Pattern of Cervical Lymph Node Metastasis in Squamous Cell Carcinoma of Buccal Mucosa and Its Correlation for Optimal Neck Management

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ABSTRACT

Objective: To document cervical node metastasis in oral squamous cell carcinoma (OSCC) of buccal mucosa and analyze the oncological necessity of most suitable neck dissection, in population of a tertiary care hospital.

Study Design: Descriptive cross-sectional study.

Place and Duration of Study: Maxillofacial department, Abbasi Shaheed Hospital, Karachi Pakistan, from Jul 2018 to Jul 2020.

Methodology: It was a study of 110 histopathologically proven patients of Oral Squamous Cell Carcinoma of buccal mucosa. Non-probability sampling technique was used and sample size was calculated with help of WHO software using 8% prevalence of cervical metastasis in oral squamous cell carcinoma of buccal mucosa, 95% confidence interval, 7% margin of error. Patients aged 18-75 years, either gender, resectable tumor with or without lymph node involvement were included. Patients treated previously, with distant metastasis, unfit for general anesthesia and not willing to give consent were excluded. Tumor resection with selective neck dissection was done by one experienced surgeon and specimens were sent to same laboratory for histopathology. Data was collected on a proforma and analyzed using SPSS version 26.

Result: Out of 110 patients 93 (84.5%) were male and 17 (15.5%) were female. Mean age was 43 years ± 12.75. Occurrence of occult metastasis was 41.8%. According to histopathologically positive metastatic node, highest incidence was in level I 21 (19.1%) followed by levels I, II, III 12 (10.9%) and levels I-II 7 (6.4%), while positive levels I, II, III, IV were seen in only 2 (1.8%) cases.

Conclusion: Oral Squamous Cell Carcinoma of buccal mucosa is an aggressive pathology with high incidence of occult metastasis mainly involving level I, II, III, therefore selective neck dissection I-III should be performed routinely even in early-stage patients.

Keywords: Buccal mucosa, Cervical lymph nodes, Metastasis, Oral Squamous cell carcinoma (OSCC).

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INTRODUCTION

In head and neck region oral cavity is the most common subsite that harbors squamous cell carcinoma (SCC) and was attributed as a disease of elderly population in the past.[1] It is the eighth most common malignancy in the world but in Pakistan according to literature it is the second most common.[2-4]

The higher incidence of oral squamous cell carcinoma buccal mucosa (OSCC) in Indo-Pak is attributed to the cultural use of tobacco, betel quid, areca nut and gutka chewing, especially in younger age groups.[2,3]

Treatment modalities for management of oral squamous cell carcinoma of buccal mucosa include surgery, radiotherapy, chemotherapy or any combination of these modalities.[4] Treatment plan depends upon various factors such as site of tumor, size, proximity to bone, histological grade, depth of invasion, status of cervical lymph nodes and distant metastasis. Other factors which are considered in treatment planning are surgeon and patient related.[4]

In human body almost one third of the total lymph nodes are located in the head and neck region.[5] Just a single metastatic lymph node is associated with greater risk of recurrence and reduced rate of survival.[5] Survival rate in oral squamous cell carcinoma is strongly related to cervical metastasis. There are various predictive factors of cervical metastasis which include; site and size of tumor, depth of invasion, histological grading, perineural and perivascular invasion.[6] There have been a few studies regarding the nodal metastasis pattern of oral squamous cell carcinoma buccal mucosa in our population. It is described that 20-37% occult metastasis occurs in cervical lymph nodes in patients presenting with oral squamous cell carcinoma of buccal mucosa.[6] According to another study nodal metastases was most common in level I (100%), followed by level II (32%), level III (16%), and level IV (8%) respectively.[7]

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The treatment of neck nodes for oral squamous cell carcinoma has always been a topic of much controversy.[8] One school of thought among authors suggest that selective neck dissection in cN0/cN+ oral squamous cell carcinomais a safe management strategy. However, several studies support the idea of primary tumor resection followed by wait and watch policy before going for neck dissection.[8,9]

The aim of this study wasto analyze our data on the pattern of cervical lymph node metastasis and the distribution in different levels of neck nodes in patients with oral squamous cell carcinoma of buccal mucosa presenting to Abbasi Shaheed Hospital, Karachi, in order to develop a foundation based on findings of our local population for selecting the most suitable type of neck dissection during treatment planning.

