

Epidemiological and clinical correlates of oral squamous cell carcinoma in patients from north-west Pakistan

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Abstract

Objective: To investigate the association of oral squamous cell carcinoma with demographic variables and oral health indicators.

Methods: The observational case-control study was conducted at the Institute of Radiotherapy and Nuclear Medicine, Peshawar, Pakistan, from November, 2015, to August, 2016. Pathologically confirmed patients with oral cancer represented the cases, while the controls were ethnically and linguistically-matched subjects without any oral pathology. Demographical, clinical and pathological data was taken down to assess variables, risk factors, and oral health indicators. Descriptive statistics and logistic regression modelling were employed for data analysis.

Results: Of the 551 subjects, 341 (62%) were males, and 210 (38%) were females. Of the total, 276 (50.1%) were cases and 275 (49.9%) were controls. The mean age of the cases was 55.0 ± 13.4 years and that of the controls was 52.8 ± 14.9 years ($p=0.073$). Poor oral hygiene, periodontal diseases, material of toothbrush, and no use of mouthwash were significant predictors of oral cancer ($p<0.05$ each). Smoking and using smokeless tobacco were also significant variables.

Conclusion: Oral health indicators in combination with smoking conferred an increased risk of oral cancer.

Keywords: Oral cancer, Oral squamous cell carcinoma, Oral hygiene, Smoking, Smokeless tobacco, Epidemiology, Case-control, Pakistan. (JPMA 69: 1074; 2019)

Introduction

Oral squamous cell carcinoma (OSCC), generally known as oral cancer, is presented with tumours in the oral cavity, pharynx and larynx. OSCC, when not managed properly, may lead to severe morbidity and mortality and it has been estimated that the overall five-year survival rate is below 50%.¹ Oral cancers account for approximately 6% of the cancer incidence worldwide, with 650,000 new cases and 350,000 deaths per year.^{2,3} The regions with the highest incidence of oral cancer are southeast Asia and some countries in southern and central Europe.^{4,5}

The risk of developing oral cancers is associated with several factors, including ethnicity, geographical location, lifestyle, exposures, and genetic background. Some of the common aetiological factors are tobacco, smokeless tobacco (naswar), poor oral hygiene, alcohol, and human papilloma virus.^{6,7} In Pakistan, smokeless tobacco is commonly used in forms of naswar, betel leaf (paan), and areca nut (gutka).⁴ A study in Lahore demonstrated that lip and oral cavity cancers were the

second most prevalent types, and the commonest addictions were smoking, alcohol, naswar and paan consumption.⁸

Poor oral hygiene is one of the several factors that have an additive adverse outcome on oral cancer together with tobacco and alcohol.⁹ Poor oral hygiene causes the development of chronic inflammation such as periodontitis which may lead to oncogenesis and OSCC.¹⁰ Common indicators of oral hygiene include tooth brushing, use of mouthwash and dental floss, wearing of denture, missing teeth, and gum bleeding.⁷ Studies highlighting the association of oral hygiene with OSCC among Pakistani subjects are scarce. The current study was planned to assess the potential role of oral hygiene as a contributing factor to oral cancer in the background of smoking and use of naswar in Pakistani subjects.

Subjects and Methods

The observational case-control study was conducted at the Institute of Radiotherapy and Nuclear Medicine, Peshawar, Pakistan, from November, 2015, to August, 2016. The 'cases' were pathologically confirmed and currently registered patients suffering from oral carcinoma. Patients with tumours of other organ-systems were excluded.

An age, ethnically and linguistically-matched 'control'

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comprised the general visitors to the hospital outpatients department (OPD) without any oral pathology. Subjects who were alcohol users or in the habit of paan-chewing were excluded.

Both the cases and the controls belonged to Peshawar or its suburban areas. Approval was obtained from the ethics committees of Hazara University, Mansehra, and Quaid-i-Azam University, Islamabad. Prior to data collection, informed consent was taken from every participant.

