



## Incidence of Oral Cancer and Outcome of Treatment in a Single Institution Based Retrospective Study

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### Abstract

*Oral cancers have a very high incidence in males. But at present the incidence is also on the rise in females due to smoking, chewing tobacco and betel nut habit or addiction. The basic aim of our study is to compare both the sexes clinically, epidemiologically, etiologically, histopathologically and also as per the biological behavior of the tumor, regarding out-come of the different modalities of treatment to determine if any difference exists between the males and females.*

**Keywords:** Oral cancer, addiction, epidemiology, biological behavior.

### Introduction

The global cancer burden is estimated to have risen to 18.1 million new cases and 9.6 million deaths in 2018. The increasing cancer burden is due to several factors, including population growth and ageing as well as the changing prevalence of certain causes of cancer linked to social and economic development. Global pattern shows that for men and women combined nearly half of the new cases and more than half of the cancer deaths worldwide in 2018 are estimated to occur in Asia, in part because the region has nearly 60% of the global population<sup>1</sup>. The incidence of oral cancer is ranked among the top three types of cancer in the country<sup>2</sup>. In

comparison with the U.S. population, where oral cavity cancer represents only about 3% of malignancies, it accounts for approximately 12 % of all malignancies in India<sup>3</sup>. According to Globacon 2018, incidence of Lip and oral cavity cancer is 119,992, rank 2 (11.42%), with cumulative risk 1.02%. Death rate due to Lip and Oral cancer is around 72,616, ranked 2nd for causing cancer death and 5 years prevalence rate (all ages) is 265,255<sup>1-3</sup>. It is a major oncological problem in the regions of the world where tobacco habits in the form of chewing and/or smoking with or without alcohol intake are common. Cigarette and Bidi smokers are presently 5.7% and 9.2% of adults respectively and 10.3% and

16% males and 0.8 %, 1.9% of females respectively<sup>4-5</sup>. Consumption typically occurs in exaggerated form in the elderly men during the fifth through eighth decade of life and 9.6% of adolescent consume tobacco in any form in between age group 15 -17 years. Most studies have yet to find a difference if any between male and female oral cancers, if any such difference exists<sup>6-7</sup>. This retrospective study in a single urban based Oncology and associate units at Govt Medical College & Hospital, aims at finding any such differences.

### Materials and Methods

A retrospective analysis of the patients with oral cancer presented at our oncology and Ear, Nose, Throat (E.N.T) and Dental Department at Urban based Govt Medical College & Hospital, between October, 2014 to September, 2017, was carried out. Data extraction was carried from the case registers. Inclusion criteria were patients with oral cancer attending OPD of Radiotherapy, E.N.T and Dental department.

Exclusion Criteria- included patients with terminal cancer not amenable to any form of treatment other than palliative care and no consenting patients i.e. refusing any form of treatment.

The anatomical sites reviewed in this study included lip, buccal mucosa, upper and lower alveolus, hard palate, anterior 2/3 of tongue and floor of mouth.

Variables analyzed for each patient included age, sex, history of tobacco and alcohol abuse, history of any cancer in the first-degree family members, nutritional and socioeconomic status, oral hygiene, presence of premalignant lesions, histology, clinical extent and lymph node involvement at the time of presentation, surgery, role of radiotherapy and chemotherapy, disease free survival and follow-up.

All variables were entered in a database for analysis. Simple charts and tables were used for tabulating the data for analysis.

The treatment of the patients was divided into 3 categories:-

Group A- these patients underwent upfront surgery only. Only those with

clinical Stage I,II,III, and operable IVA

Group B- Upfront surgery was followed by adjuvant therapy based on high risk

Features- 1. Positive margins 2. pT3, pT4 primary 3. N2, N3 nodal disease 4.Extracapsular nodal spread 5. Vascular /perineural invasion

Group C- Concurrent Chemo radiotherapy was given- Patients had locally advanced disease not amenable to resection.

The patients were followed up initially monthly for 1 year and the 3 monthly subsequently. DFS was calculated from the time of completion of treatment till the time of recurrence, both local and distal. Overall survival was calculated from the time of diagnosis till death or till the last follow up.

