CORRELATION OF LEVELS OF LYMPH NODE, NODE INVOLVEMENT, GENDER PREDILECTION AND HISTOPATHOLOGY IN SURGICAL PATHOLOGY SPECIMEN OF ORAL SQUAMOUS CELL CARCINOMA

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Introduction:

Oral cancer is a common type of tumour seen in the head and neck region (38%) with an incidence of 75% in male patients above 60 years of age and almost 95% of the cases examined are of squamous cell carcinomas [1].Oral squamous cell carcinoma is an invasive lesion that frequently metastasises to the cervical lymph nodes [2]. Lymph node metastasis occurs in about 40% of patients with oral cancer [3]. Lymph node involvement is considered as the first indication for metastatic spread and is a strong prognostic factor [4].
Therefore the regional lymph nodes play an important role in the diagnosis, treatment and management of a disease. The development of new and highly sensitive detection methods such as immunohistochemistry and molecular analysis have been associated with an increase in the incidence of metastasis in the past few years thereby facilitating the prognosis of oral squamous cell carcinoma [1,5]. In this study, the surgical pathology specimen of regional lymph nodes in patients with squamous cell carcinoma are assessed on the grounds of gender, histopathology and the levels of lymph nodes involved and the relation between these aspects is analyzed.

Materials and methods:

This study was approved by the Scientific Review Board, Saveetha Dental College and Hospitals and was conducted over a period of 3 years in the same hospital. 19 cases of oral squamous cell carcinoma was obtained which involved metastasis to the regional lymph nodes. The inclusion criteria consisted of cases involving lymph node metastasis in oral squamous cell carcinoma. Exclusion criteria consisted of cases of oral squamous cell carcinoma in the early stages with no involvement of the regional lymph nodes. The data was collected and tabulated under the variables of gender, lymph node involvement, histopathology of the lesion and the levels of lymph nodes involved. Data analysis was done using the Chi square test or the Fischer's exact test.

Results:

This study was conducted to ascertain the correlation of histopathology, lymph node architecture and levels of lymph node involved which may serve as a prognostic factor.
19 cases of squamous cell carcinoma with lymph node involvement were seen over the period of last three years in the Department of Oral Pathology, Saveetha Dental College and Hospitals out of which 11 were males and 8 were females. Based on histopathological grading, it was seen that 18 cases out of the 19 cases showed the well differentiated variant of squamous cell carcinoma whereas only 1 case of the 19 cases showed moderately differentiated variant of squamous cell carcinoma.

Gender predilection and histopathological grading were assessed which showed that 100% of males showed well differentiated variant of oral squamous cell carcinoma and 87.5% and 12.5% of females showed the well differentiated variant of squamous cell carcinoma and moderately differentiated variant of squamous cell carcinoma respectively. The comparison between gender predeliction and histopathological grading was found to be not statistically significant as $p>0.05$(Table1)

The comparison between gender predilection and levels of lymph node involvement showed that 63% of the males showed level 1 lymph node involvement and 25% of females showed only level 1 involvement of lymph nodes and 25% of females showed only level 2 involvement of lymph nodes. This comparison was found to be not statistically significant as $p>0.05$. Level 1 involvement of lymph nodes was seen in 47.4% of cases and the involvement of level 2 lymph nodes was seen in 15.8% of cases. (Table2)

The comparison between histopathology and levels of lymph node involved showed that 50% of cases of well differentiated squamous cell carcinoma showed only level 1 involvement of lymph nodes and 11.1% of the cases of well differentiated squamous cell carcinoma showed only level 2 involvement. This comparison was also found to be not statistically significant as $p>0.05$. (Table3)

The comparison between lymph node involvement and gender showed that 45% of the males showed lymph node with malignant cells effacing the entire lymph node architecture and 18% of the males showed malignant cells effacing the entire lymph node architecture until the subcapsular region. Also 37% of females showed lymph node with malignant cells effacing the entire lymph

node architecture and 50% showed malignant cells effacing the lymph node upto the capsular and subcapsular region. This comparison was found to be statistically insignificant as p>0.05.(Table4)

The comparison between lymph node involvement and histopathology showed that 44% of the cases of well differentiated squamous cell carcinoma showed entire lymph node involvement whereas 22% of the cases of well differentiated squamous cell carcinoma showed malignant cells effacing the entire lymph node architecture infiltrating upto the subcapsular region. This comparison in this study was however found to be not statistically significant as p>0.05. (Table5)

The comparison between level of lymph node involved and extent of lymph node involvement showed that 62.5% of the cases that showed entire lymph node involvement belonged to the level 1 group of lymph nodes. 12.5% of the cases with malignant cells effacing the entire lymph node architecture showed involvement of level 2 group of lymph nodes and 12.5% of the cases showing entire lymph node involvement belonged to both level 1 and level 2 lymph nodes. This comparison was found to be not statistically significant as p>0.05. (Table6)

Histopathology	Gender					
	Male		Female		Total	
	N	%	N	%	N	%
Well differentiated	11	100.0	7	87.5	18	94.7
Moderately differentiated	0	.0	1	12.5	1	5.3
Total	11	100.0	8	100.0	19	100.0

