

Patterns of Lymph Node Metastasis in Buccal Carcinoma

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Abstract

Buccal carcinoma appears to be the most frequent malignant neoplasm of the oral cavity in South Asia, particularly in Bangladesh, because of widespread consumption of tobacco and betel nut. Lymph node metastasis is an important factor for prognosis, staging and planning of treatment in buccal carcinoma. A cross-sectional, descriptive study was conducted in the Department of ENT and Head-Neck Surgery, in collaboration with the Department of Pathology, Dhaka Medical College Hospital, Bangladesh, to evaluate the pattern, rate and distribution of metastasized lymph nodes in patients with buccal carcinoma. Between January 2023 and December 2024, a total of 57 histopathologically proven cases of buccal carcinoma were included in the study. Nodal involvement was determined using clinical examination, radiological review and histopathological evidence. The mean age of the patients was 53.7±9.6 years and male-female ratio was 3:1. Out of 57 patients, 35(61.4%) had histopathologically confirmed lymph node metastasis, while 22(38.6%) showed no nodal involvement. Among those with metastasis, unilateral cervical lymph node involvement was most frequent (52.6%), while bilateral metastasis was found in 8.8% of patients. Level I (submandibular) lymph nodes were the most commonly affected, observed in 40.3% of patients, followed by Level II (upper deep cervical) nodes in 29.8%. Involvement of Level III nodes was seen in 15.7%, and only a few patients showed metastasis to Levels IV and V (7% and 3%, respectively). 15 out of 20 Stage III patients (75%) and 14 of 17 Stage IV patients (82.3%) had nodal metastasis, whereas only 6 of 20 patients (30%) in Stage II exhibited nodal spread. Poorly differentiated carcinomas showed the highest incidence of nodal involvement (77%) compared to moderately (54%) and well-differentiated tumors (29%).

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Introduction

Buccal carcinoma, which is a predominant form of oral squamous cell carcinoma (OSCC) poses a severe global health challenge in the majority of developing countries, particularly in South and Southeast Asia. Oropharyngeal tumors represent 30-40% of head and neck cancers in this area, with buccal carcinoma among the most common subtypes.^{1,2} It is well known to have high prevalence in countries such as Bangladesh, India and Pakistan where the habit of chewing betel quid, areca nut, tobacco and slake lime is common. Nitrosamines and polycyclic aromatic hydrocarbons are potential carcinogens in these materials, whose chronic epithelial irritation and genetic mutations play a role in malignant transformation.³ In the case of Bangladesh, poor oral hygiene, low socioeconomic status and delayed presentation to treatment which lead to advanced stage at diagnosis makes the matter

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worse.^{4,5} Buccal mucosa is sensitive to malignant transformation, secondary to chronic exposure of the mucosa to mechanical or 10 chemotherapeutic treatments at first visit chemical irritants. The carcinoma commonly starts with leukoplakia or non-healing ulcers on the buccal mucosa which develop gradually into infiltrative lesions affecting deeper tissues. After the tumor breaks through the basement membrane, lymphangiogenesis also plays a crucial role in association with metastasis.^{6,7} Lymphatic spread of the buccal mucosa is mainly to submandibular and upper deep cervical lymph nodes, which are the most frequent site for secondary deposits. Thus, the status of lymph node metastasis is an important predictor that has a major impact on both disease stage and treatment outcomes.⁸ Lymph node metastasis not only reflects the progression of disease, but also has an influence on patient survival and recurrence. Survival has been significantly lower in patients with nodal involvement.⁹ The complex anatomy of the cervical lymph node compartment enables tumor cells to be disseminated through multiple pathways, which leads to different metastatic distributions according to primary site location, size and biological behavior.^{10,11} Involvement of Level I and II nodes is most common in buccal carcinoma, while Level III nodes or contralateral side may also be involved in later stages.¹² A knowledge of these patterns is important for surgical oncologists to determine how extensively the neck should be treated, without under-treating or providing excess morbidity with an extensive operation. Apart from anatomic factors, many histopathologic and molecular variables influence the prognosis of buccal carcinoma. Tumor thickness, non-pharmacological methods (NPMs), poorly differentiated tumors, perineural invasion (pNI), LVE and tumor 4mm have been found as highly correlated with nodal

spread.^{13,14} Only few studies have investigated regional spread pattern in buccal carcinoma in Bangladesh. This investigation will therefore provide critical information on the incidence, distribution and association of lymph node metastasis with various clinical and pathological factors among patients in Dhaka Medical College Hospital, one of the largest tertiary hospitals in Bangladesh. The results from the study can serve as evidence-based knowledge to optimize the surgical practice, especially for individualized selection between elective neck dissection and prognostic estimation on buccal carcinoma treatment.