### Observations

A total of 100 patients with oral cancer in the 2-year period from October'2015-September'2017 were retrospectively analyzed. Buccal mucosa was the commonest site identified in 16 (62%) females and 35 (48%) males.

There were 73 (73%) males and 27 (27%) females, with a male to female ratio of 2.7:1.

The median age at presentation was 50 years in the females and 48 years in the males.

Incidence of young patients (<40 years) was lower in the females 19% compared to 34% amongst the male patients.

The median time to presentation was 4 months in females and 2 months in males.

Socioeconomically, among the females, 6 patients were belonging to above poverty line and these included 1 patient in stage 0, 2 patients in stage I, and 3 patients in stage II.

Of the patients in below poverty line (n=21), only 1 patient was in stage I, the rest 20 were all in stage III and stage IV (74%).

Among the male patients, 33 patients were above poverty line of whom, 4 patients were in stage 0, 11 patients in stage I, and 18 patients in stage II.

Of the patients in below poverty line (n=40) only 2 patients were in stage I, 5 patients were in stage II and the remaining 33 patients were all in stage III and stage IV (45%) (chart-1).

Concerning oral hygiene, halitosis was found in 10 female patients, dental caries in 11 patients and both were found in 3 patients. Among the male patients, halitosis and dental caries were found in 30 and 15 patients respectively and both were found in 5 patients.

Concerning precancerous lesions, OSMF was found in 33% females compared to 14% males. Leucoplakia was found in 26% females compared to 20% in males (chart-1).

More than 50% patients in either group (67% of females, and 90% males) were habituated to tobacco chewing, smoking, bidi, gutkha and alcohol (chart-1).

The median duration of addiction in either group was 15 years in females and 30 years in the males

Family history of cancer was found in only 10% females and 11% males.

Histologically, only squamous cell carcinoma was found. Among females incidence of low grade tumours was 26%, (compared to 25% in males), incidence of intermediate grade tumours was 33 % compared to 64% in males, and incidence of high grade tumours was 41 %, compared to 11% in the males (chart-1).

Stage wise distribution of patients was as follows-  
For females-

Stage 0- 4%, n=1; Stage I - 7%, n=2; Stage II - 15%, n=4 ; Stage III- 37%, n=10;