Data was collected regarding demographic variables, oral health condition and risk factors through a standard questionnaire. To assess the overall oral hygiene, visual inspection of each subject was performed by specialist doctors. Questions were asked on oral health, including the frequency of tooth brushing, material used for cleaning teeth (miswak and/or dandasa; chewing sticks and walnut-tree peel product), use of dental floss and mouthwash, gum bleeding, number of missing teeth, and use of dentures. A detailed history of smoking and naswar consumption was taken.

Clinical data was analysed against demographic variables and significance of difference was detected through Chi-test statistics ($p < 0.05$). For the evaluation of risk factors, odds ratios (OR) and 95% confidence interval (CI) were

calculated. Multivariate analyses were carried out through logistic regression and all independent variables (coded as dichotomous) were assessed against the disease status. Oral health indicators were assessed in a two-step approach. The initial analyses through contingency test statistics demonstrated that the differences in the distribution of cases and controls regarding various variables. In order to evaluate the combined effect of independent variables, a stepwise logistic regression model was adopted.

Results

Of the 551 subjects, 341(62%) were males, and 210(38%) were females. Of the total, 276(50.1%) were cases and 275(49.9%) were controls. The mean age of the cases was 55.0 ± 13.4 years and that of the controls was 52.8 ± 14.9 years ($p = 0.073$). Overall, 496(90%) subjects had Pashto ethnicity, 468(85%) belonged to poor socioeconomic background, 375(68%) had rural origin and 297(54%) were illiterate. There were no statistically significant differences between the two groups with respect to demographic attributes ($p > 0.05$).

Among the cases, cancer of oral cavity was the most common presentation, followed by involvement of larynx, hypopharynx, oropharynx and pharynx (Table-1).

Table-1: Clinical and pathological features of male and female patients.

Features	Male (n=177)		Female (n=99)		Total		P value
	n	%	n	%	n	%	
Tumour location							
Oral cavity	115	65	55	56	170	61	0.021
Larynx	27	15	8	8	35	13	
Hypopharynx	14	8	18	18	32	12	
Oropharynx	16	9	12	12	28	10	
Pharynx	5	3	6	6	11	4	
Total	177	100	99	100	276	100	
Stage of cancer (n=165)							
Well differentiated (diff.)	46	41	23	43	69	42	0.030
Moderately diff.	62	56	24	44	86	52	
Low grade diff.	0	0	3	6	3	2	
Poorly diff.	3	3	4	7	7	4	
Undergone oral surgery							
No	93	53	45	45	138	50	0.259
Yes	84	47	54	55	138	50	
Family history of cancer							
No	165	93	87	88	252	91	0.131
Yes	12	7	12	12	24	9	
Method of cancer ascertainment							
Biopsy	127	72	79	80	206	75	0.215
Incisional biopsy	24	14	8	8	32	12	
Excision biopsy	13	7	3	3	16	6	
Others	13	7	9	9	22	8	

Table-2: Oral health indicators in cases and controls*.

Characteristics	Cases (n=276)		Controls (n=275)		OR	CI (95%)	P value
	n	%	n	%			
Oral hygiene							
Good	1	0	85	31	Reference		
Fair	34	12	112	41	25.80	3.46-192.4	<0.0001
Poor	241	88	78	28	262.6	35.96-1918	<0.0001
Toothbrush (time/day)							
>2	5	2	26	9	Reference		
1	34	12	101	37	1.75	0.62-4.92	0.284
<1	57	21	61	22	4.86	1.75-13.52	0.001
Never	180	65	87	32	10.76	3.99-28.98	<0.0001
Material used to clean teeth							
Tooth brush	96	35	188	69	Reference		
Miswak and/ordandasa	134	49	81	29	3.24	2.24-4.69	<0.0001
None	46	17	6	2	15.01	6.19-36.41	<0.0001
Use of mouthwash							
Yes	5	2	32	12	Reference		
No	271	98	243	88	7.14	2.74-18.61	<0.0001
Periodontal diseases							
No	97	35	219	80	Reference		
Yes	179	65	56	20	7.22	4.92-10.59	0.0001
Missing teeth							
None	58	21	158	58	Reference		
1-10	158	57	112	41	3.84	2.61-5.66	<0.0001
>10	60	22	5	1	32.69	12.5-85.5	<0.0001
Use of denture							
No	240	87	264	96	Reference		
Yes	36	13	11	4	3.60	1.79-7.23	0.0001

*only significant variables are mentioned; 'gum bleeding' and 'use of dental floss' were not significant. OR: Odds ratio; CI: Confidence Interval.

