

## Detection of Cervical Lymph Node Metastasis on Histopathology in Stage cN<sub>0</sub> after Elective Neck Dissection in Oral Carcinoma

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### ABSTRACT

**Objective:** To detect the frequency of lymph node micro-metastasis in clinically negative nodes (cN<sub>0</sub>) after elective neck dissection in patients of oral cavity carcinoma.

**Study Design:** Cross sectional descriptive study. This was a multi-center study conducted at four hospitals of Karachi, including Dow University Hospital, PNS Shifa Hospital, Zubaida Medical Center and Hashmani's Hospital, over a period of two years from June 2013 to June 2015.

**Materials and Methods:** A total of 48 patients were included in this study. Inclusion criterion was all patients of squamous cell carcinoma of the oral cavity with clinically negative nodes (cN<sub>0</sub>). Surgery was done in all the cases for the primary tumour as well as elective neck dissection. The neck specimen was sent for histopathology after marking the different level.

**Results:** The overall positive neck nodes were found in 17 out of total 48 cases (35.4%). The incidence was found to be highest in level II lymph nodes (64.7%) followed by level Ib lymph nodes (58.8%). Level IV lymph node was not involved in any case. Lower alveolus and palatal carcinoma has the highest incidence for nodal metastasis (50% each) followed by tongue (42.6%), upper alveolus (40%) and lowest in buccal carcinoma (22.7%).

**Conclusion:** The incidence of cervical lymph node metastasis in oral carcinoma is fairly high, so elective neck dissection should be routinely performed in oral carcinoma. Secondly most of the metastasis is in level I, II and III, so classical supra-omohyoid neck dissection is enough in most cases.

**Key words:** Oral carcinoma, neck dissection, supra-omohyoid neck dissection, squamous cell carcinoma

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### INTRODUCTION

Carcinoma of the oral cavity is the sixth most common cause of cancer related deaths around the globe<sup>1</sup> and it accounts for 200,000 deaths per year<sup>2</sup>. The most significant factor affecting the overall prognosis in oral carcinoma is still the presence of lymph node metastasis as a century ago<sup>3</sup>. If the cervical lymph nodes are involved by the tumour, the overall survival rate decreases about 50% regardless of the primary

tumour size<sup>4</sup>. In 1880, Kocher was the first surgeon who described the concept of removing the lymph nodes<sup>5</sup> while in 1906; George presented the technique of classical radical neck dissection and published a series of 132 cases<sup>6</sup>.

The commonly used tools in clinical practice for staging purpose, often cannot predict accurately about the absence of cervical lymph node metastasis<sup>7</sup>. Clinical examination of the neck, ultrasonography, CT scan and MRI, each have its own limitation with both false positive and false negative rates<sup>8</sup>. The most accurate method and the gold standard for the detection of cervical lymph node metastasis is the histopathology of the surgical specimen after elective neck dissection<sup>9</sup>. The management of clinically and radiologically negative cervical lymph nodes in patients of oral carcinoma especially in early cases remains a matter of debate. The majority of the studies favor the role of elective neck dissection for treatment of oral carcinoma in clinically negative nodes (cN<sub>0</sub>).

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The objective of the present study is to find out the frequency of positive micro-metastasis cases, in clinically negative cervical lymph nodes (cN0), operated by elective neck dissection along with the wide excision of the primary tumour with reconstruction.

## MATERIALS & METHODS

This study was conducted over a period of two years from June 2013 to June 2015 at four hospitals of Karachi including Dow University Hospital, PNS Shifa Hospital, Zubaida Medical Center and Hashmani's Hospital. A total number of 48 cases of oral carcinoma have been included where along with the surgery for primary tumour, elective neck dissection was performed. Sampling technique was convenient and sequential sampling.

### Inclusion criteria

Inclusion criteria included all cases of oral carcinoma with clinically negative neck nodes (cN0) where surgery was done for the primary tumour along with elective neck dissection.

### Exclusion criteria

Exclusion criteria from the study were as follows:

- Clinical suspicion of cervical lymph node metastasis.
- Detectable nodes on sonography of the neck
- Detectable nodes on CT scan of the neck with contrast.
- Patients whose histo-pathological report of the specimen of elective neck dissection was not available.

