

Locoregional Recurrence of Oral Squamous Cell Carcinoma-A Retrospective Analysis

Oral
Squamous
Cell
Carcinoma

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ABSTRACT

Objective: This study was undertaken to evaluate the loco regional recurrence cases of OSCC in the twin cities of Pakistan during the period of 2015 to 2018.

Study Design: A retrospective, descriptive, cohort study

Place and Duration of Study: This study was conducted at the Islamic International Dental College, Islamabad from August 2019 to July 2020.

Materials and Methods: A sample size of 40 patients with OSCC was calculated. Data was collected from the clinical and histopathological reports of the OSCC patients. Demographic data regarding age, gender along with clinic-pathological variables such as tumor stage, primary tumor site, treatment type, recurrence site, histological grade, tumor resection margins, and lymph node involvement were investigated to deduce the significance of these variables in recurrence.

Results: The mean age of the patients was 55.25 and the sample predominantly had females (62.5%). Most common tumor site was found to be the lower alveolar ridge. Out of 40 patients, 8 showed recurrences (20%) with majority on the primary tumor site. Owing to the small sample size, the variables although having a potential of inference did not come out to be statistically significant.

Conclusion: Although a high recurrence rate of 20% was seen; however none of the studied variables showed any statistically significant co-relation.

Key Words: OSCC, clinicopathological variables, loco regional, recurrence rate

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INTRODUCTION

Oral squamous cell carcinoma is the most common subtype of head and neck cancer. Accounting for nearly 3% of all cancers worldwide with 263,000 newly diagnosed cases and 128,000 registered deaths per year. According to Collective Cancer Registry of the Shaukat Khanum Memorial Cancer Hospital & Research Center, Pakistan, Oral and lip cancers are reported to be the 3rd most common cancer registered among adults in both sexes from a data of 24 years i.e. Dec 1994 to Dec 2018. Whereas amongst adults (> 18 years), it landed being the 2nd commonest malignancy.

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Most oral squamous cell carcinomas are located on the tongue, the floor of mouth and the gingiva in almost equal proportions. Like most cancers of the upper aero digestive tract, it is strongly associated with tobacco use and alcohol consumption. In Pakistan, Betel nut chewing, and tobacco were the commonly identified risk factors.

Of the known prognostic factors TNM stage, histological grade and depth of tumor invasion are well recognized. Therapeutic choices include surgery, chemotherapy, radiotherapy and brachytherapy with similar intent for recurrences as well.

Despite advances in surgery and radiotherapy, which remain the standard treatment options, the mortality rate has remained largely unchanged for decades, with a 5-year survival rate of around 50%.

The main reason of poor prognosis is the recurrence of OSCC due to aggressive local invasion and metastasis decreasing the survival rate from 90 to 30%. Recurrence most often is classified as local, regional, loco regional and distant. The risk of loco regional recurrence varies with some features of the primary tumor such as tumor stage, histological differentiation; patient characteristics such as age, alcohol use and smoking status; treatment factors such as positive resection margins.^{2,8} The different biological growth

patterns of malignancies mean that the identification of the clinic pathological risk factor is still of utmost importance for predicting recurrence.^{1,2} For the past many decades, the single most important prognostic indicator of survival for this disease is the regional spread to the ipsilateral and contra lateral neck nodes.

In regard to this, the objective of this study was to evaluate the incidence of loco regional recurrence and to identify significant risk factors for it through clinico-pathological data and follow-up data of patients with OSSC in the twin cities of Pakistan.

MATERIALS AND METHODS

A retrospective Cohort study was carried out at the Islamic International Dental College and hospital. The study involved all the patients with the diagnosis of a primary OSCC and if any subsequent recurrence.

The clinical and histopathological variables were studied to analyze the pattern of loco-regional recurrence of oral squamous cell carcinoma ranging from 2015 to 2018. The ethical approval was taken from the Research Ethical Board (REB) of Islamic International Dental College, Reference No.IIDC/IRC/2020/008/004. The sample size was calculated by WHO calculator as 40 and the technique applied was non-probability convenience sampling. Recurrence was defined as a tumor of similar histology appearing in the same anatomical site as primary malignancy with a minimum interval of more than six months after successful initial treatment.

Inclusion criteria were patients with treatment naive OSCC and primarily curative intended surgery, based on radical tumor resection with neck dissection. Un-resectable disease, lesions arising in less than 6 months, secondary primary tumors and inadequate information on clinicopathological characteristics served as exclusion.

