

## PATTERN OF ORAL SQUAMOUS CELL CARCINOMA — A STUDY

\*MUSLIM KHAN, BDS (LUMHS) (Sindh), FCPS (Oral Surgery)

\*\*NADIA MANSOOR, BDS (Pesh)

\*\*\*MUHAMMAD RIZWAN MEMON, BDS (LUMHS) (Sindh)

\*\*\*\*ABDUS SALAM, BDS (Pesh) MDS (Punjab) FCPS (Pak)

### ABSTRACT

*The study was carried out on a total of 312 biopsy proved patients of oral squamous cell carcinoma over a period of 3 years i.e., from 1<sup>st</sup> January 2004 to 31<sup>st</sup> December 2006 in Oral and Maxillofacial Surgery Unit of Khyber College of Dentistry, Peshawar. The aim of the study was to evaluate different patterns of oral squamous cell carcinoma in the North West Frontier Province. Amongst these 312 patients 214 were males (68.59%) and 98 (31.41%) were females. Male to female ratio was 2.18:1. The age range was from 11 years to 77 years, with the mean age of 58.8 years; SD  $\pm$ 12.69. While the most commonly involved age group was 7<sup>th</sup> decade of life (35.57%) followed by 6<sup>th</sup> and 8<sup>th</sup> decade (28.20%) and (15.38%) respectively. Mandibular left gingivolabial sulcus was the most commonly involved site i.e., 41.34%, followed by mandibular right gingivolabial sulcus (18.27%). The most common histological grade of the tumour was G1 i.e., well differentiated Squamous Cell Carcinoma (74.68%) followed by G2 i.e., moderately differentiated (21.15%) and G3 i.e., poorly differentiated oral squamous cell carcinoma (4.16%). 84% of patients had a positive history of Niswar dipping.*

**Key words:** Niswar, Oral Cancer, Khyber College of Dentistry, Snuff Dipping, Oral Squamous Cell Carcinoma, Oral Malignancy.

### INTRODUCTION

Squamous cell carcinoma is the most frequently occurring malignant tumor of the oral structures, accounting for about 90% of the malignant oral lesions, therefore, oral squamous cell carcinoma can be designated as "Oral Cancer" Epidemiological studies have shown that the incidence of oral cancer varies significantly amongst the continents and within developed and developing countries.<sup>1</sup>

The current hypothesis in oral carcinogenesis is that there is an accumulation of genetic mutations in the oral epithelial cells, with tobacco and betel quid mutagens identified as aetiological agents. It is esti-

mated that 75% of all intra-oral cancers in western countries can be attributed to smoking and alcohol.<sup>2</sup> However, only a small proportion of individuals who use tobacco, alcohol or betel quid develop oral cancer and there is an emerging population of oral cancer patients who lack exposure to these agents. Infection of the oral keratinocytes with human papilloma virus (HPV) may be involved in the development of oral cancer in some patients. A role for HPV in oral cancer is supported by findings of HPV in tumour tissue and by studies showing that HPV immortalizes oral keratinocytes in vitro.<sup>3,4</sup> HPV immortalized oral keratinocytes become tumorigenic in mice following exposure to tobacco related chemicals in vitro.<sup>5</sup> The E6

\* Assistant Professor, Oral and Maxillofacial Surgery Unit, Sardar Begum Dental College and Hospital, Peshawar. E Mail. muslim177@hotmail.com muslim\_khan177@yahoo.com Ph. 0300-5846906 091-2561081

\*\* Resident, Oral and Maxillofacial Surgery Unit, Khyber College of Dentistry, Peshawar

\*\*\* Resident, Prosthodontics Unit, Khyber College of Dentistry, Peshawar

\*\*\*\* Professor and Dean, Post Graduation Dentistry, Gandhara Institute of Health Sciences, Sardar Begum Dental College and Hospital, Peshawar

and E7 genes of HPV 16 and HPV 18 encode proteins that are involved in the direct destruction of p53 and retinoblastoma (pRb) growth-regulatory proteins respectively.<sup>3</sup> In contrast, mutagens in tobacco, alcohol and betel quid are thought to damage important growth regulatory genes in oral keratinocytes resulting in cancer formation. Chronic infection of oral keratinocytes with *Candida Albicans* may have a role in oral carcinogenesis. *Candida albicans* stimulates epithelial cell proliferation in vitro and oral lesions of chronic hyperplastic candidosis (candidal leukoplakia) show epithelial dysplasia and may undergo malignant transformation.<sup>6</sup> Furthermore, *Candida Albicans* was shown in rates to be an effective promoter of 4-nitro-quinoline-1-oxide (4NQO)-initiated oral mucosal squamous cell carcinoma.<sup>7</sup>