METHODOLOGY

This descriptive cross-sectional study was conducted at the Department of Oral and Maxillofaical surgery, Abbasi Shaheed Hospital/Karachi Medical and Dental College, Karachi Pakistan, from July 2018 to July 2020. An approval of Institutional ethical and scientific review committee was taken before data collection (Ref: 005/18). A total of 110 patients of oral squamous cell carcinoma (OSCC) of buccal mucosa were included in the study using non-probability consecutive sampling technique, sample size was calculated with help of WHO software using 8% prevalence of cervical metastasis in oral squamous cell carcinoma of buccal mucosa, 95% confidence interval, 7% margin of error.[7] Informed consent was taken from all patients. Inclusion criteria was patientsaged 18-75 years, irrespective of gender,histopathologically proven cases of squamous cell carcinoma of buccal mucosa i.e. site of origin is buccal mucosa, clinical tumor size T1 to T4a (resectable tumor), with or without clinical lymph node involvement cNo, cN+. Exclusion criteria consisted of patients who werepreviously treated (surgery or irradiated), had systemic metastasis (detected on radiological investigations) orunfit for general anesthesia.

After a detailed history and clinical examination including palpation of cervical lymph nodes and radiological investigations, patients fulfilling inclusion criteria were admitted and prepared for surgery. Grading of the tumor among all patients was done according to the American Joint Committee on Cancer (AJCC) 8th edition Tumor, Node , Metastasis (TNM) classification.

One experienced surgeon performed tumor resections along with selective neck dissection. In cN0 patients the extent of selective neck dissection was level I-III and upto level I-IV in cN+ patients. Silk orientation sutures were placed for markings of primary tumor and neck node specimens i.e., level I marked with one silk suture, level II with two silk sutures, level III with three silk sutures and level IV with four silk sutures respectively. The marked specimens were placed in formalin and sent to the same laboratory along with biopsy form for histopathological examination in which presence or absence of metastatic tumor cells was noted in different levels of cervical lymph nodes. The demographic variables (i.e. age, gender) and all above information was recorded on a profoma.

Data was analyzed using SPSS version 26. Mean and ± standard deviation (SD) was calculated for quantitative variable like age. Frequencies and percentages were computed for qualitative variable like gender, affected side, tumor size, clinical node status and lymph node level involved by metastasis. Cervical metastasis was stratified by tumor size and pathological neck node level involved. Post stratification chi-square test was applied keeping *p*-value ≤0.05 as significant.

RESULTS

Hundred and ten patients of oral squamous cell carcinoma of buccal mucosa were included. There were 93 (84.5%) male patients and 17 (15.5%) female patients. Mean age of the patients was 43 years ± 12.75. Maximum age was 72 years and minimum age was 23 years. The frequency of oral squamous cell carcinoma with gender distribution of the study participants according to age groups is illustrated in Figure.

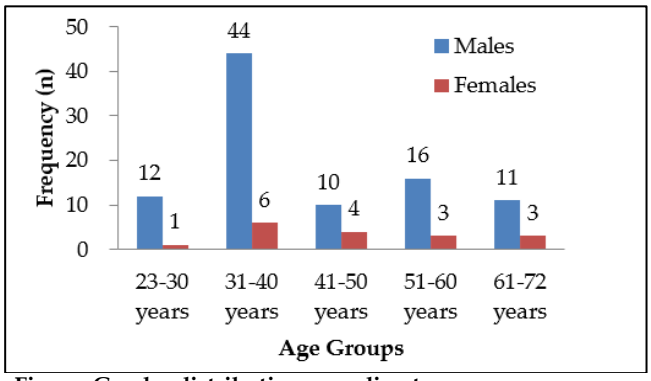

Figure: Gender distribution according to age groups.

The baseline properties of the patients included in study are summarized in Table-I. According to metastatic lymph node, the highest incidence of histopathologically positive lymph node level was level I 21 (19.1%) followed by positive levels I, II and III 12 (10.9%) and on third number was positive levels I and II 7 (6.4%) while only 2 (1.8%) cases were of positive

levels I, II, III and IV lymph node levels (Table-II). Out of 26 (29.5%) of clinical neck negative patients cN0 had cervical metastasis, mostly in only one cervical level (12.5%). Level IV was not found positive in T3 and T2 lesions (Table-III).

Table-I: Baseline properties.