Clinicopathological data were collected from medical records that include post-treatment notes and histopathological reports. The statistical analysis was performed by SPSS 23.0 for Windows. All variables in

the data with recurrence was run through Chi-square test to calculate p-value, while for all variables where there was at least 1 case less than 5, Fisher Exact was applied with an arbitrary value of 0.5.

RESULTS

Of the total population of 40 patients with OSCC 25 (62.5%) were female and 15 (37.5%) were male. Recurrences had similar pattern with 5 females and 3 males making a sum of 8 patients with collective recurrences i.e., 20% of the sample. The peak age of the patients was 51-60 years. The mean age calculated was 55.25 years. The primary tumor site included alveolar ridges, palate, buccal mucosa, lip and oropharynx with maximum number of cases associated with the lower alveolar ridge. 75% of recurrences were on the primary site and whereas only 25% were on sites other than the primary tumor site.

33 OSCC patients were treated with curative surgery alone out of which 6 showed recurrences with 3 (27.27%) out of 11 having positive resection margins. Tumor staging was done, and maximum numbers of recurrences were associated with primary tumors of stage 4. The most common histological grade among the patients was I, however most cases of recurrence were associated with grade II.

5 (35.71%) out of 14 patients with recurrent OSCC showed lymph node involvement while 17 patients with OSCC who had undergone supra-omohyoid neck dissection only 2 (11.76%) showed recurrence pattern. Of the 4 patients who were deceased only 1 had shown recurrence.

The statistical analysis was carried out, Fisher’s exact test was applied and none of the association was statistically significant except the site of recurrence which was the same as that of primary tumor in 6 out of 8 cases of recurrent OSCC with a p value of less than 0.000.

Further details regarding the characteristics of the cohort study are shown in Table 1.

Table No.1: Association between Clinic-Pathological Variables of OSCC and Recurrence

Clinico-Pathological Variables		Recurrence Status			P-Value
		Yes	No	Total	
Tumor stage	STAGE I	1	7	8	0.243
	STAGE II	0	8	8	
	STAGE III	1	5	6	
	STAGE IV	6	12	18	
Primary tumor site	UPPER ALVEOLAR RIDGE	0	12	18	0.728
	PALATE	1	1	2	
	BUCCAL MUCOSA	2	10	12	
	TONGUE	2	4	6	
	LIP	0	2	2	
Treatment type	SURGERY	6	27	33	0.147
	RADIOTHERAPY + SURGERY	0	2	2	

	CHEMOADJUVANT + SURGERY	2	0	2	
	CHEMO-NEOADJUVANT	1	1	2	
	CHEMOTHERAPY + RADIOTHERAPY + SURGERY	0	1	1	
Recurrence site	PRIMARY SITE	6	0	6	0.000
	OTHER THAN PRIMARY	2	0	2	
Histological grade	GRADE I	6	21	27	1.000
	GRADE II	2	10	12	
	GRADE III	0	1	1	
Positive resection margins	YES	3	8	11	0.660
	NO	5	24	29	
Lymph node involvement	YES	5	9	14	0.102
	NO	3	23	26	
Neck dissections	NO NECK DISSECTION	2	2	4	0.206
	SUPRAOMPHYOID	2	15	17	
	RADICAL NECK	4	15	19	

DISCUSSION

The recurrence of OSCC is a major contributing factor resulting in the increased mortality rate. Our study findings showed an increased frequency of OSCC in females (62.5%) as compared to males (37.5%). However, on the contrary a similar Pakistani study showed an increased prevalence in males' verses females. One retrospective study conducted over 20 years in Mexico on the trends in frequency and prevalence of OSCC showed a similar finding as that of present study with slight female predominance due to increase trend in smoking habits by women in the last decade. Likewise, increased trend of smoking, pan and gutka in our region might explain the increase in the incidence of OSCC in females. A study carried out in India to demonstrate the smoking trends verified an alarming growth in the prevalence of smoking among women in developing countries. However, patient habits have not been taken in account in our study.

With regard to age of the studied patient sample, mean age of 55 was observed, this is comparable to a similar study conducted in India. These findings were also consistent with 2-year study done in SKMCH&R (Lhr) and AFIP (Rwp), Pakistan, stating that most patients diagnosed with OSCC were above the age of 50 years.

