ORIGINAL ARTICLE

Oral Squamous Cell Carcinoma with Cervical Lymph Node Metastasis: A Study in Dhaka Dental College and Hospital

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Abstract:

An observational study of 29 cases of oral squamous cell carcinoma with cervical lymph node metastasis was done among the patients attended in Dhaka Dental College and Hospital from January 2006 to December 2007. Majority of the patients (34.5%) belonged to the age group of 40-49 years. 58.6% of the patients were male, while remaining 41.4% were female. 51.7% of the lesions were located in the alveolar ridge where the other common sites were buccal mucosa (27.6%) and retro molar area (13.8%). Half of the study subjects (51.7%) were habituated to betel quid chewing followed by 37.9% and 10.3% were habituated to smoking and betel quid-smoking respectively. The majority of the (SCC) cases presented as ulcers where others were exophytic and verrucous in nature. Grade I lesions was most prevalent (75.9%) in the patients. Majority of cases presented with Stage IV lesions (55.2%). The sensitivity, specificity, positive predictive value, negative predictive value & accuracy of Ultrasonographic technique for determining metastatic cervical lymph nodes were 93.33%, 50%, 66.7%, 87.5% and 72.4% respectively. Most of the patients are habituated with betel quid and or smoking and come in late stage of disease when treatment becomes difficult. Sonographic evaluation can improve the diagnosis of metastatic cervical lymph nodes in patients with oral squamous cell carcinoma. Early diagnosis is expected for good outcome of the disease.

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Introduction:

Oral cancer is one of the ten most common cancers and it is the second major cause of death after heart disease[1,2]. It is a major health problem in the Indian sub continent[1]. Though oral cancer represents approximately 5% of cancers in men and 2% in women in developed countries, it represents about 25% of all cancers among the people of Indian sub-continent[1]. Approximately 90% of oral cancers are squamous cell carcinoma (SCC)[1]. Oral SCC predominantly develops in middle aged and older persons, with highest incidence

in the sixth decade of life[3]. It affects males more frequently than females, although the ratio is equalizing[3]. The prevalence of oral cancer is also generally higher in ethnic minorities in other developed countries[4]. SCC typically presents as a persistent white, red or mixed lesion, mass, nodule, or indurated ulcer.

The clinical variants are ulcerative or infiltrative, exophytic and verrucous. The three most common sites of involvement are tongue, lip and floor of the mouth in developed countries, where buccal mucosa, retro-molar trigon and alveolar mucosa are mostly affected in patients of this Indian sub-continent. They can develop from pre-cancerous lesions, such as leukoplakia and erythroplakia, or apparently normal epithelium[3].

About 90% of the oral SCC in South East Asia is attributable to tobacco use in its different forms[1] and in Bangladesh it is the main etiological factor[5]. Usually people of this region use tobacco as conventional smoking, reverse smoking and smokeless tobacco as betel quid (combination of betel leaf, nut, tobacco, lime) as chewing tobacco and snuff dipping[6, 7, 8]. In developed countries alcohol also plays an important role in developing oral SCC[9,10]. Apart from these, human papilloma virus (HPV) infection, especially HPV_{16} and HPV_{18}, are found in a variable but small proportion of oral, and up to 50% of tonsillar and oropharyngeal SCC[11]. It has been realized for a long time that patients with oral SCC are at risk of second tumors in the upper aerodigestive tract, reported to occur in 10-35% of cases[3]. Histopathologically, they can be categorized into three degrees of differentiation: i) Well-differentiated disease shows greater than 75% keratinization, ii) Moderately differentiated disease contributes to the bulk of SCC and is characterized by 25% to 75% keratinization, and iii) Poorly differentiated disease demonstrates less than 25% keratinization. The degree of differentiation may vary from one part of the tumor to another. Conventional histological grade by Broader's as above correlates poorly with patient outcome and thus it has limited value for prognosis. But newer concept of Aneroth's classification of grading contributes a lot for determining prognosis of oral SCC[6,7]. Staging of tumor is done according to TNM classification. Tumor size and lymph node involvement are the most significant prognostic factors. At the time of diagnosis, the majority of patients with SCC present advanced disease (stage III-IV), and approximately one third of them show metastasis to lymph node. After curative treatment, about 50% of the patients suffer recurrences; 80% within 2 years and the remaining within 4 years[6,7].

