

Frequency of Occult Metastasis in Cervical Lymph Nodes in Patients with Squamous Cell Carcinoma of Oral Cavity

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ABSTRACT

Objective: To determine the frequency of occult metastases in cervical lymph nodes in patients with squamous cell carcinoma (SCC) of oral cavity presenting at government tertiary care facilities of Karachi and Peshawar.

Patients and Methods: This cross-sectional descriptive study was carried out at Department of Ear, Nose, Throat (ENT) and Head and Neck Surgery Lady Reading Hospital Peshawar and Jinnah Postgraduate Medical Centre, Karachi from June 2009 to February 2011. Fifty six patients were included who fulfilled the inclusion criteria after taking the informed consent.

Results: A total of 56 punch biopsy proven cases of squamous cell carcinoma of all the sub sites of oral cavity with all T-stages were included in this study. The average age of the patients was 47.7±13.06 years (95% CI: 44.2 to 51.19) and minimum age of the patients was 22 years and maximum age was 75 years. Out of 56 patients, 37 (66.1%) were male and 19 (33.9%) were female. There are two hospitals from where patients were included and 80.36% patients were in Jinnah Postgraduate Medical Centre Karachi and 19.64% patients were from Lady Reading Hospital Peshawar. Regarding site of tumor, buccal mucosa was observed in 39 (69.64%) and tumor in tongue was found in 13 (23.21%).cases. Similarly tumour in floor of mouth, lower alveolus and retromolar trigone was also found in patients. Rate of tumor stages T2 and T3 was found in 23 (41.1%) each, rate of tumor stage T1 was eight (14.3%) and stage T4 was two (3.6%). Overall occult metastases rate was 33.9% (19/56). Rate of occult metastases was above 60% in less than 42 years of age while in between 54 to 64 years of age rate of occult metastases was 38.5% and above 64 years of age, it was observed in 16.7% cases. Similarly rate of occult metastases in males was 35.1% and in females was 31.6%.

Conclusion: there is high incidence of occult metastasis with squamous cell carcinoma of oral cavity ant at least supraomohyoid neck dissection should be considered in cancers arising from oral cavity.

Key words: Oral cavity, Squamous cell carcinoma, Cervical lymph nodes.

INTRODUCTION

Oral cancer is one of the type of head and neck cancer and is a cancerous tissue growth located in the oral cavity. It may arise as a primary lesion originating in any of the oral tissues or by extension from a neighboring anatomic structure such as the nasal cavity. It may be of varied histologic types: teratoma, adenocarcinoma derived from a major or minor salivary gland or melanoma from the pigment producing cells of the oral mucosa. Oral Cancer' includes malignant neoplasms of the lip and intra-oral sites while the oropharynx, nasopharynx, hypopharynx and salivary glands are not normally included. There are several types of oral cancers but around 90% are squamous cell carcinoma, originating in the tissues that line the mouth and lips. Squamous cell carcinoma (SCC) of the oral cavity is

rare in patients of 50 and younger, being primarily a disease that occurs in males in their sixth and seventh decade^{1,2}. In the last few decades it has been suggested that the incidence of oral cancer in all age groups may be rising worldwide³. In 2008, in the United States of American (US) alone, about 34,000 individuals were diagnosed with oral cancer. 66% of the time these were found as late stage III and IV disease. Low public awareness of the disease is a significant factor but oral cancer could be found at early highly survivable stages through a simple, painless, five minute examination by a trained medical or dental professional. Although several past studies in the early 1970s have indicated that the occurrence of oral cancer has been decreasing.⁴⁻⁶ The highest rates of oral cancer in people of all ages occur in developing countries such as south and south-east Asia where oral cancer is often the first or second most common site for malignancy^{7,8,9,10}. There are several causes of squamous cell oral carcinoma and oncogenes are activated as a result of mutation of the DNA. South Asian regions chewing betel, pan and chalia is known to be a strong risk