Table-3: Smoking and naswar use among cases and controls.

Variable	Cases (n=276)		Control (n=275)		OR	CI (95%)	P value
	n	%	n	%			
Smoking							
No	207	75	243	88	Reference		
Yes	69	25	32	12	2.53	1.60-4.00	<0.0001
Smoking frequency							
Less frequent	10	68	8	56	Reference		
1-3 times/day	12	17	6	19	1.60	0.41-6.18	0.494
>3 time/day	47	14	18	25	2.09	0.72-6.13	0.175
Smoking since... (years)							
1-5	16	23	15	47	Reference		
6-10	20	29	11	34	1.71	0.62-4.72	0.303
>10	33	48	6	19	5.16	1.68-15.80	0.003
Naswar use							
No	164	59	226	82	Reference		
Yes	112	41	49	18	3.15	2.13-4.66	<0.0001
Naswar use frequency							
Less frequent	2	2	0	0	Reference		
1-3 times/day	21	19	10	20	0.41	0.02-9.33	0.336
>3 time/day	89	79	39	80	0.45	0.02-9.67	.0351
Using naswar since... (years)							
1-5	8	7	11	22	Reference		
6-10	16	14	13	27	1.69	0.53-5.45	0.376
>10	88	78	25	51	4.84	1.76-3.34	0.001

OR: Odds ratio; CI: Confidence Interval.

Table-4: Significant predictors of oral cancer as depicted by logistic regression.

Variables	OR*	P-Value	95% CI	OR	P-Value	95% CI	OR	P-Value	95% CI
	With smoking and naswar use			Without smoking and naswar use			Oral hygiene (poor) omitted		
Oral hygiene (poor)	9.45	<0.0001	5.95-15.01	8.85	<0.0001	5.55-14.09	-	-	-
Toothbrush (no)	-	-	-	1.66	0.035	1.03-2.68	2.01	0.001	1.36-3.25
Material used (none)	5.01	<0.0001	2.20-11.37	3.66	0.003	1.57-8.49	5.08	<0.0001	2.27-11.62
Mouthwash (no)	4.76	0.010	1.46-15.48	4.98	0.008	1.51-16.45	6.59	0.001	2.25-19.28
Periodontal diseases	5.04	<0.0001	3.18-8.01	4.80	<0.0001	3.02-7.61	4.05	<0.0001	2.51-6.55
Missing teeth	-	-	-	-	-	-	2.56	<0.0001	1.57-4.18
Smoking	2.27	0.008	1.24-4.16	-	-	-	2.11	0.009	1.20-3.70
Naswar use	-	-	-	-	-	-	1.74	0.024	1.07-2.82
Cons	0.02	<0.0001	0.01-0.08	0.02	<0.0001	0.01-0.08	0.02	<0.0001	0.01-0.07

*OR did not change significantly when analyses were adjusted for age or gender.

OR: Odds ratio; CI: Confidence Interval.

A significantly higher number of patients had poor oral hygiene compared to the controls ($p<0.0001$). Majority of the patients never used toothbrush compared to the controls most of whom used toothbrush once-a-day ($p<0.0001$). Regarding the material used for cleaning teeth, majority of the patients used miswak and/or dandasa for cleaning teeth, compared to the controls who used toothbrush most often ($p<0.0001$). Very few of the cases used mouthwash compared to the controls ($p=0.003$). The occurrence of periodontal diseases, number of missing teeth, and use of denture were significantly higher among the patients compared to the controls ($p=0.0001$) (Table-2).

Smoking was more prevalent among the patients compared to the controls ($p<0.0001$). A significantly higher number of patients used naswar ($p<0.0001$) and for more extended period compared to the controls (Table-3).

