

Original article

Epidemiological Patterns of Oral Squamous Cell Carcinoma and Its Variants in the Libyan Population: A 20-Year Retrospective Study

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ABSTRACT

Keywords:

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Histological Variants,
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Squamous cell carcinoma is the most common oral malignancy, accounting for more than 90% of all forms of oral cancer. This study aimed to determine the frequency and distribution of oral squamous cell carcinoma in the Libyan population, considering histological variants and grades. A retrospective analysis of all cases biopsied and diagnosed from 2000 to 2019 in the Department of Oral Medicine, Oral Pathology, Diagnosis, and Radiology was conducted. Information on the patient's age and gender, tumour type, grade, and its anatomical site was recorded and analyzed. During the study period, 105 biopsies were histologically confirmed as oral squamous cell carcinoma. Males were more commonly affected than females, giving a male-to-female ratio of 1.67:1. Most patients were older than 50, with a mean age of 57.63 ± 14.569 years. The Lateral border of the tongue was the most common site for the lesion (39%), followed by the buccal mucosa (19%). The most common histological subtype was conventional oral squamous cell carcinoma (90%), primarily well and moderately differentiated. The other histological variants were uncommon (N=8): 4 cases of verrucous carcinoma, 2 of adenosquamous carcinoma, and 2 of spindle cell carcinoma. In conclusion, oral squamous cell carcinoma constituted a considerable proportion of oral and maxillofacial lesions, with the conventional type being the most common. A higher proportion has been noted in males aged 50 years and older, with the lateral border of the tongue being the most affected site.

Introduction

Worldwide, head and neck cancer is considered one of the most common forms of cancer, with a significant geographical and epidemiological variation; in underdeveloped countries, like India, it is the most commonly diagnosed cancer in male patients, whereas in the Western world, it accounts for about 1–4% of all cancers [1]. Even within the same geographical region, the incidence may vary considerably among demographic groups defined by age, gender, or race [2].

Oral squamous cell carcinoma (OSCC) is the most common malignant neoplasm of the oral cavity, accounting for more than 90% of all forms of oral cancer. Despite the advances in diagnosis and treatment of OSCC, the overall 5-year survival remains no more than 60% due to tumour metastasis and a high rate of recurrence [3].

A variety of risk factors have been implicated in the pathogenesis of OSCC, primarily tobacco use and alcohol consumption, with a well-documented synergistic effect [4]. Furthermore, alcohol consumption has been approved as an independent risk factor for the development of oral cancer in a dose-dependent manner [5]. Additionally, the role of human papillomavirus (HPV) in the pathogenesis of OSCC has recently received special attention, particularly HPV-16, which has been recognized as an etiological agent for the development of OSCC, especially in the oropharynx of young patients [6].

Conventional oral squamous cell carcinoma (OSCC) has been graded into well, moderately, and poorly differentiated variants based on Broder's criteria for classifying conventional squamous cell carcinoma (SCC) [7]. Variants of OSCC are relatively rare; however, they do exist, including verrucous carcinoma, spindle cell carcinoma, acantholytic/adenoid SCC, adenosquamous carcinoma, basaloid SCC, and papillary SCC, each with distinctive histopathological features [8-10].

Epidemiological data have revealed variable trends in the prevalence of OSCC with respect to patients' age, gender, and anatomical site; however, most of the patients were of the relatively older age group, with a higher male predilection, and a propensity for the tumour to affect the tongue, buccal mucosa, and the floor of the mouth [2,8,9,11].

To achieve optimal patient treatment and improve overall survival and prognosis, the primary tumour should be accurately approached. This can only be accomplished by adequate knowledge of the clinical and histopathological features of OSCC and its different variants.

Worldwide, considerable research has investigated the incidence and prevalence of OSCC [2,9,10,12]. However, such studies are relatively scanty in Libya and other African countries, particularly those that consider the histological variances. So, the current study aims to determine the prevalence of OSCC in the Libyan population of Benghazi while considering tumour grading and histological variants, and to compare the results with those reported in other countries.

Materials and methods

Study design

A retrospective review of all cases operated and diagnosed at the Faculty of Dentistry, Benghazi University, which receives referrals from all regions of Libya, from 2000 to 2019. A total of 2036 patients with oral and maxillofacial lesions were reviewed through their medical records and biopsy files at the Department of Oral Medicine, Pathology, Diagnosis, and Radiology. A total of 171 cases were malignant oral lesions; of these, 105 were confirmed OSCCs, including the histological variants. Information regarding patients' age, gender, and the anatomical site of the lesion was recorded. The histological slides were re-evaluated to confirm the diagnosis according to the World Health Organization (WHO) 2022 classification [13]. Conventional OSCC was graded as well, moderately, or poorly differentiated based on Border's criteria [7]. All cases were analysed in relation to patient age, gender, and the anatomical site of the lesion.

Eligibility criteria

Inclusion criteria: Medical records of Libyan patients with a histologically confirmed diagnosis of OSCC and its variants of all ages and of both genders from the year 2000 to 2019.