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factor for developing oral cancer. In these regions where such practices are common, oral cancer represents up to 40% of all cancers, compared to just four percent in the United Kingdom (UK)^{8,11,12}. In Indian subcontinent, oral submucous fibrosis is very common. This condition is characterized by limited opening of mouth and burning sensation on eating of spicy food. This is a progressive lesion in which the opening of the mouth becomes progressively limited, and later on even normal eating becomes difficult. It occurs almost exclusively in India and Indian communities living abroad. Smoking and other tobacco use are associated with about 75 percent of oral cancer cases, caused by irritation of the mucous membranes of the mouth from smoke and heat of cigarettes, cigars and pipes. Use of chewing tobacco or snuff causes irritation from direct contact with the mucous membranes. Alcohol use is another high-risk activity associated with oral cancer. There is known to be a very strong synergistic effect on oral cancer risk when a person is both a heavy smoker and drinker. However, this risk factor is more common in western countries. Infection with human papilloma virus (HPV), particularly type 16, is a known risk factor and independent causative factor for oral cancer affecting both blacks and whites.¹³⁻¹⁵ There are several studies that have identified the prevalence and risk factors associated with oral squamous cell carcinoma and occult metastasis globally. These studies have shown an increasing trend particularly where the associated factors such as smoking, betel chewing, gutka and chalia are common. Most studies available on the pattern are from the western world and for early cancers of the tongue and floor of the mouth⁶⁻²⁰. It is clear that contrasting evidence exists in the literature as to the status of alcohol and tobacco as risk factors for oral carcinoma in young adults. Many authors have reported that risk factors of smoking and drinking, considered significant etiological agents in older patients, were also present to varying degrees in younger people. Many authors also reported a complete lack of the usual etiological factors associated with older patients. Genetic studies have indicated that patients diagnosed with SCC at a young age may exhibit predispositions to genetic instability²¹⁻²⁵.

PATIENTS AND METHODS

This cross-sectional descriptive study was carried out at Department of Ear, Nose, Throat (ENT) and Head and Neck Surgery lady Reading Hospital Peshawar, and Jinnah Postgraduate Medical Centre, Karachi from June 2009 to February 2011. Fifty six patients were included who fulfilled the inclusion criteria after

taking the informed consent. The patients who are biopsy proven cases of SCC of oral cavity and fulfilling the section criteria were enrolled through ENT and Head and Neck surgery out patient, departments (OPD) of JPMC and CHK, Karachi by a postgraduate trainee having clinical experience of at least two years in the speciality after obtaining permission from the head of the department of the respective hospitals. These patients were informed about the study and informed consent was taken after explaining risks and benefits of the surgical procedure. These clinically NO patients were subjected to supraomohyoid neck dissection (SOHND) along with excision of the primary tumour. The histopathology report of the neck specimen was followed by myself. All the information was recorded on a proforma. The collected data was analyzed in SPSS 10.

RESULTS

A total of 56 punch biopsy proven cases of squamous cell carcinoma of all the sub sites of oral cavity with all T-stages were included in this study. Histogram of age distribution is presented in Figure 1. The average age of the patients was 47.7±13.06 years (95% CI: 44.2 to 51.19) and minimum age of the patients was 22 years and maximum age was 75 years as presented in Table 1. Out of 56 patients, 37 (66.1%) were male and 19 (33.9%) were female as shown in Figure 2. There are two hospitals from where patients were included and 80.36% patients were in Jinnah Postgraduate Medical Centre Karachi and 19.64% patients were from Lady Reading Hospital Peshawar. Regarding site of tumors, buccal mucosa was observed in 39 (69.64%) and tumors in tongue was found in 13 (23.21%) cases. Similarly tumour in the floor of mouth, lower alveolus and retromolar trigone were also found in patients as presented in Figure 3. Rate of tumor stages T2 and T3 was found in 23 (41.1%) each, rate of tumor stage T1 was 8 (14.3%) and stage T4 was 2 (3.6%) as shown in Figure 4. Overall occult metastases rate was 33.9% (19/56). Rate of occult metastases was above 60% in less than 42 years of age while in between 54 to 64 years of age rate of occult metastases was 38.5% and above 64 years of age it was observed in 16.7% cases. Similarly rate of occult metastases in males was 35.1% and in females was 31.6%. Occult metastases rate in tumors stage T3 and T4 were observed in 39.1% and 50% respectively while occult metastases rate in stage T1 and T2 were found in 37.5% and 26.1% respectively (Tables 2-5)

