

STNMP Staging of Oral Squamous Cell Carcinoma in Patients Above and Below 40 Years of Age: An Institution Based Study.

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ABSTRACT

Background: A study on Oral Squamous Cell Carcinoma (OSCC) in patients above and below forty years of age.

Aims: To compare the clinicopathological features of OSCC in patients below and above 40 years using STNMP [S-site, T-Tumor, N- Node, M – Metastasis, P- Pathology] staging system.

Materials and Methods: A cross sectional study with data of patients reported with OSCC from January 2015 to September 2019 in the Department of Oral Pathology and Department of Radiotherapy, was done and analyzed using Chi-square test. The 937 study subjects obtained were categorized according to age as Group I (≤ 40 years) and Group II (>40 years). A comparative study of clinicopathological variables using STNMP staging was done.

Statistical analysis used: Statistical Package for Social Sciences (SPSS) version 23.0

Results: Of the 937 cases of OSCC, 87 were in Group I and 850 in Group II. Both the groups showed a male predilection. Tongue was the most common site among Group I and the buccal mucosa in Group II. STNMP staging of OSCC showed a higher percentage of individuals in the most advanced stage of the disease Stage IV, 42.5% and 32.2% in Group I and Group II respectively.

Conclusions: Both the study groups showed a higher percentage of OSCC presentation in Stage IV which highlights the need for routine oral screening and awareness campaigns about OSCC. Study also points out the advantage of STNMP staging system in giving a detailed information about the tumor which makes it easy for future analysis.

Key-words: Squamous cell carcinoma, STNMP, histopathology

Oral and Maxillofacial Pathology Journal (2022): <https://www.ompj.org/archives>.

INTRODUCTION

Oral Squamous Cell Carcinoma (OSCC) has been seen as a disease mainly affecting the older age group. Recently, an increasing trend in incidence of OSCC in younger individuals is concerning.^{1,2} Patients belonging to younger age group are considered by some authors to bear more aggressive clinical course when compared to the older age.^{3,4} Other investigators nevertheless have found a similar prognosis for both evaluated groups.⁵

A precise staging system for oral cancer, if it could be applied universally, would provide invaluable information regarding the extent of the tumor, presence or absence of demonstrable regional lymph nodes, distant metastases, histopathological grades and thus the prognosis of the tumor.⁶ Rapidis A. D. et al in 1976 analyzed 136 cases of intraoral carcinoma with more than 5 years follow up and proposed a new classification by adding S [Site] and P [Pathology] to the conventional TNM classification; the STNMP [S-site, T-tumor, N-node, M-metastasis, P-pathology] staging system. The greatest advantage of the system is that it enables detailed information of any malignant tumor of the oral cavity to be recorded for future analysis and also that it can be easily transferred between different treatment centres.

In the study, we compared the clinical and histopathological features of OSCC in patients above and below forty years of age using STNMP staging system and analysed whether these factors

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How to cite this article: Ambili M, Sudha S, Ajayakumar T, Varma S, Navajeevaraj M.N, Deepthi P.V. STNMP Staging of Oral Squamous Cell Carcinoma in Patients Above and Below 40 Years of Age: An Institution Based Study. Oral Maxillofac Pathol J 2022; 13(2): page no. 87-91

Source of Support: Nil

Conflict of Interest: None

and also the differences in the etiological factors may be used to explain the disease pattern of OSCC in the two age groups.

SUBJECTS AND METHODS

Relevant data of patients reported with OSCC from January 2015 to September 2019 in the Department of Oral Pathology and Department of Radiotherapy were retrospectively analyzed. A total of 937 subjects were obtained for the study. Ethical clearance from the institution was obtained prior to the study. The patients were then categorized according to age as Group

I (≤ 40 years) and Group II (>40 years). Gender, family history, trauma history, habitual history, oral hygiene status, site of the lesion, tumor size, nodal status, metastasis and histopathology of the study subjects were recorded. STNMP staging system for each subjects based on the variables were also recorded and analysed. The data were then transferred to SPSS version 23 for statistical analysis. Chi square test was carried out with statistical significance set at $p \leq 0.05$

RESULTS

The study consisted of a total of 937 cases of OSCC, of which 87(9.3%) were ≤ 40 years (Group I) and the remaining 850 (90.7%) were >40 years of age (Group II). Chi square test was done and the data was analysed with SPSS software. Both the age groups showed a male predilection with Group I having a male to female ratio of 2:1 and Group II, 1.45: 1. Gender and site predilection in each group are shown in Table 1 and 2 respectively.

