



Clinico Pathological Characteristics and Treatment Outcome in Female Patients with Carcinoma Tongue

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Abstract: Globally, oral cancer is the sixth most common cancer. In India it is the most common cancer in men and third most common cancer in women, the tongue is the most common location and accounts for approximately 25% to 40% of oral cancers. The incidence of carcinoma tongue is higher in an older age group, especially men, with a long history of tobacco use and alcohol consumption. Recently, however, there has been an increase in the incidence of oral cancer in a younger population especially in women who have not been exposed to the conventional risk factors. Although tongue cancer is not one of the most common cancers in women, this increase in occurrence has raised concern. This study intends to find out the patterns of presentation and treatment outcome in female patients who were diagnosed with carcinoma tongue at our center. This was a retrospective analysis to describe the clinic pathological characteristics and to find out the treatment outcome in female patients with carcinoma tongue treated at our center during the period 1st January 2015 to 31st December 2020. All cases of histopathologically proven tongue cancers were included in our study. The quantitative variables were summarized using descriptive statistics and the qualitative variables were summarized using number and percentages. The Kaplan- Meier method was used to find out the overall and disease free survival. The data was analyzed using statistical software SPSS version 20. A total of 295 females were diagnosed with carcinoma tongue during the study period. The median age of the study population was 62 years. 45% patients had a history of chewing tobacco. 25% patients had family history of malignancy. 43% of patients had comorbidities. The most common site of involvement was the lateral border in 82% of cases. 42% had well differentiated squamous cell carcinoma histology. 71% of patients presented with ulcer and pain. 62 % of patients presented with stage III and stage IV disease. 52% patients underwent radical intent treatment. 21% patients underwent palliative intent radiation or chemotherapy treatment and 27% patients did not undergo any treatment. Median follow up was 36.9 months. The three year DFS was 71% and 3-year OS was 76.5%. The 3 year DFS and OS for stage I disease was 80.3% and 80.5%. For stage II it was 88.7% and 95.8%. For stage III it was 69.2% and 69.8% and for stage IV it was 54.6% and 62.6% respectively. Oral tongue cancer presents in advanced stages and carries poor prognosis. Its increasing incidence in females is a growing concern. Our study showed that the clinicopathological profile and outcomes were similar to the literature data. More studies are needed to find out if there is any difference in treatment outcome with the male counterparts. Also studies are needed to find out the mechanisms involved in carcinoma development in non-habituates females.

Key words: Clinical outcome, Female tongue cancer.

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1. INTRODUCTION

Tongue cancer is one of the most common head and neck cancers.¹ The most common histological type of oral cavity cancer is squamous cell carcinoma (SCC), with the tongue being the most frequent site of occurrence.^{2,3} The standard treatment for oral cavity cancer is surgery. However, in locally or locoregionally advanced disease, combined-modality therapy with surgery followed by adjuvant radiotherapy (RT) or chemoradiotherapy (CRT) is indicated.⁴ The incidence of tongue cancer has increased significantly in both men and women, particularly in younger patients (≤ 40 years).⁵ Furthermore, there have been no improvements in 5-year overall survival (OS) and disease-free survival (DFS), which remain in the range of 50%-60%.^{6,7} The incidence of ca tongue is higher in an older age group, especially men, with a long history of tobacco use and alcohol consumption. Recently, however, there has been a reported increase in the incidence of oral cancer in a younger population especially in women who have not been exposed to the traditional risk factors for an extended period of time. Although tongue cancer is not very common in women, this increase in occurrence has caused concern. Several descriptive studies on trends in oral tongue cancer, indicating that the number of incidences has dramatically increased among young white people, mainly women.⁸ The aim of our study was to describe the clinicopathological characteristics and to find out the treatment outcome in terms of overall survival and disease free survival in female patients with carcinoma tongue treated at our center during the period 1st January 2015 to 31st December 2020.