Exclusion criteria: Metastasized tumours and those with a controversial diagnosis.

Ethical approval

The study was approved by the Ethics Committee of the Faculty of Dentistry of Benghazi University (approval number: 0397).

Statistical analysis

All descriptive and quantitative data analysis and graphs were performed using the Statistical Package for the Social Sciences (SPSS) software, version 21.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were used for the variables, including patients' age group and gender, lesion type, grade, and anatomical site. Chi-square test was used to assess statistical significance at the level of <0.05 .

Results

A total of 105 cases were confirmed as OSCC, accounting for 5% of all the biopsies during the study period and 61.4% of the malignant lesions. Males (63.8%) were more commonly affected than females (36.2%), yielding a male-to-female ratio of 1.67:1. Patients' age ranged from 18 to 93 years (mean age, 57.63 ± 14.569 years). Most of the patients were 50 years and older, with the highest percentage (28.6%) falling in the 60-69 age group (Table 1).

Table 1. Distribution of patients' age groups according to gender

Age group	Gender		Total
	male	female	
<50	16	9	25
50-59	16	7	23
60-69	16	14	30
> or =70	19	8	27
Total	67	38	105

Site-based analysis revealed that the lateral border of the tongue was the most preferred site for lesions in both genders, accounting for 35.8% in males (N=24) and 44.7% in females (N=17), followed by the buccal mucosa (16.4% in males) and (23.7% in females). The other less commonly affected sites were the mandible (13.3%), maxilla (7.6%), and the lower lip (6.7%). Statistically, there has been no association between patient gender and the anatomical site of the lesion (p-value $>.05$) (Table 2).

Table 2. Distribution of the anatomical site of the lesion according to patients' gender

Site of lesion		gender		Total
		male	female	
Lateral of tongue	Count	24	17	41
	% within gender	35.8%	44.7%	39.0%
Buccal mucosa	Count	11	9	20
	% within gender	16.4%	23.7%	19.0%
Floor of mouth	Count	1	1	2
	% within gender	1.5%	2.6%	1.9%
Gingiva	Count	1	2	3
	% within gender	1.5%	5.3%	2.9%
Ventral of tongue	Count	1	0	1
	% within gender	1.5%	0.0%	1.0%
Lower lip	Count	6	1	7
	% within gender	9.0%	2.6%	6.7%
Mandible	Count	10	4	14
	% within gender	14.9%	10.5%	13.3%
Maxilla	Count	6	2	8
	% within gender	9.0%	5.3%	7.6%
Palate	Count	2	1	3
	% within gender	3.0%	2.6%	2.9%
Upper lip	Count	1	0	1
	% within gender	1.5%	0.0%	1.0%
Submandibular	Count	2	0	2
	% within gender	3.0%	0.0%	1.9%
Missing site	Count	2	1	3
	% within gender	3.0%	2.6%	2.9%
Total	Count	67	38	105
	% within gender	100.0%	100.0%	100.0%

Pearson Chi-Square=7.050, df=10, p-value=0.721

Regarding the histological subtypes of OSCC, more than 90% of the sample was represented by the conventional OSCC, primarily well differentiated (42.9%) and moderately differentiated (41%). The remaining sample comprised 8 histological variants of OSCC, including verrucous carcinoma, constituting 3.8% of the sample, followed by adenosquamous carcinoma and spindle cell carcinoma, each of which constituted 1.9% of the total sample (Tables 3 and 4).

Table 3. Grades of OSCC

Grade		n	%
Valid	Well differentiated	45	42.9
	Moderately differentiated	43	41.0
	Poorly differentiated	9	8.6
	Total	97	92.4
Missing	System	8	7.6
Total		105	100.0

Table 4. Histological subtypes of OSCC

Type	n	%
Conventional SCC	97	92.4
Verrucous carcinoma	4	3.8
Adenosquamous carcinoma	2	1.9
Spindle cell carcinoma	2	1.9
Total	105	100.0

Discussion

Globally, OSCC is a common malignant tumour that can affect the oral cavity and oropharynx with a significant rate of morbidity due to tissue destruction, local and distant metastasis, and the tendency for recurrence [3]. Many factors were proven to be involved in the pathogenesis of OSCC, primarily tobacco and alcohol consumption, with a well-documented synergistic effect [5,14-16]. OSCC can develop as a conventional SCC, which is the predominant histological type, or exist as histological variants, each with a unique histological appearance, including verrucous carcinoma, which is a low-grade variant, spindle cell carcinoma, and adenosquamous carcinoma, both of which are considered of high-grade potential [9]. Therefore, a precise histopathological diagnosis is essential for accurate patient management, as the prognosis of each of these variants is considerably variable.

In this study, 2036 patients with oral and maxillofacial lesions were reviewed for the prevalence of OSCC using their medical records and biopsy files. Out of these, 105 cases were histologically verified OSCCs, including their variants, forming about 5% all lesions and about 61% of malignant lesions in this sample. This finding is relatively higher than that reported in Nigeria (41%) [16], but much less than that found in Jordan (84%) [17]. Egypt, on the other hand, has shown a markedly higher percentage (90%) [18], despite its geographical proximity to Libya. A possible explanation for this discrepancy is the less frequently encountered risk factors, like tobacco and alcohol consumption, particularly in women. In addition, alcohol consumption is legally prohibited in Libya, making it a less likely encountered risk factor [19].