A positive family history of any other malignancy is found in 100 individuals among the 937 studied subjects, of which 14(16.1%) were in the Group I and 86 (10.1%) in Group II. History of trauma from sharp tooth is another factor under study which showed a 28.75 positive history in Group I and 74% in Group II. Habitual history of chewing tobacco was highest among subjects in Group II while individuals without any habits were affected more with OSCC in Group II which indicates a correlation with history of trauma from sharp tooth in Group II individuals as shown in Table 3.

Site wise predilection showed tongue to be the most common site among Group I and the buccal mucosa in Group II. The correlation between site of tumor, history of trauma from sharp tooth and habitual history is shown in Table 4.

Evaluation of tumor size showed highest number of subjects with a T4 tumor size among both the study groups as shown in Table 5. Nodal status showed N2 to be the most common nodal grade in both Group I and Group II (Table 6). No metastasis (M0) as shown by most of the study subjects as shown in Table 7.

Moderate differentiation was the most common grading among Group I while well differentiated SCC showed a mild predilection among Group II as shown in Table 8.

STNMP staging of OSCC in the present study resulted with a higher percentage of individuals in the most advanced stage of the disease Stage IV, 42.5 and 32.2% in Group I and Group II respectively as shown in Table 9.

DISCUSSION

The present study was done to know whether there is any difference in the biologic behaviour of OSCC in patients below and above 40 years of age using the STNMP staging system. Out of the total 937 subjects, 87 (9.3%) were ≤ 40 years of age (Group I) and the remaining (90.7%) were above the age of 40 years (Group II). In a 5 year period, the data that 87 subjects with OSCC were below 40 years of age is definitely a serious matter of concern. Many studies show a similar trend in increasing incidence of OSCC among young.^{7,8,9,10}

An overall male predominance was found with 561 (59.9%) males and 376 (40.1%) females. In both the groups males predominated with 58 (66.7%) in Group I and 503 (59.2%) in Group II. The male to female ratio was 2:1 and 1.45:1 for Group I and II respectively. This is in accordance with the studies done by many investigators.^{11,12,13}

Out of the 937 subjects studied, 100 (10.7%) were with a positive family history of any other malignancy in which 16.1% were in Group I and 10.1% in Group II. A higher percentage of cases with positive family history of any malignancy is found among young adults in our study which is in accordance with the Toporcov T. N. et al study.¹⁴ Although we could not find a statistically significant difference in family history of any malignant neoplasm between the two age groups, there have been studies in the literature with a significant correlation between OSCC in young patients and family history of malignant neoplasm.¹² Thus those with no habitual history should be evaluated for unique genetic and environmental etiologies.

In Kerala, studies have been done which showed p53 mutation in 51.5% of tumors in young patients and an intense p53 expression in association with large sized tumors.¹⁶ This relationship greatly emphasizes the positive family history to be a risk factor with considerable weightage in young adults as it is considered that tobacco usage and alcohol consumption need a long term exposure for the OSCC to develop.

Trauma to the oral mucosa is yet another major risk factor for the development of OSCC in young adults for which two mechanisms had been suggested. One is that persistent mechanical irritation causes DNA damage and eventually cancer formation by increased activity of poly-ADP ribose polymerase. The second proposed

Table1: Gender predilection in the study groups

Study group	Count	Male	Female	Male/female
Group I	87	58	29	2:1
Group II	850	503	347	1.45: 1

Table 2: Site predilection in the study groups

		Site							
		Lip- mucous membrane	Tongue	Buccal mucosa	Palate	Floor of mouth	Alveolar process	Antrum	Central carcinoma of bone
Age	Group I	2 2.3%	41 47.1%	30 34.5%	0 0.0%	2 2.3%	9 10.3%	2 2.3%	1 1.1%
	Group II	29 3.4%	297 34.9%	311 36.6%	42 4.9%	51 6.0%	114 13.4%	4 0.5%	2 0.2%
Total		31 3.3%	338 36.1%	341 36.4%	42 4.5%	53 5.7%	123 13.1%	6 0.6%	3 0.3%