2. METHODOLOGY

This retrospective analysis included demographic details and clinicopathological variables collected from medical records. The inclusion criteria comprised patients who underwent

curative or palliative intent treatment at our center, including surgery, radiation therapy, or systemic therapy. The exclusion criteria included patients with incomplete medical records, prior cancer treatment at another center, or those with a history of neoadjuvant chemotherapy before primary treatment. At our center, all cases were reviewed in a multidisciplinary tumor board comprising surgical and radiation oncologists, radiologists, and pathologists. Treatment decisions, including curative or palliative intent, as well as the choice between surgery or radiation therapy, were made by the tumor board. The primary treatment modality was surgery, followed by adjuvant therapy, which included radiation therapy and/or chemotherapy. Adjuvant RT was administered at a dose of 60 Gy in 30 fractions. Patients deemed unfit for radical intent treatment were offered palliative radiotherapy, either 30 Gy in 10 fractions or 20 Gy in 5 fractions. Following radiation therapy, systemic chemotherapy or oral metronomic chemotherapy was provided based on age and performance status. Patients with poor general condition and performance status, unsuitable for active cancer-directed treatment, received best supportive palliative care. Overall survival (OS) was calculated from the time of diagnosis to death from any cause or the last follow-up date. Disease-free survival (DFS) was assessed in patients treated with curative intent and was calculated from the date of surgery to the occurrence of locoregional failure, distant failure, or death from any disease, whichever occurred first

3. STATISTICAL ANALYSIS

The statistical analysis was done using SPSS version 20.0. Continuous variables such as age were summarized in terms of either mean $\pm$ Standard Deviation or median (Interquartile range) depending on the statistical distribution of data. Categorical variables were expressed in terms of frequency and percentage. Survival analysis was done using Kaplan Meier curves.

4. RESULTS

A total of 295 patients were analysed. The median age of the study population was 62 years (24 to 95).

Table 1: Baseline characteristics

Habits	Yes	50.8%
	No	45.8%
	Unknown	2.4%
Family History	Yes	25%
	No	73%
	Unknown	2%
Comorbidities	Yes	43%
	No	57%

Table 2: Disease characteristics

Site	Left Lateral Border	44.7%
	Right Lateral Border	37.9%
	Anterior	10.8%
	Ventral	1.3%
	Whole	2.3%
Histology	ScC	72.8%
	Others	4.4%
	Unknown	22.7%
Differentiation	Well Differentiated	42%
	Moderately Differentiated	30.5%
	Poorly Differentiated	0.3%

Symptom	Unknown	22.2%
	Ulcer And Pain	71%
	Neck Swelling	19%
	Dysphagia	3%
	Others	7%
Stage	Stage I	18%
	Stage II	13%
	Stage III	22%
	Stage IVA	34%
	Stage IV B	5%
	Unknown	6%

Table 3:Treatment characteristics		
Treatment Intent	A	52%
	Palliative	21%
	No Treatment	27%
Treatment Modality (152) Curative	Surgery	36%
	Surgery-Adj Rt	45%
	Surgery- Adj Ctrt	15%
	Nact-Surgery	1%
	Ctrt	1%
Palliative(63)	Palliative Rt	73%
	Rt-Omct	20%
	Omct	4%
	IV Chemo	1%

4.1. Disease Free Survival

Disease free survival was analysed for those patients treated radically.152 patients underwent radical intent treatment.3 year DFS was 76.5% and 5 year DFS was.55.3%

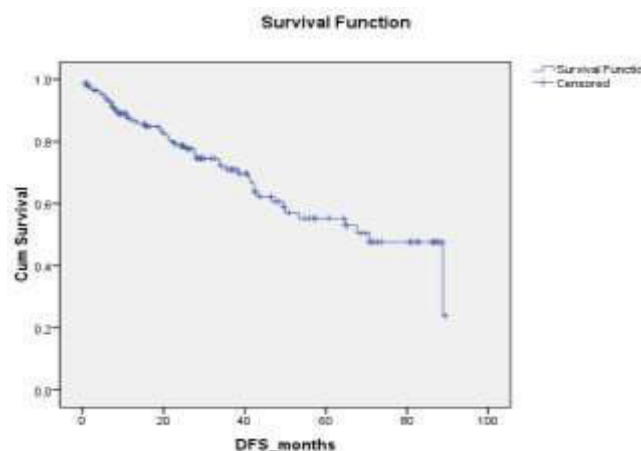


Fig 1: Graph showing disease free survival

4.2. Stage wise Disease Free Survival

Three year DFS for stage I was 80.3% and for stage II it was 88.7%. For stage III disease the DFS was 69.2%.DFS was 54.6% for stage IVA and 63.5 %for stage IV B disease.

