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Original Article

Risk factors for head and neck squamous cell carcinomas amongst patients attending a tertiary care centre of Assam

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ABSTRACT

Problem considered: Head and neck cancer in India accounts for 30% of all cancer associated with distinct demographic profile, risk factors, food habits and personnel and family history. **Methods:** A case-control study with 87 patients with head and neck squamous cell carcinoma (HNSCC) with age and sex matched controls were evaluated for possible risk factors in a tertiary care hospital. A total of 87 cases with diagnosed HNSCC underwent structured questioning using predesigned pretested schedule. Patients with cancers in oral cavity, oropharynx, nasopharynx, hypopharynx and laryngeal areas were included. Patients from outside the state of Assam were excluded. Statistical speculations were done by using univariate and multivariate analyses.

Results: Illiteracy [OR 20.88, 95% CI 1.73–251, $p = 0.017$], use of mosquito coil [OR 5.53, 95% CI 1.93–15.79, $p = 0.001$], betel nut quid retention in mouth for more than 10 min [OR 27.01, 95% CI 1.39–521.40, $p = 0.029$] and use of biomass fuel [OR 5.31, 95% CI 2.12–13.31, $p = 0.000$] had significant positive association with HNSCC.

Conclusions: Preventable risk factor needs to be addressed. Counselling all patients and screening of high risk group along with health awareness creation may be effective in risk reduction.

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1. Introduction

Cases related to head and neck squamous cell carcinoma (HNSCC) are major clinical challenge in oncology and represent the sixth most common neoplasm in the world today.¹ Worldwide about 650,000 new cases of head and neck cancer

(HNC) are reported every year.² HNC is the most common cancer in India.^{3–5} Mouth and tongue cancers are more common in the Indian subcontinent; nasopharyngeal cancer is more common in Hong Kong, as well as pharyngeal and laryngeal cancers are more common in other populations.

Smoking, tobacco and alcohol consumption are main risk factors for HNC.⁶ Epidemiological studies also reported a

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strong association with human papillomavirus (HPV) in a subset of HNSCC and in non-smoking cases.^{7,8} In South Asian countries, the risk of HNSCC is further aggravated by smoking of bidis,⁹ reverse smoking and chewing tobacco, betel quid and areca nut. In India and South East Asia, oral cancer incidence accounts for up to 40% of all the malignancies.¹⁰

The prevalence of cancer is often strikingly dissimilar in different groups of population, varies greatly from one community to another, and differs in different communities in the same geographic location, depending on the practices and lifestyles of the people in that location. Moreover, differences have been observed in the etiological, clinico-pathological and molecular pathological profiles in the tobacco smoking, chewing and alcohol associated oral cancers, particularly in the Indian subcontinent.¹¹

There is a paucity of data from North east India about risk factor distribution. Early identification and proper addressing of risk factors along with high risk screening have potential to reduce the fatality of outcomes. Therefore, this study is undertaken with an aim to investigate the risk factors for persons with HNC amongst patients attending a tertiary care hospital of Assam.

2. Methods

2.1. Setting

The study was undertaken in Assam Medical College & Hospital, Dibrugarh, which is a tertiary care government-teaching institute in the north-eastern part of India. This institute obviously involves in the treatment for almost all the cases of HNC found in this territory, as it is the only institutional hospital having radiotherapy for cancer patients in the entire upper Assam. The institute maintains the hospital tumour registry and community based tumour registries, wherein all the cases of head and neck and other malignancies are recorded.

2.2. Sampling procedure

All eligible cases of HNC who gave consent for participation were enrolled in the study after obtaining an ethical clearance from the institutional ethics committee. Equal number of age and sex matched consenting controls were enrolled. Controls were selected from patients coming for endoscopy who are not having HNC and were enrolled after getting written informed consent.

2.3. Ethical consideration

Ethical clearance was obtained from the Assam Medical College Ethics Committee (Human) and enrolment in the study was started only after ethical clearance. Informed written consents were obtained from all the participants or from a legal representative before enrolment.

2.4. Study design

A matched case-control design with equal allocation was undertaken between 2011 and 2015.

2.5. Sample size calculation

Taking current tobacco users as 60.7% amongst general population of Dibrugarh, with anticipated odds ratio of 2 and 80% power and 20% alpha error the required sample size for matched case-control is 87 with equal allocation.¹²

2.6. Outcome measurement

Risk factors distribution amongst cases and control.