There were five variables identified as significant predictors of oral cancer: poor oral hygiene, material used for brushing teeth, no use of mouthwash, presence of periodontal diseases, and smoking (Table-4).

Discussion

Oral cancer may arise as a small lesion which initially remains unremarkable. Later, it becomes conspicuous when it changes into a white or red spot or sore in the mouth. It may involve the oral cavity, including lips, gums, buccal mucosa, tongue, pharynx or larynx.³ Oral lesion or malignancy cautions immediate medical intervention. Delay in treatment for oral cancer is associated with significant morbidity and mortality.²⁻⁴

The risk of developing oral cancer increases with increasing age likely due to extended period of exposure to risk factors.^{6,11} Further, the likelihood of acquiring

mutagenic changes and epigenetic modifications also increases with age. Different studies have highlighted the preponderance of male patients in the OSCC cohorts.^{12,13} This trend has been explained in terms of increased risk of occupational, outdoor and environmental exposures, high rate of smoking and naswar use, and consumption of certain other snuff types.^{6,7}

The site of involvement of oral cancer varies in different populations and geographical areas. It may be associated with various factors, including ethnicity, age of ascertainment, the nature of exposure, and genetic background.⁷ For instance, the involvement of tongue and floor of the mouth has been witnessed in 50% cases reported in patients recruited from the Western societies, while palate, gums and buccal/labial mucosa were the least involved.¹² In the present study, OSCC was mostly presented as tumour of oral cavity (61%), followed by tumours of larynx, hypopharynx and oropharynx. Another study carried out in Pakistan showed that tumour of buccal mucosa was the most frequent (32%), followed by tumour of the tongue (22%).¹⁴ In the oral cancer, patients recruited from southern Punjab, tumour of the tongue was highly represented (50%).¹³ Nonetheless, majority of our cases presented with moderately differentiated (52%) or well-differentiated (42%) OSCCs. The patients with from southern Punjab were recruited from a tertiary care hospital.¹³ In contrast to our findings, the majority of patients in that study¹³ presented with well-differentiated oral cancers (43%), followed by moderately differentiated (38%) and poorly differentiated (20%) cases.

Good oral health is vital for achieving an overall healthy life. People are likely to suffer from a number of oral problems like oral infections, periodontal diseases, gingivitis, and loss of tooth, should there be no oral health programmes for public awareness. While analysing data

from the National Health Survey of Pakistan, a study observed that only 36% Pakistanis cleaned their teeth daily, while 8% never cleaned their teeth.¹⁵ Congruently, this study also revealed that the majority of patients scored low in the variables related to oral hygiene. For instance, a significantly high number (88%) of our patients had an overall poor hygiene. Poverty, illiteracy and poor orientation about oral health are some of the characteristics of the north-western population of Pakistan inhabiting the Khyber Pakhtunkhwa (KP) province.

Nonetheless, due to low socioeconomic conditions, the use of miswak/dandasa is a common alternative method to clean teeth in this part of Pakistan; an estimated 39% participants of this study used miswak/dandasa. A few studies have argued that miswak/dandasa do not effectively clean the teeth; thereby letting carcinogens to stay longer.¹⁶ Other researchers, however, argue that the issue is not with the use of miswak/dandasa but, in fact, the users do not clean the lingual areas and the posterior of the teeth and apply it for a short duration of time.⁹ The efficacy of miswak on the suppression of oral pathogens has been reviewed by at study.¹⁷

The current study is the first detailed attempt in Pakistani population demonstrating a range of predictors of oral cancer in a case-control setting. Risk factors like smoking and use of naswar appeared significant in univariate analyses. Curiously, however, only smoking emerged as a significant variable for oral cancer and use of naswar was not significant. Analyses were repeated while keeping smoking and use of naswar in the model and iterating the other independent variables. It was observed that use of naswar (along with smoking) appeared significant only in the absence of variable 'oral hygiene' which could be due to negative confounder effect.

Conclusion

Poor oral hygiene was the most significant risk predictor of oral cancer. The oral health indicators in combination with smoking pose a higher risk of oral cancer.

Disclaimer: The study is part of PhD research work of one of the authors.

Conflict of Interest: None.

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