Worldwide, significant geographical variations have been noted with respect to patients' age and gender, social habits, and the anatomical site of the lesion [2,12,17,18]. The results of the current study revealed a higher proportion of OSCC in males, giving a male-to-female ratio of 1.67:1. This finding is almost identical to that reported in Nigeria (1.6:1) [16] and comparable to those found in Iraq [20] and Mexico [12]. A possible explanation for this trend may be the greater tendency among men to be exposed to risk factors, such as tobacco and alcohol consumption, particularly in Arab countries, where these habits are less likely to be practised by women [19].

The majority of patients in this study were 50 years or older, with a mean age of 57.63 ± 14.569 years, and with the largest proportion (28.6%) being in their 7th decade of life. This observation is consistent with the results of previous studies, which concluded that the incidence of OSCC increases with age, particularly in patients older than 50 years [12,21-23]. However, in recent years, this trend has shown a marked change with a higher incidence of oral cancer in younger individuals, despite the absence of the associated risk factors. In fact, recent epidemiological studies have linked this trend to human papillomavirus (HPV) [22], which has been a focus of considerable research, particularly regarding its role in the pathogenesis of oropharyngeal carcinoma. In 2017, Sharma and Singh demonstrated another plausible explanation addressed by the significant shift in lifestyle habits in recent years, including early exposure to smoking [23]. In the current study, the youngest age group constituted only 24% of the total sample, so our results continue to demonstrate predominance among older patients.

OSCC can develop at any anatomical site of the oral mucosa, and large tumours can invade several adjacent areas. In this study, the lateral border of the tongue was the most affected site (39%), which agrees with those reported in Egypt [18], Brazil [24], and Mexico [11], followed by the buccal mucosa (19%) and the mandible (13.3%). However, evidence from India consistently indicates that the buccal mucosa is more commonly affected, owing to the widely practised use of smokeless tobacco in this country [25,26].

SCC is grossly classified into three histologic grades based on Border's criteria, including well, moderately, or poorly differentiated SCC, based on the degree of differentiation [7]. Our study revealed a higher proportion of well and moderately differentiated SCC (42.9%) and (41%), respectively, which is in accordance with previous studies [17,24].

The majority of cases in this study were conventional SCC (92.4%), which is in agreement with the literature [10,27]. There have been eight histologically confirmed OSCC variants, including verrucous carcinoma, adenosquamous carcinoma, and spindle cell carcinoma.

Verrucous carcinoma is a well-differentiated low-grade variant of SCC affecting older individuals, and is said not to metastasize. This variant carries an excellent prognosis with more than 70% five years survival; however, aggressive behaviours have been observed in some long-standing lesions [9]. In this study, we

identified 4 cases of verrucous carcinoma in men, affecting the mandible and buccal mucosa, all of whom were over 50 years old. These findings align with those of previous studies [10,28]. The other four variants comprise two adenosquamous carcinomas and two spindle cell carcinomas. Adenosquamous carcinoma is an aggressive, high-grade variant of SCC that exhibits both squamous and glandular differentiation and has a poor prognosis due to regional and distant metastasis [29]. This lesion is typically reported in older individuals, most commonly in their sixth and seventh decades of life [29]. In this study, however, the two lesions were found in two young male patients aged 18 and 32, highlighting a rare deviation from the typical age distribution.

The other histological variant found in this study was spindle cell carcinoma (sarcomatoid carcinoma), a rare variant of poorly differentiated SCC composed of spindle-shaped epithelial cells, hence the name (sarcomatoid). Importantly, this variant of OSCC is easily confused with a true sarcoma, so immunohistochemistry and ultrastructural studies are essential to confirm the diagnosis [30]. This study identified two cases of spindle cell carcinoma affecting the lateral border of the tongue in two patients aged 60 and 63. This finding is consistent with a previous report from India describing the occurrence of this lesion in older patients [31].

Conclusion

Conventional OSCCs constituted the largest proportion of the study sample (90%), with the majority being well to moderately differentiated. Males were more commonly affected than females, yielding a male-to-female ratio of 1.67:1, and most patients were aged 50 and older (mean age, 57.63 ± 14.569 years). The Lateral border of the tongue was the predominant site for the lesion (40.2%), followed by the buccal mucosa (19.6%). Eight histological variants of OSCC have been identified in this study: verrucous carcinoma (N=4), spindle cell carcinoma (N=2), and adenosquamous carcinoma (N=2). This study would provide valuable information regarding the prevalence of OSCC in the Libyan population while focusing on the different histological variants and their distribution; however, data regarding tumour clinical staging and patients' overall prognosis are still required. Therefore, future work is encouraged to include these important variables to better define OSCC and its variants in the Libyan population.

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Conflicts of interest:

Nil

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