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TOBACCO SMOKING AND THE RISK OF HEAD AND NECK CANCER: A DESCRIPTIVE EPIDEMIOLOGICAL STUDY IN NISHTAR HOSPITAL MULTAN, PAKISTAN.

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Abstract

Aim: The purpose of this study was to find out the relationship of smoking with demographic and clinical features of Head and Neck Cancer (HNC) patients visiting Nishtar Hospital Multan, Pakistan. Even though there has been a lot of studies conducted regarding the many aspects of HNC around the world, but Southern Punjab, Pakistan, no online information is available to our knowledge. **Materials and methods:** Demographic and clinical information from HNC patients was obtained and analyzed with respect to smoking. **Results:** In this study, male patients (65.3%) were more common than female patients (34.7%). Among smoker patients, males were more frequent (88.70%) than females (11.29%). The habit of smoking was identified in 51.2% patients. Among demographic factors, there were statistically significant differences in age, smoking and income ($p \leq 0.05$) in both patient groups. Most of smoker patients (88.70%) were from low-income families. In terms of education of patients, a non-significant difference was reported ($p=0.987$). A significant difference was found according to the all HNSCC subsites ($p=0.005$). The rate of larynx cancer was more in smoker patients (53%) and hypopharynx cancer was more in non-smoker patients (47%). Squamous cell carcinoma (96.6%) was dominant. Regarding clinical features of HNC, the percentage of stage III cancer (54.54%) and moderately differentiated tumour (82.64%) was the highest. Among TNM classification, T3-4, N0 and M0 were more frequent. **Conclusion:** Smoking may be a key risk factor for HNC in addicts.

Keywords: Head and Neck Cancer, Smoking, Larynx Carcinoma, TNM classification, Squamous Cell Carcinoma.

INTRODUCTION

Head and Neck Carcinoma (HNC) is linked to heterogeneous cancers that affect the salivary glands, pharynx, larynx, oral nasal canals and paranasal sinuses [1, 2]. As cancer registries are not maintained in many developing nations with large disease burdens, such as India [3], it is difficult to estimate the real frequency of the disease, or the number of HNC patients. The prevalence of HNC as a whole is expected to increase by 30% yearly by 2030. Both advanced and poor countries have seen an increase in HNC [1, 2, 4]. Chewing areca nuts (betel quid), either with or without tobacco, is linked to an especially high prevalence of oral cancer in Southeast Asia and the Asia-Pacific area. As a result, it is anticipated that oral cancer would increase in Southeast Asia [5]. The

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Epstein-Barr virus (EBV) and human papillomavirus (HPV) infections, smoking, drinking alcohol, diet are the risk factors more frequently linked to HNC [1]. Smoking is significant in HNC patients and it has a major impact on treatment and survival [6]. Eighty percent or more of HNC patients have a background of smoking, drinking alcohol or both, particularly those with malignancies of the larynx, hypopharynx, oral cavity and oropharynx [7]. Smoking in the form of cigars, cigarettes, chewing tobacco, pipes, snuff (powdered tobacco) are the central causes of HNC. In addition, passive smoking has also role in development of HNC [8]. It has been observed that in exhaled smoke of smoker, there are around forty eight hundred identified compounds, out of which sixty nine are carcinogenic [9]. It has been found that certain carcinogenic compounds are naturally found in the tobacco plant, whereas others are made during cigarette combustion. According to previous research, the frequency and intensity of using smokeless tobacco, tobacco and alcohol consumption all increase the likelihood of developing HNC [10]. The frequency of HNC in Pakistani male is 32.62% and in female 15.12% and most prevalent in men and 2nd in women [11]. In this current study, the HNC patients who had no history of usage of betel leaves, betel nuts, alcohol and tobacco were also included to find the possible risk factors. The goal of the current study was to ascertain whether smoking and other potential risk factors were related to HNC in patients visiting Nishtar Hospital Multan, Pakistan.

