ORIGINAL RESEARCH PAPER

Volume - 11 | Issue - 08 | August - 2022 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

TO ASSESS ROLE OF WORST PATTERN OF INVASION,DEPTH OF INVASION AND EXTRANODAL SPREAD IN PREDICTING RECURRENCE IN 1000 CASES OF SQUAMOUS CELL CARCINOMA IN ORAL CAVITY-SINGLE TERTIARY CANCER CENTER STUDY

Oncopathology

Dr Anjali Sharma Senior Consultant & Head, Department of Pathology, Bhagwan Mahaveer Cancer Hospital & Research Center, Jaipur

Dr Ankita Gupta* Oncopathology Fellow, Department of Pathology, Bhagwan Mahaveer Cancer Hospital & Research Center, Jaipur * Corresponding Author

ABSTRACT

The incidence of oral squamous cell carcinoma (OSCC) remains high .Oral and oro-pharyngeal carcinomas are the sixth most common cancers in the world. **Aim-** The present study was conducted in a tertiary care cancer hospital in India to evaluate recurrence in squamous cell carcinoma of oral cavity. **Material And Methods-** The present study was carried out in department of pathology at regional cancer tertiary centre from . February 2011 to June 2021 .The cases were selected on basis of inclusion and exclusion criteria. **Results-** The average age of the patients suffering from oral squamous cell carcinoma (48.8 years) with male predominance (M:F =9.7:1). Recurrence rate was 23.6%. Most common site of presentation was buccal mucosa. The most common grade in recurrent as well non recurrent cases was moderately differentiated . 388 patients out of 1000 had pathologically node positive disease. The recurrence rate among node positive was 27.5 % (107 out of 388). Non-cohesive pattern was more common in recurrent cases (55.92%) . Risk of recurrence was 82.62% with depth of invasion > 5 mm . Extranodal extension was seen in 34 cases (14.40%) . Perineural invasion , lymphovascular invasion and bone invasion was seen in 44.5% , 26.7% and 22.45% respectively . Out of total 236 recurrent cases, 3 year survival rate was 64.8%, 5 year survival rate was 34.7% and disease free survival rate was 81%. **Conclusion-** Squamous cell carcinoma of oral cavity has poor overall prognosis with high tendency to recur. Risk factors for recurrence are -lymphatic permeation, depth of invasion – 5 mm or more, poorly differentiated tumor, non- cohesive pattern of invasion .

KEYWORDS

Squamous Cell Carcinoma, Recurrence, Prognosis.

INTRODUCTION

The incidence of oral squamous cell carcinoma (OSCC) remains high [(1)]. Oral and oro-pharyngeal carcinomas are the sixth most common cancers in the world [(2)]. It is one of the highest occurring cancers where tobacco consumption is common.

The AJCC 8th TNM staging system, revised in 2017, has introduced two histological characteristics [(3)] includes depth of invasion (DOI) and extra nodal extension (ENE). Other histopathological characteristics, include perineural invasion (PNI), lymphovascular invasion (LVI), status of the surgical margins ,worst pattern of invasion (WPOI), bone invasion and inflammatory response.

Depth of invasion is defined as distance between normal mucosal surface and the deepest point of invasion. It has been considered a valuable parameter for regional nodal involvement and survival in OSCC [(4)]. There is no official agreement on the optimal cut off point in DOI analysis, but a 4-mm cut off value is widely used [(5)] However, more recent studies have suggested 5 mm as the most useful cut off point in early oral cancer [(6)].

Extranodal extension is defined as extension of metastatic tumor, present within the confines of the lymph node, through the lymph node capsule into the surrounding connective tissue, with or without associated stromal reaction [(7)]. It is measured from the external aspect of the lymph node capsule to the most distant tumor focus. Its presence correlates with the risk of regional recurrence, distant disease and overall survival.

WPOI at the tumor host interface is a modification of the pattern of invasion[(8)] and is prognostic for patient survival in early stage OSCC. The pattern of invasion can be assessed by using Anneroth et al., and Bryne et al., criteria. Grade 1 tumours had well-delineated "pushing or cohesive" borders . In Grade 2 tumors , the advancing edge of tumour infiltrated in solid cords, bands or strands. Grade 3 tumours had margins that contained small groups or cords of infiltrating cells. In Grade 4, there is marked dissociation in small groups or even single cells(non-cohesive)[(9)]. Grade 5 tumors are recognized by a dispersed, discontiguous growth pattern. LVI and PNI show a significant association with tumor size, histological grading, invasive front, nodal involvement and overall prognosis and survival. The purpose of this study was to correlate histological factors with the recurrence in oral cavity squamous cell cancers. These factors include worst pattern of invasion , depth of invasion, extranodal extension , PNI,LVI.