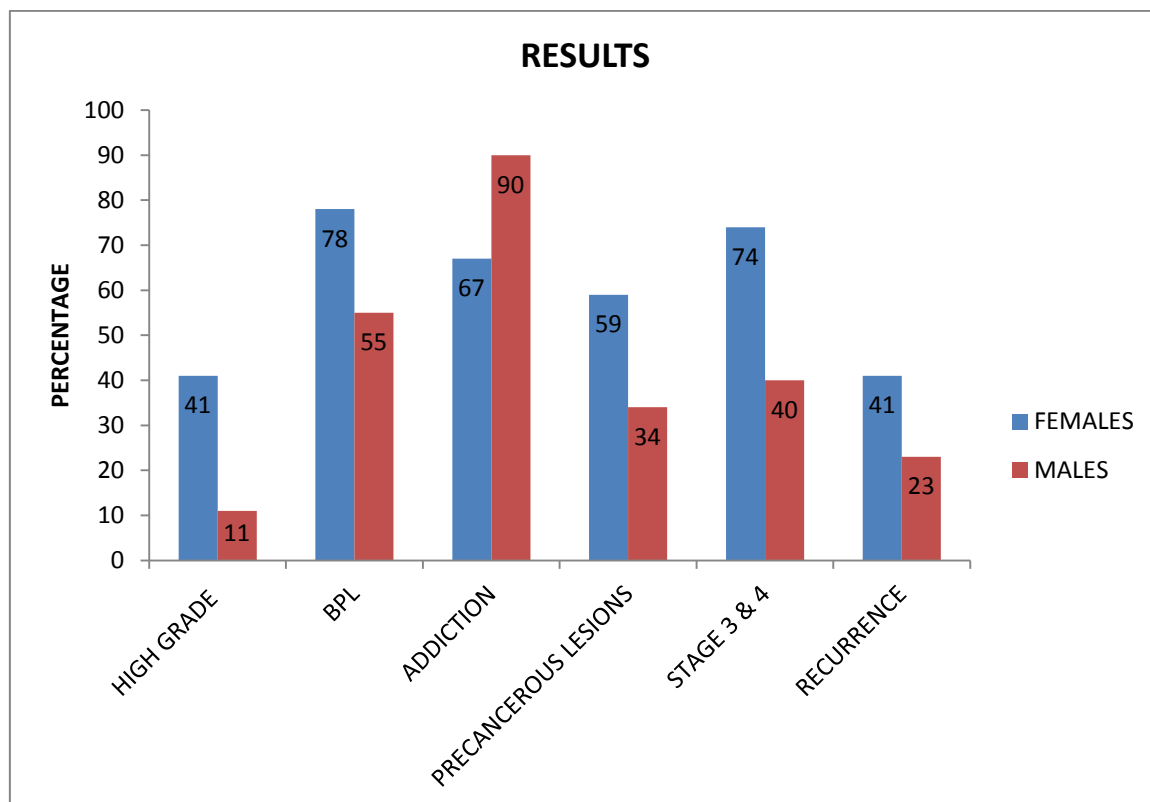
Stage IV- 37%, n=10

For male-

Stage 0- 5%, n=4; Stage I - 19%, n=1 ; Stage II - 32%, n=2; Stage III- 14%, n=10

Stage IV- 26%, n=19

(chart-1) .



**Chart-1**

Upfront surgery only was performed in 19% females and 38% males [GROUP-A]. Surgery followed by adjuvant treatment was done in 70 % females and 55% males [GROUP-B]. Concurrent

CTRRT was offered to 11% females and 7% males, only a few of whom underwent subsequent surgery[GROUP-C] (chart-2).

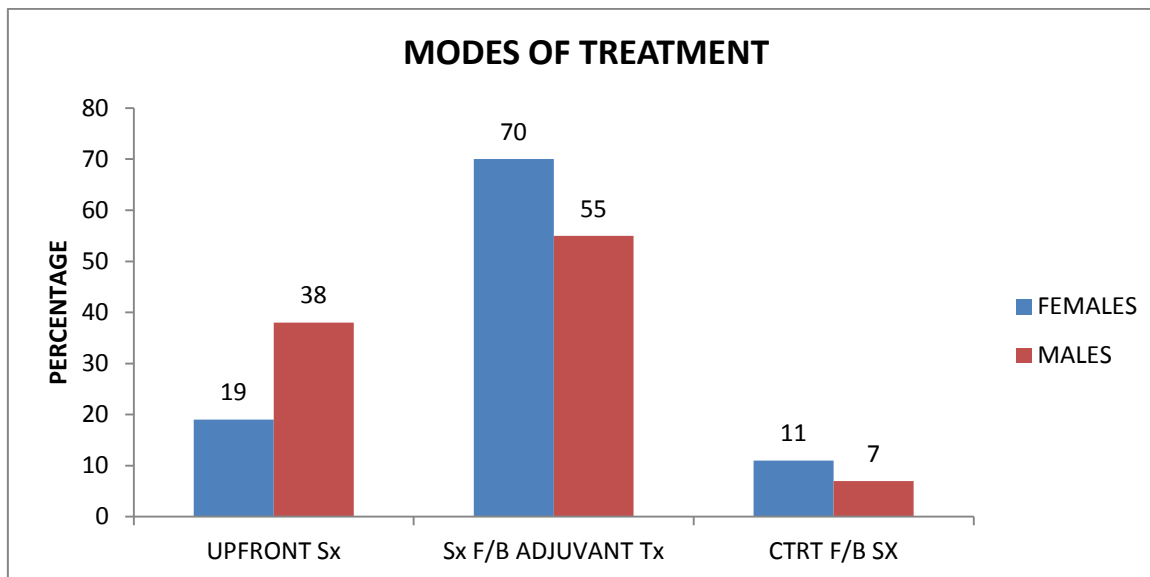


Chart-2

After the completion of treatment overall 25 out of 100 (25 %) patients developed recurrences. 41% of the females and 23% of the males developed recurrences. Among the recurrences, all the females developed loco regional recurrences. This was similar to the male patients except for one who developed a systemic recurrence. For the recurrent lesions, surgery and chemotherapy were the options in the management as all of them had already been subjected to radiotherapy. Amongst the females, 10 patients were put on palliative chemotherapy due to inoperable recurrence of whom 9 people died and one is alive with disease with empirical treatment with oral TKI. 1 Patient

was treated with surgery due to resectable recurrence and is alive at present. Amongst the males, only 2 were offered resurgery due to resectable recurrence, the rest (n=12) were put on palliative chemotherapy or best supportive care (chart-1).