METHODOLOGY

Information of HNC patients was obtained from Nishtar Hospital Multan, Pakistan during the period of three years. After collecting the histopathology reports and confirmation from the competent medical professionals, the HNC patients were recruited for the molecular study. After taking the consent from the patient, all details regarding gender, age, smoking, use of betel leaves, betel nuts (Paan, Chalia) naswar, alcohol consumption, social status and other demographic aspects were directly recorded from patients or their relatives on a predesigned questionnaire. The information regarding clinical features like TNM classification, tumour stage, tumour grade, HNC sites and subsites were taken from histopathology reports. The criteria for smokers included was that if a patient used betel leaves, betel nut or any tobacco product at least once/day for at least one year or more throughout their lifetime. If a patient had never used alcohol, betel leaves, betel nuts, or any tobacco product in their lifetime, they were included as non-smokers. betel leaves and betel nuts (Paan, Chalia), Naswar, Cigarettes and hubble-bubble (Huqqa) were among the tobacco products. Ethical approval of study was obtained from University Research Ethics Committee (UREC) of The Women University Multan via letter No: WUM/UREC/00014. The Chi-square test was used to assess associations between the smoker and non-smoker patient groups. Differences that had a p value of ≤0.05 were deemed statistically significant. SPSS software (version 20), was used to execute statistical analyses (SPSS, Chicago, IL).

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RESULTS

A total of 121 HNC biopsies and blood samples were collected for molecular and epidemiological studies. In current study, 62 HNC patients were found as smokers and 59 patients were non-smokers and various parameters were analyzed between smoker and non-smoker HNC patients. A highly significant difference was found regarding gender ($p<0.001$) between smoker and non-smoker patients. There was more percentage of male smoker patients (88.70%) as compared to female smoker patients (11.29%). Mean age of smoker patients was 54.46±15.18 years and 47.64±16.80 years for non-smoker patients. The statistical analysis indicated that there was a significant difference in age among smokers and non-smoker patient groups ($p=0.009$), with smokers being on general more aged than non-smokers. Smoker patients accounted for a larger percentage of the population in the ≥55 age group (46.77%) but non-smoker patients were more common in the >35-55 age group (40.67%). The smoking pack years was divided into less than and equal to fifteen years, greater than fifteen years to forty five years and greater than forty five years. As far as smoking pack years was concerned, the number of smokers (n=41) was highest in pack years between >15-45 and lowest (n=4) in pack years >45 years (Figure 1). According to monthly income, three socioeconomic status categories were made category 1 (PKR 10,000–25,000), category 2 (PKR >25,000–41,000) and category 3 (PKR >41,000–57,000). Income group was found to differ significantly in both smoker and non-smoker patients ($p=0.010$). Most of smoker patients (88.70%) were from low-income families. In terms of education, a non-significant difference was reported ($p=0.987$) among smoker and non-smoker patient groups. The majority of smoker patients with educational backgrounds were observed in education level of 8^{th} class (42.10%) and no one was found in graduation level. The educational level of the both patient groups showed a non-significant difference ($p=0.301$) (Table 1).

Table 1: Demographic features of HNC patients

Features	Smokers n=62 n (%)	Nonsmokers n=59 n (%)	p-value
Age			<0.009**
≤ 35	5 (8.06)	11 (26.19)	
>35-55	28 (45.16)	24 (40.67)	
>55	29 (46.77)	18 (30.50)	
(Mean ± SD)	54.77±15.96	44. 31±14.79	0.020[a]
Gender			<0.001***
Male	55 (88.70)	24 (40.67)	
Female	7 (11.29)	35 (59.32)	
Income			0.010**
PKR 10,000-25,000	55 (88.70)	42 (71.18)	
PKR >25,000-41,000	6 (9.67)	7 (11.86)	
PKR. >41,000-57,000	1 (1.61)	10 (16.94)	
Education			0.987
Uneducated	43 (69.35)	41 (69.49)	
Educated	19 (30.64)	18 (30.50)	

