FREQUENCY OF CERVICAL LYMPH NODE METASTASIS IN EARLY STAGE SQUAMOUS CELL CARCINOMA OF THE TONGUE AND ITS ASSOCIATION WITH TUMOR DEPTH.

Rehana[1], Sameer Qureshi[2], Uneeba Rehman[3], Uzma malik[4], Muhammad Sibtain Shah[5], Zafar Abbas[6].

ABSTRACT

INTRTODUCTION: Approximately half-hour of malignancies of the top and the neck square measure oral fissure cancers and ninety-fifth of those being epithelial cell carcinomas (SCCs). It's rated as sixth most typical cancer within the world **OBJECTIVE:** to see the frequency of the cervical node metastasis in an epithelial cell the malignant neoplastic disease of an oral tongue and its comparison with depth of the neoplasm to ascertain the association of the cervical nodal metastasis with completely different depth of the neoplasm.**METHOD:** it was a descriptive cross sectional study conducted from January 2016 till June 2017 and 85 patients with SCC of oral tongue with stage 1 or stage 2 were enrolled in study after fulfilling inclusion criteria and they all underwent resection of tumor along with ipsilateral neck dissection. Association between tumor thickness and neck nodal metastasis was calculated from final histopathology reports. **RESULTS:** Between January 2016 till June 2017. Total of 85 patients were enrolled and neck node metastasis was present in 28 (32%) patients. In patients with tumor thickness of >5mm it was found that out of 36 patients 28 (77.78%) patients were positive for nodal metastasis (p-value <0.0001). **CONCLUSION:** Based on our study findings, it is seen that depth of tumor is strongly associated with chances of cervical lymph node metastasis and prophylactic neck dissection can play a strong role in increasing the overall survival in the early stage squamous cell carcinoma of tongue as neck node metastasis has strong impact overall disease free survival.

KEYWORDS: Cervical Node Metastasis, Squamous Cell Carcinoma, Tumor Depth, Oral Tongue Carcinoma.

1. Senior Registrar, Department of ENT and Head & Neck Surgery, Fatima Hospital, Baqai Medical University Karachi.
2. Head of Department ENT, Head & Neck Surgery Department, JPMC, Karachi.
3. Senior Registrar Department of ENT, Head & Neck Surgery, Fazaia Hospital, Ruth Pfau Medical College Karachi.
4. Senior Lecture, Department of Radiation Oncology, SIUT Karachi.
5. Assistant Professor, Oncology Medical Unit I, PUMHSW Nawabshah.
6. In charge, Intense Care Unit (ICU), Memon Hospital Karachi.

How to cite this article: Rehana[1], Qureshi S[2], Rehman U[3], Malik U[4], Shah MS[5], Abbas Z[6]. **FREQUENCY OF CERVICAL LYMPH NODE METASTASIS IN EARLY STAGE SQUAMOUS CELL CARCINOMA OF THE TONGUE AND ITS ASSOCIATION WITH TUMOR DEPTH.** *JPUMHS; 2021:11:03, 07-11.* http://doi.org/10.46536/jpumhs/2021/11.03.307

For Corresponding: Rehana**,** Senior Registrar, Department of ENT and Head & Neck Surgery Fatima Hospital, Baqai Medical University Karachi. dr_gr8_2009@hotmail.com

Received April 23rd 2021, Accepted On 25th July 2021, Published On 30th September 2021

INTRODUCTION

Approximately half-hour of malignancies of the pinnacle and neck square measure rima oris cancers and ninety-fifth of those being epithelial cell carcinomas (SCCs). It's rated as sixth-commonest cancer within the world [1]. It was calculable that within the year 2018, carcinoma occurred globally in regarding 355,000 people, and resulted in 177,000 deaths [2]. In Asian landmass carcinoma is one among the most-common varieties of cancer because of its association with consumption of smoking (tobacco, bidi), true pepper quid and alcohol. Regionally incidence varies, with the highest rates in South Asia region notably Asian nation, India, Bangladesh, Sri Lanka, and Islamic State of Afghanistan [3], with tongue and buccal mucosa being among most common site of OCSCC. Neck node metastasis is a common feature of oral cavity cancers with incidence being reported approximately 20% to 40% in most cases, which remains undetectable by physical and radiological examination in many cases and in these cases the controversy arises whether to go for neck dissection specially in early stage cancers where no detectable nodal