At the last follow up, amongst the female patients, 63% were alive without any evidence of disease, 33% were dead while 4% were alive with disease, undergoing further treatment .Of the male patients, 79% were alive without any evidence of disease, 19% were dead while 1% was alive with disease, undergoing treatment with oral TKI(chart- 3).

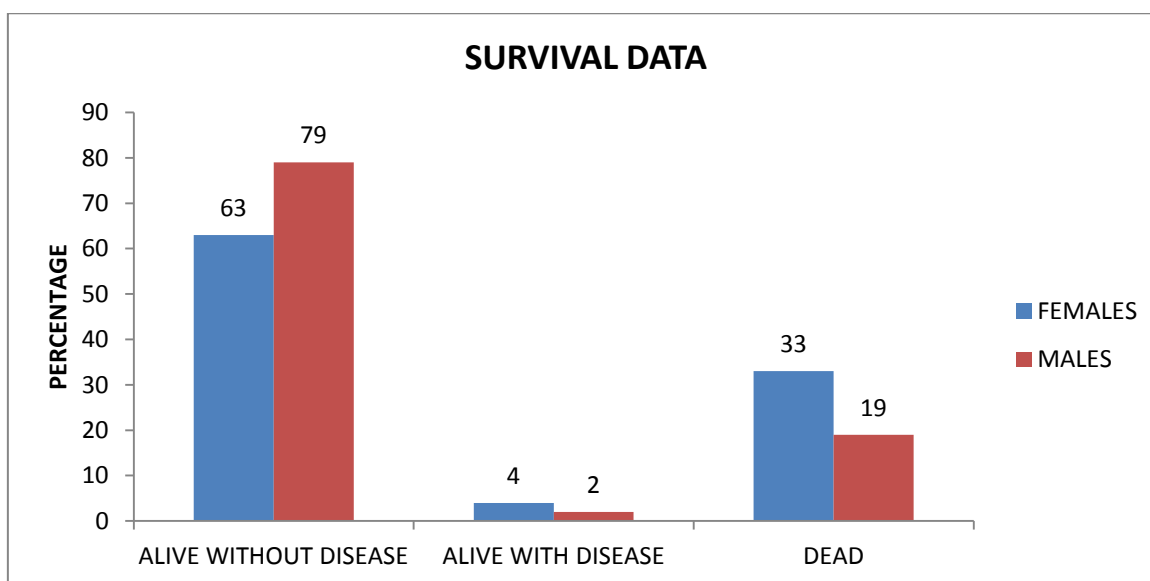


Chart-3

Site Specific incidence of mortality in females was highest for buccal mucosa, 50% cases followed by 17% each for tongue, lip and central arch. For the male patients, Site Specific incidence of mortality was highest for buccal mucosa, 57% followed by 14% for tongue, central arch and lower alveolus.

The median disease free survival (DFS) in this study group at 3 years was 12 and 14 months respectively in the females and males. The median overall survival was also 12 and 16 months respectively in females and males (chart 4 & 5).

