

# Frequency of Lymph Node Metastasis in Oral Cavity Cancer with Clinically Node Negative

Lymph Node  
Metastasis in  
Oral Cavity  
Cancer

Allah Bux Mushtaq<sup>1</sup>, Abdul Waheed<sup>2</sup> and Mukhtar Ibrahim<sup>3</sup>

## ABSTRACT

**Objective:** To determine the frequency of lymph node metastasis in oral cavity cancer with clinically node negative (No).

**Study Design:** Descriptive / cross sectional study.

**Place and Duration of Study:** This study was conducted at the Department of Otolaryngology, Sindh Government Lyari General Hospital, Karachi from January 2015 to June 2016.

**Materials and Methods:** All patients with aged 20 years or more with either gender presented with more than 3 months oral cavity cancer with clinically No diagnosed on histopathology having stage T1 or T2 were enrolled. Presence of abnormal cells in lymph nodes was taken as metastasis positive.

**Results:** Mean age of the patients was  $43.93 \pm 7.87$  years. Male preponderance was found to be higher 71 (75.50%) as compared to females 23 (24.50%). Betel quid chewing was found in majority 56 (59.60%) patients followed by cigarette smoking 52 (55.30%), areca nut 42 (44.70%), gutka 36 (38.30%) and naswar 33 (35.10%). Lymph node metastasis was found in 39 (41.50%) patients.

**Conclusion:** The frequency of lymph node metastasis was noted in 41.50% oral cavity cancer with clinically node negative (No).

**Key Words:** Lymph Node Metastasis, Clinically Node Negative, Oral Cavity Cancer

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## INTRODUCTION

Oral cancer is one of the most common types of tumor in the head and neck (38%) with an incidence of 75% in male patients over age 60 years old, while about 95% of cases are squamous cell carcinomas.<sup>(1)</sup> Oral squamous cell carcinoma is an invasive lesion with the presence of perineural growth. It has a significant recurrence rate and frequently metastasizes to cervical lymph nodes.<sup>(2)</sup> Lymph node metastatic tumors occur in about 40% of patients with oral cancer. Clinically, their manifestations are hidden in rates of 15% to 34%.<sup>(3-4)</sup> However, despite significant advances in surgery and chemotherapy achieved over the past decades, oral cancer is still characterized by poor prognosis and a low survival rate.<sup>(5-6)</sup>

In patients diagnosed with tumors at an advanced stage, there is a high occurrence of invasion to surrounding tissues, with lymph node and distant metastasis, and a peculiarly high risk of second malignancy during the patient's lifetime.<sup>(7)</sup>

The rationale of the study is that cervical metastasis is the major determinant of prognosis and management of early stage cancer is still controversial. Therefore, actual magnitude of lymph node metastasis has to be known that will help in decision making for management of early stage oral cavity cancer.

## MATERIALS AND METHODS

The study was conducted at Department of Otolaryngology, Sindh Government Lyari General Hospital, Karachi from January 2015 to June 2016. The study design was Descriptive Cross sectional study. The inclusion criteria were patients of Oral cavity cancer with clinically NO diagnosed on histopathology, Stage T1 and T2, Duration of symptoms 3 months or more, Aged 20 years or more and Either gender.

The Exclusion criteria was Patients with T3, T4, N+ve, Recurrence of Oral cavity cancer, Site of origin of cancer other than oral cavity and Received any prior treatment. Patients of Oral cavity cancer with clinically NO meeting the inclusion criteria admitted in the department of Otolaryngology of the institute were included in the study. Prior to inclusion the pros and cons of the study was explained to the patient and

<sup>1</sup>. Department of ENT, Layari General Hospital Karachi.

<sup>2</sup>. Department of ENT, Khairpur Medical College, Khairpur Mirs.

<sup>3</sup>. Department of ENT, Indus Medical College, Tando Muhammad Khan.

Correspondence: Dr. Allah Bux Mushtaq, ENT Specialist Layari General Hospital Karachi.

Contact No: 0345-3925788

Email: drallahbux@yahoo.com

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written informed consent was taken for inclusion in the study and for surgery.