Baseline Properties	Oral Squamous Cell Carcinoma of Buccal Mucosa, n (%)
Mean Age ± SD Range (min-max)	43 years ± 12.749 23-72 years
Gender	
Male	93 (84.5%)
Female	17 (15.5%)
Laterality of Tumor	
Right side	58 (52.7%)
Left side	52 (47.3%)
Tumor Size	
T1	10 (9.1%)
T2	42 (38.2%)
T3	35 (31.8%)
T4	23 (20.9%)
Clinical node status	
cN0(clinical neck nodes negative)	88 (80%)
cN+ (clinical neck nodes positive)	22 (20%)
Pathological node status	
pN0 (pathological neck nodes negative)	64 (58.2%)
pN+ (pathological neck nodes positive)	46 (41.8%)

Table II: Metastatic lymph node levels.

Metastatic Lymph Node Levels	n (%)
None	64 (58.2%)
I	21 (19.1%)
I, II, III	12 (10.9%)
I, II	7 (6.4%)
I, II, III, IV	2 (1.8%)
II	2 (1.8%)
I, III	1 (0.9%)
II, III	1 (0.9%)

The association between T and metastatic node, showed that the incidence was highest in T4a n=19/23 level I was 6/19 (31.5%), level I, II was 3/19 (15.7%), level I, II, III was 4/19 (21%) and level I, II, III, IV was 2/19 (10.5%). For T3 n=19/35 nodal metastasis in level I was 10/19 (52.6%), Level I, II was 2/19 (10.5%) and level I, II, III was 7/19 (36.8%). T2 n=8/42 lesions metastasis in level I was 5/8 (62.5%), level I, II was 2/8 (25%) and level I, II, III was 1/8.

DISCUSSION

The treatment success of oral squamous cell carcinoma pivots around the optimal management of cervical neck nodes, as occult metastasis is prevalent in OSCC and it is the prime prognostic indicator.[10] OSCC buccal mucosa has a slightly lower incidence of neck metastasis as compared to tongue, floor of the mouth and dento-alveolar gingiva.[11] Evidence based knowledge in local population about predictability of nodal spread of a tumor helps in formulating an adequate treatment plan and increases chances of a disease free survival.

Interestingly, the present study showed that most of the cases 63 (57.3%) were reported in younger age groups i.e. between 23-40 years. This is alarming as the findings of previous studies show more cases in middle age population.[12] The mean age was 43 years in our sample. In contrast, a study by Caritiet al6 shows mean age to be 60.13 and Essig *et al*,[7] reported that the mean age was 56.5 years.

The present study documents that most tumors were located in the right buccal mucosa 58 (52.7%) while 52 (47.3%) were on the left side. Our study showed a prevalence of male patients 84.5%, as compared to female patients 15.5%. These findings are same as reported in previous studies and can be attributed towards a more common habit of betel quid chewing and smoking in males.[3,13]

In general, for OSCC literature documents that the rate of locoregional spread of metastasis to cervical nodes is 34-50%.[13] According to studies by Sagheb *et al*,[14] and Cariti *et al*,[6] OSCC buccal mucosa presents with regional metastases in 24-32% cases which is quite lower as reported for OSCC tongue 37-55% and floor of mouth 10-65% respectively. In present study, a much higher incidence of cervical lymph node metastasis was present in 41.8% of cases.

Our results show a significant difference between the clinical versus pathological neck node metastasis

Table-III: Association between tumor size and metastatic neck levels.

Tumor Size	Neck Levels									*p*-value
	None	I	II	I, II	I, II, III	I, II, III, IV	I, III	II, III	Total	
T1	10 (100%)	-	-	-	-	-	-	-	10	<0.001
T2	34 (81%)	5 (62.5%)	-	2 (25%)	1 (12.5%)	-	-	-	42	
T3	16 (45%)	10 (52.6%)	-	2 (10.5%)	7 (36.8%)	-	-	-	35	
T4a	4 (17.1%)	6 (31.5%)	2 (10.5%)	3 (15.7%)	4 (21%)	2 (10.5%)	1 (5.3%)	1 (5.3%)	23	

status, 80% were cN0 and 20% were cN+ cases, whereas 58.2% had pN0 disease while 41.8% had pN+ disease. We found that 26 (29.5%) of clinical neck negative patients cN0 had cervical metastasis, mostly in only one cervical level. On the other hand metastatic lymph nodes were present in 20 (90.9%) clinical neck positive patients cN+ and it was observed that more than one cervical level had nodal metastasis. Above-mentioned results coincide with the findings reported by Patil *et al,*[13] in their study.