Chi-Square Tests	Value	P-Value
Fisher's Exact Test	-	0.421

Table1: Comparison of histopathological differentiation with gender

Level of lymph node involvement	Gender					
	Male		Female		Total	
	N	%	N	%	N	%
Leve-I	7	63.6	2	25.0	9	47.4
Leve-II	1	9.1	2	25.0	3	15.8
Leve-III	1	9.1	0	.0	1	5.3
Leve-I, II	0	.0	1	12.5	1	5.3
Leve-II, III	1	9.1	0	.0	1	5.3
Leve-II, IV	0	.0	1	12.5	1	5.3
Leve-I, II, III	0	.0	1	12.5	1	5.3
Leve-I, II, V	0	.0	1	12.5	1	5.3
Leve-I, III, IV	1	9.1	0	.0	1	5.3
Total	11	100.0	8	100.0	19	100.0

Chi-Square Tests	Value	P-Value
Fisher's Exact Test	9.340	0.190

Table2: Comparison of gender with level of lymph nodes involved

Level of lymph node involvement	Histopathology					
	Well differentiated		Moderately differentiated		Total	
	N	%	N	%	N	%
Leve-I	9	50.0	0	.0	9	47.4
Leve-II	2	11.1	1	100.0	3	15.8
Leve-III	1	5.6	0	.0	1	5.3
Leve-V	0	.0	0	.0	0	.0
Leve-I, II	1	5.6	0	.0	1	5.3
Leve-II, III	1	5.6	0	.0	1	5.3
Leve-II, IV	1	5.6	0	.0	1	5.3
Leve-I, II, III	1	5.6	0	.0	1	5.3
Leve-I, II, V	1	5.6	0	.0	1	5.3
Leve-I, III, IV	1	5.6	0	.0	1	5.3
Total	18	100.0	1	100.0	19	100.0

Chi-Square Tests	Value	P-Value
Fisher's Exact Test	12.625	0.526

Table3: Comparison between histopathological differentiation with level of lymph node involvement

Lymph node involvement	Gender					
	Male		Female		Total	
	N	%	N	%	N	%
Entire	5	45.5	3	37.5	8	42.1
Subcapsular	1	9.1	1	12.5	2	10.5
Medullary	1	9.1	0	.0	1	5.3
Entire & Capsular	0	.0	2	25.0	2	10.5
Entire & Subcapsular	2	18.2	2	25.0	4	21.1
Subcapsular & Medullary	1	9.1	0	.0	1	5.3
Extracapsular	1	9.1	0	.0	1	5.3
Total	11	100.0	8	100.0	19	100.0

Chi-Square Tests	Value	P-Value
Fisher's Exact Test	4.980	0.421

Table4: Comparison between gender and the extent of lymph node invasion

Lymph node involvement	Histopathology					
	Well differentiated		Moderately differentiated		Total	
	N	%	N	%	N	%
Entire	8	44.4	0	.0	8	42.1
Capsular	0	.0	0	.0	0	.0
Subcapsular	2	11.1	0	.0	2	10.5
Medullary	1	5.6	0	.0	1	5.3
Entire & Capsular	1	5.6	1	100.0	2	10.5
Entire & Subcapsular	4	22.2	0	.0	4	21.1
Subcapsular & Medullary	1	5.6	0	.0	1	5.3
Extracapsular	1	5.6	0	.0	1	5.3
Total	18	100.0	1	100.0	19	100.0

Chi-Square Tests	Value	P-Value
Fisher's Exact Test	9.559	0.368

Table5: Comparison between the histopathological differentiation with level of lymph node involvement

Level of lymph node involvement	Lymph node involvement																	
	Entire		Capsular		Subcapsular		Medullary		Entire & Capsular		Entire & Subcapsular		Subcapsular & Medullary		All lymp node		Total	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Leve-I	5	62.5	0	.0	1	50.0	1	100.0	0	.0	2	50.0	0	.0	0	.0	9	47.4
Leve-II	1	12.5	0	.0	1	50.0	0	.0	1	50.0	0	.0	0	.0	0	.0	3	15.8
Leve-III	0	.0	0	.0	0	.0	0	.0	0	.0	0	.0	1	100.0	0	.0	1	5.3
Leve-V	0	.0	0	.0	0	.0	0	.0	0	.0	0	.0	0	.0	0	.0	0	.0
Leve-I, II	1	12.5	0	.0	0	.0	0	.0	0	.0	0	.0	0	.0	0	.0	1	5.3
Leve-II, III	0	.0	0	.0	0	.0	0	.0	0	.0	1	25.0	0	.0	0	.0	1	5.3
Leve-II, IV	0	.0	0	.0	0	.0	0	.0	0	.0	1	25.0	0	.0	0	.0	1	5.3
Leve-I, II, III	1	12.5	0	.0	0	.0	0	.0	0	.0	0	.0	0	.0	0	.0	1	5.3
Leve-I, II, V	0	.0	0	.0	0	.0	0	.0	1	50.0	0	.0	0	.0	0	.0	1	5.3
Leve-I, III, IV	0	.0	0	.0	0	.0	0	.0	0	.0	0	.0	0	.0	1	100.0	1	5.3
Total	8	100.0	0	.0	2	100.0	1	100.0	2	100.0	4	100.0	1	100.0	1	100.0	19	100.0

Chi-Square Tests	Value	P-Value
Fisher's Exact Test	65.862	0.270

Table6: Comparison between level of lymph node involvement and extent of lymph node invasion.