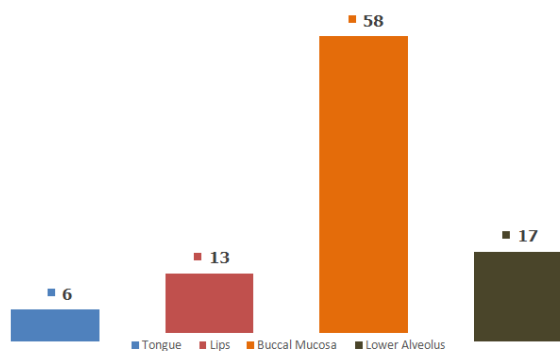
History of the patients regarding the duration of symptoms and factors leading to oral cavity cancer was taken and local examination was done by the principal investigator. Surgery was performed by consultant having more than 2 years of post-fellowship experience under general anaesthesia.

Specimen of regional lymph nodes was sent to the institutional laboratory for histopathology. Report of the histopathology was followed and presence of abnormal cells in lymph nodes was taken as metastasis positive. This information along with stage of tumour, duration of symptoms, factors leading to it, age and gender was noted.

Statistical package for social sciences for windows was used for data entry and analysis. Data was double entered, cleaned and coded. Frequencies and percentages were calculated and presented for qualitative data like gender, stage of tumour, site of tumour and associated factors. Mean $\pm$ S.D was calculated and presented for quantitative data like age, duration of symptoms and size of tumour. Multivariate analysis was done to address the effect modifiers like gender, age, stage, site, duration of symptoms, size of tumour and associated factors. 95% confidence interval was also calculated.

## RESULTS

Mean age of the patients was  $43.93 \pm 7.87$  years. Majority of the patients 81 (86.2%) were presented with  $>40$  years of age. Male preponderance was found to be higher 71 (75.50%) as compared to females 23 (24.50%). Mean duration of symptoms was  $4.02 \pm 0.74$  months. Majority of the patients 67 (71.30%) were presented with  $\leq 4$  months of duration of symptoms. Mean tumor size was  $2.64 \pm 0.78$  cm.



**Figure No.1: Site of Tumor**

Majority of the patients 76 (80.90%) had  $\leq 3$  cm of tumor size. There were 54 (57.40%) patients with T1 stage of tumor while 40 (42.60%) had T2 stage of tumor. Majority of the patients 58 (61.70%) had buccal mucosa site cancer followed by lower alveolus 17 (18.10%), lips 13 (13.80%) and tongue 6 (6.40%).

Betel quid chewing was found in majority 56 (59.60%) patients followed by cigarette smoking 52 (55.30%), areca nut 42 (44.70%), gutka 36 (38.30%) and naswar 33 (35.10%). Lymph node metastasis was found in 39 (41.50%) patients.

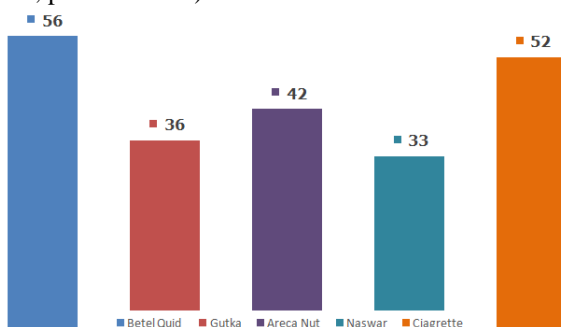
**Table No.1: Regression Analysis**

Variables	Univariate Analysis			Multivariate Analysis		
	OR	95% CI	p-value	AOR	95% CI	p-value
Age, in years	1.05	0.95-1.05	0.841	-		
Gender						
Male	-		0.234	-		
Female	1.77	0.68-4.58				
Duration of Symptoms						
≤4 months	-		0.31	-		
>4 months	0.61	0.24-1.56				
Stage of Tumor						
T1	-		0.06	-		
T2	2.21	0.95-5.11				
Site of Tumor						
Tongue	0.41	0.06-2.81	0.36	-		
Lips	0.66	0.14-3.07	0.6			
Buccal Mucosa	0.51	0.16-1.64	0.26			
Lower Alveolus	-					
Betel Quid						
Yes	-		0.001	-		0.001
No	0.09	0.03-0.28		0.13	0.04-0.43	
Gutka						
Yes	-		0.08	-		
No	0.47	0.20-1.10				
Areca Nut						
Yes	-		0.151	-		
No	1.85	0.79-4.29				
Cigarette Smoking						
Yes	-		0.001	-		0.001
No	0.09	0.03-0.26		0.12	0.04-0.39	

OR: Odds Ratio, AOR: Adjusted Odds Ratio, CI: Confidence Interval

Multivariate analysis showed that people who did not chew betel quid were 87% less likely to have lymph node metastasis as compared to the people who chew

betel quid (OR: 0.13, 95% CI: 0.04-0.43, p-value 0.001) and people who smoke cigarette were 88% less likely to have lymph node metastasis as compared to the patients who smoke cigarette (OR: 0.12, 95% CI: 0.04-0.39, p-value 0.001).