MATERIALAND METHOD

The study was conducted after obtaining approval from scientific and research committee followed by approval from the institutional Ethical Committee.

Study Site: Department of Pathology , Bhagwan Mahaveer Cancer Hospital and Research Centre, Jaipur, Rajasthan.
Study Population: All cases of oral squamous cell carcinoma received during study period & fits in study criteria.
Type of Study: Retrospective, Observational, Single centre study.
Study Design: Cross –sectional study
Sample Size: 1000 consecutive cases
Study Duration: 10 years (2011 to 2021)

Statistical Methods

Continuous variables will be summarized as Mean & Standard deviation, whereas Nominal/categorical variables will be expressed as Proportions (%). Unpaired T test, One-way Anova test & Pearson correlation test will be used for analysis of continuous variables while Chi-square test & Fischer exact test will be used for analysis of nominal/categorical variables. P value <0.05% will be taken as significant. Medcalc 16.4 version software will be used for all statistical calculations.

Inclusion Criteria

1. All cases of squamous cell carcinoma of oral cavity diagnosed & treated at BMCHRC during study period.
2. All age group cases and both genders.
3. Cases given consent to be a part of study.

Exclusion Criteria

1. All non-malignant cases.
2. Carcinoma of oropharynx and nasopharynx.
3. Outside operated cases.

RESULTS

Table 1: Age Wise Distribution Of Total Cases

AGE	NUMBER	PERCENTAGE
21-40 YEARS	277	27.7%
41-60 YEARS	571	57.1%
61-80 YEARS	147	14.7%
81-100 YEARS	5	0.5%

Table 2 : Gender Wise Distribution In Total Cases

GENDER	NUMBER	PERCENTAGE
MALE	907	90.7%
FEMALE	93	9.3%
TOTAL	1000	

Table 3 : Recurrence Versus Non Recurrence Cases

CASES	NUMBER	PERCENTAGE
RECURRENT	236	23.6%
NON-RECURRENT	764	76.4%
TOTAL	1000	

Table 4 : Site Wise Distribution Of Cases

SITE	RECURRENT CASES	NON-RECURRENT CASES	TOTAL
BUCCAL MUCOSA	106	364	470
TONGUE	62	203	265
RMT	16	46	62
ALVEOLUS	24	50	74
LIP	01	12	13
ANGLE OF MOUTH	00	07	07
FLOOR OF MOUTH	00	09	09
GBS	18	45	63
HARD PALATE	03	05	08
MAXILLA	01	05	06
PYRIFORM FOSSA	00	02	02
SOFT PALATE	02	14	16
CENTRAL ARCH	03	05	08
TOTAL	236	764	1000

Table 5 : Histological Grading In Total Case

GRADE	NON-RECURRENT CASES	RECURRENT CASES	TOTAL	PERCENTAGE
WELL-DIFFERENTIATED	308	103	411	41.1%
MODERATELY-DIFFERENTIATED	440	128	568	56.8%
POORLY-DIFFERENTIATED	16	5	21	2.1%
TOTAL	764	236	1000	

Table 6: wpoi Pattern In Total Cases

WPOI	RECURRENT CASES	NON-RECURRENT CASES	TOTAL
PATTERN 1	0	13	13
PATTERN 2	1	64	65
PATTERN 3	103	422	525
PATTERN 4	123	242	365
PATTERN 5	9	23	32
TOTAL	236	764	1000

P=<0.05 (significant) df=4 chi square=47.18

Table 7: Doi In Total Cases

DOI	RECURRENT CASES	NON-RECURRENT CASES	TOTAL	PERCENTAGE
1-5MM	41	238	279	27.9%
6-10MM	93	273	366	36.6%
>10MM	102	253	355	35.5%
TOTAL	236	764	1000	