Discussion:

Cervical node metastasis exhibit variable incidence and is widely accepted as one of the major prognostic factors in oral squamous cell carcinoma patients [6]. The rate of metastasis in cervical lymph nodes has been reported to be 35.3-60% in oral squamous cell carcinoma patients and is known to be an indicator of poor prognosis in patients with oral cancer [7].

In this study, the relationship between the levels of lymph node, node involvement, gender predilection and histopathology in surgical pathology specimen of oral squamous cell carcinoma is assessed.

Metastasis to the lymph node is more commonly seen in males than females as is the incidence of squamous cell carcinoma as seen in the study by Alkaisi et al (2014) [8]. When gender was compared to histopathological grading it was observed that 100% of the male patients and 87.5% of females showed well differentiated squamous cell carcinoma and 12.5% of females showed moderately differentiated squamous cell carcinoma.

The comparison between gender predilection and levels of lymph node involvement showed that a majority of males showed level 1 lymph node involvement. 25% of females showed only level 1 involvement of lymph nodes and 25% of females showed only level 2 involvement of lymph nodes. 47.4% of the total number of cases showed level 1involvement and the involvement of level 2 lymph nodes was comparatively lesser i.e., 15.8%. This relationship between gender, histopathological grading and level of lymph node involvement is not statistically significant as only one female patient showed moderately differentiated variant of

squamous cell carcinoma and p>0.05.

When histopathological grading was compared to the level of lymph node involvement it was seen that 50% of cases of well differentiated squamous cell carcinoma showed only level 1 involvement of lymph nodes and 44% of the cases of well differentiated squamous cell carcinoma showed entire lymph node involvement whereas 11.1% of the cases of well differentiated squamous cell carcinoma showed only level 2 involvement 22% of the cases of well differentiated squamous cell carcinoma showed malignant cells effacing the entire lymph node architecture infiltrating upto the subcapsular region. There was only one case of moderately differentiated squamous cell carcinoma involving the level 2 lymph nodes with invasion of the entire lymph node architecture upto the subcapsular region. Hence, well differentiated squamous cell carcinoma is associated with better prognosis as it mostly involved level 1 lymph nodes with comparatively lesser involvement of the subcapsular and medullary involvement. Moderately differentiated squamous cell carcinoma is associated with a poor prognosis as it involved the level 2 lymph nodes with subcapsular invasion. Medullary involvement was seen in level 4 lymph nodes and hence indicating poor prognosis. This result is substantiated by the study conducted by Chandavarkar et al (2015) where highest percentage of invasion in the form of islands was seen in WDSCC (73.9%) followed by MDSCC (50%) and PDSCC (40%) [9]. Though this study substantiates the results of similar previous studies, it is not statistically significant as there was only 1 case of moderately differentiated squamous cell carcinoma and p>0.05.

When the extent of lymph node involvement, gender and level of lymph node involved was compared it was seen that 45% of the males showed lymph node involvement with malignant cells effacing the entire lymph node architecture and 62.5% of the cases that showed entire lymph node involvement belonged to the level 1 group of lymph nodes. 18% of the males showed lymph nodes with malignant cells effacing the entire lymph node architecture until the subcapsular region. 37% of females showed lymph node with malignant cells effacing the entire lymph node architecture and 25% and 25% of females showed malignant cells effacing the lymph node architecture upto the capsular and subcapsular region respectively.
12.5% of the cases with malignant cells effacing the entire lymph node architecture showed involvement of level 2 group of lymph nodes and 12.5% of the cases showing entire lymph node involvement belonged to both level 1 and level 2 lymph nodes. In level 1 and level 2 lymph nodes there was an equal prevalance of capsular and subcapsular involvement. Therefore, level 1 involvement of lymph nodes with invasion of the entire lymph node architecture has a better prognosis than involvement of level 1, level 2 or level 3 involvement with invasion of malignant cells upto the capsular or subcapsular region. This result is however not statistically significant as p>0.05.

We believe that the node related parameters should be assessed for every oral squamous cell carcinoma patient and according to the findings, the patients should be categorized into the relevant risk categories. Assessment of these parameters would help the pathologist to send the surgeon referred a more informative report for assessing patient prognosis and formulating a more comprehensive treatment protocol. Further studies with larger sample sizes have to be done on lymph node related pathologic parameters to assess their prognostic signifcance with greater certainty.

Conclusion:
This study is the first of it's kind involving the comparison of levels of lymph node, node involvement, gender predilection and histopathology in surgical pathology specimen of oral squamous cell carcinoma.
The results obtained in this study were not definitive and the values were not statistically significant as the total number of cases observed was less with p>0.05. Similar studies can be conducted on a larger scale with a larger sample size to reach a definitive conclusion and to substantiate the results obtained in this study.

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