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Education level			
Primary	6 (31.57)	5 (27.77)	0.301
Middle	8 (42.10)	5 (27.77)	
Matric	5 (26.31)	4 (22.22)	
Graduation	0 (0.0)	4 (22.22)	

* p≤0.05= significant; **p≤0.01=highly significant; ***p≤0.001= very highly significant; p-value=Chi-square test;

a= Students's t-test; n= Number of patients

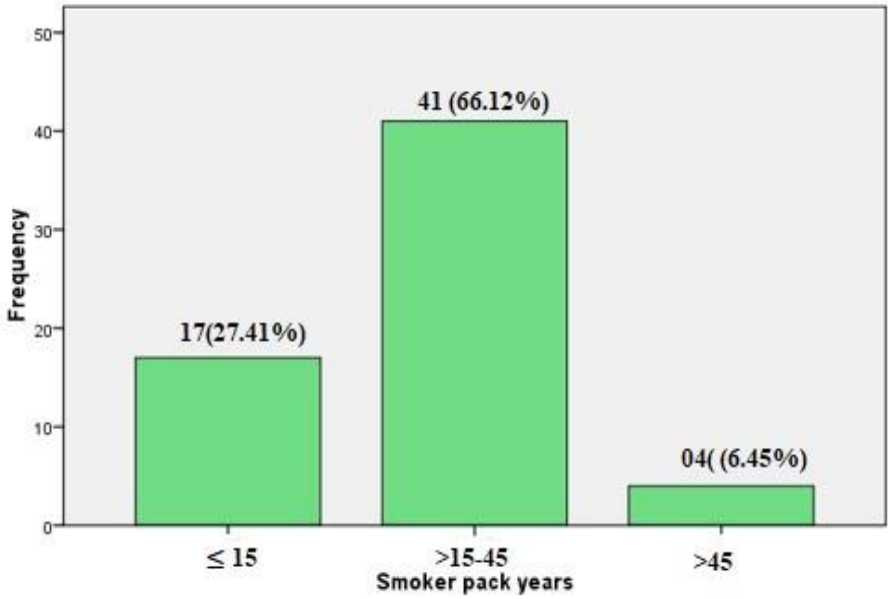

Figure 1: Graphical representation of smoking pack years of HNC patients

A significant difference was found between patient groups in all HNC subsites for smoking (P=0.005). Graphical representation of all HNC sites according to smoking is shown in Figure 2. The larynx site (n=50) (including the glottic, supraglottic, and subglottic subsites) was the most commonly affected site among smokers (n=33) with HNC. The second most prevalent site, the hypopharynx (n=41) (including the subsites postcricoid, pyriform sinus, and post-pharyngeal wall), was higher in non-smokers (n=28). HNC was divided into four subsites with regard to the skin. Total patients with squamous cell carcinoma were 116, equally affecting (n=58) both non-smokers and smokers. Regarding skin, a non-significant difference was observed between the smoker and non-smoker patient groups (p=0.403) (Table 2).

