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Clinicopathological Parameters and its Correlation with Recurrence, Distant Metastasis and Death Rate in Oral Cancer a Retrospective Study

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Original Research Article

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Abstract: The incidence of oral squamous cell carcinoma remains high in India due to the social and cultural habit of tobacco, it accounts for about 5%of total cancer of the body. Despite evolution in management,the overall survival of patients has not been improved significantly during the past 20 years. Several clinicopathological parameters have been implicated in the prognosis, recurrence and survival, following oral cancer. This retrospective study aims at the study of clinicopathological parameters including regional lymph nodes and distant metastasis and its correlation with recurrence and death rates in patients with oral squamous cell carcinoma. In this retrospective study data collected from the registry of cancer ward, Victoria hospital and Government dental college, Bangalore from 2007-2014(8 years) in total, 283 patients with oral squamous cell carcinoma were included. The clinical staging and histopathological reports were analysed and chest X ray, MRI was used to assess the distant metastasis and these findings were correlated with recurrence and death rates of the patients.Statistical analysis was carried out using chi square test. Among 283 patients 159 were males (56.2%) and 124 were females (43.8%). Most of the identified squamous cell carcinomas were T_4 (42%) and N2 (40.6%). Recurrence was identified in 40 patients, 85(30%) had regional nodal metastasis and 9 had distant metastasis, and 40 patients died out of 283.Squamous cell carcinoma of the oral cavity has a poor overall prognosis with a high tendency to recur at the primary site and extend to involve the cervical lymph nodes.

Keywords: Oral squamous cell carcinomas, regional lymph node, distant metastasis, recurrence, death rate.

INTRODUCTION

Oral cancer is a major global health problem being the sixth most common cancer worldwide which accounts for 45% of cancers in India [1]. Tobacco chewing along with smoking and alcohol are the main reasons for the increasing incidence rate of Oral Cancer. Squamous cell carcinoma of the oral cavity has a poor overall prognosis despite of advances in radiotherapy and chemotherapy, with a high tendency to recur at the primary site and extend to inolve the lymph nodes and/or distant metastasis.It has been suggested that a number of factors may influence the development of distant metastases, such as tumor size, primary site of the disease, histological differentiation, and locoregional spread of the tumor. Survival after a diagnosis of distant metastasis is almost poor in most of the oral cancer patients [2]. Thus in this retrospective study we intend to study the clinicopathological parameters including regional lymph nodes, distant metastasis and its correlation with recurrence, death and survival rates in patients with oral squamous cell carcinoma.

AIM AND OBJECTIVES

- To study the prevalence, clinical presentation, staging and histopoathological grading of oral cancer.
- To correlate the clinical presentation and histopathological grading with regional , distant metastasis, recurrence and survival rate in oral cancer

MATERIALS AND METHODS

This is a retrospective study conducted using the medical records which were retrieved from cancer ward ,Victoria hospital Bangalore and Government dental college Bangalore. An ethical clearance from the institution was taken prior to the conductance of the study.

The inclusion criteria for enrollement were

- Medical records of histologically proven, documented cases of oral squamous cell carcinoma above 18 years of age
- Patients who underwent treatment for oral cancer (surgical or radiotherapy and/or both).

The exclusion criteria for enrollement were

- History of HIV patients who are on antiviral therapy
- Patients with carcinoma of other systems.

Based on the above selection criteria,the records for a period of 8years(2007-2014) were analysed.283 medical records of patients with oral cancer were selected out of total 1185 available records.the medical reco information collected included demographic data, habits, symptoms, lab tests, imaging studies including chest radiograph and MRI, TNM stage, histopathological grading,recurrence, distant metastasis, treatment modalities, follow-up details, death and cause of death. The data thus collected were tabulated and statistically analysed.

RESULTS

Among 1185 cancer patients 283 were having oral cancer. Out of 283 patients 159 were males (56.2%) and 124 were females (43.8%). Their mean age of diagnosis of oral cancer was 54.47(SD-12.633 years, Min 25 years, Max 89 years). Primary sites were mainly buccal mucosa (32.9%), alveolus (20.8%), tongue (16.3%), base of tongue (9.2%), soft palate (8.8%), valleculla (5.7%),maxilla (4.6%), retromolar region (0.7%), floor of mouth (0.7%) and lip (0.1%).