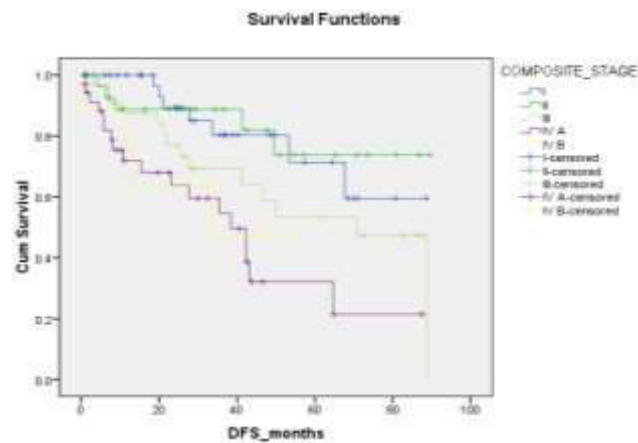


Fig II: Graph showing stagewise disease free survival

OVERALL SURVIVAL

Median follow up was 36.9 Months. The three year OS was 76.5% and five year overall survival was 62.4%.

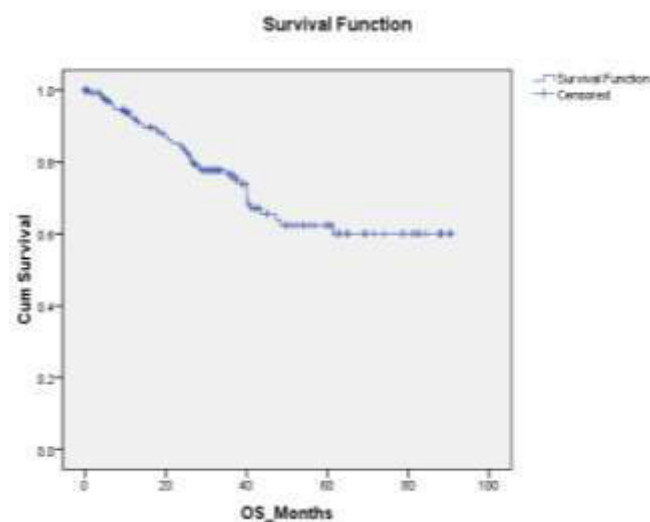


Fig III: Graph showing overall survival

4.3. Stagewise Overall Survival

The three-year overall survival for stage I disease was 80.5%. For Stage II it was 95.8% and stage III it was 69.8.7% .For stage IVA it was 62% and 72.9% for stage IV B .