Studies on OSCC buccal mucosa report that tumor size is one of the main prognostic factors.[15] Majority of the cases in our sample were T2 sized lesions followed by T3, T4a and T1 in descending order. These findings differ substantially from a study which document 64.2% cases in T1/T2 sized lesions while only 35.9% cases presented as T3/T4 lesions.[6] In OSCC due to its aggressive nature cervical lymph node metastasis can occur in T1 or T2 cases as reported in different studies.[11,15] It has been highlighted in literature that even small lesions pose a great threat of nodal spread16. However, according to the present study T1 cases were free of nodal involvement, whereas metastasis was found in 19% T2 cases.

The lymph flow pattern is well-delineated and the patterns of nodal metastasis from a primary squamous cell carcinoma of oral cavity have shown cervical lymph node levels I, II and III to be at a higher risk.[17] Lymph from buccal mucosa enters primarily into submandibular nodes (level I) and then descends into superior jugular nodes (level II).[18] We document in the ipsilateral neck isolated level I (19.1%) was the most common, followed by level I-III (10.9%).

The rate of skip metastasis in OSCC buccal mucosa is very rare and sparsely reported in literature.[19] In present study 4 (3.6%) cases of skip metastasis to level II and III were recorded, isolated level IV involvement was not seen in any case.

The doctrines of neck dissection have been evolving over the years, starting from a more radical approach to an inclination towards selectivity of removal of the known neck node levels at risk.[20] D'Cruz *et al,*[21] in a study found that a reduced proportion of patients 9.9% developed nodal recurrence who underwent elective neck dissection as compared to 42.5% in the patients who were kept under observation of the neck. Another argument regarding the decision to perform elective neck dissection in clinically neck negative patients is based on the incidence of occult metastasis if it is greater than 20%.[22] In our study level IV involvement was seen in only 1.8% cases, another study reported that the incidence of level IV involvement inclinically neck positive patients of OSCC buccal mucosa is very low.[7] Henceforth, removal of level IV in all cN+ cases seems unnecessary in buccal mucosa cancer unless there is a strong clinical or radiological indication of metastasis.

In the light of existing literature and our findings we recommend selective neck dissection level I, II, III as an optimal treatment modality for OSCC buccal mucosa. As this disease has become more common in younger population,therefore patients will benefit from an early intervention with neck dissection focused at the lymph nodes levels at high risk. A few limitations of our study include small sample of patients presenting at a single center, short study duration which does not include long term follow up for 5 years to ascertain the benefit of selective neck dissection in terms of quality of life and rate of survival.

CONCLUSION

Oral squamous cell carcinoma of buccal mucosa is an aggressive pathology with high incidence of occult metastasis mainly involving level I, II, III. Furthermore, this study emphasizes that selective neck dissection I-III should be considered as a routine management strategy even in early-stage patients of OSCC buccal mucosa.

Conflict of Interest: None.

Authors' Contribution

SHR:, SA:, MT: Conception or design of work, acquisition, analysis, or interpretation of data drafting or revising it critically, final approval agreement to be accountable for all aspects of work.

REFERENCES

1. Kruaysawat W, Aekplakron W, Chapman RS. Survival, time, prognostic factors of oral cancer in Ubon Ratchatani Cancer Center. J Med Assoc Thai 2010; 93(3): 278-284.
2. 2.Akram S, Mirza T, Mirza MA, Qureshi M. Emerging patterns in clinico-pathological spectrum of Oral Cancers. Pak J Med Sci 2013; 29(3): 783.
3. Bhurgri Y, Bhurgri A, Hussainy AS, Usman A, Faridi N, Malik J, et al. Cancer of the oral cavity and pharynx in Karachi-identification of potential risk factors. Asian Pac J Cancer Prev 2003; 4(2): 125-130.
4. Bhurgri Y, Bhurgri A, Pervez S, Bhurgri M, Kayani N, Ahmed R, et al. Cancer profile of Hyderabad, Pakistan 1998-2002. Asian Pac J Cancer Prev 2005; 6(4): 474.
5. Thakare E, Gawande M, Chaudhary M. Detection of micrometastasis in lymph nodes of oral squamous cell carcinoma: A comparative study. J Oral Maxillofac Pathol 2013; 17(3): 374–380.
6. Cariati P, Cabello Serrano A, Marin Fernandez A, Julia Martinez M, Fernandez Solis J, Martinez Lara I. Behavior of buccal mucosal squamous cell carcinoma: a retrospective study of 53 carcinomas of this anatomical region. Craniomaxillofac Trauma Reconstr 2019; 12(1): 8-13.