It was not been possible to prove conclusively a causative association between specific etiologic factors and oral cancer (Oral SCC). This is partly because the quality of cancer statistics is very much variable and partly because the etiology of the malignancy is complex and multifactorial, causative factors operate over a long period and the process of malignant change is so slow that there is a prolonged lag period before the disease appears.<sup>8</sup>

Oral SCC is a common problem in the region because of use of smokeless tobacco in the form of Niswar, low socio-economics, lack of dental motivation, bad oral hygiene and professional delays. The rationale of the study is to evaluate different patterns of oral SCC in a population of North West Frontier Province (NWFP) and to make the people of the region realize that snuff (Niswar) is a strong risk factor in the aetiology of oral SCC. The study may provide evidence

for recommendation of possible preventive measures and early diagnosis and management of this grave disease..

## MATERIALS AND METHODS

The study was carried out in Oral and Maxillofacial Surgery Unit of Oral and Dental Hospital, Khyber College of Dentistry, Peshawar over a period of three years i.e., from 1<sup>st</sup> January 2004 to 31<sup>st</sup> December 2006. This Unit is a tertiary care centre for the treatment of oral and dental diseases in NWFP. The study was carried out on 312 biopsy proved oral SCC patients. All the patients irrespective of age and sex, confirmed on biopsy and histopathological findings as Oral SCC were included in the study.

A standard history and clinical examination chart was completed for each patient. All the information about the variables of the study like, age, gender or sex, site distribution, positive or negative history of snuff (Niswar) dipping were recorded.

## RESULTS

The mean age of the patient in the present study was of 58.8 years; SD  $\pm 12.69$ , the age range was from 11 years to 77 years. 10.575% of patients were suffering from Oral SCC below 40 years of age. The most commonly involved age group was the 7<sup>th</sup> decade 35.57% followed by 6<sup>th</sup> and 8<sup>th</sup> decade (28.205%) and (15.38%) respectively. (Table 1). 89.4% of patients were aged above 40 years. Oral SCC was common predominantly in males (68.59%), as compared to females (31.41%). The male to female ratio was. 2.18:1 (Table. 1)

Mandibular left gingivolabial sulcus (Fig. 2) was the most common site of oral SCC, (41.346%) which was

Age in years	Sex		Total	Percentages
	Males	Females		
11-20	3	None	3	.96%
21-30	10	2	12	3.84%
31-40	12	6	18	5.77%
41-50	23	9	32	10.25%
51-60	52	36	88	28.2%
61-70	77	34	111	35.57%
71-80	37	11	48	15.38%

TABLE 1: AGE AND GENDER DISTRIBUTION OF ORAL SCC PATIENTS

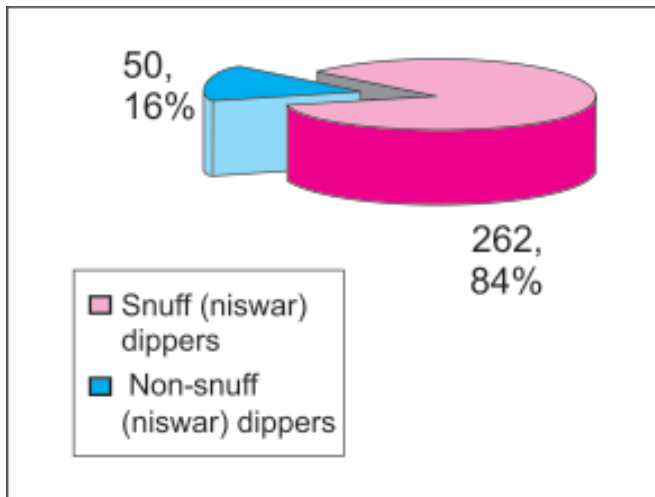


Fig. 1. Snuff dippers and non-snuff dipper Oral SCC Patients



Fig. 4: SCC of the cheek ucosa (non-Snuff dipper female patient)