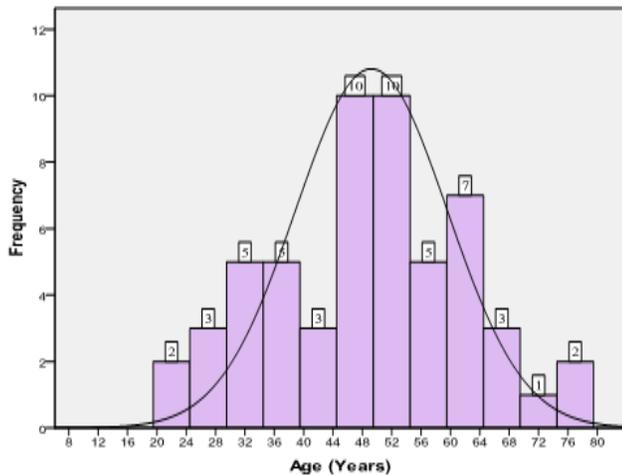


Fig. 1: Histogram of age distribution (n=56)

Table 1: Descriptive statistic of age (n=56)

Statistics	Age (years)
Mean±SD	47.70±13.06
95% CI	44.2 to 51.19
Median (IQR)	49.5 (21)
Maximum age	75
Minimum age	22

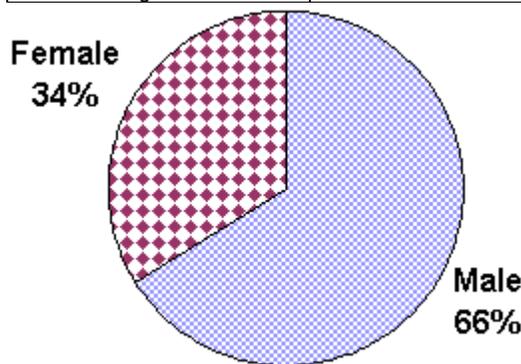


Fig. 2: Percentage of genders

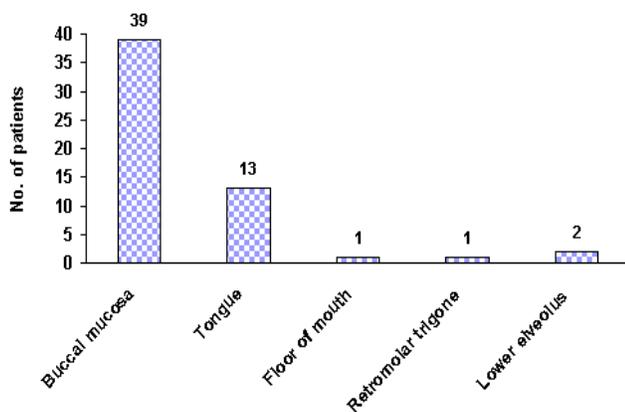


Fig. 3: Site of tumour

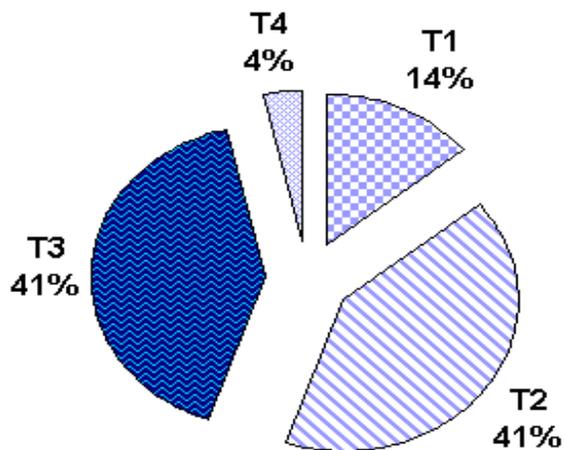


Fig. 4: Stage of primary tumour

Table 2: Statistics of age with respect to occult metastases present and absent (n=56)

Statistics	Occult metastases	
	Present	Absent
Mean±SD	46.53±12.59	18.30±13.42
95% CI	40.45 to 52.60	43.82 to 52.77
Median (IQR)	45 (19)	50 (21)
Maximum age	68	75
Minimum age	22	24

Table 3: Frequency of occult metastases with respect to age groups

Age (years)	No.	Occult metastases present (n = 19)	%age
≤30	7	2	28.6
31 - 41	11	6	54.5
42 – 53	19	5	26.3
54 – 64	13	5	38.5
>64	6	1	16.7

Table 4: Frequency of occult metastases with respect to tumour stage

Tumour stage	No.	Occult metastases present (n = 19)	%age
T1	8	3	37.5
T2	23	6	26.1
T3	23	9	39.1
T4	2	1	50.0

Table 5: Frequency of occult metastases with respect to gender

Gender	No.	Occult metastases present (n = 19)	%age
Male	37	13	35.1
Female	19	6	31.6