Most of the identified squamous cell carcinomas were T_4 (42%) and N2 (40.6%) with 30% of nodal metastasis. Histopathologically 108 ($38_{\%}$) patients were diagnosed as well differentiated oral squamous cell carcinoma and 73(25.8%) patients had poorly differentiated carcinoma.

Recurrence was identified in 40 patients out of 283 in which males were 24(15.1%) and 16(12.9%) were females. most common site of recurrence was floor of mouth, with $T_2N_2M_0$ stage and 22 patients (p=0.000) had poorly differentiated carcinoma. among 40 patients 22 had nodal metastasis(p=0.000) ,3 patients had distant metastasis and 14 patients died due to oral cancer(p=0.000).

Out of 283 patients 85(30%) had regional nodal metastasis and 9 had distant metastasis, Common primary site being base of tongue(p=0.003) involving the lungs (77%) and thyroid (22.2%). Total 5 out of 9 patients who had distant metastasis were diagnosed as moderately differentiated squamous cel carcinoma with $T_4N_2M_0$ staging. out of 9 patients 3 had recurrence and 6 patients(p=0.000) died of oral cancer.

Among 283 patients 40 were died in which 28 were males and 12 were females. An interesting finding was that 12 patients who died had primary disease on buccal mucosa (p=0.180), 19 patients had tumor size of T_4 (p=0.807), 17 patients had nodal involvement of N_2 (p=0.896) , 24 had poorly differentiated carcinoma (p=0.000), 16 patients had nodal metastasis (p=0.138),14 patients had recurrence (p=0.000) and 6 patients had distant metastasis. The mean of overall survival days of 40 patients was 1125 days (3.08 years) with a min of 245days (6 months) and maximum of 2392 days (6.5 years).

Table-1: **clinical and histological parameters of 283 patients**

Parameters	No of patients
Age (range)	25-89 years
Sex	
Male	159 (56.2%)
Female	124 (43.8%)
Tumor site	
Buccal mucosa	93 (32.9%)
Alveolus	59 (20.8%)
tongue	46 (16.3%)
Base of tongue	26 (9.2%)
Valleculla	16 (5.7%)
Soft palate	25 (8.8%)
Maxilla	13 (4.6%)
Retromolar trigone	02 (0.7%)
Floor of mouth	02 (0.7%)
Lip	01 (0.4%)
Tumor size	
T_1	14 (4.9%)
T_2	89 (31.4%)
T_3	61 (21.6%)
T_4	119 (42%)
Nodal involvement	
N_0	69 (24.4%)
N_1	77 (27.2%)
N_2	115 (40.6%)
N_3	20 (7.1%)
N_4	2 (0.7%)
Histopathological grading	
Well differentiated	108 (38.2%)
Moderately differentiated	102 (36%)
Poorly differentiated	73 (25.8%)
Nodal metastasis	85 (30%)
Distant metastasis	09 (3.2%)
Recurrence	40 (14.1%)
Death	40 (14.1%)

Table-2: **Showing percentage distribution of age and gender in patients with oral cancer**

	Gender		Total
	Male	Female	
<30 yrs	2	2	4
	50.0%	50.0%	100.0%
30-39 yrs	12	19	31
	38.7%	61.3%	100.0%
40-49 yrs	34	32	66
	51.5%	48.5%	100.0%
50-59 yrs	51	21	72
	70.8%	29.2%	100.0%
60-69 yrs	42	29	71
	59.2%	40.8%	100.0%
70-79 yrs	14	17	31
	45.2%	54.8%	100.0%
80-89 yrs	4	4	8
	50.0%	50.0%	100.0%
Total	159	124	283
	56.2%	43.8%	100.0%

Table-3: **Showing percentage distribution of site of occurrence in oral cancer patients**