metastasis is found pre operatively. Despite these controversies, it's thought-about that management of neck return when a amount of observation is way tougher as a results of hyperbolic incidence of high stage neck sickness at the side of additional capsular unfold and salvage rates for this cluster area unit extraordinarily poor. However, on the opposite hand a routine policy of elective neck treatment would subject a big proportion of patients to associate degree unnecessary procedure. at this time we have a tendency to don't have precise predictors of nodal metastases from carcinoma however many studies have instructed that the dimension, i.e. neoplasm thickness or depth of invasion is a very important risk issue for cervical metastasis in patients with HNSCC [4, 5, 6,7,8,9.10]. The increasing depth of invasion and also the small tube-shaped structure proliferation caused by growth growth would possibly confirm proximity to blood vessels and lymphatics, therefore facilitating the tumor's ability to spread.[11] Neck dissection leads to vital morbidity to patient in terms of cosmetic and useful outcomes however at an equivalent time Elective neck dissection provides pathologic data on the standing of neck nodes, therefore serving to to work out the necessity for extra medical aid, and might additionally take away occult cancer cells spread to the body fluid vessels . Few studies, however, have shown the worth of the dimension in association with cervical metastasis in patients with Stage I/II SCC of the oral tongue which showed that prevalence of node metastasis was 47.7% overall, in which it was 12% in <5mm tumor thickness and in 5mm or >5mm tumor thickness it was 70%[12]. Present study can valuate the histopathological feature of oral tongue epithelial cell cancer of tongue that is said to the dimension of growth i.e. growth thickness in patients with Stage I/II oral tongue SCC treated with radical surgery with none pre-surgical native or general medical aid in a trial to outline their utility as predictors of cervical nodal metastasis.

METHODOLOGY:

This was a prospective study conducted in ENT and head & neck surgery department of JPMC from January 2016 till June 2017. Cases of early stage squamous cell carcinoma of tongue were enrolled in the study after informed consent, purpose of study was explained to the patients. A Performa was made which included bio data, addiction, depth of tumor, grade of trismis, symptoms related to the tumor like pain, bleeding etc. After informed consent all patients who fulfill inclusion criteria were enrolled. All patients underwent partial or hemi-glossectomy with ipsilateral neck dissection. Medical record number, clinico-pathological features including age, gender, clinical and histopathological staging were evaluated to see whether nodes removed by neck dissection were positive for metastasis or not. Node-positive cases during this study means that the cases during which positive cervical nodes were known supported a microscopic anatomy designation once a neck dissection. Depth was marked as less than or equal to 5mm, and more than 5mm. All demographical and histopathological features were recorded in pre-structured Performa.

Data was stored and analyzed using SPSS 22.0, Mean ±SD was reported for quantitative variables i.e. age, duration of symptoms and tumor size. Frequency and percentages were calculated for gender, duration of symptoms, type of addiction and clinical stage, tumor depth (<5mm or ≥ 5mm) and cervical lymph node metastasis (positive/negative). Cervical lymph node metastasis was compared with different depth of tumor using Chi-square test. Effect modifiers like age, gender, duration of symptoms, clinical stage, type of addiction like Pan, Chalia, Gutka, Niswar, Tobacco chewing, Alcohol were controlled through stratification. Post stratification Chi-square test was applied using P≤ 0.05 as significant.

RESULT:

In this study 85 patients were included to assess frequency of cervical node metastasis in squamous cell carcinoma of oral tongue and its comparison with different depth of tumor and the results were analyzed as Mean ± SD of age was 43.65 ±3.28 with C.I (42.94…….44.35) years as shown in (**Table 1).** Mean ± SD for duration of symptoms was 8.56 ±2.48with C.I (8.02…….9.09) weeks as shown in (**Table 2**).

Out of 85 patients 66 (77.64%) were male and 19 (22.35%) were female.

In distribution for type of addiction 13(15.2%) were pan addicted, 60(70.5%) both pan and gutka addicted, 7 (8.2%) were niswar addicted and 12(5.8%) both gutka and cigarette addicted as shown in (**TABLE 3).**

In frequency of clinical stage out 85 patients 23 (27.05%) had T1 and 62(72.94%) had T2 stage.In frequency of tumor depth 49(57.64%) had ≤5mm and 36(42.35%) had > 5mm and patients with T1 stage 20 patients(87%) had tumor thickness ≤5mm and 3(13%) patients had tumor thickness of >5mm, among 62 patients with T2 lesion 29 (46.77%) had tumor thickness ≤5mm and 33(54.88%) patients had tumor thickness of >5mm. By comparing lymph node metastasis to depth of tumor 49 patient with tumor depth

of ≤5mm had negative nodal metastasis ,while among 36 patients with tumor depth of >5mm 28 patients(77.78%) had positive metastasis while 8 patients were negative for nodal metastasis which was statically significant (p <0.0001).(**TABLE 4).**

Among 86 patients positive cervical node metastasis was found in 28(32%) patients while 57(68%) were negative for nodal metastasis. **Table 5.** While figure 1 shows LN mets.