Methods

This cross-sectional, descriptive study was conducted in the of Department of ENT and Head-Neck Surgery in collaboration with the Department of Pathology, Dhaka Medical College Hospital, Bangladesh over a period of 2 years from January 2023 to December 2024. A total of 57 patients were enrolled with confirmed histopathology of buccal carcinoma. We included men and women of 30-80 years. Demographic profile, clinical history, hazards like tobacco chewing/smoking/betel nut use and information on tumor presentation and duration were documented. All patients were subjected physical examination focusing on oral cavity examination and palpation of cervical lymph nodes. Diagnostic imaging with USG, CT or MRI scans were used to assess the primary tumor extent and nodal involvement.

Our inclusion criteria were patients aged 18 years or older with histologically confirmed squamous cell carcinoma of the buccal mucosa, newly diagnosed, previously untreated cases, and who consented to surgical intervention and follow-up. Exclusion criteria were: patients with recurrent buccal carcinoma or

prior head and neck malignancy, those who had undergone previous head and neck surgery, chemotherapy, or radiotherapy, already having distant metastases, and non-squamous histological variants or secondary malignancies involving the buccal mucosa. Radiologic evaluation was then performed to identify the extent of tumor and cervical node involvement. According to the TNM stage, patients were treated by surgery (wide local excision of the primary and neck dissection – selective, modified or radical). Immediately after operation, all resected specimens were fixed in 10% formalin and sent for histopathological examination. The lymph nodes of neck dissection specimens were meticulously dissected and classified according to the American Head and Neck Society (AHNS) classification system by anatomical level (I–V). Metastasis, extracorporeal organ support (ECOS) and perineural Invasion (pNI) were assessed microscopically with H&E staining. Clinicopathological features which included tumor size, histologic grade, perineural invasion and lymphovascular invasion were recorded. The TNM staging was according to the American Joint Committee on Cancer (AJCC), 8th edition. A particular focus was on assessing the presence of occult lesions in clinically node-negative (N0) patients.

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) version 26.0 for Windows (IBM Corp., Armonk, NY, USA). Descriptive statistics including frequency and percentage was calculated to express demographic and clinical variables. Data was presented in tabulated form.

The study was approved by the Ethical Review Committee of Dhaka Medical College, Dhaka, Bangladesh.

Results

The age of the patients ranged from 30 to 80 years, with a mean age of 53.7 ± 9.6 years. The majority of the patients (61.4%) were between 50 and 65 years of age. A significant male predominance was observed, with 43 males (75.4%) and 14 females (24.6%), resulting in a male-to-female ratio of approximately 3:1 (Table-I). Out of 57 cases, 35(61.4%) had histopathologically confirmed lymph node metastasis, while 22(38.6%) showed no nodal involvement (Table-II). Among those with metastasis, unilateral cervical lymph node involvement was most frequent (52.6%), while bilateral metastasis was found in 8.8% of patients. Level I (submandibular) lymph nodes were the most commonly affected, observed in 40.3% of patients, followed by Level II (upper deep cervical) nodes in 29.8%. Involvement of Level III nodes was seen in 15.7%, and only a few patients showed metastasis to Levels IV and V (7% and 3%, respectively). 15 out of 20 Stage III patients (75%) and 14 of 17 Stage IV patients (82.3%) had nodal metastasis, whereas only 6 of 20 patients (30%) in Stage II exhibited nodal spread (Table-III). Poorly differentiated carcinomas showed the highest incidence of nodal involvement (77%) compared to moderately (54%) and well-differentiated tumors (29%) (Table-IV).

Table-I: Age and gender distribution of patients with buccal carcinoma (n=57)

Variables	Frequency	Percentage
Age group (in years)		
30–39	5	8.8
40–49	10	17.5
50–59	24	42.1
60–69	11	19.3
≥70	7	12.3
Gender		
Male	43	75.4
Female	14	24.6

Table-II: Distribution of tumor stage and nodal involvement (n=57)

Stage	Total Case	Nodal Metastasis	Percentage
Stage II	20	6	30.0
Stage III	20	15	75.0
Stage IV	17	14	82.3

Table-III: Frequency of metastasis in cervical node levels

Node Level	Frequency	Percentage
Level I (Submandibular)	23	40.3
Level II (Upper Deep Cervical)	17	29.8
Level III (Mid-Jugular)	9	15.7
Level IV (Lower Jugular)	4	7.0
Level V (Posterior Triangle)	2	3.5

Table-IV: Distribution of tumor grade with lymph node metastasis

Tumor grade	Total case	Cases with metastasis	Percentage
Well differentiated	21	6	28.6
Moderately differentiated	24	13	54.2
Poorly differentiated	12	9	75.0