The most important factor in determining prognosis of oral cancer is presence of regional nodal metastasis. Survival rates decrease by 50% when nodal metastasis are present; a contra lateral node reduces survival by an additional 50%. Consequently bilateral nodal involvement reduces survival actually by 75% and extra nodal involvement reduces this by another 50%[12]. Furthermore, the presence of cervical lymphadenopathy has been correlated with an increase in the rate of distant metastasis[13,14].

Pre-operative assessment of the cervical lymph nodes helps in planning suitable surgical management of the neck, wherein the justification to operate the neck is being questioned more often than not, owing to the fact that only about 30% of clinically negative necks are histopathologically positive once

operated[15]. Evaluating neck metastasis based on physical examination findings has been the classic method for patients of new tumors in the head and neck. Unfortunately clinical palpation of the neck demonstrates a large variation of findings by various examinations. Although inexpensive to perform and repeat, palpation findings are generally accepted as inaccurate. Here sensitivity and specificity are in the range of 60 – 70%, depending on the tumor studied. Because of the knowledge of sensitivity and specificity of palpation, a neck side without palpable metastasis is still at risk of harboring occult metastasis, with the risk determined by the characteristics of the primary tumor. The incidence of false negative (occult) nodes based on physical examination varies from 16-60%[15]. Before the introduction of diagnostic imaging, clinical palpation was shown to be inadequate for detecting cervical lymph node metastasis. Soko et al reported that only 28% of occult cervical metastases were found by clinical palpation. Fischbein et al. have found clinical examination to have only 70% accuracy at best[16].

Imaging modalities of different types are used in evaluating the status of lymph nodes in oral cavity cancer, ranging from Ultrasound imaging, Contrast Enhanced Computed Tomography (CECT), Magnetic Resonance Imaging (MRI) to 2-Fluoro-2-deoxy-glucose (FDG), Positron Emission Tomography (FDG-PET) and Lymphoscintigraphy. Ultrasound is reported superior to clinical palpation for detecting lymph nodes and metastasis. The advantage of ultrasound over other imaging modalities is price, low patient burden, and possibilities for follow up[17,18,19].

Often fine needle aspiration cytology (FNAC) is performed for confirmation of regional lymph node metastasis. In some centers Ultrasound-guided fine-needle aspiration cytology is also preferred. In these situations false-negative results are the possibilities, so in practical terms, ipsilateral, firm or hard, enlarged regional lymph nodes in a patient with an obvious oral carcinoma are likely to include metastases.

The study highlighted the clinico-pathologic characteristics of oral SCC of patients irrespective of race and religion with evaluation of metastatic cervical lymph nodes of the patients by ultrasonography and histopathology.

Materials and method:

A study of 29 cases of oral squamous cell carcinoma was done from January 2006 to December 2007. Patients having histologically confirmed oral squamous cell carcinoma (SCC) attending at Dhaka Dental College and Hospital were selected for the study. By convenient sampling, 29 cases of oral SCC patients were selected and evaluated clinically and by High Resolution Sonography (HRSG) for neck metastasis. Standard treatment was provided to all patients being included in the study.

Inclusion Criteria:

1. All patients diagnosed histologically as squamous cell carcinoma in oral cavity
2. Patients of oral squamous cell carcinoma with or without clinical evidence of metastatic cervical lymph nodes

Exclusion Criteria:

1. Patient of oral squamous cell carcinoma denied for investigation and treatment.
2. Patient of oral squamous cell carcinoma denied being included in the study.

Data were collected through written questionnaire, clinical examination and relevant investigations. After processing data was analyzed using computer software SPSS version 12.

Results:

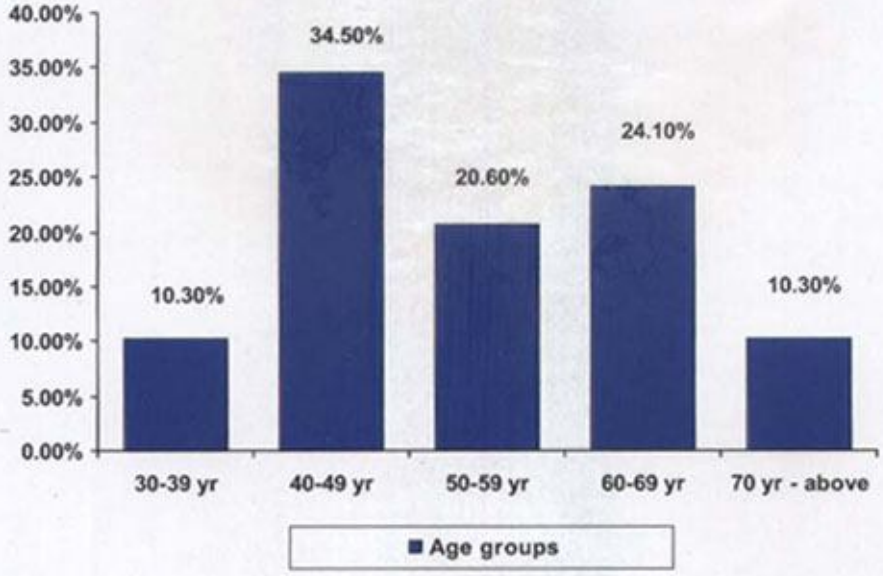

Figure-1: Age distribution of the patients (n=29)

Figure 1 shows that majority of the study subjects belonged to the age group of 40-49 years (about 34.5%) followed by the age group 60-69 years (about 24.1%). The age of the study subjects who fulfilled the inclusion criteria ranged from 35 - 85 years (Mean age ± SD=53.48 ± 12.45 years).

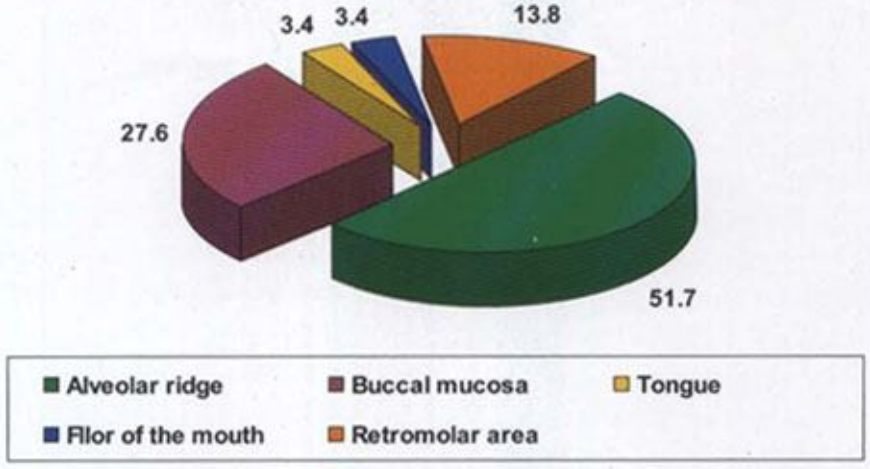

Figure-2: Figure-2: Site distribution of study patients

Figure-2 shows that about half (51.7%) of the lesions located in the alveolar ridge. Beside the alveolar ridge the other common sites were buccal mucosa (27.6%) followed by retro molar area (13.8%). Tongue and floor of the mouth were affected with the same frequency (3.4%).

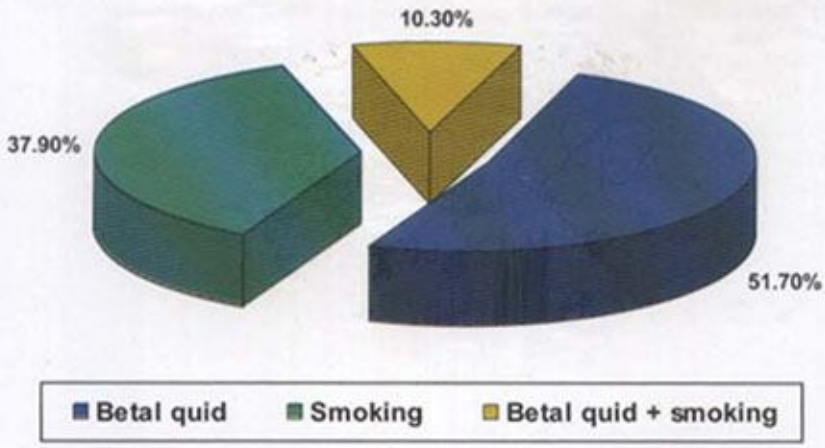

Figure-3: Distribution of patients by their habits (n=29)

Figure-3 shows that about half of the study subjects (51.7%) were habituated to betel quid chewing followed by 37.9% and 10.3% habituated to smoking and betel quid-smoking respectively.