Our study indicated that the Primary sites were the alveolar ridges, buccal mucosa, and lip, similar findings were reported by conducted at Patel Hospital lower alveolar ridge was the most common site of recurrence.¹² A significant proportion of reported literature on OSCC however shows that tongue was reported to be the most commonly affected primary site in the western countries as their tobacco exposure is more related to smoking rather than chewing¹⁷ followed by buccal mucosa in the subcontinent due to betel quid/tobacco chewing habits.**Error! Bookmark not defined.** In our study majority of the recurrences

were on the primary site and so was the case with other studies conducted in Germany and Pakistan that had primary site recurrences specifically on the tongue.¹⁸

It is widely believed that the most significant factor influencing the rate of survival is tumor stage although this alone is not sufficient to predict prognosis.¹⁹ Our study has the maximum number of cases reported with Stage 4 at diagnosis (45%). A plausible cause of this is the late diagnosis of OSCC which is consistent with the Cohort study carried out in Denver, Colorado where most patients had T3-T4 category tumor at diagnosis (42.3%)¹⁴. The relation of recurrence to tumor staging in our study was analyzed and most number of recurrences were also associated with Stage 4 (33.33%) which although explicable was still not statistically significant owing to the small sample size. A study at Agha Khan University Hospital, Karachi established that a significant higher recurrence was observed with higher tumor stages, the maximum being seen in stage 4.¹²

Histological grading when co-related with the frequency and patterns of recurrence showed a unique pattern with most number of cases showing recurrence to be of Grade 1 (well differentiated) followed by Grade 2 (16%) and no recurrences in Grade 3. This peculiar pattern owes to the fact that the sample included only one patient with Grade 3 while most patients were also lost to follow-up. Although grading is potentially subjective and the observer validation debatable, previous literature has suggested an eminent importance of grading of patients with OSCC.**Error! Bookmark not defined.** A retrospective study carried out in India to demonstrate the relation between histological differentiation and disease recurrence substantiated the higher recurrence and lower survival rate of poorly differentiated tumors in comparison to well and moderately differentiated tumors.²⁰

In our study, out of all patients who received surgery only 18% showed reoccurrence of the disease indicating that surgery remains a good prognosis factor for OSCC supporting most literature present on OSCC suggesting that surgery alone is the most well established mode of initial definitive treatment for the majority of OSCC.^{16,19} These findings could also be as a result of good prognosis of the disease itself. At the same time a more aggressive treatment regime is opted for patients with advanced disease stage.¹⁵ Patients who received a combination of both radiotherapy and surgery, none showed recurrence. Two retrospective studies on OSCC, one conducted in University of Maryland, USA and the other conducted in Karachi, Pakistan both concluded that radiotherapy in addition to surgery was successful in achieving good disease control.^{12,21} Poor outcomes despite multimodal treatment may suggest combination of a more advanced disease at initial presentation, limited salvage options or a resistant tumor biology.²²

Our study results are compatible with positive margins more likely to cause recurrence as compared to negative resection margins. 2.5-fold increase in risk of distant metastasis in presence of positive margins is reported, supporting prognostic importance in distant disease control.¹⁴ Pathologic positive margins has proven to be an adverse prognostic factor for OSCC patients Study in India concluded that high emphasis should be given on margin of tumor clearance as comparable with western population studies.²³ Surgical clear margins >5mm are recommended to prevent local recurrence and overall survival rate.^{16,19}

A significant association of lympho-vascular invasion is seen with increasing tumor size, histological grading, nodal involvement and overall prognosis and survival.¹⁵ Out of the 40 patients in our study, lymph node invasion was expressed in 14 patients. Out of those 14 patients, 55.5% of them had some form of recurrence after the primary tumor resection. Our data is in accordance with the previous data exhibiting increased prevalence of recurrence in patients with lymphatic involvement. According to a study lymph node involvement is found in more than 50% of the patients with OSCC.²³ Status of cervical metastasis is the single most important factor in survival of the patients with OSCC.²⁴

The treatment of OSCC is aimed at treating the primary tumor and regional neck metastasis, and neck dissection is an essential treatment element.¹⁴ A general trend among the surgeons was observed for preferring selective neck dissection rather than radical neck dissection as no significant contrast was seen in the prognosis of the disease, hence minimally invasive dissection was favored. SND has been accepted as the most successful staging and therapeutic procedure for OSCC clinically negative neck.²⁵

CONCLUSION

The recurrence rate of OSCC cases studied was 20%, however none of the factors included in this study were found to be statistically significant.

Author's Contribution:

Concept & Design of Study:	Nadia Zaib
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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