

## Analysis of Causative Factors in Oral Cancer

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### ABSTRACT

**Objective:** To analyse different causative factors leading to oral cancer.

**Study Design:** Descriptive type of study.

**Setting:** This study was conducted at the department of E.N.T, DUHS, Karachi.

**Study Period:** From Jan 2008, to October 2008.

**Subjects & Methods:** Fifty histopathologically proven patients of oral cancer were selected and analyzed regarding predisposing and causative factors. Patients having premalignant oral disease, post operative, post radiotherapy patients and patients with inconclusive reports of histopathology were not included in this study.

**Results:** The analyses of 50 cases of oral cancer revealed that the majority of the patients were indulged in the habit of Paan, Betel nut, Naswar, Tobacco Chewing and smoking. 42 out of 50 patients (84%) had history of indulgence into these habits. Only eight out of 50 cases (16%) had no habit of Pan, Betel nut, Naswar and smoking. Early tertiary care hospital presentation was only 36% and patients presented with stage II or I. Sixty four percent (64%) patients who reported at Civil Hospital Karachi (CHK) had stage III or IV.

**Conclusion:** The analysis of fifty patients of oral cancer revealed that majority of the patients were indulged in different chewing and smoking habits. Betel nut, Tobacco, Naswar and Paan Chewing were different causative and predisposing factors of oral cancer.

**Key Words:** Oral cancer, causative factors.

### INTRODUCTION

Since the beginning of last century, it has been well recognized that the oral cancer is one of the commonest cancers in subcontinent. In western world, oral cancers constitute 10% of all malignant tumors, standing second only to bronchogenic

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carcinoma in males and breast cancer in females and is the sixth most common cancer in the world<sup>(1)</sup>. The developing world had a different pattern, showing higher incidence of cancer of mouth, it is more common in the subcontinent than the western world. Another report describes oral cancer as number one amongst men and number three among women in the subcontinent.<sup>2</sup>

Oral cancers constitutes 20-35% of all cancers seen in various public sector hospitals in Karachi and

slightly less in other regions of Pakistan. Nevertheless it is a major killer in our population<sup>3</sup> It has been identified that the habit of Naswar, betel nuts and tobacco chewing and smoking are the major contributing factors in the occurrence of this malignancy. The (IARC) regards the chewing of betel quid to be a known carcinogen. Certain studies have tried to prove that regular chewers of betel nut have a high risk of damaging their buccal mucosa and acquiring cancer of the mouth.<sup>4</sup> However, it is not scientifically proven that chewing of the nut alone can be carcinogenic.<sup>5</sup> Studies have shown that chewing the nut along with tobacco (which is a known carcinogen), lime and betel leaf might be carcinogenic. Studies have found tobacco and caustic lime increase the risk of cancer from betel nut preparations.<sup>6</sup>

Studies exist of the use of a "pure" *paan* preparation: areca nut, betel leaf, and lime. While a single recent study claimed that unprocessed areca nuts, at high doses, displayed a very weak carcinogenicity.<sup>7</sup> In contrast, since 1971 many studies have found betel nut extracts to cause cancer in rodents.<sup>8</sup> In 2003 the (IARC) concluded that the habit of chewing betel quid with or without tobacco is carcinogenic to humans.<sup>9</sup> Support to this is provided by a recent study which found that paan even without tobacco is a risk factor for oral cancer. They found that paan with or without tobacco increases oral cancers risk, 9.9 and 8.4 times, respectively.<sup>10</sup>

According to several studies, the ingredients of Betel nut, Naswar and Tobacco act as oral carcinogens. Lack of education and awareness prevent people from reporting to a tertiary care hospital at an early stage. The delayed presentation to a specialized hospital poses a challenge to manage this disease. The spectrum of oral cancer varies from

place to place irrespective of country. Places within our country have various trends which gives chance to the causative and predisposing factors, causing oral cancers.