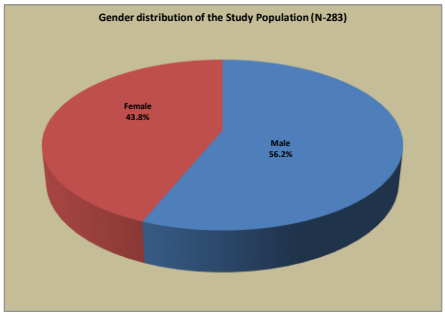
	Site										Total
	Alveolus	Base of Tongue	Buccal Mucosa	Floor of Mouth	Lip	Maxilla	Retromolar Trigone	Soft Palate	Tongue	Vallecula	
Male	16	23	33	2	1	4	2	23	39	16	159
	10.1%	14.5%	20.8%	1.3%	.6%	2.5%	1.3%	14.5%	24.5%	10.1%	100.0%
Female	43	3	60	0	0	9	0	2	7	0	124
	34.7%	2.4%	48.4%	.0%	.0%	7.3%	.0%	1.6%	5.6%	.0%	100.0%
Total	59	26	93	2	1	13	2	25	46	16	283
	20.8%	9.2%	32.9%	.7%	.4%	4.6%	.7%	8.8%	16.3%	5.7%	100.0%

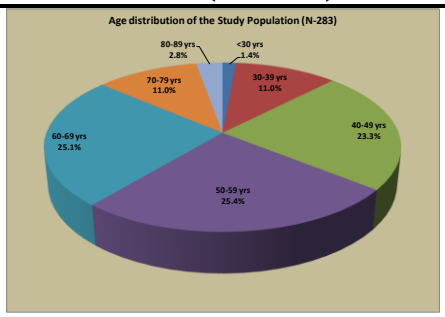
Table-4: **Showing percentage distribution of tumor size**

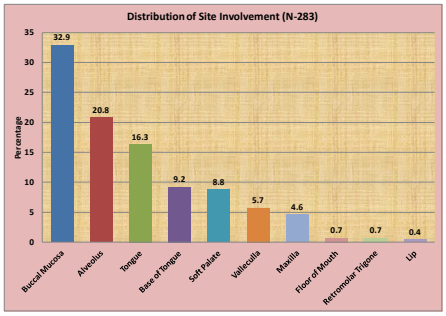
	Tumor Size				Total
	T1	T2	T3	T4	
Male	10	49	40	60	159
	6.3%	30.8%	25.2%	37.7%	100.0%
Female	4	40	21	59	124
	3.2%	32.3%	16.9%	47.6%	100.0%
Total	14	89	61	119	283
	4.9%	31.4%	21.6%	42.0%	100.0%

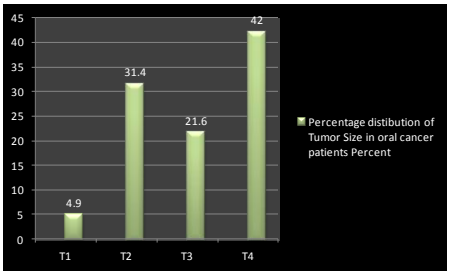
Table-5: **Showing percentage distribution of histopathological staging in oral cancer patients**

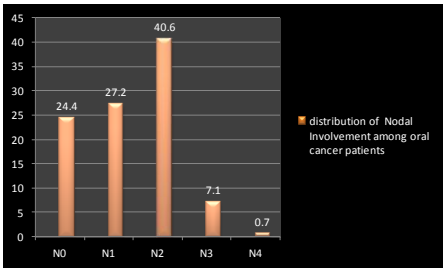
	Histopathological Staging			Total
	Well Differenciated	Moderatly Differenciated	Poorly Differenciated	
Male	59	68	32	159
	37.1%	42.8%	20.1%	100.0%
Female	49	34	41	124
	39.5%	27.4%	33.1%	100.0%
Total	108	102	73	283
	38.2%	36.0%	25.8%	100.0%