P=<0.05 (significant) df=2 chi square=18.121

Table 8: Correlation Of Ene In Total Number Of Cases

ENE	RECURRENT CASES	NON-RECURRENT CASES	TOTAL	PERCENTAGE
SEEN	34	46	80	08%
NOT SEEN	202	718	920	92%
TOTAL	236	764	1000	

P=<0.05 (significant) df=1 chi square=17.22

Table 9: Correlation Of Pni With Recurrence

PNI	NUMBER	PERCENTAGE
SEEN	105	44.5%
NOT SEEN	131	55.5%
TOTAL	236	

Table 10: Correlation Of Lvi With Recurrence

LVI	NUMBER	PERCENTAGE
SEEN	63	26.7%
NOT SEEN	173	73.3%
TOTAL	236	

Table Number 11 : Correlation Of Involvement Of Underlying Bone With Recurrence

BONE INVASION	NUMBER	PERCENTAGE
PRESENT	53	22.45%
ABSENT	183	77.54%

Table 12: T Staging In Total Cases

T-STAGING	RECURRENT CASES	NON-RECURRENT CASES	TOTAL	PERCENTAGE
T1	43	196	239	23.9%
T2	101	290	391	39.1%
T3	32	138	170	17%
T4	60	140	200	20%
TOTAL	236	764	1000	

P=<0.05 (significant) df=3 chi square=11.94

Table 13: N Staging In Total Cases

N-STAGING	RECURRENT CASES	NON-RECURRENT CASES	TOTAL	PERCENTAGE
N0	129	483	612	61.1%
N1	34	117	151	15.1%
N2	50	124	174	17.4%
N3	23	40	63	6.3%
TOTAL	236	764	1000	

P=0.013 (significant) df=3 chi square=10.62

Table 14:Association Of Doi And Nodal Status

DOI	N0	N1	N2	N3
1-5MM	218 (35%)	29 (19%)	28 (16.1%)	6 (9.5%)
6-10MM	219 (35%)	69 (45.3%)	47 (27.1%)	25 (39.6%)
>10MM	174 (28.4%)	54 (35.5%)	98 (56.64%)	32 (50.7%)

P=<0.05 (significant) df=6 chi square=75.12

Table 15: Survival Rate In Recurrence Cases

SURVIVAL	NUMBER	PERCENTAGE
1-3 YEAR	153	64.8%
4-5 YEAR	82	34.7%
>5 YEAR	68	28.8%

DISCUSSION

The present study was carried out in department of pathology at Bhagwan Mahaveer Cancer Hospital and Research Centre, Jaipur from February 2011 to June 2021.

Demographic Factors

The most common age group suffering from oral squamous cell carcinoma in present study was between 41-60 years (57.1%) with average diagnostic age 48.8 years.(Table-1). Male to female ratio was 9.7:1 .(Table-2) It is due to high prevalence of tobacco chewing habits, more among males than females. Recurrence rate in the present study was 23.6% .(Table-3) The most common site in the present study was buccal mucosa (Table-4).

Differentiation (table-5)

It is based on the level of cell differentiation and the proportion of differentiated cells in the tumor.Tumor differentiation is a significant predictor of loco-regional failure and tumor recurrence[10]. Multivariate analysis study showed that tumour grade was significantly related to nodal disease at the time of diagnosis[11]. In present study, moderately differentiated (56.8%,54.2%) followed by well differentiated (41.1%,43.6%) & poorly differentiated (2.1%,2.1%) were most

common in total as well as in recurrent cases respectively similar to the study by Jerjes et al[12] in which half of the patients had moderately-differentiated SCC .

WPOI (Table-6)

In the present study out of 236 recurrent cases, non-cohesive pattern (WPOI PATTERN 4 and PATTERN 5) showed 55.92% similar to the study done by Jerjes et al[12] in which total recurrent cases were 43 out of which 17 cases show non – cohesive pattern.

Depth Of Invasion (Table-7)

In the present study patients were grouped accordingly to the AJCC cut off points in 8th edition for depth group A: 1–5 mm, group B: 6–10 mm and group C: > 10 mm .Out of total 1000 cases 72.1% cases had depth of invasion > 5 mm. Risk of recurrence for Group A was 17.37%, group B was 39.40%, and group C was 43.22%. similar to the study by Faisal m et al[13]. It is now widely accepted that thickness is more accurate predictor of sub-clinical nodal metastasis, local recurrence and survival[14].

Extranodal Extension (Table-8)

In the present study out of 236 recurrence cases, ENE was seen in only 14.4% cases . ENE do not show any significant relevance with the recurrence in the present study. In a study done by Kwon M et al [15] out of 438 patients, 219 (50%) showed positive nodal status, and ENE was identified in 84 (19.6%) and found that ENE-positive patients had a higher risk of recurrence and a lower overall survival rate; however, multivariate analysis failed to identify a significant difference in cancer-specific survival between those with and those without ENE.