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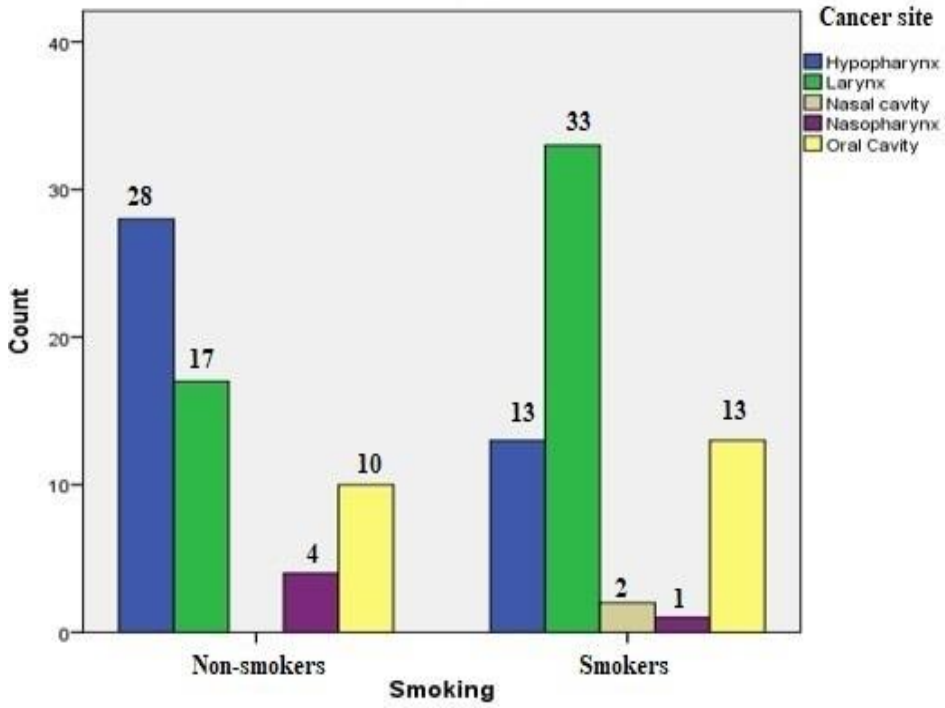

Figure 2: Graphical representation of different subsites of cancer in HNC patients according to smoking.

Table 2: Tumour location in HNC patients according to smoking.

Site n (%)	Subsite n (%)	Frequency n (%)		P value
		Smokers n=62	Nonsmokers n=59	
HNC site				0.005*
1. Larynx 50 (41.32)	Glottic 27 (54.0)	15 (24.19)	12 (20.38)	0.229
	Supraglottic 17 (34.0)	13 (20.96)	4 (6.77)	
	Subglottic 6 (12.0)	5 (8.06)	1 (1.69)	
2. Hypopharynx 41 (33.88)	Postcricoid 23 (56.0)	5 (8.06)	18 (30.50)	0.099
	Pyriform sinus 14 (34.14)	5 (8.06)	9 (15.25)	
	Postpharyngeal wall 4 (9.75)	3 (4.83)	1 (1.69)	
3. Oral Cavity 23 (19.0)	Anterior tongue 13 (56.52)	8 (12.90)	5 (8.47)	0.580
	Buccal mucosa 10 (43.47)	5 (8.06)	5 (8.47)	
4. Nasopharynx 5 (4.13)	----------	1 (1.61)	4 (80.0)	-----
5. Nasal Cavity 2 (1.65)	----------	2 (3.22)	0 (0.0)	------

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Skin type	Squamous Cell Carcinoma 116 (95.86) Basal Cell Carcinoma 2 (1.65) Adenocarcinoma 1 (0.82) Lymphoma 2 (1.65)	58 (93.54) 2 (3.22) 1 (1.61) 1 (1.61)	58 (98.30) 0 (0.0) 0 (0.0) 1 (1.61)	0.403

For statistical details and abbreviations see Table I.

Overall tumour stage-III (n=66) was the most prevalent as compared to tumour stage-II (n=24), stage-IV (n=20) and stage-I (n=11) in both smoker and non-smoker patients (Figure 3). The frequency of tumour garde 2 (Moderately differentiated tumour) was highest (n=49) among smoker patients. Among tumour size and nodal status, T3-4 (n=86) and N0 (n=64) were most common in both smoker and non-smoker patients. The statistical analysis showed no significant difference in tumour stage, grade, size and nodal status between smoker and non-smoker patient groups (p≤0.05). The metastatic status M1 was observed only in non-smokers (n=05). The metastatic status M0 was the most frequent in both smoker and non-smoker patients. A significant difference was found in the metastatic status between the patient groups who did smoking and those who did not (p=0.019) (Table 3).

