

# Squamous cell carcinoma of upper alveolus: An experience of a tertiary care center of Northeast India

Nizara Baishya, Tashnin Rahman, Ashok Kumar Das, Chandi Ram Kalita<sup>1</sup>, Jagannath Dev Sharma<sup>2</sup>, Manigreeva Krishnatreya<sup>3</sup>, Amal Chandra Kataki<sup>4</sup>

## Abstract

**Objective:** The main objective of this study was to analyze the clinical behavior and the impact of nodal metastasis on the prognosis of upper alveolus squamous cell carcinoma (SCC). **Materials and Methods:** The medical records of 110 patients with SCC of the upper alveolus (International Classification of Diseases-10-C03.0) diagnosed during 2010–2015 were reviewed. Survival analysis was done using the Kaplan–Meier method and was compared using log rank-test.  $P < 0.05$  was considered statistically significant. **Results:** Of the 110 patients, 59 were males and 51 were females. Forty-six (41.8%) patients presented with lymph node metastasis. Fifty-three (51.8%) patients presented in Stage IVA, thirty (27.3%) patients in Stage IVB, ten (9.1%) patients in Stage III, 12 (10.9%) patients in Stage II. The 5-year overall survival (OS) was 71.1% in Stage II, in Stage III it was 65.6%, in Stage IV it was 56.7%, and in Stage IVB it was 19.4% ( $P = 0.02$ ). The 5-year OS for node negative compared with node positive was 66.3% versus 37.3%, respectively ( $P = 0.019$ ). **Conclusion:** Presence of lymph node metastasis is associated with lower survival rates. Adequate surgical resection with adjuvant treatment, where necessary, offers the best chance of disease control.

**Key words:** Aggressive, cancer, neck node, prognosis, upper alveolus

## Introduction

Head-and-neck cancers (HNCs) are the sixth most common malignancy worldwide. Approximately, half of the reported head and neck malignancies are oral cavity squamous cell carcinomas (SCCs), with an estimated 300,000 new cases every year globally.<sup>[1]</sup> Oral cancer (OC) is a common cancer in the Southeast Asia region. According to the National Cancer Registry Programme of India, among males, Ahmedabad Urban Cancer Registry and East Khasi Hills Cancer Registry in females have recorded the highest age-adjusted incidence rates of OC.<sup>[2]</sup> This higher prevalence of OC may be attributed to the high consumption of areca nut and tobacco in any form in these regions. Because of the close proximity of the upper alveolar (ridge) mucosa with the upper gingivo-buccal sulcus or the upper part of the buccal mucosa, cancer of the upper alveolus may spread to these adjacent sites and thus making it difficult to localize the exact origin of the disease.<sup>[3]</sup> Upper gingival cancers accounted for only 3.5% of all OCs.<sup>[4]</sup> SCC of the oral cavity has a predilection for regional lymph node metastasis. However, only few studies have been conducted regarding the regional metastasis of SCC upper alveolus.<sup>[5]</sup> Upper gingival–buccal cancers (UGBCs) are biologically more aggressive than lower gingival–buccal cancers, which have a comparatively better disease-free survival even in advanced stages.<sup>[6]</sup> The aggressive behavior is possibly because of late presentation of UGBC and early invasion of the infratemporal fossa.<sup>[3]</sup> We herein present our 6-year experience of treating upper alveolus at a tertiary care cancer center.

## Materials and Methods

The study has been approved by the Institutional Ethics Committee of the institute. The study was a retrospective analysis of patients with SCC upper alveolus (International Classification of Diseases-10 [ICD-10]-C03.0) diagnosed from January 1, 2010 to December 31, 2015, in a tertiary care cancer center in the North East India. A total of 194 patients with SCC upper alveolus

were diagnosed in the study period. Each patient's medical records were reviewed for clinical and demographic parameters. Staging was performed according to the criteria for OC developed by the American Joint Committee on Cancer 7<sup>th</sup> Edition.

## Inclusion criteria

1. Previously untreated patients
2. Histologically proven SCC
3. Tumours confined to upper alveolus and UGBC.

## Exclusion criteria

1. Patients with tumors extending to the upper alveolus from adjacent areas (e.g., tonsil, soft palate) were excluded
2. Synchronous primary tumours
3. Patients who did not underwent treatment.

Patients were followed up by hospital revisit records, telephonic calls, and home visits. All patients were followed up for at least 5 years. Data were analyzed using Statistical Package for Social Sciences (SPSS 19.0, IBM Inc., Chicago, IL, USA). Kaplan–Meir method was used for survival analysis and was compared using log rank-test.  $P < 0.05$  was considered statistically significant.