2.7. Measurement tool

A total of 87 cases with diagnosed HNSCC underwent structured questioning using predesigned, pretested schedule. Patients with cancers in oral cavity, oropharynx, nasopharynx, hypopharynx and laryngeal carcinomas were included.

2.8. Statistical analysis used

Univariate and multivariate analyses were done for risk factor distribution in the participants for calculation of rates, ratios and proportions. Results were considered to be statistically significant at $p < 0.05$.

3. Results

Majority of the study subjects were married, Hindu by religion and studied up to middle school (Table 1). According to the site of primary lesion, majority of the cases were having hypopharyngeal lesions (33%), followed by oral cavity (25%), oropharynx (18%) and nasopharynx (4%), respectively (Fig. 1). Blood pressure, height, weight and waist circumferences were significantly different in the cases and control groups. Systolic BP was found to be significantly higher in cases while weight was found to be significantly lower in case group, though BMI difference was non-significant. Waist circumference was also found to be lower amongst cases (Table 2).

Table 1 – Socio-demographic distribution of study subjects.

Variable	Case, n (%)	Control, n (%)
Sex		
Male	76 (87.4)	75 (87.4)
Female	11 (12.6)	11 (12.6)
Marital status		
Unmarried	5 (5.7)	1 (1.1)
Married	81 (93.1)	86 (98.9)
Widowed	1 (1.1)	0 (0.0)
Religion		
Hindu	79 (90.8)	75 (86.2)
Islam	8 (9.2)	12 (13.8)
Education status		
Illiterate	16 (18.4)	1 (1.1)
Primary	21 (24.1)	24 (27.6)
Middle	30 (34.5)	44 (50.6)
Secondary	11 (12.6)	18 (20.7)
College & above	8 (10.3)	0 (0.0)

Fig. 1 – Distribution of study subjects according to sites of primary lesion.

In the univariate analysis, the *p* values were found to be significant for illiteracy, exposure to mosquito coils, history of tobacco chewing, tobacco or cigarette user, chewing betel nut both in the past and at present, duration of chewing betel nut for 20–>30 yrs, betel nut quid retention in mouth (1–>10 min), duration of chewing tobacco (1–>30 yrs), tobacco quid retention in mouth (in 1–10 min), tobacco chewing practice (with or without spitting), tobacco quid retention during sleep and duration for consumption of alcoholic beverages >30 yrs (Table 3).

Multivariate analysis shows that illiteracy [OR 20.88, 95% CI 1.73–251, *p* = 0.017], use of mosquito coil [OR 5.53, 95% CI 1.93–15.79, *p* = 0.001], betel nut quid retention in mouth for more than 10 min [OR 27.01, 95% CI 1.39–521.40, *p* = 0.029] and use of biomass fuel [OR 5.31, 95% CI 2.12–13.31, *p* = 0.000] are the risk factors of significance in our study (Table 4).

4. Discussion

A men preponderance of cancer occurrence was observed in our study, suggesting that men most often indulged in the habits that are risk factors for HNC. L Addala et al. also observed similar male preponderance and risk factor distribution in Andhra Pradesh, in 2012.¹¹ In the univariate analysis, the '*p*' values were found to be significant for illiteracy, exposure to mosquito coils, history of tobacco chewing, tobacco or cigarette user, chewing betel nut both in the past and at present, duration of chewing betel nut for 20–>30 yrs, betel nut quid retention in mouth (1–>10 min), duration of chewing tobacco (15–>30 yrs), tobacco quid retention in mouth (in 1–10 min), tobacco chewing practice (with or without spitting), tobacco quid retention during sleep and drinking duration for alcoholic beverages >30 yrs. Multivariate analysis shows illiteracy, use of mosquito coil, betel nut quid retained in mouth for more than 10 min and use of biomass fuel found significant positive associations. The world's highest incidence of cancers associated with tobacco use was found in different districts of northeast, central and southern regions of India. With HNC being highly preventable, the main emphasis should, therefore, be on preventing the onset and detecting the disease at an early stage.¹³ Commonest HNC in our participants occurred in the area is hypopharynx, followed by oral cavity, oropharynx and nasopharynx, respectively. Consolidated report of population based cancer registries (ICMR) (2008) of National Cancer Registry Programme, hypopharyngeal lesions were found to be 34.5% in Dibrugarh which were the major contributor was found similar to our study.¹⁴ The HNC is a common cancer in upper part of Assam, especially in Dibrugarh district (49.6%), and different risk factors for HNC are described from different places. Strategies for possible risk factor screening should be initiated for the prevention of HNC

Table 2 – Univariate analysis and distribution of study subjects according to blood pressure and anthropometric characteristics.