MEAN	43.65 (years)
±SD	3.28
95% Confidence Interval	42.94…….44.35

TABLE # 1 DESCRIPTIVE STATISTICS OF AGE n=85

MEAN	8.56 (weeks)
±SD	2.48
95% Confidence Interval	8.02….9.09

TABLE # 2 DESCRIPTIVE STATISTICS FOR DURATION OF SYMPTOMS n=85

TYPE OF ADDICTION	FRFEQUENCY
Pan	13 (15.2%)
Chalia	75 (88%)
Pan and Gutka	60 (70.5%)
Cigarette smoking	5(5.8%)
Niswar	7 (8.2%)
Alcohal	8 (9.4%)

TABLE # 3 FREQUENCY FOR TYPE OF ADDICTION n=85

TUMOR DEPTH	LYMPH NODE METASTASIS		P-VALUE
	POSITIVE	NEGATIVE	
< 5mm	0	49 (100%)	0.0001
≥ 5mm	28 (77.77%)	8 (22.22%)	

TABLE # 4 COMPARISON OF CERVICAL LYMPH NODE METASTASIS WITH DEPTH OF TUMOR n=85

CLINICAL STAGE	LYMPH NODE METASTASIS		P-VALUE
	POSITIVE	NEGATIVE	
T1	0	23 (100%)	0.0001
T2	28 (45.2%)	34 (54.83%)	

TABLE # 5 STRATIFICATION CLINICAL STAGE WITH RESPECT TO CERVICAL LYMPH NODE METASTASIS n=85

T stage	<5mm	>5mm
T1	20(86%)	3(13%)
T2	29(46.77%)	33(54.88)

Table 6: T stage

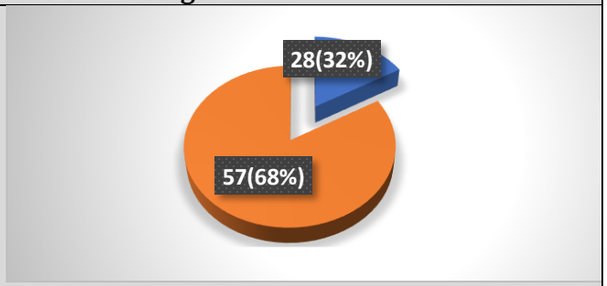

FIGURE # 1 FREQUENCY OF CERVICAL NODE METASTASIS n =85

DISCUSSION

Head and neck epithelial cell malignant neoplastic disease (HNSCC) is reportable to be the sixth most typical cancer worldwide and, as a consequence of its extremely invasive nature and proximity to very important structures, the seventh most typical reason behind cancer-induced mortality [1]. HNSCC is a heterogeneous group of tumors both from molecular [13] and clinical point of view[14]. The main clinical nonuniformity issue is that the website of the origin, that correlates with specific risk factors, symptoms, a stage at diagnosing, a tendency to the native and distant metastasis, the chemo and the radio-sensitivity and an ultimately prognosis.[13-14]. Tobacco and alcohol, which act

synergistically, are the primary etiological factors of HNSCC and account for the majority of head and neck tumors [15]. Amongst all intra-oral sites, cancers originating from oral tongue clinically behave very differently. It seems to grow faster than cancer in other sites of the oral cavity, more frequently metastasize to cervical lymph nodes, which is associated with a poorer prognosis. Indeed, despite overall improvements in surgical and medical management, clinical outcomes in patients with OTSCC have remained largely unchanged [16–18] OTSCC shows a more aggressive phenotype with properties of split invasive growth pattern, rapid local invasion, a more intense inflammatory response at the tumor interface, high proportion of lymph node positivity at the time of diagnosis and high loco-regional relapse rate[1]. Primary OTSCC spreads through lymphatic channels to the cervical lymph nodes. The reason for the aggressive growth and the nodal disease in the early stage of OTSCC can depend on the unique anatomical features of this muscular organ within the oral cavity, namely the nine extrinsic and intrinsic muscles with no relevant anatomical barrier and rich lymphatic network, with three main deep muscular lymphatic drainage pathways (Lindberg, 1972).