PNI And LVI (Table-9,10)

In a present study, out of 236 recurrent cases, PNI was seen in 105 cases (44.5%) similar to the study by Faisal et al [13] in which total recurrent cases were 29 ,out of which 11 cases show PNI (37.93%) . Lymphatic invasion was seen in 26.7% recurrent .

Bone Invasion (Table-11)

Bone and cartilage invasion affect prognosis.[16,17] . In present study only 22.45 % recurrent cases show involvement of underlying bone . According to Jerjes et al [12] only 3 patients were reported to have invasion of the mandibular cortical plate that show recurrence.

TNM System (Table-12,13)

The TNM classification of the international union against cancer relates well to the overall survival[16,17]. The earlier the tumor stage, the better the prognosis[18]. Worse prognosis is expected in patients with nodal disease[19]. In the present study, out of 1000 cases 63% were diagnosed with T1/T2 stage while 17% tumors diagnosed with T3 stage and 20% with T4 stage. Rate of recurrence of was 43.8% for T1 & T2 similar to the study done by Sieczka E et al[20] who reported out of 104 patients who were treated for buccal mucosa carcinoma, 75% had T1 or T2. Recurrence was mainly associated with n-stage disease. In our study out of 1000 cases 61.1% had N0 stage, 15.1% had N1 stage, 17.4% had N2 stage and 6.3% had N3 stage. Overall 388 patients out of total 1000 had pathologically node positive disease. The recurrence rate among those who were node positive was 27.5 % (107 out of 388). Logistic regreesion analysis revealed that the worse the pTNM , worse the prognosis. In a study done by Sharma P et al[21] 17 patients out of 60 had pathologically node positive disease, hence, the rate of occult node metastasis is 28.3%. the recurrence rate among those who were node positive is 29.4%.

Association Of Depth Of Invasion And Nodal Status (Table-14)

In the present study, out of total 1000 patients, 90.3% show DOI>5 mm in N3 stage followed by 83.74% cases in N2 stage, 80.8% cases in N1 stage and 63.4% cases in N0 stage similar to the study done by Kane et al[22] who reported increased risk of lymph node metastasis at DOI >5mm.

Survival Rate(Table-15)

In the present study out of total 236 recurrent cases, 3 year survival rate was 64.8%, 5 year survival rate was 34.7% and disease free survival rate was 81% similar to the study by Camisasca et al[23] and Wang bo et al[24].

CONCLUSION

Squamous cell carcinoma of oral cavity has poor overall prognosis with high tendency to recur .Risk factors for recurrence are-lymphatic permeation, depth of invasion – 5 mm or more, poorly differentiated tumor, non- cohesive pattern of invasion .

Abbreviations

OSCC – Oral squamous cell carcinoma
DOI- Depth of invasion
ENE -Extranodal extension
WPOI- Worst pattern of invasion
PNI- Perineural invasion
LVI- Lymphovascular invasion