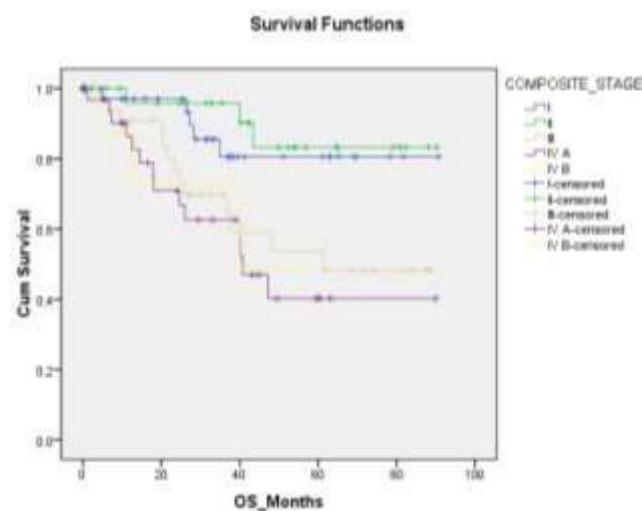


Fig IV: Graph showing stagewise overall survival

5. DISCUSSION

Oral cavity squamous cell carcinoma (OSCC) is a leading cause of death. Most of the patients in the literature are males. But recent evidence shows increasing trend in women and more specifically increasing in the subset of young, white women.⁹ This study aimed to analyze the clinicopathological characteristics and treatment outcome in female patients diagnosed with carcinoma tongue at our centre. 295 patients presented to our center with carcinoma tongue during the study period. Oral cancer typically occurs in an older age group, particularly in males, with a long history of tobacco use and alcohol consumption. This is supported by a study by Iype et al¹⁰ who reported a male to female ratio of 2:1 and Agrawal and Rajderkar¹¹ who reported a 3:1 ratio. As per our Hospital based cancer registry data the incidence of male tongue cancer was 5.2%.¹² In our study period a total of 1074 patients were registered with oral tongue malignancy during our study period. Out of them 779 were males and 295 were females. The male: female ratio in our study was 2.6:1. Clinicopathological characteristics and treatment outcome in female patients with carcinoma tongue. In a study by Jones and colleagues they reported that in patients younger than 40 years of age, females with tongue cancer outnumbered males by almost 2:1.¹² Byers et al also published similar reports.¹³ But contrary to this, the study by Clark et al.¹⁴ did not show any gender differences. In our study only 8% of cases were 40 years or younger. Oral cavity squamous cell carcinoma is common in older adults. The median age of the study population was 62 years. The age group ranged from 24 to 95 years. In their study Gangane et al¹⁵ reported the majority of oral malignancies occur in the 50 to 59 years age group. In a study done by Saraswathi et al¹⁶ the age group at presentation was 40 to 61 years. Mehrotra et al,¹⁷ reported that an increasing usage of chewing gutka and pan masala were implicated in causing oral cancer. In a study conducted in South India by Saraswathi et al Smoking and chewing were significant predictors of leukoplakia. 50% of our patients had history of tobacco chewing. According to a collaborative study in South and East Asia, chewing was more prevalent among men varying from 10.7 to 43.6% in Taiwan, Mainland China, Nepal, and Sri Lanka whereas, among women, rates were high in Malaysia and Indonesia and ranged from 29.5 - 46.8%.¹⁸ This was in concordance with our study where 50% had a history of tobacco chewing. In 2015, the International Head and Neck Cancer Epidemiology consortium conducted a large study to evaluate risk factors for Head and Neck Cancer (HNC).¹⁹ They found that a history of any cancer in any family member was associated with risk of HNC in young and older adults (> 45 years), whereas a family history of HNC was found to be associated with older adults (> 45 years) having HNC. In our study 24% of patients had family history of some cancer in their first degree relatives. Also 10% had family history of head and neck cancers. Gravello et al.²⁰ in their multicenter case control study reported that patients with at least one parent affected by HNC had a 2.3-times higher risk of cancer, whereas patients who had at least one sibling with a history of HNC were 3-times more likely to develop an oral and oropharyngeal cancer. In addition, the risk was higher when two or more relatives were affected. In our study 10% of patients had family of head and neck cancer. In a study by Najeeb et al²¹ Odynophagia and painful ulcers on the lateral border of the tongue were the main clinical symptoms with an average duration of 7 months. 71% of patients in our study presented with ulcer and pain. Rest of the symptoms documented were swelling, odynophagia, dysphagia and

