where the M:F ratio was 1.6:1 (32). OSCC prevalence in females in Jordan is noted to be higher than in the neighboring, eastern, and western countries, as Qatar (33), South Korea (3) and the USA (22) showed M:F ratios of 10.9:1, 4.4:1 and 2.52:1, respectively. This difference could be due to the difference in risk factors and the nature of the population, as Qatar for example has a high number of South Asian workers who use betel liquid. In south Korea, a significant difference in alcohol consumption among males and females makes males at more risk to develop oral cancers (36). Looking into OSCC-associated risk factors in females, smoking prevalence among females was low (15%), and most of them (75%) were unemployed. The apparent risk factor that was identified in female patients in this study was the low SES, as 80% of the females were in the low-SES category compared to 55.9%in males.

This implies that further studying the risk factors affecting females is recommended. National preventive programs may consider females to be targeted in oral health awareness programs. The effects of second-hand smoking as well as its drawbacks should also be investigated in our society and the targeted groups should be educated about these effects.

5. Conclusions

In conclusion, our pilot study revealed interesting

associations of OSCC with office working, first- and second-degree relative history of malignancy, urban residency, female gender associated factors, poor oral hygiene, educational level and socio-economic status. Targeting the high-risk groups can aid in the early detection of suspicious lesions, as early detection allows for treatment at a stage when the disease is more localized, which can significantly reduce morbidity and improve survival rates.

It is strongly advised to conduct a wide-scale, national study that considers all regions of the country in this regard and to include less commonly studied risk factors that may contribute to oral cancers. These factors include new modalities of tobacco use, like vape and e-cigarettes, the effect of COVID-19 pandemic and its vaccinations on the immunity system and the development of OSCC, as well as nutritional and biological hazards, such as irrigating plants with contaminated water or utilizing water used as a coolant for nuclear-power plants.

Conflict of Interests

The authors have no conflict of interests to declare related to this research.

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