Fig. 2: Fungating mass in mandibular Left Gingivola-bial-Sulcus in a Snuff (Niswar dipper). (The Most Common site)

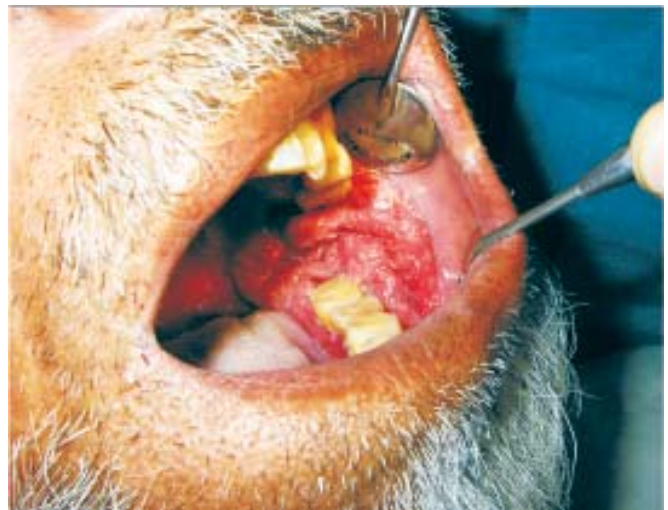


Fig. 5: SCC of the retromolar Triagone



Fig. 3: Mandibular Right Gingivolabial Sulcus (Ulceration)



Fig. 6: SCC of Posterior hard palate



Site of the lesion	No of patients	Percentage
Mandibular Left Gingivolabial Sulcus	129	41.34%
Mand Right Gingivolabial Sulcus	57	18.27%
Mand Lt & Rt Gingivolabial Sulcus alongwith the floor of mouth	43	13.78%
Floor of the mouth	7	2.24%
Maxillary Rt Gingivolabial Sulcus	4	1.28%
Maxillary left gingivolabial sulcus	3	.96%
Retromolar Triagone	11	3.52%
Buccal Mucosa	9	2.88%
Posterior lateral border of the Tongue	17	5.45%
Anterior lateral border of the tongue	14	5.48%
Ventrum of the tongue	3	.96%
Tip of the tongue	1	.32%
Anterior hard palate	9	2.88%
Posterior hard palate	5	1.6%

TABLE. 2: SITE DISTRIBUTION OF ORAL SCC PATIENTS

Grading	No of Patients	Percentages
G1	233	74.68%
G2	66	21.15%
G3	13	4.16%
Total	312	100%

TABLE 3: HISTOPATHOLOGICAL GRADATION OF ORAL SCC PATIENTS

also the most common site of Niswar dipping in both male and female patients. The other sites where the lesion had occurred were mandibular right gingivolabial sulcus, (18.27%), mandibular left and right gingivolabial sulcus along with the floor of the mouth (13.78%). The least involved site was the tip of the tongue (.32%). (Table 2).

Out of 312 patients of Oral SCC, (84%) had a positive history of snuff (Niswar) dipping, while 16% had not (Fig 1). The habit of Niswar dipping was found more

common in male sufferers than female sufferers. Most of the tumours were well differentiated Squamous Cell Carcinomas i.e. G1 (74.68%) followed by moderately differentiated i.e. G2 (21.15 %) and poorly differentiated i.e. G3 (4.16%) (Table 3).

## DISCUSSION

Oral cancer is the sixth most common cancer worldwide.<sup>9</sup> The incidence rate of oral cancer in United States is about 11 cases per 100,000 persons per year, and the incidence increasing with age.<sup>10</sup> Oral cancer is responsible for 2% of all cancer deaths in United States. Sixty percent of these cancers are well advanced by the time they are detected. Therefore, cancers of the oral mucous membranes continue to cause considerable mortality and morbidity in the United States, with a 5 years survival rate of about 30%.<sup>11</sup>

Oral cancer is also a common problem of Pakistan and other South and South East Asian countries. This is most probably due to tobacco chewing habits of a vast cross section of population of these countries.<sup>12</sup> The present study and the past study conducted in the same Unit some 20 years back (*Khadim 1985*)<sup>13</sup> suggests that oral SCC is a common problem in the region.