DISCUSSION

Squamous cell carcinoma (SCC) of the oral cavity and oropharynx is rare in patients of age 50 and

younger, being primarily a disease that occurs in males in their sixth and seventh decade. Younger patients (arbitrarily aged less than 45 years) account for approximately six percent of all oral cancers¹. Oral Cancer includes malignant neoplasms of the lip and intra-oral site. The nasopharynx, hypopharynx and salivary glands are not normally included in the term. If facial skin is excluded, the majority of malignant neoplasms of the orofacial region (over 80%) are squamous cell carcinomas of the buccal mucosa, tongue and lip². The relative rarity of these tumours occurring in young adults and the diversity in reporting age criteria, sites, stages and possible aetiology, make comparisons problematic. This in turn makes the determination of contributing factors and the development of appropriate preventative health messages difficult for this population. It has even been suggested that oral cancer in the young may be a disease distinct from that occurring in older patients with a different aetiology and disease progression²⁴.

More than 50% of patients with squamous cell carcinoma of the oral cavity have lymph node metastases and histological confirmation of metastatic disease is the most important prognostic factor. Among patients with a clinically negative neck, the incidence of occult metastases varies with the site, size and thickness of the primary tumour. The high incidence rate of occult cervical metastases (>20%) in tumours of the oral cavity is the main argument in favour of elective treatment of the neck²⁵. The occult metastasis rate of squamous cell carcinoma of tongue increases with the elevation of clinical stage and elective neck dissection could be considered for N0 patients staged over T₂ to improve neck control and survival rate and regional resection alone of primary lesion could be considered for T1N0 patients to improve quality of life if closely followed up is conducted²⁶.

Our study included 56 punch biopsy proven cases of oral squamous cell carcinoma. The mean age was around 47.78 years with predominant male population of around 66%. The overall occult metastasis in the sample cases was 33.9%. The most common sites of primary occurrence were buccal mucosa (69.64%) and tongue (23.21%); however, the conversion rates from primary tumor to occult metastasis were low only 30.76% and 30.8% respectively for these tumors, as compared to other tumors. The floor of mouth, and retromolar trigone had 100% conversion rates while lower alveolus had 50%, however, contributing to <1% of the tumors, in terms of site of location. Most of the tumors were of T2 and T3 stages 41.07 and 41.07% respectively. T4 primary stage tumors have 50% conversion rates to

occult metastasis, but conversion rates varied for T1, T2 and T3.

A Chinese study retrospectively evaluating 165 cN0 patients with squamous cell carcinoma of the tongue found that there were 42 cases of occult metastasis and the overall rate of occult metastasis was 25.45%, 34 were homolateral metastasis and four were contralateral metastasis. However, the prevalence rate in our study was slighter higher around 34%. This may be due to later identification of cases that is advanced stages of tumor present in our study. Further the rate of occult metastasis increased with the elevation of clinical T stage, similar to our study with T4 has the highest conversion rate of 50%²⁶.

A study by Zbaren et al records 100 patients with cancer of the oral cavity. The results found that occult metastases were detected in 34 of 1814 lymph nodes. Thus, 20 of 100 patients presented with occult metastases (20%), as compared to 34% in our study. The difference may be due to our late identification of squamous cell carcinomas of oral cavity as compared to advanced settings where it is diagnosed earlier. The study results also shown that some 4 of 27 T1 (14%), 10 of 55 T2 (18%) and in 6 of 18 T3 (35%) occult metastases were observed, that is the highest conversion rate for T3 (39%) similar to our study and 100% conversion rate for T4. The study also showed occult metastases was detected in 11 neck specimens of 60 (18%) tongue carcinomas, in eight of 30 (26%) tumors of the floor of the mouth and in one of 10 (10%) tumors of other locations in the oral cavity. However, our study showed low rates of occult metastasis for buccal mucosa and tongue than floor of mouth, lower alveolus and retromolar trigone.²⁷