Discussion

Lymph node involvement is still one of the most important prognostic factors for survival and rate of recurrence in buccal cancer. The current study found lymph node metastases in 61.4% of patients, in agreement with other regional and international studies.^{11,12} This is in that it emphasize the aggressive characteristic of buccal squamous cell carcinoma (SCC) and its early spread to lymphatics. The predilection of metastasis in level I and II is in agreement with the predictable lymphatic drainage of

buccal mucosa, thus confirming findings reported in the previous studies that the first that submandibular and upper deep cervical nodes are the most frequent metastatic stations.^{8,13} The lower percentage found in our study for levels IV and V serve to harden the idea of a step-by-step lymphatic spread of buccal carcinoma within the cervical chain.

The pattern and incidence of lymph node metastasis are influenced by several factors, such as tumor size, depth of invasion, histological differentiation and perineural or lymphovascular invasion.¹⁴ In the current analysis, poorly differentiated tumours showed significantly greater rates of nodal metastasis (75%), consistent with several previous reports.^{11,13,15} Moreover, tumor stage was strongly positively associated with nodal involvement; Stage II and IV tumors had far higher rates of metastasis than early-stage lesions. Our data is consistent with the previous study results. Significantly, perineural and lymphovascular invasion were associated with nodal metastasis.^{12,15} These findings are well-established indicators of tumor aggressiveness, reflecting the potential of cancer cells to invade neurovascular spaces and access regional lymphatics.^{12,16} The presence of these features on histopathology must indicate clinicians to take more aggressive approach in surgery and adjuvant treatment. In addition, occult metastasis in patients with clinically node-negative (N0) disease was also significant and suggests that clinical examination or imaging underestimates the actual nodal burden.^{8,14} Male predominance as found in the present study, which in agreement with gender-based exposure to carcinogenic agents inhaled from air, particularly a fact that have been observed an epidemiologically around South Asia.^{9,11} Our results also affirmed the importance of early screening and public health intervention to reduce exposure to oral carcinogens. National health campaigns focusing on

prevention of tobacco and betel nut would have a positive impact, as life-style habits were associated with buccal carcinoma occurrence. In addition, it is crucial to establish multidisciplinary management among surgeons, pathologists, and oncologists to attain the best treatment results. To summarize, this series confirms the anatomically predictable pattern of metastatic lymph nodes in buccal carcinoma predominantly at Levels I and II with increasing incidence in progressive and undifferentiated tumors. Awareness of these trends can help the surgeon in deciding what would be the best extent of neck dissection and also for planning individualized therapeutic interventions to achieve overall survival benefit and minimize recurrence.^{14,16}

Despite the useful findings from this study, a few limitations need to be considered. Potential limitations include a small sample size of 57 patients for application to the population at large. Further multicentric studies are warranted to validate the trends obtaining and establish patterns of lymph nodal metastasis in buccal carcinoma. Secondly, the study was single-institution in Dhaka Medical College with regional differences in lifestyle, genetic susceptibility and environmental effects. Therefore, the broader disease spectrum could be reflected by aggregated data from several centers from across Bangladesh and other South Asian countries. Furthermore, this study was mostly based on clinical, radiological, and histopathological findings instead of employing advanced diagnostic tools (like positron emission tomography-computed tomography (PET-CT)) or molecular marker analysis the use of which could not be implemented mainly because financial and resource constraints. The lack of such state-of-the-art tools may have resulted in under detection of micro metastases or skip lesions that could not be identified by conventional imaging or routine

histopathology. Over that same period, long-term follow-up of patients for survival study, the rate of relapse and disease-free interval were not incorporated into the study so as to evaluate impact over time was restricted.

Conclusion

Results from the present study conclusively reveal extensive metastasis in lymph nodes among individuals afflicted with buccal carcinoma, mostly submandibular (Level I) and upper deep cervical (Level II). This patterned spread helps to demonstrate the lymphatic drainage of the buccal mucosa and highlights the need for regional staging at diagnosis. The results also confirm that more advanced T-stage, deeper tumor invasion and poorer histological differentiation are powerful independent predictors of nodal metastasis demanding strict treatment policy. On the clinical side, this study highlights the importance of diligent preoperative work-up and collaboration between surgeons and pathologists for optimal patient management. The relatively high incidence of nodal involvement, even among clinically node-negative (N0) patients, suggests potential benefits for elective neck dissection in some of these individuals. This approach may limit regional recurrence, improve local disease control, and result in better survival. Additionally, histopathological characteristics including perineural and lymphovascular invasion need to be identified as high-risk features for which treatment should be aggressive with intimations of close follow-up.

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