## Results

One hundred and ten patients with SCC of the upper alveolus were included in the present study. Of the 110 patients' cohort, 59 were males and 51 were females (male:female ratio was 1.16:1). The median age of presentation was 55 years, with a range from 32 to 80 years. Thirty-two (29.1%) patients were below 50 years and 78 (70.9%) were 50 years and above [Table 1].

Of the 110 patients, 71 (64.5%) patients were diagnosed histologically as well-differentiated SCC (WDSCC), 28 (25.5%) patients with moderately differentiated SCC (MDSCC), and 11 (10.0%) patients with poorly differentiated SCC (PDSCC) at the time of final diagnosis. On clinical and radiological examination, 14 (12.7%) tumors were classified as T2, 13 (11.8%) as T3, 53 (48.2%) as T4a,

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Departments of Head and Neck Surgery, <sup>1</sup>Hospital Based Cancer Registry, <sup>2</sup>Pathology, <sup>3</sup>Cancer Registry and Epidemiology and <sup>4</sup>Gynecologic Oncology, Dr. B Borooah Cancer Institute, Guwahati, Assam, India  
**Correspondence to:** Dr. Nizara Baishya,  
E-mail: nizara.baishya@gmail.com

and 30 (27.3%) as T4b. Forty-six (41.8%) patients presented with cervical lymph nodes metastasis and 64 (58.2%) patients did not had regional cervical lymph node metastasis. Of the patients with positive lymph nodes, two were T2-tumors, eight were T3-tumors, 19 were T4a-tumors, and 17 patients had T4b-tumors ( $P = 0.019$ ). Furthermore, in tumor grade differentiation of patients with positive lymph nodes, 30 (65.2%) were seen as WDSCC, 12 (26.0%) as MDSCC, and four (8.6%) as PDSCC. Fifty-three patients (51.8%) presented in Stage IVA, thirty (27.3%) patients presented with Stage IVB, ten (9.1%) patients in Stage III, twelve (10.9%) patients in Stage II and one patient (0.9%) presented in Stage IVC with distant metastasis to the liver. The patients who received treatment were categorized as follows: 32 (29.1%) patients received radiotherapy (RT), 49 (44.5%) patients underwent surgery followed by external beam RT, eight (7.3%) patients were treated by only chemotherapy (CT), 10 (9.1%) underwent surgery followed by concurrent chemo-RT (CRT), and five (4.5%) patients underwent only surgery. One (0.9%) patient was treated by surgery followed by CT as shown in Table 1.

Out of 110 patients, 24 (21.82%) patients were dead at the closing period of follow-up and 86 (78.18%) were either alive or censored. The 5-year overall survival (OS) was higher among the patients in Stage II (71.1%) compared to those who

were in Stages III (65.6%), Stage IVA (56.7%), and Stage IVB (19.4%) ( $P = 0.02$ ) [Figure 1]. At the 5-year closing period of follow-up, the OS was higher among the patients with node negative (N-) than those with node positive (N+) (66.3% versus 37.3%,  $P = 0.019$ ) [Figure 2]. The median OS in patients with N+ was 18 months (95% confidence interval [CI] = 8–28). Further, OS stratified by tumor grade differentiation is shown in Figure 3. Five-year OS was 64.2% in patients with WDSCC, 32.0% in MDSCC, and 32.8% in PDSCC ( $P = 0.313$ ).

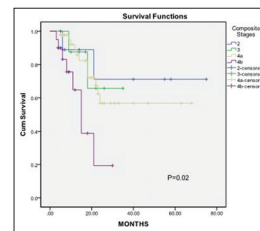
## Discussion

The alveolar processes of the maxilla and the overlying mucosa covering it constitute the upper alveolar ridge. The mucosal covering of the upper alveolar ridge extends laterally to gingivo-buccal sulcus and then to the buccal mucosa. International Classification of Disease (ICD-10) groups them together as C03.0. In oral oncology, the terms “upper alveolus” and “upper gingiva” have been used more or less synonymously. Morris *et al.* had observed that upper alveolus tumors were more common in females.<sup>[7]</sup> However, in our study, it was observed that males were more predominantly affected than females. In the West, the mean age of presentation of OC is in the seventh decade. But in the Indian and South East Asian context, the peak age frequency of OC is a decade earlier, which may be attributed to the high prevalence of tobacco consumption in our population. WDSCC of the upper alveolus was the most common grade of tumor differentiation (64.5%) in our study. However, this was in contrast to a study done by Pathak *et al.* where moderately differentiated variant was the most common type of upper alveolus SCC.<sup>[3]</sup> Nearly 75.5% of the patients in our study cohort have had T4 disease in contrast to another study by Kumar *et al.* from northern India.<sup>[8]</sup> It has been observed and well documented that, the incidence of lymph node metastasis in carcinoma of the tongue and floor of mouth is higher (30%).<sup>[9]</sup> But, reports on lymph node metastasis from SCC upper alveolus is rare. It was seen from our study that cervical lymph node metastasis was 41.8% (46/110) in patients presenting with upper alveolus SCC. This finding is much higher than the study done by Li *et al.* where it was 40%.<sup>[10]</sup> From this study, it can be seen that the chance of nodal metastasis increases with increase with the tumor T-stage ( $P = 0.019$ ). Treatment approach for oral SCC include single management