7. Essig H, Warraich R, Zulfiqar G, Rana M, Eckardt AM, Gellrich NC, et al. Assessment of cervical lymph node metastasis for therapeutic decision-making in squamous cell carcinoma of buccal mucosa: a prospective clinical analysis.World J Surg Oncol 2012; 10(1): 1-6.
8. 8.Rani P, Bhardwaj Y, Dass PK, Gupta M, Malhotra D, Ghezta NK. Neck dissection for oral squamous cell carcinoma: our experience and a review of the literature. J Korean Assoc Oral Maxillofac Surg 2015; 41(6): 299-305.
9. Qureshi S, Tirmizi S, Hussain A, Rehman A. Is supraomohyoid neck dissection effective in clinically negative node in T3 and T4 oral tumor.Pak J otolaryngol 2007; 23(2): 71-73.
10. Ahmed SQ, Junaid M, Awan S, Choudhary MM, Kazi M, Masoom A, et al. Relationship of tumor thickness with neck node metastasis in buccal squamous cell carcinoma: an experience at a tertiary care hospital. Int Arch Otorhinolaryngol 2017; 21(3): 265-269.
11. Massey C, Dharmarajan A, Bannuru RR, Rebeiz E. Management of N0 neck in early oral squamous cell carcinoma: a systematic review and meta-analysis. Laryng 2019; 129(8): E284-298.
12. Warnakulasuriya S. Global epidemiology of oral and oropharyngeal cancer. Oral Oncol 2009; 45(4): 309-16.
13. Patil LS, Arjun MA, Hanumanthappa BN. Clinico-pathological correlation of pattern of cervical lymph node metastases in oral cavity cancers. Int J Surg 2019; 3(1): 337-44.
14. Sagheb K, Blatt S, Kraft IS, Zimmer S, Rahimi-Nedjat RK, Al-Nawas B, et al. Outcome and cervical metastatic spread of squamous cell cancer of the buccal mucosa, a retrospective analysis of the past 25 years. J Oral Pathol Med 2017; 46(6): 460-464.
15. DeConde A, Miller ME, Palla B, Lai C, Elashoff D, Chhetri D, et al. Squamous cell carcinoma of buccal mucosa: a 40-year review. Am J Otolaryngol 2012; 33(6): 673-677.
16. Huang SF, Tung-Chieh Chang J, Liao CT, Kang CJ, Lin CY, Fan KH, et al. The role of elective neck dissection in early stage buccal cancer. Laryng 2015; 125(1): 128-133.
17. Farmer RW, McCall L, Civantos FJ, Myers JN, Yarbrough WG, Murphy B, et al. Lymphatic drainage patterns in oral squamous cell carcinoma: findings of the ACOSOG Z0360 (Alliance) study. Otolaryngol Head Neck Surg 2015; 152(4): 673-677.
18. Chakraborty PS, Das AK, Vatsyayan A, Rahman T, Das R, Medhi SK et al. Metastatic involvement of level IIb nodal station in oral squamous cell carcinoma: A clinicopathological study. Natl J Maxillofac Surg 2019; 10(1): 8-12.
19. Patel S, Singh I, Gulati A, Khurana N. A Study on Neck Nodes in Oral Cancers, with Special Reference to Skip Metastasis. Ind J Otolaryngol Head Neck Surg 2019; 71(1): 474-481.
20. Thiele OC, Seeberger R, Flechtenmacher C, Hofele C, Freier K. The role of elective supraomohyoidal neck dissection in the treatment of early, node-negative oral squamous cell carcinoma (OSCC): a retrospective analysis of 122 cases. J Craniomaxillofac Surg 2012; 40(1): 67-70.
21. D'Cruz AK, Vaish R, Kapre N, Dandekar M, Gupta S, Hawaldar R, et al. Elective versus therapeutic neck dissection in node-negative oral cancer. N Engl J Med 2015; 373(6): 521-529.
22. Capote A, Escorial V, Muñoz-Guerra MF, Rodríguez-Campo FJ, Gamallo C, Naval L. Elective neck dissection in early-stage oral squamous cell carcinoma-does it influence recurrence and survival?. Head Neck 2007; 29(1): 3-11.