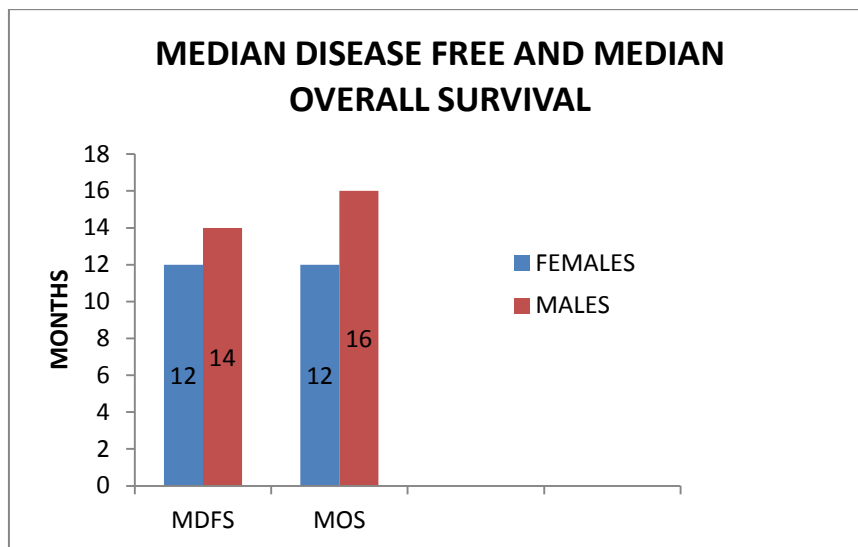


Chart-4

Survival in stages 0, I,II,III and IV were respectively 24,15,15, 9 and 6 months in females

compared to 22,18,12 and 8 months in males (chart-4).

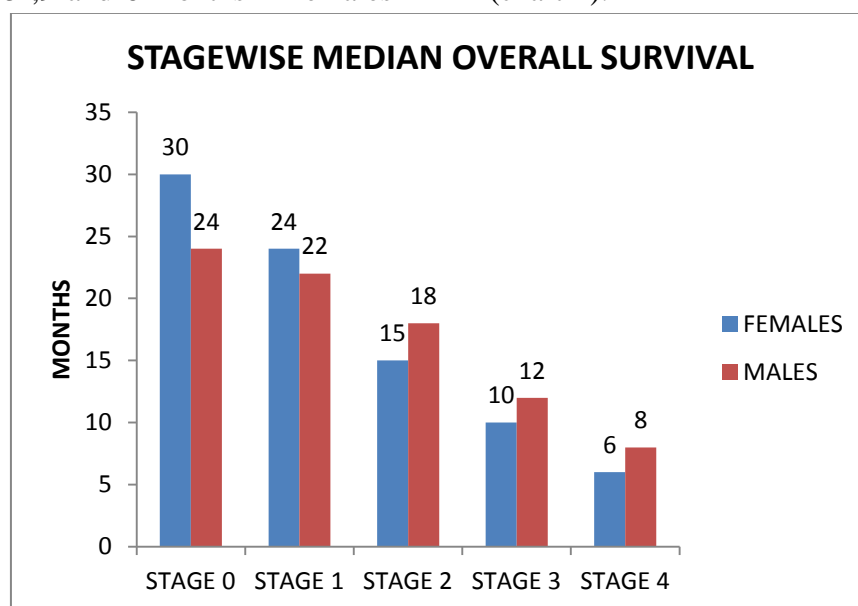


Chart- 5

**Discussion**

Oral cancer in female patients constituted 18% of all cases presenting at our institute over the period of 3 years from October 2014 to September 2017. There is an overall male predominance 2.7:1. Shakaranarayanan et al<sup>8</sup> and Swati Sharma<sup>9</sup> et al

study shows a sex ratio of 2: 1 in favor of male patients . Incidence of young patients (<40 years) was lower in the females, that is 19% compared to 34% amongst the male patients. Overall incidence of oral cancers below 40 years of age was found to be- 30%. Kapil et al<sup>10</sup> and Gupta PC<sup>11</sup> et al

showed that substantial number of the patients in their study were young adults (below 40 years age) .

The median age at presentation was higher in the females by 2 years (50 years in the females and 48 years in the male patients). The median time to presentation was also 2 months later in the females (4 months in female patients and 2 months in male patients).

Buccal mucosa was found to be the commonest site in both males and females with females having an incidence of 62%, compared to 48% in the males. This is in keeping with other recent studies like Riaz Abdulla and Soniya Adyanthaya et al, where the incidence of buccal mucosal cancers was 27.9% and tongue 29.0 %<sup>[11-12]</sup>.