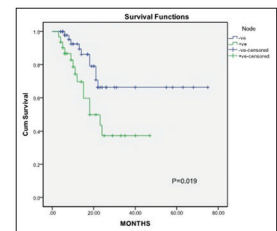
**Table 1: Demographic and clinical information of the patients included in the study cohort**

Parameters	n (%)
Gender	
Male	59 (53.6)
Female	51 (46.4)
Age group	
<50	32 (29.1)
50 and above	78 (70.9)
Differentiation	
WDSCC	71 (64.5)
MDSCC	28 (25.5)
PDSCC	11 (10.0)
T stage	
T2	14 (12.7)
T3	13 (11.8)
T4a	53 (48.2)
T4b	30 (27.3)
Node	
N0	64 (58.2)
N+	46 (41.8)
Composite stage	
Stage II	12 (10.9)
Stage III	10 (9.1)
Stage IVA	57 (51.8)
Stage IVB	30 (27.3)
Stage IVC	1 (0.9)
Treatment types	
Surgery	5 (4.5)
Radiotherapy	32 (29.1)
Chemotherapy	8 (7.3)
Surgery + radiotherapy	49 (44.5)
Surgery + chemotherapy	1 (0.9)
Radiotherapy + chemotherapy	5 (4.5)
Surgery + radiotherapy + chemotherapy	10 (9.1)

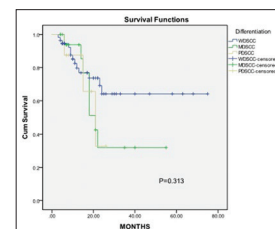
WDSCC=Well differentiated squamous cell carcinoma, MDSCC=Moderately differentiated squamous cell carcinoma, PDSCC=Poorly differentiated squamous cell carcinoma



**Figure 1: Five-year overall survival among different stages of cancer**



**Figure 2: Five-year overall survival between positive and negative nodal metastasis**



**Figure 3: Five-year overall survival among different grades of differentiation**

with surgery, RT (external beam RT and/or brachytherapy), or adjuvant systemic therapy as CT and/or target agents, and with various combination of these modalities depending on the disease presentation and pathological findings.<sup>[11]</sup> Neo-adjuvant CT may be used to downstage the disease in case of borderline operability. In our study, 45% of patients were treated by surgery followed by RT, which remained as the single largest treatment modality.

In our study, the 5-year OS was higher among the patients in Stage II (71.1%) compared to those who were in Stages III (65.6%), Stage IVA (56.7%) and Stage IVB (19.4%). This finding is similar to other studies.<sup>[7]</sup> Wang *et al.* on both univariate and multivariate analyses had not found tumor differentiation to be an important prognostic factor.<sup>[12]</sup> In our present study, tumor differentiation in terms of WDSCC had better 5-year OS. However, the survival differences between MDSCC and PDSCC were clinically not significant. Cervical lymph node metastasis is the most important prognostic factor in patients with HNCs, and advanced N-stage is correlated with a poor prognosis. In our study, we have observed that OS was higher among the patients with N- than those with N+ (66.3% vs. 37.3%). This finding is similar to the study done by Li *et al.*<sup>[10]</sup>

#### Limitations of the study

Major limitation of the present study is that the information on disease-free survival could not be obtained from the data, as the patient follow-ups for the present study were mostly done by telephonic calls. Moreover, it was a retrospective study. The strength of the present study is that, it was done on a relatively rare group of OC and there is absence of definitive insight into the natural history and outcome of these tumors.

#### Conclusion

The malignant upper alveolus tumors present in advanced stages. Presence of cervical lymph node metastasis is associated with the decreased OS. SCC of the upper alveolus should be treated by adequate surgical resection with adjuvant treatment if necessary and it offers the best chance of disease control.

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#### Conflicts of interest

There are no conflicts of interest.

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