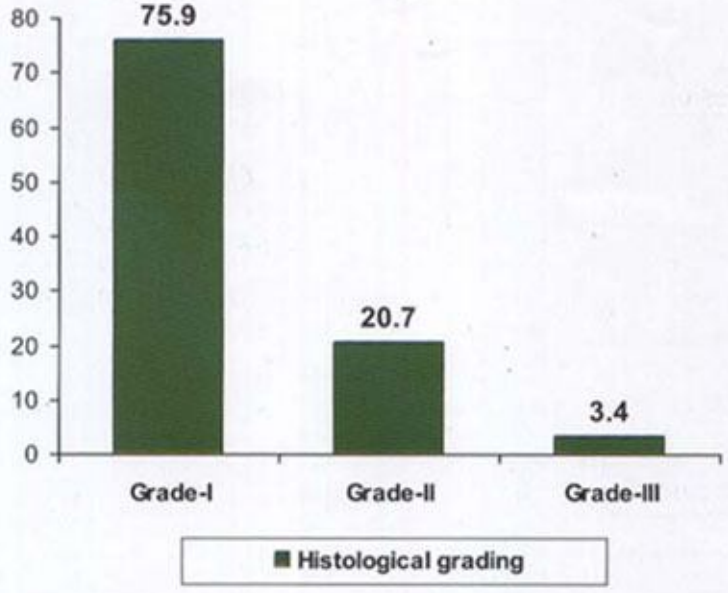

Figure-4: Histological grading of lesion (n=29

Figure-4 shows that Grade I lesions was most prevalent in the study subjects (75.9%). 20.7% and 3.4% of the lesions were Grade II and Grade III respectively in the conventional grading system.

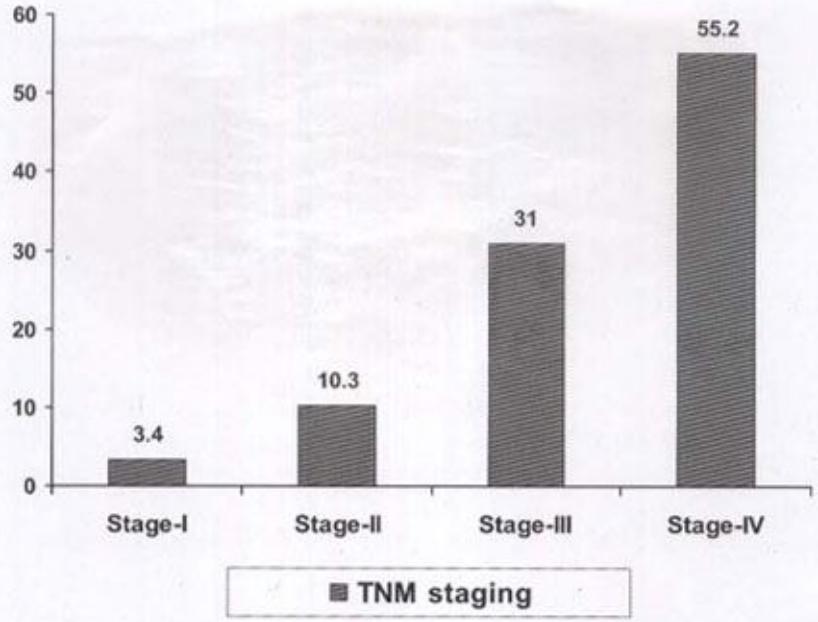

Figure-5: Distribution of patients by TNM Staging (n=29)

Figure 5 shows that most of the cases were Stage IV (55.2%) followed by 31% Stage III, 10.3% Stage II and 3.4% Stage I lesion in TNM Staging system.

Table-I: Distribution of study subjects by clinical type & grading of primary lesion (n=29)

Clinical type of lesion	Grading			Total
	Grade I	Grade II	Grade III	
Ulcerative	16 (76.2%)	4 (19.0%)	1 (4.8%)	21
Exophytic	4 (66.7%)	2 (33.3%)	0 (0%)	6
Verrucous	2 (100%)	0 (0%)	0 (0%)	2
Total	22 (75.9%)	6 (20.7%)	1 (3.4%)	29

Table-I shows that most of the ulcerative lesions were Grade-I (76.2%), which is similar to exophytic and verrucous lesions.