**Figure No.2: Associated Factors**

## DISCUSSION

From Darwinistic point of view, Metastasis was construed as a process wherein cell heterogeneity is strengthened by the genetic unsteadiness of primary tumor, allowing few metastatic clones to show and spread cancer at distance.<sup>(8)</sup> This accounts for the most overwhelming malignancy stage and the vital factor of cancerous death. Metastasis comprises chronological events involving spread, spur of angiogenesis, mobility, inflow into bloodstream and interaction with ingredients of the fresh micro-habitation, involving functional inflammatory and stromal cells.<sup>(9-10)</sup>

Apparently slight malignant cells portion under-take metastatic track, owing to an inter-play between inherent features of cancer cells and host factors; hence metastasis may depict cells escaping the unfriendly atmosphere created by them, i.e. paucity of O<sub>2</sub> and required nutrients, immunity attacks and inflammation.<sup>(11-13)</sup> Lymph node metastatic growth cells are identified in around 40% patients having oral cancer.

Their appearances are from 15% to 34%.<sup>(14-15)</sup> However, regardless of major advancements in surgery/chemotherapy obtained over the past periods, a low endurance rate and poor prognosis is its characteristic.<sup>(6)</sup> Where patients having tumors diagnosed at complex level, increased incidence of invasion in adjoining tissues, having distant metastasis/lymph node, as well as abnormal increased risk of 2nd malignancy during the lifetime is likely.<sup>(4,7)</sup>

Moreover, because of the fact that lymphatic metastasis occurs frequently that affects prognosis, a treatment decision of neck lymph nodes has to be made in every patient, even metastases are clinically absent. In case of patient possessing metastases of local lymph node needs to be critically assessed. It is established that the mechanism of palpation is an ineffective method to identify cancer stage in neck.

Current study shows that more than twenty percent likelihood of neck metastases-occult (in neck that is palpatory negative) is found suggestive of elective neck treatment, suggesting for radiative therapy and also surgery as it seems effective. This Occult metastasis likelihood, that can appear in neck from both sides, is established through primary tumor features i.e. site and size, alongwith various biological touchstones.<sup>(15)</sup>

Owing to the enhanced nodal metastases risk, even in necks that are clinically negative, most patients having tumors at T2 stage or more than that undergo any neck treatment (elective). A shortfall in this method is that the major number of patients do not carry metastases, thus were rendered to the morbid management. By analysing otherwise occult adenopathy, advanced imaging methods may show higher sensitization to positive nodes detection which accordingly reduce occult metastasis likelihood below twenty percent.

In case this is achieved, the surgeon has option to avoid a neck dissection/ radiative therapy, and pursue a wait/watch approach alongwith sensitive follow-up for analysing metastasis of neck as earlier as it is apparent.<sup>(16)</sup> The major feature of oral carcinoma's prognosis is the metastasis (cervical). This is commonly established that more enhanced oral tumors be dealt through elective neck dissection, however stage I disease handling is debatable till yet. In non-presence of clinical neck disease, oral cancer (stage I) is mostly dealt through primary tumor resection as well as regular check-up.

Moreover, studies reflect an incidence of occult neck metastases in stage I and II being as upwards as forty two percent.<sup>(17)</sup> In this study, betel quid chewing was found in majority 56 (59.60%) patients followed by cigarette smoking 52 (55.30%), areca nut 42 (44.70%), gutka 36 (38.30%) and naswar 33 (35.10%). Metastasis of lymph node was identified in 39 (41.50%) patients.

