

Head and Neck Cancer

A Study of Head and Neck Cancer Patients with Reference to Tobacco Use, Gender, and Subsite Distribution

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Abstract



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Context Head and neck cancer (HNC) is very common in India, constituting 30% of all the cancers because of the widespread use of tobacco across India. The prevalence and pattern of tobacco use vary in different regions and states of the country. Although predominantly seen in males, studies have reported that the male-to-female ratio varies worldwide and also by anatomical subsite.

Aims This study was done with an aim to determine the difference in pattern and prevalence of tobacco use in male and female patients with HNCs and compare them with different subsites' involvement in our region.

Methods and Materials This is a retrospective analysis of 500 consecutive biopsy-proven HNC patients from a large comprehensive cancer hospital from Bihar during the period of January 2019 to June 2019. Data collected for the study included age, gender, site of the disease, and use of tobacco. The categorical data were analyzed by a chi-square test using SPSS (version 16).

Results Our study showed a male-to-female ratio of 8.43:1 with tobacco addiction in 84.40% patients. Smokeless tobacco was used by 52.20%, combustible form by 12.80%, and both by 19.40% of the patients. Tobacco use was seen in 87.25% of male patients as compared with only 60.38% of female patients (p -value = 0.0001). Oral cavity cancer was seen in 60.85% of male patients and 37.74% of female patients (p -value = 0.0012), whereas oropharyngeal cancer was seen in only 11.63% of male patients as compared with 25.83% of female patients (p -value = 0.0008). The subsite analysis showed that in patients with oral cavity cancers, no addiction was found in only 10.29% of male patients as compared with 30% of the female patients (p -value = 0.008).

Conclusions Our study confirms a high prevalence of tobacco use among HNC patients. So, we need to continue our efforts to create awareness against tobacco use. Besides, there is also a need for more studies to look into other etiological factors among nontobacco users.

Keywords

- ▶ tobacco
- ▶ male
- ▶ female
- ▶ oral cavity
- ▶ oropharynx

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Introduction

Worldwide, head and neck cancer (HNC) is the seventh most common cancer overall (the fifth most common in men and the 12th most common in women), accounting for an estimated 888,000 new cases and 453,000 deaths in 2018.¹ HNCs originate from squamous cells located in the mucosal epithelium inside the head and neck and are further classified by the anatomical area in which they arise. Head and neck squamous cell carcinoma (HNSCC) includes tumors of the oral cavity, nasopharynx, oropharynx, hypopharynx, and larynx.² Overall 57.5% of global HNCs occur in Asia, especially in India where it accounts for 30% of all cancers.^{3,4} With 1,19,992 new cases and 72,616 deaths due to oral cancers in 2018, India has the highest oral cavity cancer patients in the world.¹ This could be related to the widespread use of tobacco in India.⁵ Tobacco use has been identified as a risk factor in 80 to 90% of patients of oral cancer.⁶ According to the recent Global Adult Tobacco Survey data, 42.4% of men, 14.2% of women, and 28.6% (266.8 million) of all adults in India currently use tobacco.⁷ Tobacco use in India is characterized by a high prevalence of combustible (in the form of smoking) and smokeless tobacco use, with dual use also contributing a noticeable proportion.⁸ Further, India's tobacco problem is very complex, with a large use of a variety of smoking forms and smokeless tobacco products. Combustible tobacco includes beedis, cigarettes, cigars, tobacco rolled in maize leaf and newspaper, hookah, pipes, chillum, and chutta. Smokeless tobacco includes tobacco leaf, betel quid with tobacco, khaini or tobacco lime mixture, gutkha, pan masala with zarda, gul, gudaku, and mishri.^{9–11} The prevalence and pattern of tobacco use vary in different regions and states of the country, which ranged from 9.7% in Goa to 64.5% in Tripura in 2016 to 2017.⁷ The state of Bihar also has a high prevalence of use of tobacco, especially that of chewing tobacco.⁷ However, there are few studies showing the prevalence and pattern of tobacco use among HNC patients of the state. Further, HNCs are predominantly seen in males, but the male-to-female ratio varies worldwide and also by anatomical site.^{12–14} Therefore, this study was done with an aim to determine the difference in pattern and prevalence of tobacco use in male and female patients with HNCs and compare them with different subsites' involvement.