difficulty in speech. Most tongue cancers occur on the lateral border, making cancer of the dorsum very rare, with an incidence of 2.9–5.0 %. Albuquerque et al.²² found that the lateral borders of the tongue were the most frequent carcinoma locations (59.7%). Falaki et al.²³ analyzed 158 cases of oral squamous cell carcinoma (OSCC) and found that the most common site of involvement was the tongue (66%) and lateral border of the tongue. These results are similar to the present study as we also found the most frequent site to be the lateral border of the tongue in 81 % of cases. Regarding histopathology 73% had squamous cell carcinoma (SCC), 5% had other histology and the histopathology report was not available for 22% of patients. Among them well differentiated squamous cell carcinoma was found in 42% of cases followed by moderately differentiated in 30% of cases. Agarwal et al.²⁴ found that 55.5% of cases were well-differentiated SCC and 22.2% were moderately differentiated SCC in his analysis. In a study by Selvamani et al²⁵ well-differentiated SCC accounted for 44.2%, while moderately differentiated SCC was seen in 55.8% cases. In a recent study from India, 82% of OSCC cases, significantly presented in the later stages²⁶. A study by Chu et al in Asian and Pacific Islanders showed that patients with low socioeconomic status were most likely to be diagnosed with more advanced disease at presentation²⁷. A multicentre study including Malays, Indians, and Indigenous people showed the presence of late stage tumors to be 72 –78%, whereas the Chinese displayed a widespread distribution trend of all the stages. The 68% Indian and 70% Malay patients presented with T3 and T4 tumors²⁸. In our study also 62% of patients presented with stage III or Stage IV disease. In our study majority 52% of the patients underwent radical intent treatment 21% patients underwent palliative intent radiation or chemotherapy treatment and 27% patients did not undergo any treatment. Either they were offered best supportive care or they did not report back for further treatment. Among the patients treated with curative intent, 37 % patients underwent surgery alone, 46% had surgery followed by adjuvant RT, 15% patients had surgery followed by adjuvant chemoradiation, 1% cases had neoadjuvant chemo followed by surgery and 1% had radical chemoradiation. In a single institution experience reported by Shirazi et al²⁹ 50 % of the patients were treated with surgery followed by a combination of chemotherapy and radiotherapy 29% received surgery followed by adjuvant radiotherapy alone, 20 % did not undergo surgery and were treated with definitive radiotherapy with or without chemotherapy. Mroueh et al³⁰ reported on patients treated with palliative intent treatment in carcinoma tongue. In their study palliative radiotherapy was administered to 24% of all patients. In our study 21% of patients underwent palliative intent treatment either palliative radiation, oral chemotherapy or both. Palliative radiotherapy schedules included 20 Gy in 5 fractions, 30 Gy in 10 fractions or 8 Gy single fraction. Palliative oral metronomic chemotherapy practiced in our center includes combination of Erlotinib, Methotrexate and celecoxib. Median follow up in our study was 36.9 months. Disease free survival was analyzed for those patients treated with a curative intent. 152 (52%) patients underwent radical intent treatment. 3 year DFS was 71% and 5 year DFS was 55.3% in our study. In a study conducted by Ukrani et al³¹ the 5 year disease free survival was 59%. In their study majority were males and most common stage was stage II. In our study majority of the patients had locally advanced disease. In a study by sharma et al³² the 3- and 5-year locoregional control rate was 68.5% and 58.3%, respectively. Median follow up in our study was 36.9 Months. The 3 year OS was 76.5% and 5 year OS was 62.4%. In a study by Shirazi et al²⁹ the five-year disease-free

survival and overall survival were 65.7 and 72.5 per cent, respectively. When we analyzed stage wise overall survival it was found that the three year overall survival for stage I disease was 80.5%. For Stage II it was 95.8%, and stage III it was 69.8%. For stage IVA it was 36.2% and stage IVB it was 72.9%. The 5-year overall survival from developed countries in all the stages combined ranges from 30 to 70%³³⁻³⁷. Those with early stages (stages I and 2) have a better survival rate of up to 80%, whereas patients with advanced stages of cancer have a lower survival rate (30–50%).

6. CONCLUSION

The increasing incidence of oral tongue cancer in females, especially when not associated with the traditional risk factors of tobacco and alcohol use, is a growing concern. Our study showed that the clinicopathological profile and outcome in females were similar to males as per literature. But we suggest conducting more studies to assess the prognostic factors and

the molecular mechanisms involved in carcinogenesis in non-habituante females.

7. AUTHORS CONTRIBUTION STATEMENT

Akhil P Suresh conceptualized and designed the study. Joneetha Jones and Vinin N V contributed to data collection and analysis. Geetha M and Nabeel Yahiya were involved in drafting the manuscript and interpreting the clinical data. Bindu Anilkumar supervised the statistical analysis and provided critical revisions to the manuscript. Jyothi Rejeesh offered overall guidance and final approval of the manuscript. All authors read and approved the final version of the manuscript.

8. CONFLICTS OF INTEREST

Conflict of interest declared none.

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