The incidence of OTSCC seems to be increasing among young adults (≤40years) [19–22], particularly women [23].The main objective of our study was to correlate the chances of neck nodal metastasis with the depth of tumor and the results of our study were comparable to the study done by others and in one study by Keski-Säntti et al., in 2007 assessed the predictive value of histopathologic parameters in early OSCC in 73 patients. They terminated that depth of infiltration foreseen occult nodal unwellness, however its price in clinical higher cognitive process is proscribed owing to poor specificity once employing a cutoff price that gives cheap sensitivity for locating the patients with occult nodal unwellness. [24] Study done by Balasubramanian et al., in 2014 compared the TT as a predictor of nodal metastases in early stage SCC of oral tongue and floor of mouth. They concluded that thin FOM tumors (2.1–4 mm) have a high rate of nodal metastases. They also suggested neck dissection in FOM tumors >2 mm thick and tongue tumors of more than 4 mm thickness. [25]

In 2016 Tarsitano et al. conducted a retrospective longitudinal study to determine a cutoff value of infiltration depth for predicting the risk of cervical lymph node metastasis in surgically treated patients pf stage T1 to T2 oral SCC of the tongue. The mean infiltration depth of the N negative cluster was found to be two.4 millimetre that was well totally different from the norm ascertained within the N positive cluster at five.5 mm. A important cutoff was known at associate degree infiltration depth worth of four millimetre.[26] Kejia Wang et al. in 2016 a retrospective review of prospectively collected data and set up a cut off thickness of 4mm and concluded that even tumors with thickness of 2-3.9mm also has propensity of cervical node metastasis and patients in this category require close monitoring if their neck dissection is not done in primary surgery. [27]

CONCLUSION

In conclusion, our study shows that out of 85 patients with squamous cell carcinoma of oral tongue, 20(23.53%) diagnosed to have cervical node metastasis while 65 (76.47%) did not have metastasis. Male had higher proportion of metastasis than female. Based on our study findings, it is suggested that there is a strong association between depth of tumor and nodal metastasis so depth of tumor is a strong predictor of elective neck dissection and has a significant impact on overall survival as well. However, there is a need to conduct more studies using large sample size with multiple study sites in Pakistan to validate these results.

ETHICS APPROVAL: The ERC gave ethical review approval

CONSENT TO PARTICIPATE: written and verbal consent was taken from subjects and next of kin

FUNDING: The work was not financially supported by any organization. The entire expense was taken by the authors

ACKNOWLEDGEMENTS: We would like to thank the all contributors and staff and other persons for providing useful information.

AUTHORS' CONTRIBUTIONS: All persons who meet authorship criteria are listed as authors, and all authors certify that they have participated in the work to take public responsibility of this manuscript. All authors read and approved the final manuscript.

CONFLICT OF INTEREST: No competing interest declared.

REFERENCES:

1. Supic G, Kozomara R, Jovic N, Zeljic K, Magic Z. Hypermethylation of RUNX3 but not WIFI gene and its association with stage and nodal status of tongue cancers. Oral Dis. 2011 Nov; 17(8):794-800.
2. "Cancer today". Gco.iarc.fr. Retrieved 9 June 2019.
3. Rao, Sree Vidya Krishna; Mejia, Gloria; Roberts-Thomson, Kaye; Logan, Richard (30 October 2013). "Epidemiology of Oral

Cancer in Asia in the Past Decade- An Update (2000-2012)". Asian Pacific Journal of Cancer Prevention. Asian Pacific Organization for Cancer Prevention. **14** (10): 55675577. doi:10.7314/apjcp.2013.14.10.5567. ISSN 1513-7368. PMID 24289546

