ASSOCIATION OF TOBACCO WITH NECK NODE METASTASIS IN SUPRA-GLOTTIC CARCINOMA OF LARYNX.

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Abstract

Background: *Carcinoma larynx is one of the most common cancers in the head neck region. Mortality and morbidity in this disease is still high in spite of modern treatment modalities. Smoking and Alcohol is recognized as common predisposing factor for carcinoma larynx. Neck node metastasis increases the mortality twice than the primary alone. Most of the Laryngeal carcinoma patient with neck node metastasis are smoker in our country. Stopping the consumption of tobacco may reduce both mortality and morbidity of carcinoma larynx. Metastasis is more common in supraglottic carcinoma of larynx. This study is carried to observe the association of tobacco with lymph node metastasis in supra-glottic carcinoma of larynx.*

Materials and Methods: *This cross sectional study was conducted in Otolaryngology and head Neck surgery department of Dhaka Medical College and Mitford Hospital of Dhaka, Bangladesh from June 2013 to June 2015. 212 cases of supraglottic carcinoma age ranging from 35 year to 90 years (mean age 63.6 ±11.65) was included in this study.*

Results: *Sixty two percent patients were diagnosed with cervical lymph node metastasis. 83.28% patients with nodal metastasis were above 60 years of age and 75.67% patients were manual worker.100% node positive patients were smoker. Smoking for longer period (>30yrs) and higher in number (>30 sticks/day) were found in advanced stage. Significant association was found between site, size, macroscopic features, cellular differentiation and demographic factors of patient with neck node metastasis in supraglottic carcinoma larynx.*

Conclusion: *As neck node metastasis significantly reduces prognosis so we must be more attentive towards factors that increase the chance of nodal metastasis to avoid the advancement of the disease.*

Key words: *Carcinoma larynx, Supraglottic carcinoma, Neck node metastasis, Prognosis.*

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Introduction:

Carcinoma of larynx is one of the common malignancies in Bangladesh (Rashid et al, 2007). Squamous cell carcinoma (SCC) is the commonest type, comprising more than 97% of all laryngeal malignancy (Birchal et al, 2008).Cervical lymphatic plays an active role in controlling biologic behavior of head and neck carcinoma (Shaha et al, 1990). Malignant cells are trapped by nodes, where they proliferate which often leads to uncontrolled regional disease and eventual demise of the patient (Subranium et al, 2006).

Different factors such as site, size, shape, histological type and grade, habit, occupation, habitant were considered as important predictors

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of lymph node metastasis. Probability of cervical metastasis and delayed contralateral metastasis is directly proportional to the size of primary lesion (i.e. the T stage) (Mc Gavran1961). Supraglottic lesions presenting with a clinically positive cervical node 2 cm in diameter or more, possibility of contralateral neck metastasis is 40% or higher (Som 1970). Because of profuse lymphatic network supraglottic carcinoma metastasizes frequently to cervical lymph nodes and failure of treatment is usually a result of metastasis rather than local disease. Histological features of Head Neck carcinoma have correlation with nodal metastatic potential. Non-keratinizing and poorly differentiated carcinomas are more aggressive. Although degree of cellular differentiation is not thought to be the most significant factor in tumor grading, it has been reported to correlate with probability of cervical metastasis (Lauma1971), which in turn has a strong impact on survival (Spiro 1974). A substantial number of those patients with clinically negative necks are found to have histological disease, as demonstrated when neck dissection is performed, or if left untreated they convert to clinically positive necks (Shaha et al. 1974). Over 60% of patients of supraglottic carcinoma will have neck disease at presentation. 20-25% of supraglottic carcinoma may present only as a neck mass in their primary presentation (Shaha et al, 1974 & Hansen 1975).

The most important prognostic factor in this case is the status of cervical lymph node.. 5 years survival rate reduces to 50% and is responsible for 50% to 95% of recurrence of disease when there is involvement of regional lymph nodes (Candellaet al.1985).

For these reasons, a key issue in laryngeal oncology is to assess metastasis to cervical lymph node and it's potentiality at diagnosis. This cross sectional observational study was based on, selected patients (positive histopathological report of supraglottic carcinoma of larynx) and tried to correlate association of tobacco with metastatic behavior of it.The result of this study hope to provide us knowledge about the incidence of neck node metastasis and it's association with tobacco, which may help in predicting the prognosis of diseases, choice of appropriate treatment modalities and it's prevention.

Methods and Study design:

Cross sectional (Observational) study conducted in Dhaka Medical College Hospital and Sir Salimullah Medical College and Mitford Hospital, Dhaka from January 2013 to June 2015.Total 212 patients who fulfilled the inclusion criteria and allowed for direct endoscopic examination with biopsy from the primary sites were included in this study.