mechanism being chronic mucosal trauma results in inflammation thereby releasing chemical mediators like cytokine, prostaglandins and Tumor Necrosis Factor and eventually leads to oxidative stress. Inflammation may thus act at different steps, inducing genetic and epigenetic changes and result in cancer formation.¹⁷ Trauma can be either from a sharp tooth, from an ill fitting denture, faulty restoration or any other intraoral prosthesis. In our study, a positive trauma history was found in 88 (9.4%) of the patients with OSCC in which 25 were in Group I and 63 were in Group II. 28.7% of the young adults and 7.4% of the older adults are with a positive trauma history in the current study. This is in concordance with the study by Dholam K.P et al in which 33% of the case samples have had dental trauma compared with the 45 in the control group, thus showing the role of dental trauma as a risk factor for OSCC.¹⁸ In our study, a statistically significant difference with a p value 0.000 was obtained which emphasizes the role of dental trauma as a causative agent of OSCC in young age.

Another interesting finding was out of the 88 cases with the trauma history 51 were without any habits and this further emphasizes the role of chronic mucosal trauma. In the contrary, in a review by Monkman et al, they concluded that trauma as a single factor has no evidence to cause OSCC but in combination with other factors may act as a co-carcinogen. Singhvi H. R. et al in his review on role of chronic mucosal trauma in oral cancer very well explains the increased risk of developing oral cancer due to repeated trauma from ill-fitting denture in an altered mucosal site

which had already undergone field cancerization due to previous habits.¹⁷

Evaluation of habitual history revealed a total of 280 (29.9%) patients with more than one habit. Unfortunately 27 (31%) of the 87 patients in Group I were with the habit of tobacco chewing. Also 20 (23.0%) are having more than one type of habit history. This can be due to the lack of awareness among patients from the rural areas. Much of the patients in the present study were from a low socioeconomic group and that too from tribal areas (121 cases) with the habit of tobacco chewing which further emphasizes the need for conducting camps and awareness classes about the ill effects of tobacco and alcohol on oral mucosa and the potential for developing OSCC. Out of the 937 study subjects 338 (36.1%) were with the habit of chewing tobacco mainly in the form of betel quid. A study by Salian V et al concluded betel quid chewing to be the most important etiological agent of OSCC.¹⁹

Buccal mucosa was found to be the most frequently affected site with 341(36.4%) out of the 937 subjects. This was immediately followed by tongue with 338(36.1%) of the cases. Our study showed a similar finding as the Yashna Gupta et al study on site predominance where their study also showed a predominance of buccal mucosa followed by tongue.²⁰ On the contrary some studies showed a predominance of tongue.²¹ On individual analysis of both the groups, buccal mucosa remained the predominant site of occurrence of OSCC in Group II, but tongue was found to be the one with highest occurrence in Group I. Studies show tongue and buccal mucosal carcinoma to have a different prognostic and therapeutic significance since p16 and p21 are found down regulated in tongue carcinoma and weak/ negative telomerase activity irrespective of stage of the disease.²²

A higher percentage (28.7%) of patients with OSCC in Group I were found to have a trauma history and since tongue is the mobile muscular organ of oral cavity, trauma to the tongue is more likely. This very well correlates the higher incidence of OSCC of tongue in Group I which is in accordance with many studies in the literature. (4,23–25) A higher percentage of involvement of buccal mucosa (36.4%) and alveolar mucosa (13.1%) may be due to the pouching of tobacco/ betel quid between the buccal mucosa and retromolar trigone region which was found to be the most predominant habit in the study.

A higher number of the study subjects (399 cases, 42.6%) presented with a tumor size of T4 grade in the present study. A

Table 3: Distribution of study subjects with habit and history of trauma from sharp tooth

Habits	Group I	Group II	History of trauma from sharp tooth	
			Absent	Present
Tobacco smoking	8	81	11	78
Tobacco chewing	27	311	10	328
Alcohol drinking	-	5	2	3
More than one	20	260	14	266
No habits	32	193	51	174

Table 4: Correlation of site of tumor, history of trauma from sharp tooth and habitual history

Site of tumor from sharp tooth	Group I	Group II	Presence of trauma	Habits				
				Tobacco smoking	Tobacco chewing	Alcohol drinking	More than one	No habits
Lip	2	29	3	2	15	-	8	6
Tongue	41	297	60	48	85	2	93	110
Buccal mucosa	30	311	18	15	170	1	102	53
Palate	-	42	-	6	15	1	13	7
Floor of mouth	2	51	-	9	5	1	27	11
Alveolar process	9	114	5	8	48	-	34	33
Antrum	2	4	-	-	-	-	3	3
Central carcinoma of bone	1	2	-	1	-	-	-	2



higher grade at the time of presentation very well points the lack of awareness about the risks and prognosis due to delay in diagnosis and treatment of these type of lesions. In the study by Kademani D et al on the influence of histologic grade as a prognostic factor in intraoral SCC, primary tumor size and cervical lymph node status were considered to be the two most significant factors in patient survival.²⁶