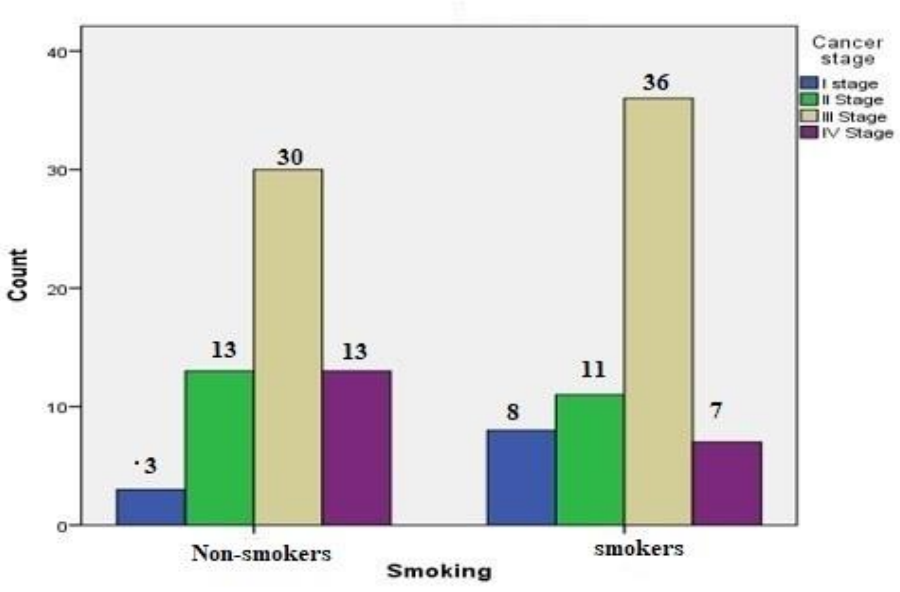

Figure 3. Graphical representation of cancer stage of HNC patients according to smoking.

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Table 3: Clinical characteristics of HNC patients according to smoking

Characteristics	Type n (%)	Frequency n (%)		P value
		Smokers n=62	Non-smokers n=59	
Tumour Stage				0.194
	Stage I 11 (9.09)	8 (12.90)	3 (5.08)	
	Stage II 24 (19.83)	11 (17.74)	13 (22.03)	
	Stage III 66 (54.54)	36 (58.06)	30 (50.84)	
	Stage IV 20 (16.52)	7 (11.29)	13 (22.03)	
Tumour grade				0.540
	Grade 1 6 (4.95)	4 (6.45)	2 (3.38)	
	Grade 2 100 (82.64)	49 (79.03)	51 (86.44)	
	Grade 3 15 (12.39)	9 (14.51)	6 (10.16)	
TNM classification				
Tumour size				
	T1-2 35 (28.92)	18 (29.03)	17 (28.81)	0.979
	T3-4 86 (71.07)	44 (70.96)	42 (71.18)	
Nodal status				
	N0 64 (52.89)	37 (59.6)	27 (45.76)	0.125
	N+ 57 (47.10)	25 (40.3)	32 (54.23)	
Metastatic status				
	M0 116 (95.86)	62 (100)	54 (91.52)	0.019*
	M1 5 (4.13)	0 (0.0)	5 (84.7)	

For statistical details and abbreviations see Table I.

DISCUSSION

HNC is seventh most prevalent cancer globally, which accounts for 5% of all malignancies. There are 350,000 deaths and 650,000 new cases of HNC each year worldwide [1, 2, 12, 20], but it is the 2nd most frequent cancer in Pakistan [13], Mean age of smoker patients was above 46 years and this is similar to finding of [14, 15,16] and contrary to the study of [16] where it was 59 years. In current study, non-smoker patients were found to be younger similar to the findings of [14]. Majority smoker patients were found in >55 age group as found in the study of [17]. In many other countries of world, higher rate of HNC has also been found at age of 40 to 60 years [18]. So this study suggests that older age (≥50 age) should be included as a risk factor of HNC and this is according to findings of [19, 20]. The frequency of male smoker patients was more as compared to female smoker patients, consistent with the studies of [14, 16, 17, 18]. Increased use of naswar and smoking, as well as increased exposure to environment and occupational risk factors, are all possible explanations for why males develop HNC more than women [21]. This study confirmed findings from previous studies that non-smoker HNC patients seem to be younger females [14] and this may be due to malnutrition. In this study, majority of smoker HNC patients were identified in >15-45 smoking pack years as confirmed by different studies in which majority of HNC patients had high smoking