Table 1 Gender wise distribution of head and neck cancer patients

Gender	Total No. of patients	Percentage (%)	Ratio
Male	447	89.40%	8.43
Female	53	10.60%	1

Materials and Method

This is a retrospective analysis of 500 consecutive biopsy-proven HNC patients of Mahavir Cancer Sansthan, Patna, who reported during the period of January 2019 to June 2019. The subsites included in the study were oral cavity, oropharynx, hypopharynx, nasopharynx, and larynx. All the patients had squamous cell carcinoma. Data collected for the study included age, gender, site of the disease, and use of tobacco.

Data were entered in Microsoft Excel and the categorical data were analyzed by a chi-square test using SPSS (version 16). The association of tobacco use with gender and subsite of cancer was reviewed and compared. A *p*-value of less than 0.05 was accepted to be statistically significant.

Results

A male predominance was seen with a male-to-female ratio of 8.43:1. Among the 500 patients, 447 (89.4%) were males and only 53 (10.6%) were females. The age range of the patients was from 26 to 84 years. The most common age group was from 51 to 60 years followed by 61 to 70 years, 41 to 50 years, and 31 to 40 years with 26.60, 21.60, 21.40, and 18.40% of the patients, respectively. A similar pattern of age distribution was seen among male patients. However, among the female patients, majority belonged to the age group of 41 to 70 years with only 3.77% of the patients in the age group of 31 to 40 years. This difference in age pattern was not statistically significant (*p*-value = 0.066; [Tables 1 and 2](#)).

Tobacco addiction in any form was seen in 422 (84.40%) out of the 500 patients. The pattern of tobacco use showed that 52.20% of the patients used smokeless tobacco, 12.80%

Table 2 Distribution of cases based on sex and age group (*n* = 500)

Age group	Total No. of patients, <i>n</i> (%)	Male, <i>n</i> (%) ^a	Female, <i>n</i> (%) ^b	<i>p</i> -Value ^c
20–30	20 (4.00%)	19 (4.25%)	1 (1.89%)	0.066
31–40	92 (18.40%)	90 (20.13%)	2 (3.77%)	
41–50	107 (21.40%)	91 (20.36%)	16 (30.19%)	
51–60	133 (26.60%)	116 (25.95%)	17 (32.08%)	
61–70	108 (21.60%)	94 (21.03%)	14 (26.42%)	
71–80	34 (6.80%)	31 (6.94%)	3 (5.66%)	
81–90	6 (1.20%)	6 (1.34%)	0 (0.00%)	

^aPercentage of all male age groups.

^bPercentage of all female age groups.

^c*p*-Value obtained by a chi-square test.

Table 3 Distribution of habits according to the gender ($n = 500$)

Group	Total No. of patients ($n = 500$)	Male ($n = 447$), n (%) ^a	Female ($n = 53$), n (%) ^b	p -Value ^c
No addiction	78 (15.60%)	57 (12.75%)	21 (39.62%)	0.0001
Smokeless	261 (52.20%)	249 (55.70%)	12 (22.64%)	0.0001
Smoking	64 (12.80%)	51 (11.41%)	13 (24.53%)	0.0069
Both	97 (19.40%)	90 (20.13%)	7 (13.21%)	0.2279

^aPercentage of all male age groups.^bPercentage of all female age groups.^c p -Value obtained by a chi-square test.

smoked, and 19.40% used both smokeless and smoking tobacco. In male patients, the addiction was seen in 87.25% of the patients as compared with only 60.38% of female patients, with a highly significant p -value of 0.0001. Use of smokeless tobacco was the most common addiction seen in 55.70% of male patients, whereas in the female population, beedi smoking was the most common form of tobacco addiction, seen in 24.53% of the patients. Use of chewable or smokeless tobacco was seen in only 22.64% of the female patients as compared with 55.70% of male patients with a significant p -value of 0.0001 (→Table 3).