Sampling technique: Purposive

Inclusion Criteria:

1. Supraglottic laryngeal cancer diagnosed histologically.
2. Neck node metastasis proved cytologically.

Exclusion Criteria:

1. Carcinoma of larynx where primary site was in confusion.
2. When patient had multiple malignancies

Variables: a) Age, b) Sex, c) Occupation d) Smoking and e)primary lesion in the Larynx (size, type and cellularity)

Data Processing and Statistical Analysis

Collected data were coded, kept confidential, processed and analyzed using computer software SPSS (Statistical Package for Social Sciences) and Sigma stat 3.1.

Results:

In this cross sectional study total 212 patient of supraglottic carcinoma of larynx who were fulfilling the certain inclusion and exclusion criteria were included. Of which 196(92%) males and only 16(8%) females, age ranged from 35 to 90 years with mean63.6yrs±11.6SD.

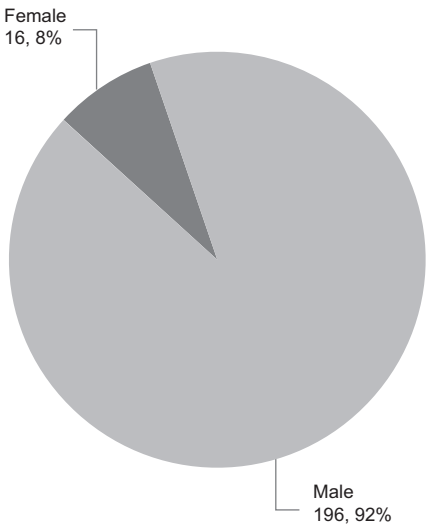

Figure 1: *Sex distribution of supraglottic carcinoma of larynx.*

Table-I

Relationship of sex with neck node metastasis.

Sex	Node +ve(n)	Node-ve(n)	p-value
Male	142(97.20%)	55(85.93%)	<0.001
Female	06(2.80%)	09(14.07%)	<0.001
Total	148(100%)	64(100%)	

Chi-square= 31.519 with 1 degrees of freedom. (P = <0.001).There was significant association with nodal presentation and sex.

Table-II

Age and cervical lymph node metastasis in laryngeal carcinoma.

Age	Node +Ve	Node -Ve	p-value
<60yrs	17(16.22%)	46(87.5%)	0.031
>60yrs	131(83.78%)	18(12.5%)	0.025
Total	148(100%)	64(100%)	

Chi-square= 18.372 with 1 degrees of freedom. There was significant relation between the age of the patient and the neck node metastasis.

Table-III

Nodal metastasis and habitat of patients

Habitat	Node +Ve	Node -Ve	p-value
Rural	127(85.81%)	13(20.32%)	0.025
Urban	21(4.19%)	51(79.68%)	0.035
Total	148(100%)	64(100%)	

Significant association was found in the habitat of patient with neck node metastasis.

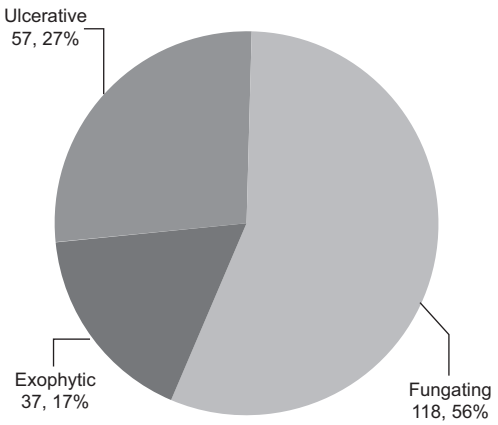

Figure 2: *Macroscopic variation of supraglottic Carcinoma of larynx.*

Table-IV

Association of nodal metastasis with T stages of supraglottic lesion.

Nodal status	T (early stage)	T (advanced)	p-value
Node +ve	16(47.06%)	132(74.15%)	<0.001
Node –ve	18(62.94%)	46(25.85%)	
Total	34(100%)	178(100%)	

Chi-square= 5.176 with 1 degrees of freedom.. There were significant association among different T stage with the nodal metastasis of (p<0.001).

Table-V

Relationship of nodal metastasis with macroscopic appearance of growth.

Nodal	Exophytic	Ulcerative	Fungating	p-value
Node +Ve	18(48.64%)	17(29.83%)	103(87.29%)	<0.001
Node –Ve	19(51.26%)	40(70.17%)	15(12.71%)	<0.001
Total	37(100%)	57(100%)	118(100%)	

Chi-square= 58.884with 1 degrees of freedom..Significant associations found between the macroscopic appearance with nodal involvement (p<0.001).