Table-II: Association between clinical staging and pathological staging of lymph node

Clinical staging of lymph node	Pathological staging of lymph node			Total
	N_0	N_1	N_2	
N_0	6 (100%)	0 (0%)	0 (0%)	6 (100%)
N_1	6 (31.6%)	12 (63.2%)	1 (6.3%)	19(100%)
N_2	0 (0%)	1 (25%)	3 (75%)	4 (100%)
Total	12 (41.4%)	13 (44.8%)	4 (13.8%)	29 (100%)

Table-II shows the cross tabulation between clinical staging of lymph nodes and pathological staging of lymph nodes. Clinically suspected all N_0 neck was confirmed by histological examination. 63.2% of clinically suspected N1 case was confirmed by histological examination where 31.6% become N_0 and 6.3% become N_2.

Table-III: Relationship between palpation finding and Histological finding of lymph node

Palpation finding of lymph node	Histological finding of lymph node		Total
	Positive	Negative	
Positive	14 (73.7%)	5 (26.3%)	19 (100%)
Negative	1 (10%)	9 (90%)	10 (100%)
Total	15 (51.7%)	14 (48.3%)	29 (100%)

It was found that sensitivity, specificity, positive predictive value, negative predictive value and accuracy of palpation method for determining metastatic cervical lymph node were 93.33%, 64.29%, 73.68%, 90% & 79.3% respectively.

The sensitivity, specificity, positive predictive value, negative predictive value & Accuracy of Ultrasonographic technique for determining metastatic cervical lymph node were 93.33%, 50%, 66.7%, 87.5% and 72.4% respectively

Table-IV: Relationship between Ultrasonographic finding and Histological finding of lymph node

Ultrasonographic finding of lymph node	Histological finding of lymph node		Total
	Positive	Negative	
Positive	14 (66.7%)	7 (33.3%)	21 (100%)
Negative	1 (12.5%)	7 (87.5%)	8 (100%)
Total	15 (51.7%)	14 (48.3%)	29 (100%)

Discussion:

The study of 29 cases of oral squamous cell carcinoma fulfilling the inclusion criteria was done with the aim of evaluating the clinical and pathological characteristics of oral squamous cell carcinoma with cervical lymph node metastasis in Bangladeshi patients.

In analysis, 58.6% of patients were male which corresponded to other studies on Bangladeshi patients as 53% by Sitan[20], 56.5% by Adhikari[21]. The age ranged from 35 to 85 years where majority of the patients (34.5%) belonged to the age group of 40-49 years. The data showed similarity with Shaheed[5] et al and other researchers[20,21,22]. On clinical examination it was found that half of the lesions (51.7%) were located in the alveolar ridge where other common sites were buccal mucosa (27.6%) followed by retro molar area (13.8%). Tongue and floor of the mouth were affected with the same frequency (3.4%). The distribution were almost similar to Sitan[20] 2006 but showed disparity with Richard[23] et al and Hsie[24] et al. Habit of betel quid chewing was present among 51.7% patients, which were almost similar to other investigators[5,20,21,25,26]. The second most

common habit was smoking (37.9%), which was followed by both betel quid, and smoking (10.3%).

Histologically 75.9% of SCC were well differentiated, 20.7% were moderately differentiated and 3.4% were poorly differentiated. The finding was almost similar to Shaheed[3] et al, which is 72%, 18% and 6% respectively. The study showed that most of the cases were Stage IV (55.2%) followed by 31% Stage III, 10.3% Stage II and 3.4% Stage I lesion in TNM Staging system which is almost similar to other studies[20,21].

The cross tabulation between clinical staging of lymph nodes and pathological staging of lymph nodes show that clinically suspected all N_0 neck was confirmed by histological examination. 63.2% of clinically suspected N1 case was confirmed by histological examination where 31.6% become N_0 and 6.3% become N_2.

Lymph node metastasis in neck was one of the most important factors in the prognosis and treatment of patients with head and neck squamous cell carcinoma[12, 13]. In addition, because lymphatic metastasis was a frequent event that impacts prognosis, a decision to treat the lymph nodes in the neck had to be made in almost all patients, even if metastases were not diagnosed clinically. It was therefore important to assess whether a patient had regional lymph node metastases or not. The presence of cervical lymph node metastasis in oral squamous cell carcinoma often also changes the extent of surgical treatment or radiotherapy and chemotherapy.