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pack years [17, 22]. So in this study, smoking was highly associated with HNC among smoker patients as confirmed by different studies [15, 20, 24, 25] and in contrast to the study of [23] where smoking frequency was very less. Similar to the findings of different studies, the prevalence of HNC in smoker patients was higher among the low income patients [17, 15, 28]. That might be due to the fact that the data of current study was taken from a government hospital where the most of the patients came from low-income families. Additionally, according to various studies, nicotine increases physical activity and metabolic rate while lowering hunger in smokers [26]. As a result, poor people use tobacco to stifle their appetites, which may contribute to malnutrition and HNC. It is found in current study that study that tumour can also develop in persons who don't drink or smoke. This demonstrates that additional risk factors may function either independently or as co-factors in the development of HNC. Thus, extensive research is required in Southern Punjab to identify any potential risk factors in non-smoker HNC patients.

Majority of the smoker HNC patients were uneducated as confirmed by different studies [15, 18, 23] and among education level, most of the patients were found in middle or less education level similar to one study of Pakistan [15] and contrary result was found in other study[18] in which majority of patients completed secondary school of education. Educated patients have more awareness about HNC and visited the hospital in early stage. In contrast to educated individuals, people with low levels of education or no education at all are more likely to have late-stage cancer because of low awareness. This study showed that lower income and fewer years of schooling may be linked to a higher risk of developing HNC disease.

In contrast to findings from different studies [24, 25, 27, 28] who observed the larynx as the second most prevalent cancer site, the percentage of laryngeal cancer was highest in this study and primarily targeted the area of the glottis. as observed in different studies [15, 17]. According to an analysis of the risks for various subsites, the risk for laryngeal cancer was most closely associated with smoking. Thus, smoking is the main contributor to the risk of laryngeal cancer [1]. Our study found that the prevalence of hypopharynx was higher in non-smoker patients as compared to smokers, is in accordance with the research done in Pakistan [17] and in contrast to [24] who reported it more prevalent in smoker patients. In current study, squamous cell carcinoma ranked first among tumour skin types, as it has been observed in other studies [25, 28].

Tumour stage III was the most common type in both patient groups in this study and similar to the many findings [25, 27] and in contrast to the Pakistani researches [15, 28] where tumour stage IV was the most prevalent. Most of the patients in current study had tumour of grade 2 (Moderately differentiated) and several researchers revealed the similar findings [15, 24, 27]. In this study, the frequency of tumour size T3-4 and nodal status N0 was more and that is in consistent with work of [23, 27, 29] respectively. Similarly regarding metastatic status, the frequency of distant metastasis M1 was very low in current study groups as found in different studies [30].

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CONCLUSION

It can be concluded from this data analysis that smoking may be a key risk factor for HNC in addicts, whereas there are no major causative factor of HNC has been found in non-smokers. The results showed that there are numerous differences regarding HNC in smoker and non-smoker patients. Particular patient features that differ between the two patient groups include gender, age, income and the location of HNC incidence. These findings are crucial because clinicians need to be aware that a growing number of HNC patients do not use tobacco products and that HNC is not just limited to tobacco only. Long-term prevention and management of certain tumour may benefit from knowing these variations. Patients arrived at the hospital at a later stage of HNC due to lack of knowledge and a poor family background. The healthcare system in a developing nation is more burdened by this illness. In order to better control the disease, it is necessary to educate the public. A large-scale research is necessary, particularly in Nishtar hospital Multan as no descriptive study of HNC and smoking has been done before.

Conflict of Interest: Authors declare no conflict of interest

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Compliance with Ethical Standards

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