Table-VI

Nodal involvement of cancer with the Smoking habit of the patient.(n=212)

Smoking habits	Node +ve	Node –ve	Total	X^2 Test	
Smoking (sticks/day)				X^2	p-value
Lower (<20S/D)	10	28	38	2.205	<0.001
Middle (20-30S/D)	48	26	74		
High(>30S/D)	91	09	100		
Total	149	63	212		
Duration of smoking (years)				26.895	<0.001
<20 yrs	18	26	44		
20-30 yrs	55	19	74		
>30yrs	76	18	94		
Total	149	63	212		

Discussion:

In this cross sectional study two hundred and twelve [212] consecutive cases of supraglottic laryngeal carcinoma, fulfilling the certain inclusion and exclusion criteria were studied in the Department of ENT and Head-Neck Surgery, Dhaka Medical College Hospital and Mitford Hospital, Dhaka June'2013 to June'2015 to observe the association of tobacco

and certain clinico-pathological factors with the development neck node metastasis.

Among 212 of patients 196 (95.4%) were males and 16(4.6%) females the male female ratio were 12:1(Fig-1), which was similar to the findings of other study in Bangladesh(Amin et al 1990, Alauddin et al 1997,Haqueet al 2002). Among node positive patients 142(97.20%) were male and 06(2.80%) were female which was statistically significant. Age ranged from 35 - 90 years (mean 63.6 ±11.65SD). Nodal involvement was higher among elderly patients. In this study 16.22 % patients were below 60 years and 83.78% were above 60 years. Among node negative 83.78% were below 60 years of age. Analysis of habitat revealed 72(34%) from urban area and 140(66%) from rural area(Table-III) this situation was reverse to the international data. It might be due to the pattern of life style, knowledge of patient, consciousness, habit and other socio-demographic variants that might influence over the occurrence of carcinoma in our country. Most of the swelling in the neck (67.445%) of adult patients were metastatic neck nodes. In this study 22.41% presented with neck mass as their primary presentation, where in different literature it was shown that 20% patient of supraglottic carcinoma may present only as a neck mass as their primary presentation. (Chakraborty et al 1992. Verma et al 1990).

Incidence of carcinoma of larynx is strongly related to cigarette smoking. Tobacco smoke act as a promoter and initiator in carcinogenesis. Smoking alone accounted for 95% of all cases of laryngeal cancers. This malignancy is very uncommon among nonsmokers. Reduction in smoking has been associated with reduced incidence of laryngeal cancer (Tuyns1988).In this study 197(92.92%) patients with carcinoma larynx were smoker, 102(48.13%) patients of supraglottic group used to smoke more than 30 sticks per day and 72 patients smoked for more than 30 years. Among 148 patients with positive neck node 141 were smoker, Data revealed more number of cigarettes (>30 sticks/ day) have more chance of neck metastasis..In this study 71% patient with smoking >20 years shown node positivity (*table-VIII*). This results is similar to the study of Tuyns,1988.

.Among 212 patients of supraglottic carcinoma 24% were in T (early) and 76% were in T(advanced) stage. Incidence of palpable node increases with the size of primary tumor. Neck node metastasis was less common in T_{1-2}(24%) stage than T_{3-4} stage (76%)(Table-IV). Microscopic metastases was found in T_1 (<5%), T_2 (7%), T_3 (14%) and T_4 (33%).In this series 148(69.81%) patient had cytologically proved metastatic lymph node (s). In a previous study in Bangladesh this was found 70.09% in supraglottic (Alauddinet al.1997) andit was closer to the findings (85.7%) of study result of Bhowmik et al conductedin 2007. This is because, most of the patients complaining about their neck lump rather than laryngeal functional problem.

In this observational study 87.29% of fungating growth developed enlarged neck node whereas 70.17% of all ulcerative lesion had no metastatic node *(Table-V).* This study result is consistent with the findings of Amin et al, 1990 and of Kashima 1975. Histological grading has great impact on staging. It influences the development of neck node that was shown in different study. In this study 95.31% of moderate to poorly differentiated group had positive neck node. 69.05% patient of well differentiated group had no positive lymphadenopathy (*Table-VI*). This result is similar to the study of Hirabayashi et al 1991. Supraglottic and subglottic carcinoma are usually diagnosed at advanced histological grade and have more chance of neck metastasis.

Conclusion: In this cross sectional study some clinlinicopathological (site, type, extension and microscopical feature) along with demographic (age, sex, habitat) and causative factors like smoking were observed. Significant association was found between smoking with the development of nodal metastasis in supraglottic carcinoma of larynx.

Recommendations: Awareness must be created among general people in regarding the ill effects tobacco. Law makers should come forwards to ban on the use of tobacco related products. Peoples of urban and rural area should encourage to adopt healthy life style. Screening program should be installed to diagnose the disease at earlier stage to reduce mortality and

morbidity and hence reducing burden over national health system.

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