### Methodology

A detailed history and thorough clinical examination of the primary tumour and neck nodes palpation was done in all the cases after taking written informed consent and fulfilling all ethical considerations. Biopsy of the primary lesion was done and all the cases have squamous cell carcinoma. Ultrasonography of the neck was done in all the cases while CT scan with contrast was done in all the cases. Other baseline investigations for general anesthesia and surgery purpose were done in all the cases accordingly. Complete surgical excision of the primary tumour from buccal mucosa, lower and upper alveolus, palate and tongue with reconstruction was done in all the cases along with elective neck dissection. The extent of elective neck dissection from level I to IV was decided by the site and size of the primary tumour and per-operative assessment of the neck. The specimen of the neck dissection was marked for levels and sent for histo-pathology in all the cases. All the data was recorded and analyzed on SPSS version 15.

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Informed consent was obtained from all patients for being included in the study.

## RESULTS

A total of 48 cases of oral carcinoma have been included in this study after assessing the inclusion and exclusion criteria. There were 38 males (79.2%) and 10 female (20.8%) patients. The age ranges from 34 years to 66 years with the mean age of 49.35 years ( $\pm 8.06$ ). Fig. I demonstrate the age group and gender distribution of the patients in this study, where majority of the patients were in age group of 41 to 50 years (16 males and 4 females). Fig. II shows the site of primary tumour and its T status, where majority of the patients had T1 buccal mucosa tumour (10 males and 3 female patients). Out of 48 patients, 26 (54.2%) had T1 lesion while 19 (39.6%) had T2 and only 3 patients (6.3%) had T3 lesion. All the patients had no cervical or distant metastasis, either clinically or radiologically.

Elective neck dissection of level 1 to 3 was performed in majority of the cases (45 patients, 93.8%) while neck dissection from level 1 to 4 was done in 3 patients (6.3%). In 43 patients (89.6%) neck dissection was done on the ipsilateral side while bilateral neck dissection was done in 5 cases (10.4%). Overall cervical lymph node metastasis was detected on histo-pathology in 17 out of 48 cases (35.4%). Out of these 17 patients 9 (52.94%) had metastasis at only one level of lymph nodes while the 8 patients (47.06%) has more than one level of lymph nodes involved by the disease. Fig. III shows that level II lymph nodes were involved in majority of the cases i.e. 11 cases (41%), while level Ib was involved in 10 cases (37%), level Ia in 3 cases (11%) and level III in 3 cases (11%). Table I shows the details of level of lymph nodes involved along with their primary site and gender distribution.

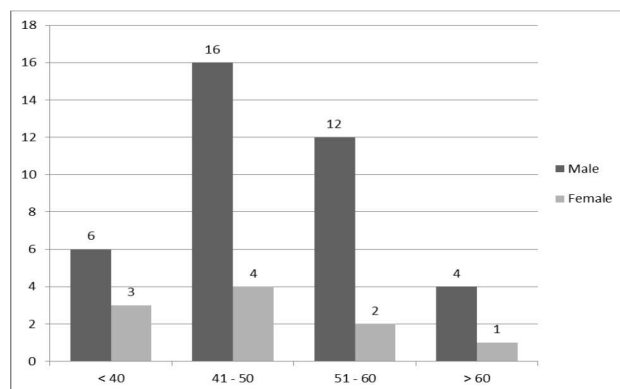


Fig. I: Age group and gender distribution (n = 48)

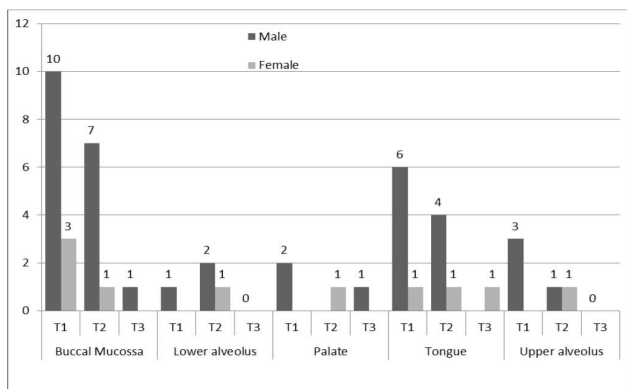


Fig. II: Site of primary tumour and its T status (n = 48)