Oral cavity was the most common site of disease, seen in 58.4% of the patients followed by larynx, oropharynx, hypopharynx, and nasopharynx in 17.2, 13.4, 7, and 4% of the patients, respectively. The incidence of oral cancer further increased to 60.84% in the male patients as compared with only 37.74% in the female patients (p -value = 0.0012). However, the female patients showed a high incidence of oropharyngeal cancer as compared with the male patients, 28.30 vs. 11.63% (p -value = 0.0008; →Table 4).

The subsite analysis showed that in patients of oral cavity cancers, no addiction was found in only 10.29% of male patients as compared with 30% of the female patients (p -value = 0.008). Use of smokeless tobacco was found in 62.50% of the male patients and in 45% of the female patients (p -value = 0.1209). Prevalence of smoking and smoking with the use of smokeless tobacco was comparable in both groups of the patients (→Table 5).

In the laryngeal subsite, two-thirds of the female patients had no addiction as compared with only 13.16% of male

patients without any addiction (p -value = 0.0001). None of the female patients used smokeless tobacco in this group as compared with 47.37% of their male counterparts (p -value = 0.01). Smoking was the only addiction seen in 25% of the female patients (→Table 5).

The oropharyngeal subsite had the maximum number of male patients without any addiction. In this group, 23.08% of the patients had no addiction with almost comparable number of patients in the smokeless, smoking, and the group addicted to both smoking and smokeless tobacco. A total of 40% of the female patients in this group were addicted to smoking. However, there was no significant difference in the tobacco addiction pattern between male and female patients with oropharyngeal cancer. The hypopharyngeal subsite had 12.90% male patients with no addiction as compared with 50% of the female patients without any addiction. Smokeless tobacco was being used by 61.29% of the male patients. Smoking was the only addiction found in female patients. It was seen in 50% of the female patients as compared with 9.68% of the male patients (p -value = 0.03). The nasopharyngeal subsite had the least number of patients with a nonsignificant difference seen in the pattern of addiction in both male and female patients (→Table 5).

Discussion

HNSCC is an epithelial malignant disease arising from the mucosa of the upper aerodigestive tract (oral cavity, larynx, oropharynx, and hypopharynx).² It has been classically described as a disease of older and middle-aged adults

Table 4 Distribution of cases based on the site of disease in male and female cancer patients ($n = 500$)

Site	Total No. of patients ($n = 500$)	Male ($n = 447$), n (%) ^a	Female ($n = 53$), n (%) ^b	M/F ratio	p -Value ^c
OC	292 (58.40%)	272 (60.85%)	20 (37.74%)	13.6	0.0012
OPX	67 (13.40%)	52 (11.63%)	15 (28.30%)	3.46	0.0008
LNx	86 (17.20%)	76 (17.00%)	10 (18.87%)	7.6	0.7336
HPX	35 (7.00%)	31 (6.94%)	4 (7.55%)	7.75	0.8688
NPX	20 (4.00%)	16 (3.58%)	4 (7.55%)	4	0.1634

Abbreviation: HPX, hypopharynx; M/F, male/female; NPX, nasopharynx; OC, oral cavity; OPX, oropharynx; LNx, larynx.

^aPercentage of all male age groups.^bPercentage of all female age groups.^c p -Value obtained by a chi-square test.