Cigarettes contain many cancer-causing agents (carcinogens). These include, tar, arsenic, benzene, cadmium, formaldehyde and polonium-210. Tar, the brown residue that stains smoker's teeth and fingers is a collection of solid particles. The risk of oral cancer increases depending since how long a person has been smoking and how often he or she smokes.<sup>12</sup>

Long term exposure to cancer-causing agents in cigarettes alters normal functions of oncogenes and tumor suppressor genes in oral tissues. These changes will eventually lead to uncontrolled cell growth and the onset of oral precancer. Several studies have found links between chemicals in cigarette smoke and cancer, by looking at the footprints, these chemicals leave on our genes for example, one study showed that benzo [a] pyrene, a chemical in cigarette tar, damages a key gene called p53.<sup>11</sup> The researchers found that p53 in cancer patients was damaged in exactly the same way as in their experiments.<sup>12</sup>

## **PATIENTS & METHODS:**

This study was conducted at the department of E.N.T Head & Neck Surgery, DUHS and CHK, which is a 1800 beds' tertiary care hospital. Fifty (50) histopathologically proven cases of oral cancer were selected during the period of 10 months. Patients having premalignant oral disease and patients with inconclusive reports of histopathology were not included in this study. A detailed and comprehensive history including the details and duration of symptoms were taken. A comprehensive

past history including surgical and medical illnesses, radiotherapy, chemotherapy and medication history was also taken.

Special emphasis was given on the personal history like habits and addiction. Betel nuts, Paan, Tobacco chewing, Smoking and Naswar addiction were inquired. Quantity of pan, tobacco, betel nuts and Naswar per day was also asked. In smokers, number of cigarette smoked per day and duration of indulgence into these habits were also recorded. Finally we took family and socioeconomic history. Complete clinical examination including Ear, Nose, Throat, Neck, Systemic CVS, CNS, respiratory and abdominal examinations were performed. Baseline routine hematological, biochemical and serological laboratory tests including CBC,Urine D/R,BT,CT, Hepatitis B and C viral screening, LFT and UCE were performed for every patient. Imaging studies included x-ray chest, P.A View, ultra sound and MRI from skull base upto the root of neck were also done. Ultimately a panendoscopy was done under general anaesthesia especially for second primary. Neck palpation was also done.

**Table 1:** Risk factors for squamous carcinoma

<ul style="list-style-type: none"> <li>· Betel nut and tobacco chewing</li> <li>· Naswar</li> <li>· Submucosal fibrosis</li> <li>· Smoking</li> <li>· alcohol intake</li> <li>· Malnutrition</li> <li>· Avitaminosis</li> <li>· Chronic glossitis</li> <li>· Plummer-Vinson syndroms</li> <li>· Hot spicy foods</li> <li>· Chronic dental diseases</li> <li>· Alcoholic mouth washes</li> <li>· Leucoplakia</li> <li>· Syphilis</li> <li>· Cirrhosis</li> <li>· Lichen planus</li> <li>· Chronic hyperplastic candidiasis</li> <li>· Human immunodeficiency virus (HIV)</li> <li>· Xeroderma pigmentosa</li> <li>· Dyskeratosis congenita</li> </ul>
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## RESULTS

A total of fifty (50) patients with oral cancer during 6-months period were analyzed.

Forty two patients out of fifty cases (84%) were habituated to either betel nuts, tobacco, naswar and smoking. Only eight, out of fifty cases (16%)there had no habit of these things.

Ten out of fifty cases (20%) were addicted to two things Paan(betel nuts & tobacco) and cigarette smoking. This study also shows dose-response relationship with respect to duration (time period in years) and frequency (number of times per day) of betel nut with tobacco chewing.

Majority of cases belong to low socioeconomic status (80%) Thirty one (31) out of fifty (50) cases i.e. 62% chew betel nut with tobacco with or without paan. Seven (14%) chew betel nut with tobacco for less than or upto 10 years. While twenty four cases (48%) chew for more than 10 years.

Fourteen percent (14%), chew for not more than 10 years, while Forty eight (48%) chew betel nut with tobacco for more than 10 years. This shows strong dose-response relationship to duration of betel nut with tobacco chewing (with / without paan) Only one oral cancer patient (02%) chew betel nut with tobacco for not more than 5 times a day, while 20 cases(40%) chew more than 5 times a day. This also shows very strong dose-response relationship with respect to frequency of betel nut with tobacco chewing (with / without paan). Urban (70%) to rural (30%) ratio was 7:3.

**Table 2: Habits**

Habits	Number of patients	Percentage
Betel nuts, Chewing, paan chewing with or without tobacco chewing	31	64%
Naswar	10	20%

**Table 3: Sex Incidence.**

Gender	Number of patients	Percentage
Male	38	76%
Female	12	24%

**Table 4: Site Involvement.**

Site involved	Number of patients	Percentage
Buccal mucosa	31	62%
Tongue	15	30%
Lips	5	10%
Floor of month	10	20%
gums & alveolus	5	10%
Hard palate	5	10%

**Table 5: Histopathological variants of squamous cell Carcinoma N=50**

Variant	No: of patients	Percentage
BWell differentiated	41	82
Moderately differentiated	06	12
Poorly differentiated	01	02
Carcinoma in situ	02	04