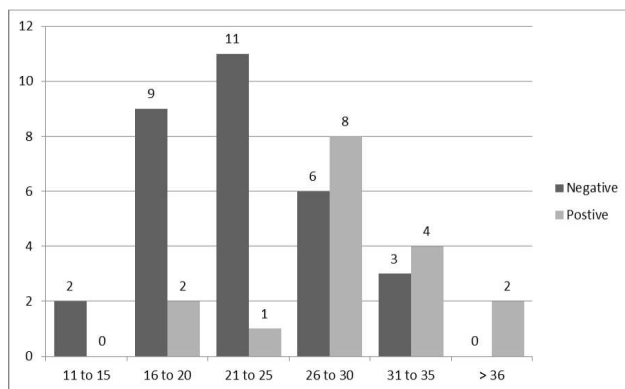


Fig. IV: Total number of lymph nodes identified on histo-pathology with negative or positive nodes

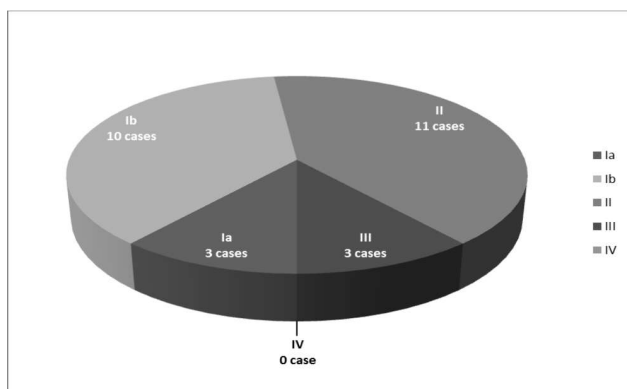


Fig. III: Levels of lymph nodes found positive for metastasis

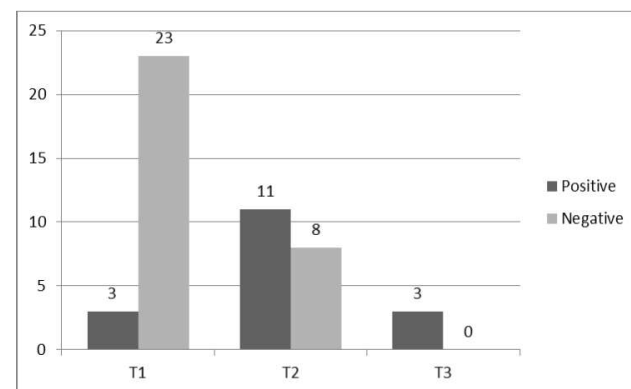


Fig. V: Relationship of T status of the primary lesion with negative or positive cervical lymph node metastasis (n=48)

Table I: Level of lymph nodes affected according to primary site and gender (n=48).

Lymph nodes level	Buccal mucosa		Lower alveolus		Palate		Tongue		Upper alveolus		Total
	M	F	M	F	M	F	M	F	M	F	
Ia	---	---	---	---	---	---	---	---	---	1	1
Ia, Ib	---	1	---	---	---	---	---	---	---	---	1
Ia, Ib, II	---	---	---	---	1	---	---	---	---	---	1
Ib	1	---	---	1	---	---	1	---	1	---	4
Ib, II	---	1	1	---	---	---	---	1	---	---	3
Ib, II, III	1	---	---	---	---	---	---	---	---	---	1
II	1	---	---	---	---	1	1	1	---	---	4
II, III	---	---	---	---	---	---	2	---	---	---	2
Total cases	3	2	1	1	1	1	4	2	1	1	17
Positive nodes	5 (22.7%)		2 (50%)		2 (50%)		6 (46.2%)		2 (40%)		
Total cases	15	2	2	0	2	0	6	1	3	0	31
Negative nodes	17 (77.3%)		2 (50%)		2 (50%)		7 (53.8%)		3 (60%)		
Total	18	4	3	1	3	1	10	3	4	1	48
	22		4		4		13		5		

The number of lymph nodes removed in each case varies from minimum of 14 nodes to maximum of 37 nodes with a mean of 25.10 (± 5.86). Total number of lymph nodes removed in all the cases were 1205. Fig. IV shows the relationship of number of lymph nodes removed with negative and positive nodes on histo-

pathology report. Fig. V shows the relationship of T status with positive or negative cervical lymph node metastasis. In T3 disease 100% of the patient showed nodal metastasis (3 out of 3). In T2 11 out of 19 (57.8%) had cervical metastasis while in T1 lesion only 3 had cervical metastasis out of 26 patients (11.5%).