Variable	Mean + SD	Mean difference	95% CI	t	p-value
Age (yrs)					
Control	57.1 + 11.0	1.10	2.434–4.618	0.618	0.542
Case	58.2 + 12.6				
BP systolic (mm Hg)					
Case	129.3 + 10.3	9.89	6.48–13.31	5.723	0.000
Control	119.2 + 12.4				
BP diastolic (mm Hg)					
Case	74.7 + 6.6	8.47	5.77–11.16	6.220	0.000
Control	83.1 + 10.8				
Weight (kg)					
Case	51.3 + 9.0	6.35	3.46–9.24	5.770	0.000
Control	57.6 + 10.2				
Waist circumference (cm)					
Case	77.7 + 5.7	3.81	0.42–7.20	2.224	0.027
Control	81.5 + 14.9				
Hip circumference (cm)					
Case	82.4 + 5.8	3.96	0.36–7.56	2.175	0.031
Control	86.4 + 15.9				
BMI (kg/m ²)					
Case	24.4 + 3.5	0.67	0.46–1.61	1.095	0.275
Control	23.8 + 3.3				

Table 3 – Distribution of demographic and behavioural risk factors and corresponding odds ratios (95% CIs) amongst cases and matched controls based on univariate logistic regression analysis.^a

Variables	Total cases	Case (n = 87)	Control (n = 87)	OR (95% CI)	p-value
Religion					
Islam	20 (11.5)	8 (40.0)	12 (60.0)	Reference	
Hindu	154 (88.5)	79 (51.3)	75 (48.7)	1.58 (0.61–4.08)	0.345
Education					
Secondary	38 (21.8)	20 (52.6)	17 (47.4)	Reference	
Middle	74 (42.5)	30 (40.5)	44 (59.5)	0.61 (0.27–1.34)	0.224
Primary	45 (25.9)	21 (46.7)	24 (53.3)	0.78 (0.33–1.87)	0.588
Illiterate	17 (9.8)	16 (94.1)	1 (5.9)	14.40 (1.73–119.76)	0.014
Exposure to mosquito coils					
No	124 (71.3)	49 (39.5)	75 (60.5)	Reference	
Yes	50 (28.7)	38 (76.0)	12 (24.0)	4.84 (2.31–10.18)	0.000
Tobacco history					
Never used	26 (14.9)	4 (15.4)	22 (84.6)	Reference	
Formally or currently user	148 (85.1)	83 (56.1)	65 (43.9)	7.02 (2.31–21.39)	0.001
Chewing habits (betel nut/tobacco)					
Never	50 (28.7)	9 (18.0)	41 (82.0)	Reference	
Chewing in past but not present	99 (56.9)	64 (64.6)	35 (35.4)	8.33 (3.62–19.12)	0.000
Chewing at present	25 (14.4)	14 (56.0)	11 (44.0)	5.79 (1.98–16.89)	0.001
Duration of chewing betel nut (yrs)					
0	50 (28.7)	9 (18.0)	41 (82.0)	Reference	
0–15	35 (20.1)	7 (20.0)	28 (80.0)	1.13 (0.38–3.41)	0.816
16–30	31 (17.8)	20 (64.5)	11 (35.5)	8.28 (2.95–23.21)	0.000
>30	58 (33.3)	51 (87.9)	7 (12.1)	33.19 (11.38–96.7)	0.000
Betel nut quid retained in mouth (min)					
Never take	50 (28.7)	9 (18.0)	41 (82.0)	Reference	
1–10	102 (58.6)	60 (58.8)	42 (41.2)	6.55 (2.86–14.80)	0.000
>10	22 (12.6)	18 (81.8)	4 (18.2)	20.50 (5.57–75.34)	0.000
Chewing practice betel nut					
Never take	50 (28.7)	9 (18.0)	41 (82.0)	Reference	
Spitting	87 (50.0)	65 (74.7)	22 (25.3)	13.46 (5.64–32.07)	0.000
Swallowing	23 (13.2)	8 (34.8)	15 (65.2)	2.43 (0.79–7.45)	0.121
Both	14 (8.0)	5 (35.7)	9 (64.3)	2.53 (0.68–9.37)	0.165
Tobacco chewing					
Never	62 (35.6)	20 (32.3)	42 (67.7)	Reference	
Chewing in past/present	112 (64.4)	67 (59.8)	45 (40.2)	3.12 (1.62–6.01)	0.001
Duration of chewing tobacco (yrs)					
0	62 (35.6)	20 (32.3)	42 (67.7)	Reference	
0–15	29 (16.7)	4 (13.8)	25 (86.2)	0.33 (0.10–1.09)	0.071
16–30	29 (16.7)	16 (55.2)	13 (44.8)	2.58 (1.04–6.38)	0.040
>30	54 (31.0)	47 (87.0)	7 (13.0)	14.10 (5.42–36.68)	0.000
Tobacco quid retain in mouth (min)					
Never take	62 (35.6)	20 (32.3)	42 (67.7)	Reference	
1–10	93 (53.4)	52 (55.9)	41 (44.1)	2.66 (1.36–5.21)	0.004
>10	19 (10.9)	15 (78.9)	4 (21.1)	7.87 (2.31–26.80)	0.001
Tobacco chewing practice					
Never take	62 (35.8)	20 (32.3)	42 (67.7)	Reference	
Spitting	76 (43.9)	55 (72.4)	21 (27.6)	5.50 (2.64–11.44)	0.000
Swallowing	23 (13.3)	8 (34.8)	15 (65.2)	1.20 (0.40–3.07)	0.826
Both	12 (6.9)	3 (25.0)	9 (75.0)	0.70 (0.17–2.87)	0.620
Tobacco quid retain during sleep					
Never used tobacco	62 (35.6)	20 (32.3)	42 (67.7)	Reference	
No	84 (48.3)	51 (60.7)	33 (39.3)	3.24 (1.62–6.46)	0.001
Not always/always/most often	28 (16.1)	16 (57.1)	12 (42.9)	2.80 (1.11–7.01)	0.028
Smoking habits					
Never	93 (53.4)	46 (49.5)	47 (50.5)	Reference	
Smoking at past/present	81 (46.6)	41 (50.6)	40 (47.1)	1.04 (0.57–1.90)	0.879
Smoking duration (yrs)					
0	93 (53.4)	46 (49.5)	47 (50.5)	Reference	
1–15	9 (5.2)	7 (77.8)	2 (22.2)	3.57 (0.70–18.12)	0.124
16–30	28 (16.1)	9 (32.1)	19 (67.9)	0.48 (0.19–1.18)	0.110
>30	44 (25.3)	25 (56.8)	19 (43.2)	1.34 (0.65–2.76)	0.422
Drinking habits					
Never	84 (48.3)	41 (48.8)	43 (51.2)	Reference	
Drink at past/present	90 (51.7)	46 (51.1)	44 (48.9)	1.09 (0.60–1.98)	0.762