According to the present study Oral SCC is a disease of old age, 89.4% of the patients were aged more than 40 years. The most common age group was the seventh decade of life i.e. 35.57%. Other studies confirm these findings like Jusawala<sup>14</sup>, Cawson RA, Odell EW<sup>15</sup> and Zaidi SH.<sup>16</sup> Oral SCC is predominantly a disease of the male patients (68.59%) than the females (31.41%), with male to female ratio of 2.18:1. the study correlates with the Khadim's study in which 71.42% were the male sufferers and 28.42% were female. But contrary to the study of *Johan Isaac Usha Isaac and Naveed R Qureshi (2004)*,<sup>17</sup> a recent study conducted at (*LUMHS*) *Liaquat University of Medical and Health Sciences Jamshoro*, the female patients (59.25%) outnumber males (40.74%). In the United Kingdom the male to female prevalence of Oral cancer was 5:1 in 1932-1939, but has become 1:1 by 1960-1969.<sup>18</sup>

The most common site for the Oral SCC according to the present study is the lower left gingivolabial sulcus 41.346% which is also the most favorite site for the habitual placement of Niswar, followed by mandibular right gingivolabial sulcus (18.27%). 84% of the

patients were snuff (Niswar) dippers. This analysis correlates with *Hirsch JM, Heyden G and Thilander H (1982)*<sup>19</sup> study that the oral effects of the smokeless tobacco are typically seen on the mucosal surfaces where the product is placed i.e. the primary site of placement of the smokeless tobacco. Based on numerous studies, the consensus is that smokeless tobacco use causes oral cancer, typically 20-50 years of use is required to cause the malignant changes in the oral mucosa. According to a study by Winn DM, Blot WJ,<sup>20</sup> on oral cancer among women in Southern United States, snuff dipping over the years results in the buccal sulcus carcinoma directly adjacent to the site where it is habitually placed (primary site of placement). Recent studies have also shown a trend of increasing percentages of ridge and gingival cancers.<sup>21,22</sup> In Taiwan, they occur most often on the buccal mucosa (40.8%) then on the tongue (25.6%), the lower gums (17.1%).<sup>23</sup> Martin reported that approximately 10% of all malignant tumours of the oral cavity occur on the gingiva, and that the tumours arise more commonly on the edentulous areas, although they may develop at sites where teeth are present.<sup>24</sup> It is generally agreed that carcinomas of the mandibular gingiva are more common than those of the maxillary gingiva<sup>25</sup> and 60% of these are located posterior to the premolars.<sup>26</sup>

The term differentiation refers to the extent the tumour cells resembles their mother cells (cells of origin) i.e. cells of stratified squamous epithelium both structurally and functionally. And according to the degree or grade of differentiation of its neoplastic cells, Oral SCC graded as follows.<sup>27</sup>

G0- Grade cannot be assessed

G1- Well differentiated oral SCC

G2- Moderately differentiated oral SCC

G3- Poorly differentiated oral SCC

Most of the tumours were well differentiated SCC, i.e. G1 (74.68%) followed by moderately differentiated, i.e. G2 (21.15 %) and poorly differentiated i.e. G3 (4.16%) the present study is consistent with that of the John Isaac study<sup>17</sup> as far as the histopathological gradation is concerned. Histopathological features of oral SCC vary from well differentiated to moderately differentiated to poorly differentiated. Poorly differentiated oral SCC has the worst prognosis. Understand-

ing the biological behaviour of tumours is established through histopathological investigations.<sup>28</sup>

This is of interest for oral oncologists and surgeons because there has been a correlation between histopathology and prognosis. This finding has got a great bearing on prognosis and 5 year survival because the prognosis for poorly differentiated and undifferentiated tumours is poor as compared to well differentiated tumours. Histopathology of the tumour is favorable, i.e., most of the tumours are predominantly well differentiated but it is very unfortunate that most of these patients present at a later advanced stage (stage III and IV), making the prognosis and five years survival poor. . Silent (painless) nature of the disease, difficult examination (lesion in the posterior one third of the tongue), low socio-economics, lack of dental motivation, bad oral hygiene and professional delay (lack of properly trained dental professionals in the far flung areas of the province) are some of the factors responsible for late presentation of this deadly tumour.<sup>29</sup>

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