## DISCUSSION

The biological behavior of squamous cell carcinoma of the oral cavity is uncertain and many of these tumours have an aggressive behavior in their early stage which results in early cervical lymph node metastasis<sup>10</sup>. Blood supply and lymphatic drainage of the oral cavity is very rich which promote early metastasis especially to draining lymph nodes. Occult or sub-clinical metastasis may be present in the draining lymph node which is otherwise not possible to detect on commonly used clinical and radiological assessment. Micro-metastasis is defined as tumour deposit in the lymph node, larger than 0.2 mm but not exceeding 2.0 mm. Isolated tumour cells (ITC) are small cluster of tumour cells smaller than 0.2 mm or cluster of cells not exceeding 200 cells in a single cross section<sup>11</sup>. The prognostic significance of isolated tumour cells (ITC) is not clear but the presence of micro-metastasis is clinically very significant<sup>12</sup>. The overall survival rate of patients with cN0 with micro-metastasis is worse as compared to patients without micro-metastasis<sup>13</sup>.

The management of patient of oral squamous cell carcinoma with clinically negative nodes is a controversial issue. Most of the studies favor elective neck dissection rather than wait and watch policy due to high incidence of occult or sub-clinical micro-metastasis. However on the other hand, theoretically many patients are being over treated by this elective neck dissection. The other newer option is sentinel lymph node biopsy, where the functional outcome and complications rates are much better than neck dissection<sup>14</sup>. If the sentinel biopsy comes positive than further neck dissection is required thus the patient is undergoing a second surgery. Another problem with this policy is the presence of skip metastasis which may not be diagnosed on sentinel lymph node biopsy but later on will lead to regional recurrence of the disease.

In our study cervical lymph node metastasis was detected in 17 patients out of 48 (35.4%) which is much similar to many international<sup>15-17</sup> and local cases studies<sup>18-19</sup>. The majority of the cervical metastasis in this study were found to be in level II nodes (11 out of 17 or 64.7%) followed by level Ib nodes (10 out of 17 or 58.8%). This is in accordance with another local study of Pakistan, where in squamous cell carcinoma of the tongue and floor of the mouth showed highest nodal metastasis of 30% in level I and II and 23% in level II alone<sup>10</sup>. In both level Ia and level III there were 3 cases each (17.6%) in our study. In three patient level IV lymph nodes were also removed due to per-operative suspicion of the disease but none of them found to be

positive on histo-pathology. This is also in accordance with the two local studies where no isolated involvement or skip lesion of level IV or V was found<sup>10,18</sup>.

According to the site of primary lesion, the incidence of positive nodes was highest in carcinoma of the lower alveolus and the palate (50% in each) followed by tongue (42.6%), upper alveolus (40%) and lowest in buccal carcinoma (22.7%, see table IV). The cervical lymph node metastasis incidence increases with the increase in the size of the primary tumour. In this study we also had the similar findings. In T3 disease 100% of the patient showed nodal metastasis (3 out of 3). In T2 lesions, 11 out of 19 (57.8%) showed cervical metastasis while in T1 lesion only 3 had cervical metastasis out of 26 patients (11.5%). This is in contrast with many studies who mentioned that the size of the primary tumour does affect the pattern of drainage to any specific level and the prevalence of cervical metastasis is not significantly co-related with the primary site and T status<sup>3,20,21</sup>.

Table V is showing that there was also a direct relationship of number of nodes removed with positive nodes histo-pathology in this study. The incidence of positive nodes was higher in group where the number of removed nodes was higher. The total number of lymph nodes in a specimen appears to be strongly dependent on the harvesting protocol and the extent of the neck dissection<sup>3</sup>. The mean number of lymph nodes removed in our study was 25.1, which is fairly similar to other studies<sup>3,22</sup>.

Patients with lateralized oral carcinoma have a very low rate of isolated contralateral neck metastasis. A recent study showed recurrence in the contralateral neck in 14 patients out of 481 (2.9%)<sup>23</sup>. In our study, bilateral neck dissection was done in 5 cases in which the primary disease was either close to midline or has crossed the midline but none of them found to be positive of histopathology. Patients with poorly differentiated carcinoma and pathologically proven ipsilateral neck metastasis are at significantly higher risk of contralateral failure.

## CONCLUSION

In our view overall incidence of cervical lymph node metastasis in oral carcinoma is fairly high in this study, so elective neck dissection should be performed routinely in all cases of oral carcinoma. Secondly most of the metastasis are in level I, II and III and no patient in this study had skip metastasis at level IV, so classical supra-omohyoid neck dissection is enough in most cases. Level IV or V lymph nodes should only be removed if there is any per-operative suspicion of the disease in these lymph nodes.

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