Table 3 (Continued)

Variables	Total cases	Case (n = 87)	Control (n = 87)	OR (95% CI)	p-value
Drinking duration (yrs)					
Never drink	84 (48.3)	41 (48.8)	43 (51.2)	Reference	
1–15	18 (10.3)	7 (38.9)	11 (61.1)	0.66 (0.23–1.88)	0.446
16–30	49 (28.2)	21 (42.9)	28 (57.1)	0.78 (0.38–1.59)	0.507
>30	23 (13.2)	18 (78.3)	5 (21.7)	3.77 (1.28–11.10)	0.016
Biomass fuel					
LPG	104 (59.8)	34 (32.7)	70 (67.3)	Reference	
Wood	70 (40.2)	53 (75.7)	17 (24.3)	6.41 (3.24–12.80)	0.000

^a Values are numbers (percentages) of participants unless stated otherwise.

in a community. The present case–control study was done in a government-run tertiary care teaching institution in Assam on the histologically confirmed cases of HNC patients, irrespective of their disease status, and along with the cases, controls were taken after age and gender matching. We enrolled all consenting consecutive cases of HNC fulfilling inclusion and exclusion criteria. These cases were selected as well as enrolled, and structured questionnaire were used to find out the presence or absence of different possible risk factors in them. Similarly, unrelated controls without any family history of HNC were selected, and same questionnaires were used to know the risk factors' distribution. Published literatures from India show that tobacco smoking in the form of cigarettes, bidis, cigar/chutta/cheroot, dhunti (Goa), the

water pipes/hookah (north India), reverse chutta smoking (in coastal Andhra Pradesh & Orissa), Hookli (Gujarat) and chillum (Northeast part of India). Around 57% of all man and 11% of woman in India, between 15 and 49 yrs of age, use some form of tobacco. Uses of smokeless tobacco as well as betel quid (pan) are widespread in many parts of India.¹⁵