In a local study 732 patients had T1 and 62 patients had T2 lesion. In patients with T1 carcinoma, nine out of thirty two had metastases (28%), however in patients with T2 carcinoma, 21 out of 62 showed metastases (34%). Thus, the overall rate of occult lymph node metastases was high (32%).<sup>(18)</sup> González Moles et al. (1998) assessed clinical and histological parameters concerning survival, pointing out the most influential factors as the primary site, existence of metastasis of lymph node, clinical stage and intensity of differentiation of cells along with pleomorphism.<sup>(19)</sup>

## CONCLUSION

The frequency of lymph node metastasis was noted in 41.50% oral cavity cancer with clinically node negative (No).

### Author's Contribution:

Concept & Design of Study: Allah Bux Mushtaq  
Drafting: Abdul Waheed

Data Analysis: Mukhtar Ibrahim  
 Revisiting Critically: Allah Bux Mushtaq,  
 Abdul Waheed  
 Final Approval of version: Allah Bux Mushtaq

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

## REFERENCES

1. Ayas B, Saleem K, Azim W, Shaikh A. A clinico-pathological study of oral cancers. *Biomedica* 2011;27:29-32.
2. Okura M, Aikawa T, Sawai N, Lida S, Kogo M. Decision analysis and treatment threshold in a management for the N0 neck of the oral cavity carcinoma. *Oral Oncol* 2009;45:908-911.
3. Lea J, Bachar G, Sawka AM, Lakra DC, Gilbert RW, Irish JC, et al. Metastases to level IIb in squamous cell carcinoma of the oral cavity: a systematic review and meta-analysis. *Head Neck* 2010;32:184-190.
4. Fan S, Tang QL, Lin YJ, Chen WL, Li JS, Huang ZQ. A review of clinical and histological parameters associated with contralateral neck metastases in oral squamous cell carcinoma. *Int J Oral Sci* 2011;3:1890-1891.
5. Xi S, Grandis J. Gene therapy for the treatment of oral squamous cell carcinoma. *J Dent Res* 2003;82: 11-16.
6. Pereira M, Oliveira D, Landman G, Kowalski L. Histologic subtypes of oral squamous cell carcinoma: prognostic relevance. *J Can Dent Assoc* 2007;73:339-344.
7. Parkin D, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2001. *CA Cancer J Clin* 2005;55:74-108.
8. Klein A. Parallel progression of primary tumours and metastases. *Nature reviews Cancer* 2009;3: 302-312.
9. Fidler I. Critical factors in the biology of human cancer metastasis: twenty-eighth GHA Clowes Memorial Award Lecture. *Cancer Res* 1990;50: 6130-6138.
10. Nguyen D, Massague J. Genetic determinants of cancer metastasis. *Nat Rev Cancer* 2007;8: 341-352.
11. Fidler I. Tumor heterogeneity and the biology of cancer invasion and metastasis. *Cancer Res* 1978; 38:2651-2660.
12. Mani SA, Guo W, Liao MJ, Eaton EN, Ayyanan A, Zhou AY, et al. The epithelial mesenchymal transition generates cells with properties of stem cells. *Cell* 2008;133:704-715.
13. Barnhart B, Simon M. Metastasis and stem cells pathways. *Cancer and Metastasis Rev* 2007;2: 261-271.
14. Barnhart B, Simon M. Metastasis and stem cells pathways. *Cancer and Metastasis Rev* 2007;26: 261-271.
15. Okamoto M, Ozeki S, Watanabe T, Lida Y, Tashiro H. Cervical lymph node metastasis in carcinoma of the tongue: correlation between clinical and histopathological findings and metastasis. *J Craniomaxillofac Surg* 1988;16: 31-34.
16. Weiss MH, Harrison LB, Isaacs RS. Use of decision analysis in planning and management strategy for the stage N0 neck. *Arch Otolaryngol Head Neck Surg* 1994;120: 699-702.
17. Ho CM, Lam KH, Wei WI, Lau SK, Lam LK. Occult lymph node metastasis in small oral tongue cancers. *Head Neck* 1992;14:359- 363.
18. Akhtar S, Ikram M, Ghaffar S. Neck involvement in early carcinoma of tongue. Is elective neck dissection warranted? *J Pak Med Assoc* 2007; 57(6):305-307.
19. González Moles M, Rodríguez Archilla A, Caballero R, Avila I, García Anillo M, et al. Estudio de los parámetros clínicos e histopatológicos del carcinoma epidermoide del cavidad oral. Implicaciones pronósticas. *Avances Odontostomatol* 1998;14:589-610.