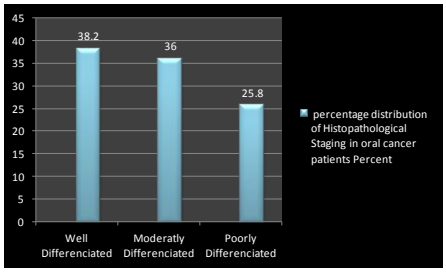


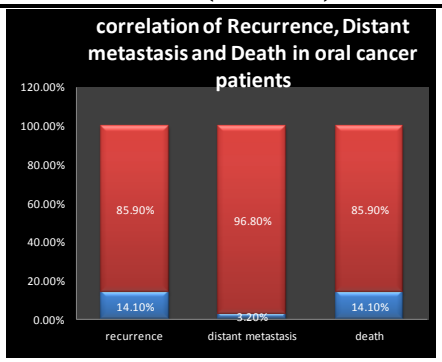

Age distribution of the Study Population (N-283)
80-89 yrs 2.8%
<30 yrs 1.4%
70-79 yrs 11.0%
30-39 yrs 11.0%
40-49 yrs 23.3%
60-69 yrs 25.1%
50-59 yrs 25.4%


Distribution of Site Involvement (N-283)
Percentage
32.9
20.8
16.3
9.2
8.8
5.7
4.6
0.7
0.7
0.4
Buccal Mucosa
Alveolus
Tongue
Base of Tongue
Soft Palate
Vallecula
Maxilla
Floor of Mouth
Retromolar Trigone
Lip


4.9
31.4
21.6
42
T1
T2
T3
T4
Percentage distibution of Tumor Size in oral cancer patients Percent


24.4
27.2
40.6
7.1
0.7
N0
N1
N2
N3
N4
distribution of Nodal Involvement among oral cancer patients


38.2
36
25.8
Well Differenciated
Moderatly Differenciated
Poorly Differenciated
percentage distribution of Histopathological Staging in oral cancer patients Percent



DISCUSSION

This retrospective study which aims to study the prevalence, clinical and histological presentation of oral cancer and its correlation with recurrence, distant metastasis and death rate, with the available data retrieved from cancer ward Victoria hospital and government dental college Bangalore for a period of 8 years (2007-2014).

In this study 1185 patients were reported according to the registry with various type of cancer in the body, amongst which 283 were with oral cancer which accounts for 25% of the total body cancer which is highly significant. The mean age of occurrence of cancer was 54.47 years with a male predominance. These results are similar to studies of *Bhurgri et al*. [3]. The highest no of oral cancer in our study was found on the buccal mucosa which is explained due to the habit of tobacco quid placement in Indian population. The result of the study is in accordance with many studies.

The treatment modality, recurrence and survival rate depends on the tumor size, regional and distant metastasis. In our study the maximum no of cases with respect to primary tumor size were T4 (42%) and maximum no of cases with cervical lymph nodes involvement were N2 (80%) and pulmonary distant metastasis was found to be 3.2%.The findigs were similar to the study conducted by Waseem Jerjes *et al*. [4].

Metastasis of oral cancer is a complex process involving detachment of cells from the tumor tissue, regulation of cell motility and invasion, proliferation and evasion through the lymphatic system or blood vessels. This process is due to reduced intercellular adhesion of tumor cells as they progress to malignancy because of loss of E-cadherin; they thereby begin to express proteins such as mesenchymal vimentin and N cadherin, promoting cell elongation and interfering with cell polarity. This morphological transition, called epithelial mesenchymal transition (EMT) leads to molecular alterations interfering with the behaviour of these cells [5].

The regional lymph node metastasis is considered as the first indication for spread and prognostic factor. Nodes are considered to be malignant if their size is greater than 1cm and they are fixed and hard [5].Distant metastasis commonly develops before, during, and after treatment for oral cancer. The lungs are the significant location for distant metastasis in 9 patients which was detected by MRI during treatment and distant metastasis significantly correlates negatively with survival rate.

In the histopathological grading, highest no of cases were well differentiated (38%) and 25% of patients had poorly differentiated squamous cell carcinoma. The recurrence rate was highest with poorly differentiated squamous cell carcinoma due to the microinvasion into the adjacent tissues which were clinically missed out. Distant metastasis was reported with moderately differentiated and the death rate was correlated with poorly differentiated squamous cell carcinoma. These results are in accordance with the study by Jerjes *et al.* [4, 5].

CONCLUSION

Squamous cell carcinoma involving buccal mucosa is highly significant. Clinical staging (T_4N_2) and poorly differentiated carcinoma is positively correlated with recurrence rate and distant metastasis.

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