Nodal status at the time of presentation is another important predictor of survival and prognosis in OSCC. Nobrega T. D. et al in their study concluded that the absence of lymphnode metastases at diagnosis and small tumor size were predictive of better survival.²⁷ Majority of our study subjects (477 cases, 50.9%) showed nodal status of N2 grade according to the STNMP classification system followed by N0 grade (394 cases, 42.0%). This was also true for the individual analysis of both the study groups with no statistically significant difference between the two. In our study, clinical evidence of distant metastases without definite histological and/or radiographic confirmation graded in STNMP staging system as M1 was reported in 4 (0.45) of which only one in Group I and the remaining 3 were in Group II. Although none of the study subjects were with proven evidence of metastases beyond the regional nodes in Group I, two from Group II presented with M2 grade.

Histopathology remains another important prognosticator for the survival and outcome of the patients with OSCC. In our study, moderate and well differentiated grades showed almost similar range of occurrence with moderately differentiated leads by only 0.1%. in Group I. A greater number of patients reported with moderately differentiated grade while Group II showed a slightly higher percentage in the well differentiated grade. This is in contrast with the Sasaki et al study where most of the subjects in the young age group showed well differentiated SCC compared to a less percentage in the older group.⁵ 58 out of the 937 subjects reported with poor differentiation, of which 56 were from Group II and only two from Group I. The poor survival rate found in patients

with moderately and poorly differentiated cancer gives a more potential prognostic significance of cellular morphology in OSCC.²⁸

STNMP staging of OSCC in the present study showed a higher percentage of individuals in the most advanced stage of the disease, Stage IV followed by Stage III. Many studies in the literature were in accordance with our finding that at the time of presentation, patients present with an advanced disease state.²⁸ TNM staging was used in many studies as it is the one which is most universally accepted. Addition of the two important prognosticators to this conventional system in STNMP staging system not only gives a detailed information about the lesion but also aids in providing an accurate indication of the prognosis. Staging showed a statistically significant difference between the two age groups in the present study

A comparison was made between STNMP and TNM staging and the results are as shown in the Table 9. The results are very well suggestive of the STNMP staging system to be accepted as an equivalent to the conventional TNM staging system.

The prognosis, recurrence and survival following OSCC is dependent on the clinicopathological parameters so far evaluated.

CONCLUSION

There is an increasing trend of OSCC involving younger males with higher STNMP stage at presentation when compared to elder patients. Locoregional differences do occur, but further studies on genetics, immune system, diet, habits and demographics are necessary to unveil the difference between younger and older patients. The STNMP system, although superficially complicated in that it involves five different variables, is, in practice, simple to use and has the advantage of providing detailed information of any malignant tumor of the oral cavity to be recorded for future analysis.

Table 5: Distribution of tumor size grading in the study groups

	Tumor size			
	T1	T2	T3	T4
Group I	16	19	11	41
Group II	110	243	139	358

Table 7: Distribution of metastasis grading in the study groups

	Metastasis		
	M0	M1	M2
Group I	86	1	-
Group II	845	3	2

Table 9: Distribution of study groups in the different stages of STNMP staging system

	Staging			
	Stage I	Stage II	Stage III	Stage IV
Group I	17	21	12	37
Group II	128	204	244	274

Table 6: Distribution of nodal status grading in the study groups

	Node					
	N0	N1	N2	N3	N4	N5
Group I	37	-	41	2	6	1
Group II	357	2	436	22	31	2

Table 8: Distribution of histopathology grading in the study groups

	Histopathology		
	Well Differentiated	Moderately differentiated	Poorly differentiated
Group I	39	46	2
Group II	422	375	56

Table 10: Comparison of the distribution of study groups in the different stages of STNMP and TNM staging system

	Group I		Group II	
	STNMP	TNM	STNMP	TNM
Stage I	17	10	128	74
Stage II	21	14	204	129
Stage III	12	22	244	268
Stage IV	37	41	274	379



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