**Table 6: Frequency Of Betel Nut With Tobacco Chewing No: Of Cases = 50**

No:	Frequency (times per day) of betel nut with tobacco chewing (with / without paan)	No: of cases	%
1	≤ 05 times per day	02	04
2	> 05 times per day	29	58

**Table 7: Betel Nut And Tobacco Chewing (With Or Without paan) No: Of Cases = 50**

No:	Betel nut and tobacco chewing	No: of cases	%
1	Yes	21	42
2	No	10	20

**Table 8: Duration Of Betel Nut With Tobacco Chewing No: Of Cases = 50**

Duration (time period) of betel nut with tobacco chewing (with / without paan)	No: of cases	%
≤ 10 years	07	14
> 10 years	24	48

**Table 9: Frequency of betel nut with tobacco chewing No: of cases = 50**

No.	Frequency (times per day) of betel nut with tobacco chewing (with / without paan)	No: of cases
1	≤ 05 times per day	01
2	> 05 times per day	20

## DISCUSSION

Karachi is the largest city of Pakistan and Civil Hospital is the largest government tertiary care hospital of this city. Patients from the neighboring regions also approach for treatment at this institute. Oral cavity cancer is one of the commonest malignancies at Karachi. Chewing of paan containing betel nut and tobacco, sweet supari and “gutka” an indigenous preparation of tobacco with slaked lime in and around Karachi is a very common social habit.

Betel nut chewing is one of the major factors for this high incidence of oral malignancy. Number of betel leaf (paan) chewed per day by an individual is also high (15-25/day) in Karachi, which acts as a continuous irritant to the oral mucosa.<sup>13</sup> Use of smokeless tobacco (Paan Parag, city gutka etc) is on the increase in Karachi. A male to female ratio of 2.3:1 was observed. Smokeless tobacco, also known as chewing tobacco or snuff, is popular in different communities of Pakistan. Many studies have shown that smokeless tobacco can also cause oral cancer.<sup>14</sup> One study found that people who used smokeless tobacco had almost 50 times higher oral cancer risks than those who didn't.<sup>15</sup>

Most dangerous chemicals in smokeless tobacco are called tobacco-specific nitrosamines (TSNAs). One

review found that people who use smokeless tobacco expose themselves to thousand times more TSNA's than non-smokers, and up to 50 times more than smokers.<sup>16</sup>

Smokeless tobacco is also addictive as cigarettes. Some studies found that the amount of nicotine absorbed from smokeless tobacco is 3-4 times greater than that from a cigarette.<sup>17</sup> The nicotine is also absorbed more slowly and stays in the bloodstream for a longer time. Tobacco use is known as a major risk factor for oral and other cancers. All tobacco products, including cigarettes, cigars, pipe tobacco, chewing tobacco, and snuff, contain toxins (poisonous substances), carcinogens (cancer-causing agents), and nicotine (an addictive substance). Each tobacco product is linked to an increased risk for specific cancers. Smokers are six times more likely than nonsmokers to develop some form of oral cancers. Cigarettes contain more than 60 cancer-causing agents.<sup>17</sup>

The study confirmed that commonest histological variety is squamous cell carcinoma. Well differentiated i.e. Grade 1 squamous cell carcinoma was the highest in our group and this was similar to the carcinoma. Findings of type who reported 52.6% of patients who had well-differentiated tumors.

The buccal mucosa was found to be the most common site involved by the malignant process and was observed in 42.57% of our patients followed by the tongue in 58(19.14%) cases.

Interpretation of data from a single Institution do have limitations. The data reflects our specific patient population reporting to the hospital and not the community as a whole. Most of the patients had similar smoking or tobacco chewing habits. The

highest rate of oral cancer is found in the developing world where oral cancer alongwith that of pharynx is the third commonest site of cancer. In Pakistan, India, Bangladesh and Srilanka, oral cancers are most common and accounts for one third of all cancers.<sup>18</sup> Cultural differences in the use of tobacco lead to the variation in the geographic and anatomic incidence of oral and pharyngeal cancers in accordance with dose response and other factors. There should be an intense public education plan and appropriate prevention and cessation strategies for smoking and smokeless tobacco products along with a social war against alcoholism to revert back the present trend of preventable oral cancers.

Primary prevention measures including education and awareness programs are on the anvil. It is high time now that an early detection scheme will be started at this institution utilizing oral self-examination, toluidine blue staining, brush biopsy and scalpel biopsy as need be.

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