Acquisition of the tobacco habit typically occurs early in life through imitation of a family member or peers. Various studies carried out across the country report that at least a third of school students less than 15 years of age have used one form or another of tobacco. Less females and more males were habituated to tobacco chewing, smoking, bidi, gutka and alcohol. The median duration of addiction in either group was less females compared to males

Socioeconomically, higher percentage females were below the poverty line (78% vs 55%) and also were associated with poorer oral hygiene (78% vs 62%).

Family history of cancer was found more in male c.t females (11% vs 10%) This was probably due to less peer effect on the females. Overall incidence of family history was 11% almost similar to Iype et al<sup>[5]</sup>, where it was 12.2%.

Histologically, only squamous cell carcinoma was found similar to Gonzalez et al.<sup>[6]</sup> Iype et al<sup>[5]</sup>, also found tumours of the minor salivary gland and soft tissue sarcomas. Ravi et al<sup>[4]</sup> found basal cell carcinoma besides SCC.

Incidence of grade I tumours amongst females and males was comparable, (26% vs 25 %), while the incidence grade II tumours was lower in females (33% vs 64%); and the incidence of grade III tumours was higher in females (41 % vs 11%).

Of the precancerous lesions, only oral submucosal fibrosis and leucoplakia were found. The incidence of these precancerous lesions was also higher in females. Overall incidence was 36%. Iype et al<sup>[5]</sup> found precancerous lesions in the form of leukoplakia, sub mucous fibrosis, lichen planus and erythroplakia, these were present in 11% patients.

Incidence of Stage 3 &4 tumours was higher in the females (74% vs 40%). Overall, 49% of the cases presented in stage III and Stage IV disease. Sankaranarayanan et al<sup>[8]</sup> .shows only 10% to 15% of cases present in localized stages. Ken et al<sup>[13]</sup> also reported that 48% of these oral cancer cases presented in stage III and IV.

Less no of female underwent upfront surgery (19%vs 38%). Incidence of locally advanced cancers considered irresectable was also higher in the female (11% vs 7%). Surgery followed by adjuvant treatment was done in a higher percentage of female (70 %) in comparison to 55% male. Concurrent CTRT was given equally to 11% female and 7% male, all of whom underwent subsequent surgery.

At the completion of treatment female recorded higher recurrences (41% vs 23%) and higher mortality (33% vs 19%).

Site Specific incidence of mortality in female was highest for buccal mucosa in both the sexes. These findings are not in agreement with Larond et al<sup>[14]</sup>(2008) showing the tongue and the floor of mouth cancer as the lower 5 year survival rate. Capilla et al<sup>[15]</sup> (2007) claims that the mandibular trigone is the worst site for survival prognosis when compared to lip, tongue and floor of mouth. DFS & OS and stage wise survival was also lower in female (12 vs 14 months & 12 vs 16 months respectively) which is similar to other study<sup>[16]</sup>.

### Conclusion

The study therefore demonstrates presents more biologically aggressive tumour in the females leading to poorer DFS and OS in spite of lower incidence and duration of addiction which is one of the prime risk factors in causing oral cancers.

More in-depth studies are needed to investigate the aetiology of intraoral cancer in female patients. Any ulcer or lesion at a younger age should not be dismissed easily, even if it is not habit related. High index of clinical suspicion in high incidence areas should lead to further investigation in order to identify the disease in early stage, which is perhaps the only way to ensure good prognosis. Improving the incidence, mortality, and survival rates of oral cancers requires a multi-tier structural approach that targets society, dentists, communities, and the individual. Efforts should be maximized to increase the early detection of localized lesions and pre-cancers, coupled with "aggressive" counselling in tobacco cessation and alcohol use for OPC outcomes to improve.

Improving overall socioeconomic status can also be beneficial in improving nutritional and educational status, thereby having long term effects in reducing risk factors of cancer.

Reducing smoking rates through the enactment of a nation-wide smoking ban would also reduce OPC, given the highly interrelatedness of smoking and OPC. Reducing alcohol and cigarette consumption should also be targeted. More randomised studies are necessary to fully study the epidemiological patterns of oral cancers in female patients as compared to their male counterparts in the Indian population for more definitive conclusions.

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