Table 5 Distribution of habits according to the gender and subsites

Site	Habit	Male	Female	p-Value
Oral cavity	No addiction	28 (10.29%)	6 (30.00%)	0.0080
	Smokeless	170 (62.50%)	9 (45.00%)	0.1209
	Smoking	23 (8.46%)	2 (10.00%)	0.8117
	Both	51 (18.75%)	3 (15.00%)	0.6767
Oropharynx	No addiction	12 (23.08%)	6 (40.00%)	0.1927
	Smokeless	15 (28.85%)	1 (6.67%)	0.0759
	Smoking	13 (25.00%)	6 (40.00%)	0.2562
	Both	12 (23.08%)	2 (13.33%)	0.4135
Larynx	No addiction	10 (13.16%)	6 (75.00%)	0.0001
	Smokeless	36 (47.37%)	0 (0.00%)	0.0100
	Smoking	12 (15.79%)	2 (25.00%)	0.5061
	Both	18 (23.68%)	0 (0.00%)	0.1204
Hypopharynx	No addiction	4 (12.90%)	2 (50.00%)	0.0639
	Smokeless	19 (61.29%)	0 (0.00%)	0.0206
	Smoking	3 (9.68%)	2 (50.00%)	0.0301
	Both	5 (16.13%)	0 (0.00%)	0.3856
Nasopharynx	No addiction	3 (18.75%)	1 (25.00%)	0.7799
	Smokeless	9 (56.25%)	2 (50.00%)	0.8222
	Smoking	0 (0.00%)	1 (25.00%)	0.0402
	Both	4 (25.00%)	0 (0.00%)	0.2636

with a long history of tobacco use.¹⁵ Being a tobacco-related cancer and a high consumption of tobacco products among the male population in India, HNCs are more common in males than in females. Studies have reported a male-to-female ratio ranging from 2:1 to 5:1 in Indian population.¹² The gender-wise distribution of our study showed a male-to-female ratio of 8.4:1, which is higher than those previously reported. The possible cause could be the social taboo associated with the use of tobacco among females in the state, which results in low prevalence of tobacco addiction.¹⁶ Another possible factor for a high prevalence of oral cancers among males than females is the difference in the working pattern seen in our state. Majority of the male population is involved in outdoor activities as they work as farmers or laborers, which means working in scorching sunlight for long hours. Oral cancer, especially lip cancer, has been related to sunlight exposure in many studies.¹⁷ International Agency for Research on Cancer has also recognized prolonged exposure to sun for long hours as a carcinogen for skin and lip cancers.¹⁸ The women of our state usually work indoor and do household chores, which protect them from prolonged exposure to direct sunrays.

Majority of our patients were in the age group of 41 to 70 years. Although the percentage of male population below the age of 40 was higher than that of the female patients, the difference seen in different age groups was not statistically significant (p -value = 0.66). Many other studies have shown

similar results and reported that HNC is more common in 4th to 6th decades of life.^{12,13} It has also been observed that males were presenting a decade earlier than females.¹⁹ Thus, we can say that the male preponderance and age of presentation seen in our study are in correlation with other studies.

Tobacco addiction was found in 84.40% of our patients. The gender-wise distribution of tobacco use showed a statistically significant higher addiction among male patients as compared with female patients, i.e., 87.25 vs. 60.38% (p -value = 0.0001). A recent study by Das et al from Northeast India reported that 82.9% of all HNCs in both genders were found to be associated with tobacco in any form. Their gender-wise analysis showed a total of 87.7% males and 64.6% females to be associated with tobacco habits, which are similar to our study results.¹⁵ A study by Kumar et al among North Indian population reported 97% of the patients being addicted to tobacco. Tobacco use has been reported to be prevalent among men, rural population, illiterates, and poor and vulnerable sections of the society.¹²

Overall, oral cavity was the most common site of cancer seen in 58.4% of our patients, followed by oropharynx, larynx, hypopharynx, and nasopharynx in 17.2, 13.4, 7, and 4% of the patients, respectively. A gender-wise distribution of subsite involvement showed a statistically significant difference in the incidence of oral cavity and oropharyngeal cancer. Oral cavity cancer was seen in 60.85% of male patients as compared with only 37.74% of female patients (p -value

= 0.0012). On the other hand, oropharyngeal cancer was seen in only 11.63% of male patients as compared with 25.83% of female patients (p -value = 0.0008). There was no statistically significant difference seen in other subsites.

This finding could probably be explained by the difference seen in the prevalence and pattern of tobacco use among our male and female patients. Among male patients, use of smokeless tobacco mainly in the form of khaini chewing was seen in 55.70% of cases followed by smoking in 11.41%, and both in 20.13% cases. Smoking mostly in the form of beedi was the most common form of tobacco addiction seen in 24.53% of the female patients. Use of smokeless tobacco was seen in only 22.64% of the female patients. This difference in the pattern of tobacco use was statistically significant with a p -value of 0.0001.