REFERENCES

1. Bagan JV, Scully C. Recent advances in Oral Oncology 2007: epidemiology, aetiopathogenesis, diagnosis and prognostication. Oral Oncol. 2008;44(2):103–8.
2. Warnakulasuriya S. Global epidemiology of oral and oropharyngeal cancer. Oral Oncol. 2009;45(4-5):309–16.
3. Amin MB, Edge S, Greene FL, Byrd DR, Brookland RK, Washington MK, et al. AJCC Cancer Staging Manual. 8th Ed. New York: Springer (2017). p. 79–94. doi: 10.1007/978-3-319-40618-3.
4. Pentenero M, Navone R, Motta F, et al. Clinical features of microinvasive stage 1 oral carcinoma. Oral dis. 2011;17(3):298-303
5. Huang SH,Hwang D, Lockwood G, Goldstein DP,O' Sullivan b (2009) Predictive value of tumor thickness for cervical lymph node involvement in SCC of the oral cavity: a meta analysis of reported studies. Cancer 115:1489-1497.
6. Ebrahimi A, Gil Z,Amit M, Yen TC, Liao CT, Chaturvedi P, Agarwal JP, Kowalski LP, Kreppel M, Cernea CR, Brandao J, Shah JP, Patel SG, Clark JR (2014) Primary tumor staging for oral cancer and a proposed modification incorporating depth of invasion: an international multicenter retrospective study. JAMA Otolaryngol Head Neck Surg 140:1138-1148.
7. Protocols for the examination of specimens from patients with carcinomas of the lip and oral cavity. College of American Pathologists.
8. Brandwein-Gensler M, Teixeira MS, Lewis CM, Lee B, Rolnitzky L, Hille JJ, Genden E, Urken ML, Wang BY (2005). Oral squamous cell carcinoma: histologic risk assessment, but not margin status, is strongly predictive of local disease-free and overall survival. Am J Surg Pathol. 2005;29(2):167–178.
9. Spiro RH, Guillamondegui O Jr, Paulino AF, Huvos AG: Pattern of invasion and margin assessment in patients with oral tongue cancer. Head Neck. 1999;21(5):408–13.
10. Kademani D, Bell RB, Bagheri S, Holmgren E, Dierks E, Potter B, Homer L:Prognostic factors in intraoral squamous cell carcinoma :the influence of histologic grade. J Oral Maxillofac Surg 2005,63(11):1599-605.
11. Larsen SR, Johansen J, Sørensen JA, Krogdahl A: The prognostic significance of histological features in oral squamous cell carcinoma. J Oral Pathol Med. 2009, 38 (8): 657-62.
12. Jerjes, W., Upile, T., Petrie, A. et al. Clinicopathological parameters, recurrence, locoregional and distant metastasis in 115 T1-T2 oral squamous cell carcinoma patients. Head Neck Oncol 2, 9 (2010).
13. Faisal M, Abu Bakar M, Sarwar A, et al. Depth of invasion (DOI) as a predictor of cervical nodal metastasis and local recurrence in early stage squamous cell carcinoma of oral tongue (ESSCOT). PLoS One. 2018;13(8):e0202632. Published 2018 Aug 22. doi:10.1371/journal. pone. 0202632.
14. Woolgar JA: Histopathological prognosticators in oral and oropharyngeal squamous cell carcinoma. Oral Oncol 2006,42(3):229-39.
15. Kwon M, Roh JL et al Extranodal extension and thickness of metastatic lymph node as a significant prognostic marker of recurrence and survival in head and neck squamous cell carcinoma April 2015 Journal of cranio-maxillo-facial surgery: official publication of the European Association for Cranio-Maxillo-Facial Surgery 43(6) DOI:10.1016/j.jcms.2015.04.021 .
16. Scully C, Bagan JV: Recent advances in oral oncology 2008; Squamous cell carcinoma imaging, treatment, prognostication and treatment outcomes. Oral Oncol. 2009, 45 (6): e25-30.
17. Scully C, Bagan J: Oral squamous cell carcinoma overview. Oral Oncol. 2009, 45 (4-5): 301-8.
18. Schroeff MP van der, Baatenburg de Jong RJ: Staging and prognosis in head and neck cancer. Oral Oncol. 2009, 45 (4-5): 356-60.
19. Greenberg JS, El Naggar AK, Mo V, Roberts D, Myers JN: Disparity in pathologic and clinical lymph node staging in oral tongue carcinoma. Implication for therapeutic decision making. Cancer. 2003, 98: 508-515.
20. Sieczka E, Datta R, Singh A, Loree T, Rigual N, Orner J, Hicks W Jr. Cancer of the buccal mucosa: Are margins and T- stage accurate predictors of local control? Am J Otolarynol.2001 Nov-Dec;22(6):395-9.doi: 10.1053/ ajot.2001.28067. PMID:11713724 .
21. Sharma P, Shah SV, Taneja C, Patel AM, Patel MD. A prospective study of prognostic factors for recurrence in early oral tongue cancer. J Clin Diagn Res. 2013;7(11):2559-2562.
22. Kane SV, Gupta M, Kakade AC, et al. Depth of invasion is the most significant histological predictor of subclinical lymph node metastasis in early squamous carcinoma of the oral cavity. Eur l surg Oncol 2006;32(7):795-803. DOI:10.1016/j.ejso.2006.05.004.
23. Camisasca DR, Silami MA, Honorato J, et al. Oral squamous cell carcinoma clinicopathological features in patients with and without recurrence. ORL J Otorhinolaryngol Relat Spec. 2011;73:170–176.
24. Wang, Bo et al. —The recurrence and survival of oral squamous cell carcinoma: a report of 275 cases. Chinese journal of cancer vol. 32,11(2013):614-8.doi:10.5732/cjc.012.10219.