Clinical palpation is an inaccurate technique to stage cancer in the neck[27]. Risk of occult neck metastases (in a palpatory-negative neck) above 20% was found to be indicative for elective neck treatment, either radiation therapy or surgery. The risk of occult metastasis, which can occur in both sides of the neck, was determined by characteristics of the primary tumor such as size, site, and several biological criteria. Because of the increased risk of nodal metastases, even in clinically negative necks, most patients with tumors staged as T2 or larger undergone some form of elective neck treatment. The disadvantage was that the majorities of patients do not harbor metastases and, therefore, will be subjected to the morbidity of unnecessary treatment. By detecting occult adenopathy, modern imaging techniques have increased sensitivity for detecting positive nodes, and consequently, decrease the risk of occult metastasis to below 20%. If this can be accomplished, the clinician may refrain from a neck dissection or radiation, and adapt a wait-and-see policy with careful follow-up to detect a neck metastasis as early as possible. The drawback of palpation method for evaluating neck lymph node is that it is a subjective method that depends on operator and experience. It can be competitive with other investigation modalities if the skill can be improved by repeated examinations of neck.

The study showed that the sensitivity, specificity, positive predictive value, negative predictive value and accuracy of palpation method for determining metastatic cervical lymph node were 93.33%, 64.29%, 73.68%, 90% and 79.3% respectively. The result was comparable to Chowdhury[28] et al where the results are 75.6%, 60%, 88.6%, 37.5% and 72.5% and Haberal[29] et al where the results are 64%, 85%, 78%, 74% and 75%. The comparison showed that positive predictive value and accuracy rates were almost same in all studies though there were some

dissimilarity exists in sensitivity, specificity and negative predictive value. In this study, palpation method showed high sensitivity (93.33%) and specificity (64.29%), which have limited clinical value as probably many metastatic lymph nodes, were palpable. The sensitivity would have been lower if the study was limited to N_0 neck population.

Updated Imaging techniques like CT, MRI, and Sonography are more accurate than palpation. In 25% of pathologically verified tumor-positive neck dissections, micro metastases are smaller than 3 mm, which are undetectable by most techniques, are present. Lymph nodes 2–3 mm in size can be seen as nodules on CT and MR images, and may even be better seen with high-resolution scanners. Nonetheless, differentiation between benign and malignant metastatic disease still remains a problem. Recently, other techniques such as radioimmunoscintigraphy and positron emission tomography have been explored, but these expensive techniques still have to prove their value in clinical practice.

Sonographic criteria, such as nodal size and configuration of the lesion, and Doppler Sonographic criteria have been studied extensively for their value to differentiate between benign and malignant lymphatic disease in the neck. The minimal axial diameter appears to be the most accurate size criterion, compared to the maximal axial diameter and the longitudinal diameter. Regarding the aspect of lymph nodes on sonograms, the echogenic hilus appears to be a reliable parameter. The configuration (shape) of the node might be important, but some authors doubt its value. Following the above criteria the patients were evaluated with a high-resolution sonography machine with use of color and power Doppler. After clinical and sonographic evaluation the subjects were treated by neck dissection and were evaluated by histopathological examinations.

The study showed that the sensitivity, specificity, positive predictive value, negative predictive value and accuracy of the sonographic technique for determining metastatic cervical lymph nodes were comparable to other studies by Haberal et al[29], 94% accuracy by Steinkamp et al[30], 78% accuracy by Mikami et al[31] and 92% sensitivity by Naito et al. The study showed that the accuracy of sonographic technique was satisfactory (72.4%) and almost similar to other studies abroad. The important drawback of this technique is that it is operator and skill dependent as like as other investigations.

Sonography-guided fine-needle aspiration cytology (FNAC) has been shown to be very accurate in the evaluation of regional metastatic disease. It combines the high sensitivity of sonography with the excellent specificity of FNAC. The reported sensitivity of sonography-guided FNAC in the neck ranges from 48% to 73%, whereas the reported specificity is 100%. In the United States, this technique has received fewer acceptances because it is labor-intensive and operator-dependent. False-negative results may be the result of sampling the wrong node or the wrong part of the correct node. Furthermore, the cytopathologist may overlook small nests or single tumor cells.

Conclusion:

Ptients with oral squamous cell carcinoma were mostly habituated with betel quid and or smoking and came in late stage of disease when treatment becomes difficult. High-resolution Doppler sonography might be an

adjunct tool in diagnosing metastatic nodes in patients with oral squamous cell carcinoma, which was cost effective, non-invasive, fewer burdens to patient, does not create problem of overlapping with mandible and could be done repeatedly during follow up. Early diagnosis with proper evaluation of both primary lesion and metastatic cervical lymph nodes is necessary for good prognosis of the disease. Routine examination of the oral cavity by dental practitioners and other health care providers helps in the early detection of premalignant and malignant oral disease. General practitioners including dentists can play a significant role in disseminating information regarding oral cancer.

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