Our study shows that approximately 78% of all male patients used smokeless tobacco either alone or in combination with smoking as compared with only 36% of female patients. A review by Jethwa and Khariwala has reported a tremendous geographic variation in the type of tobacco product consumed worldwide.²⁰ Approximately 90% of the world's smokeless tobacco consumption has been reported in Southeast Asia with nearly 100 million people using smokeless tobacco in India and Pakistan alone.^{21,22} According to Global Adult Tobacco Survey 2 survey, approximately 29.6% of men and only 12.8% of women currently use smokeless tobacco in India.⁷

Our observation of a preponderance of oral cavity cancers among all HNCs is in accordance to the fact that chewing tobacco has a strong correlation to oral cavity cancer as compared with other subsites.^{23,24} Goud et al had reported that oral cancers caused by chewing tobacco are common in India and some parts of the Indian subcontinent with their study showing a significant association (p -value less than 0.001) between the use of Indian chewing tobacco and oral cancer.²⁵ Pednekar et al in their Mumbai cohort study also reported that smokeless tobacco use was associated with cancers of the lip, oral cavity, pharynx, digestive, respiratory, and intrathoracic organs.²⁶

In a survey conducted in 0.1 million households, the state of Bihar had the highest percentage (57%) of households consuming smokeless tobacco.²⁷ In another cross-sectional study from rural Bihar, smokeless tobacco use had 33% prevalence with khaini (57%) as the predominant choice.²⁸

Smokeless tobacco contains >30 known carcinogens with predominance of nitrosamines, aromatic amines, polycyclic hydrocarbons, aldehydes, and metals.²⁰ These carcinogens in tobacco undergo metabolic activation processes initiated by cytochrome p450 enzymes. Metabolic activation makes the carcinogens electrophilic which then react with DNA to form DNA adducts. When left unrepaired, DNA adducts can cause miscoding and permanent mutations which can activate oncogenes such as K-ras, or inactivate tumor suppressor genes such as p53 to initiate and promote carcinogenesis.^{29,30}

Thus we see that the role and pathogenesis of smokeless tobacco in oral cavity cancer have been well studied. However, our study also reported approximately 40% of the female patients with no tobacco addiction. The female

patients also had a statistically significantly higher prevalence of oropharyngeal cancer than male patients. In the past few years, strong evidence has accumulated that infection with certain human papillomaviruses (HPVs) is the cause for the increasing incidence of HNSCC despite a decrease in the use of tobacco and particularly for the oropharyngeal subsite.³¹ According to the recent World Cancer Report, 30.8% of oropharyngeal cancers have been attributed to HPV infection as compared with only 2.2% for oral cavity and 2.4% for laryngeal cancers.³² Thus, HPV could be the most probable etiological agent in our female patients who are nontobacco users. Besides, other factors like poor oral hygiene, lichen planus, iron-deficiency anemia, poor diet, gastrointestinal reflux, and genetic predisposition also have a role in causing HNC, particularly in nontobacco users.^{33–35}

The limitation of this study is that being retrospective in nature we could only analyze the categorical data we had at our disposal. Details regarding many other etiological factors like use of alcohol, poor oral hygiene, chronic oral infection, nutritional status, and sexual history for evaluating HPV infection risk were not available. Further, limited analyses could be done at subsites like larynx, hypopharynx, and nasopharynx because of a small number of female patients which further decreased when it was distributed according to subsites and tobacco use.

Conclusion

Our study confirms a high prevalence of tobacco use among HNC patients. Tobacco use is more common in males, particularly in the smokeless form. So, we need to continue our efforts to create awareness against tobacco use. In addition to this, there is also a need for more studies to look into etiological factors like HPV for HNC among nontobacco users. Good oral hygiene, proper treatment of benign oral lesions, healthy food, and lifestyle habits should also be recommended for prevention of HNCs.

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Nil.

Conflicting Interest

Nil.

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