The pattern of nodal spread in oral cancers is largely predictable and treatment of neck can be tailored with this knowledge. Most studies available on the pattern are from the western world and for early cancers of the tongue and floor of the mouth. The study by Narendra and Tankshali evaluate the prevalence and pattern of nodal metastasis in patients with pathologic T4 (pT4) buccal/alveolar cancers. The study was aimed to evaluate the prevalence and pattern of nodal metastasis in patients with pathologic T4 (pT4) buccal/alveolar cancers.²⁸ Medical records of the patients with pT4 primary buccal and alveolar squamous cell carcinomas treated by single-stage resection of primary tumor and neck dissection were taken. Fifty percent of the patients did not have nodal metastasis on final histopathology. Occult metastasis rate was 23%. Our study found that occult metastasis rate for buccal mucosa, although was lower for overall oral squamous cell carcinomas but still accounts for 30.76% of the buccal mucosa tumors. The study also

found that all of these cases occurred in levels I to III.²⁸ A Korean study retrospectively analyzed 69 patients with clinically N0 disease. The study results showed that the rates of occult metastasis were 60% for T1, 69% for T2, 100% for T3 and 39% for T4, respectively, among patients who underwent neck dissection. The risk for occult neck metastasis is high in patients with oral cavity SCC; therefore, elective neck treatment should be considered.²⁹

Squamous cell carcinoma (SCC) of the tongue is one of the most common cancers in the oral and maxillofacial region. From 2002 to 2006, 100 consecutive patients with SCC of the tongue were reviewed by analyzing the characteristics of OCLNM, diameter of the tumor, T classifications, depth of invasion, forms of growth, pathological grade and degree of differentiation.³⁰

The rate of OCLNM in 100 patients with SCC of the tongue was 22%. The most common region with OCLNM was level II in the ipsilateral neck, followed by levels I and III. There were 51.61% (16/31) of OCLNM in level II and 87.10% (27/31) of OCLNM in levels I–III. The rate of occult metastases increased with the increased pathological grade, the decreased degree of differentiation and the increased depth of invasion. The most common regions with OCLNM in cN0 patients with SCC of the tongue were levels I–III in the ipsilateral neck. Supraomohyoid neck dissection should be the elective treatment to the neck in patients with cN0 SCC of the tongue by consideration of the clinical and pathological factors for the depth of invasion, forms of growth, pathological grade, and degree of differentiation.³¹

To determine the frequency of occult neck node metastasis in squamous cell carcinoma of oral cavity, a descriptive study was conducted in Karachi, Pakistan in 2007. The study included cases of untreated carcinoma of oral cavity, not crossing midline, having N0 neck. The study results showed that occult metastasis was found in 12 out of 37 cases (32.4%), this is approximately similar to our study 33.9%.³² The metastasis in tongue carcinoma was 5/14, lower alveolar ridge carcinoma metastasized in 5/18, floor of mouth carcinoma was 2/4 and buccal mucosa carcinoma was 0/1. The site of occurrence also varied from our study, as our study showed that tongue and buccal mucosa had lower rates of conversion to occult metastasis. The most interesting finding was that similar to our study in which most of the cancers belonged to stage II and III, current study also found highest rates for level II and level III. Thus supporting that no improvements in stage of diagnosing of squamous cell oral carcinomas, despite the knowledge and information campaigns and predisposing factors that are prevalent in our society.³³

Metastases of squamous cell carcinoma of the tongue and the mouth floor have been well studied. Concerning maxilla squamous cell carcinomas, however, only a few studies have been performed. The question is whether a prophylactic neck dissection should be performed in these tumors. A study in the department of Craniomaxillofacial Surgery at the University Hospital of Zurich, 30 patients who had been treated for squamous cell carcinoma of the maxilla was examined retrospectively. Out of some 59 patients with upper jaw carcinomas over nine year period, only about half (30 patients) had a squamous cell carcinoma of the upper jaw. Of those patients, 27% had an upper lesion on the right side, 33% on the left. Of the 11 patients (36.7%) presenting positive lymph nodes, four patients had direct positive lymph nodes while seven patients had later positive lymph nodes; and 71.4% of the late metastasis appeared during the first year. As 36.7% of patients presenting metastases in the cervical lymph nodes, elective neck treatment should be considered in cases even with a negative clinical examination.³⁴

CONCLUSION

Our study of a middle age sample (56 cases) with predominant male population found that majority of primary tumors are of buccal mucosa and tongue with majority belongs to T2 and T3 stage. However, the rate of occult metastases was higher for other oral sites than buccal mucosa and tongue. These findings are in line with the previous studies that have shown the similar trend. One local study also showing higher prevalences of T2 and T3 stage cancers. The most important finding was that almost all studies have shown a significant prevalence rate for occult metastasis, as similar to our study therefore favouring SOHND in cN0 patients. Though standardization, advancement in diagnosing vary according to regions but overall results and their differences are understandable. The interesting finding is despite several informative and educational media campaigns, the diagnosis of oral squamous cancers is still late than many other regions.

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