4. Shingaki S, Suzuki I, Nakajima T, Kawasaki T. Evaluation of histopathologic parameters in predicting cervical lymph node metastasis of oral and oropharyngeal carcinomas. Oral Surg Oral Med Oral Pathol1988; 66:683-8.
5. Rasgon BM, Cruz RM, HilsingerJr RL, Sawicki JE. Relation of lymph-node metastasis to histopathologic appearance in oral cavity and oropharyngeal carcinoma: a case series and literature review. Laryngoscope 1989; 99:1103-10.
6. Morton RP, Ferguson CM, Lambie NK, Whitlock RM. Tumor thickness in early tongue cancer. Arch Otolaryngol Head Neck Surg1994; 120:717-20.
7. Yuen APW, Lam KY, Wei WI, Lam KY, Ho CM, Chow TL, et al. A comparison of the prognosis significance of tumor diameter, length, width, thickness, area, volume, and clinicopathological features of oral tongue carcinoma. Am J Surg2000; 180:139-43.
8. O-charoenrat P, Pillai G, Patel S, Fisher C, Archer D, Eccles S et al. Tumor thickness predicts cervical nodal metastases and survival in early oral tongue cancer. Oral Oncol. 2003 Jun; 39(4):386-90.
9. Lodder WL, Teertstra HJ, Tan IB, Pameijer FA, Smeele LE, van Velthuysen ML, et al. Tumor thickness in oral cancer using an intra-oral ultrasound probe. Eur Radiol. 2011 Jan; 21(l):98-106.
10. Goerkem M, Braun J, Stoeckli SJ. Evaluation of clinical and histomorphological parameters as potential predictors of occult metastases in sentinel lymph nodes of early squamous cell carcinoma of the oral cavity. Ann SurgOncol. 2010 Feb; 17(2):527-3.
11. DiTroia JF. Nodal metastases and prognosis in carcinoma of the oral cavity. OtolaryngolClin North Am 1972; 5:333-42.
12. Asakage T, Yokose T, Mukai K, Tsugane S, Tsubono Y, Asai M, et al. Tumor thickness predicts cervical metastasis in patients with stage I/II carcinoma of the tongue. Cancer 1998; 82:1443-8.
13. Vandenbrouck C, Sancho GH, Chassagne D, Cachiu SD. Elective vs. Therapeutic neck dissection in epidermoid carcinoma of the oral cavity. Results of a randomized trial. Cancer 1980; 46:386-9.
14. Piedbois P, Mazeron JJ, Jaddad E, Coste A, Martin M, Levy C, et al. Stage I-II squamous cell carcinoma of the oral cavity treated by iridium-192: is elective neck dissection indicated? RadiotherOncol1991; 21:100-6.
15. Lydiatt DD, Robbins KT, Byers RM, Wolf PF. Treatment of Stage I and II oral tongue cancer. Head Neck 1993; 15:308-12.
16. Brown JS, Kalavrezos N, D'Souza J, Lowe D, Magennis P, Woolgar JA. Factors that influence the method of mandibular resection in the management of oral squamous cell carcinoma. Br J Oral MaxillofacSurg 2002; 40: 275–284.
17. Barttelbort SW, Bahn SL, Ariyan SA. Rim mandibulectomy for cancer of the oral cavity. Am J Surg 1987;154: 423–428
18. Rogers SN, Devine J, Lowe D, Shokar P, Brown JS, Vaughan ED. Longitudinal health-related quality of life following mandibular resection for oral cancer: A comparison between rim and segment. Head Neck. 2004; 26:54-62.
19. Gritz ER, Carmack CL, deMoor C, et al. First year after head and neck cancer: quality of life. J ClinOncol1999; 17:352– 60.
20. Srinivasprasad V, Dineshshankar J, Sathiyajeeva J, Karthikeyan M, Sunitha J, Ragunathan R. Liaison between micro-organisms and oral cancer. J Pharm Bioallied Sci. 2015; 7(Suppl 2):S354.
21. Rodriguez T, Altieri A, Chatenoud L, Gallus S, Bosetti C, Negri E, Franceschi S, Levi F, Talamini R, La Vecchia C. Risk factors for oral and pharyngeal cancer in young adults. Oral oncol. 2004;40(2):207-13.
22. Hassona Y, Scully C, Almangush A, Baqain Z, Sawair F. Oral potentially malignant disorders among dental patients: a pilot study in Jordan. Asian Pac J Cancer Prev. 2014; 15(23):10427-31.
23. Rodriguez T, Altieri A, Chatenoud L, Gallus S, Bosetti C, Negri E, et al. Risk factors for oral and pharyngeal cancer in young adults. Oral Oncol. 2004 Feb; 40(2):207-13.
24. Keski-Säntti H, Atula T, Tikka J, Hollmén J, Mäkitie AA, Leivo I, et al. Predictive value of histopathologic parameters in early squamous cell carcinoma of oral tongue. Oral Oncol 2007; 43:1007-13.
25. Balasubramanian D, Ebrahimi A, Gupta R, Gao K, Elliott M, Palme CE, et al. Tumour thickness as a predictor of nodal metastases in oral cancer: Comparison between tongue and floorof mouth subsites. Oral Oncol2014;50:1165-8
26. Tarsitano A, Del Corso G, Tardio ML, Marchetti C.et al. Tumor infiltration depth as predictor of nodal metastasis in early tongue squamous cell carcinoma. J Oral MaxillofacSurg2016; 74:523-7.
27. Keijia Wang, David Veivers, et al. tumor thickness as a determinant of nodal metastasis in oral tongue carcinoma.ANZ J Surg (2017); 87:720-724.