Different studies suggested that repeated exposure to carcinogens leads to an accumulation of genetic alterations that results, ultimately, in the development of multiple and independent cancers.^{6,16} The other studies mention that aetiology of HNSCC was associated predominantly with smoking and drinking alcoholic beverages.^{17,18} Alcoholic drinks were found to be a significant risk factor in the multivariate analysis in the study. The associations of

Table 4 – Distribution of demographic and behavioural risk factors and corresponding adjusted odds ratios (95% CIs) amongst cases and age and gender matched controls based on multivariate logistic regression analysis.^a

Variables	Total cases	Case (n = 87)	Control (n = 87)	Adjusted OR (95% CI)	p-value
Education					
Secondary	38 (21.8)	20 (52.6)	17 (47.4)	Reference	
Middle	74 (42.5)	30 (40.5)	44 (59.5)	0.38 (0.12–1.86)	0.096
Primary	45 (25.9)	21 (46.7)	24 (53.3)	0.70 (0.20–2.39)	0.573
Illiterate	17 (9.8)	16 (94.1)	1 (5.9)	20.88 (1.73–251.00)	0.017
Exposure to mosquito coils					
No	124 (71.3)	49 (39.5)	75 (60.5)	Reference	
Yes	50 (28.7)	38 (76.0)	12 (24.0)	5.53 (1.93–15.79)	0.001
Tobacco history					
Never used	26 (14.9)	4 (15.4)	22 (84.6)	Reference	
Formally or currently user	148 (85.1)	83 (56.1)	65 (43.9)	2.07 (0.25–16.81)	0.494
Betel nut quid retained in mouth (min)					
Never take	50 (28.7)	9 (18.0)	41 (82.0)	Reference	
1–10	102 (58.6)	60 (58.8)	42 (41.2)	11.47 (0.80–169.73)	0.071
>10	22 (12.6)	18 (81.8)	4 (18.2)	27.01 (1.39–521.40)	0.029
Smoking habits					
Never	93 (53.4)	46 (49.5)	47 (50.5)	Reference	
Smoking at past/present	81 (46.6)	41 (50.6)	40 (47.1)	1.11 (0.41–3.01)	0.832
Tobacco chewing					
Never	62 (35.6)	20 (32.3)	42 (67.7)	Reference	
Chewing in past/present	112 (64.4)	67 (59.8)	45 (40.2)	0.29 (0.03–2.75)	0.282
Drinking duration (yrs)					
Never drink	84 (48.3)	41 (48.8)	43 (51.2)	Reference	
1–15	18 (10.3)	7 (38.9)	11 (61.1)	0.66 (0.18–2.38)	0.526
16–30	49 (28.2)	21 (42.9)	28 (57.1)	0.52 (0.17–1.55)	0.245
>30	23 (13.2)	18 (78.3)	5 (21.7)	2.53 (0.59–10.81)	0.210
Biomass fuel					
LPG	104 (59.8)	34 (32.7)	70 (67.3)	Reference	
Wood	70 (40.2)	53 (75.7)	17 (24.3)	5.31 (2.12–13.31)	0.000

^a Values are numbers (percentages) of participants unless stated otherwise.

different risk factors may be explained by the concept of “field cancerization” proposed by Danelly P. Slaughter.¹⁹

The strength of our study is that it was done in a tertiary care centre, the only centre having radiotherapy facility in the region, where almost major portion of the HNC cancer patients receive treatment, though a larger sample size may give more generalizable findings. Many other atypical risk factors, such as human papilloma viral infection, or other infection and infestations could not be assessed. Chances of recall bias cannot be over rolled as a basic weakness of case-control design. Further, a large-scale study using atypical risk factors exposures like agriculture and occupation-related pesticides or chemicals especially for tea (common in upper Assam) might be able to throw some more light in the other risk factors for HNC.

5. Conclusion

Risk factors of HNC such as illiteracy, mosquito coil use, betel nut use with history of betel quid retention in mouth for more than 10 min and biomass fuel users should be given due consideration for screening as high risk group. Health awareness generation may make the population more aware to reduce preventable risk factors of HNC.

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Conflicts of interest

The authors have none to declare.

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