

A Clinicopathological Study of Laryngeal Malignancies - An Institutional Experience

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ABSTRACT

OBJECTIVE: To determine the risk factors and clinico-pathological pattern of the laryngeal malignancies

DESIGN: Descriptive case-series.

SETTING: Department of Otorhinolaryngology - Head and Neck Surgery, Dow Medical College, Civil Hospital Karachi and Dow University of Health Sciences from, March 1998 to March 2009.

METHODS: All patients of either gender having malignant lesion of larynx were included. Recurrent cases after surgery or chemoradiotherapy and benign tumours of the larynx were excluded from the study. Patients were studied with particular importance to the risk factors, mode of presentation, topography and histopathology of the tumour .

RESULTS: Out of 100 patients, 89 were males and 11 were females with male to female ratio of 8.1:1. Majority of the subjects was in 5th decade of their life. Tobacco intake in the form of smoking or chewing was present in 91%. Presenting symptoms were hoarseness, odynophagia, sore throat, dysphagia and dyspnoea/stridor. Transglottic area was the commonest site (39%) for laryngeal cancer. Squamous cell carcinoma (SCC) found in 98% of patients. Well differentiated category seen in 57% of patients.

CONCLUSIONS: SCC was the most frequent malignant lesion of larynx. Most of the patients presented in the late stages (stage III and IV). Commonest presenting symptom was hoarseness. Smoked tobacco (cigarette smoking) was found to be the major risk factor.

KEY WORDS: Head and neck tumors, Laryngeal carcinoma, Histopathology.

INTRODUCTION

Head and neck region, though a relatively small anatomical area, gives rise to a wide range of neoplastic conditions. Larynx is one of the commonest sites for carcinoma.¹ It accounts for approximately 1.2% of all new cancers diagnosed in the United States.² In Pakistan an incidence of laryngeal cancer ranges from 6.3% to 8%. In a multicentre study conducted in Pakistan by PMRC and Cancer Registry Cell Sindh, laryngeal cancer along with other head and neck cancers has been listed in the top ten.¹

Laryngeal carcinomas are identified by their location in one of three anatomic region: supraglottic, glottis, or sub-glottis. Uptill now transglottic cancer has not been included as one of the clinical classification of laryngeal cancer by UICC or AJCC. This term was first used by McGovern describing it a growth involving all three regions of larynx.³ Symptoms of laryngeal cancer vary according to location, size and degree of invasion of tumour. Tumour's location and extension pattern within one or more of these regions provide information regarding the progression of disease and expected response to treatment. The prognosis for small laryngeal cancers that do not have lymph node metastases is good with cure rates of 75-95%, depending on the site, the size of the tumor, and the

extent of infiltration. Advanced disease has worse prognosis. Supraglottic cancers usually manifest late and have a poorer prognosis.²

The vast majorities of malignant neoplasms of the larynx arise from the surface epithelium and are therefore classified as keratinizing or non-keratinizing squamous cell carcinomas (SCC). Other rare malignant forms include verrucous carcinoma, adenocarcinoma, fibrosarcoma, and chondrosarcoma.⁴

Head and neck cancer, including laryngeal cancer, is associated with exposure to environmental toxins and chemical carcinogens, such as tobacco and alcohol, asbestos, wood dust, cement, polycyclic aromatic hydrocarbons and therapeutic radiation. Gastroesophageal reflux disease (GERD), nutritional deficiencies particularly that of vitamins and iron has been linked with hypo-pharyngeal and laryngeal carcinoma.^{2,5-7} Human papilloma virus (HPV) is considered as a new etiological factor.⁸ These risk factors appear to be synergistic, and they result in a multiplicative increase in the risk of developing laryngeal cancer.

The purpose of this study was to determine the frequency of clinical presentation, identification of the risk factors, topography and pattern of histopathology of laryngeal malignancies at our institution. An inefficient referral system, prevailing poor economic climate and poor outcome of radical treatment operates

in a vicious circle to deter early presentation of patients with laryngeal carcinoma. To reverse the trend a coordinated public enlightenment programme and provision of subsidised health care delivery to indigent patients is required to gain an upper hand in the battle against laryngeal cancer.

METHODS

This descriptive case-series study was conducted at Department of Otorhinolaryngology Head and Neck Surgery, Civil Hospital, Karachi. All consecutive cases of laryngeal cancer presented from March 1998 to March 2009 were included in this study except recurrent cases after surgery or chemoradiotherapy, and cases of benign tumors of the larynx. After obtaining an informed consent, a pre-designed proforma was used to record the data regarding detailed history, physical examination, age, sex, occupation, presenting complains like change of voice, difficulty in breathing, difficulty in swallowing, pain - localized or referred, neck mass, and weight-loss. Personal history regarding habits of smoking and chewing the tobacco was also recorded. Clinical examination like laryngeal crepitus, IDL findings with respect to supraglottic, glottic, subglottic and extra-laryngeal involvement and vocal cord movement were also noted. Direct laryngoscopy^o (DL) under general anaesthesia was the gold standard in the examination of the larynx for an accurate assessment of the surface extent of the lesion. Using the biopsy forceps the lesions were palpated, and this mobility and depth of invasion were gauged. Multiple biopsies were taken from representative areas and sent for histopathological analysis. Neck examination with respect to level of lymph nodes involvement was also recorded. Imaging studies like X-ray chest PA view and CT scan of larynx (from base of skull to root of neck) were routinely done in all patients. Ultrasound abdomen was performed if metastasis was suspected. Finally staging of carcinoma larynx according to AJCC-TNM classification was decided after clinical examination and imaging studies for treatment planning.

The data were entered and analyzed on SPSS version 13. The results were presented as frequency, mean, standard deviation and percentage.

RESULTS

One hundred subjects were recruited for this study; 89 males and 11 females, with a male to female ratio of 8.1:1. The age ranged from 35-67 years (mean±SD 54±7.9 years) and majority of the cases were in their 5th decade of life.

Most of the patients belonged to urban areas and low socio-economic class.

There were 91 patients with the history of smoked/

unsmoked tobacco consumption in the form of cigarette, berri, hukka, pan and niswar. In 9 patients no history of any addiction was reported. Potential risk factors are depicted in **Table I**. The symptoms with which patients presented are shown in **Table II**. Change of voice especially hoarseness was the commonest presentation (92%). The average time duration from first appearance of symptom and referral to ENT department was 10.6±3.5 months, with shortest duration of 15 days and longest duration of 3 years. Topography of laryngeal cancers is shown in **Fig I**.

Cancer stage T1 was found in 8% cases, T2 in 12% cases, T3 in 28% cases and T4 in 52% cases. Presentation of neck nodes were observed as N0 in 84% cases, N1 in 12% cases and N2 in 4% cases. Among these 16% subjects with nodal metastasis, 8 had supraglottic, 2 had glottic and 6 had transglottic tumors. CT scan was found to be well informative and cost effective for evaluating the larynx prior to treatment for staging. (**Fig III**)

Histopathological evaluation by punch biopsies via direct laryngoscopy revealed that Squamous cell carcinoma (SCC) was present in 98% of patients – well differentiated type in 57%, moderately differentiated in 28%, and poorly differentiated in 13% patients, while chondrosarcoma found only in 2% patients.

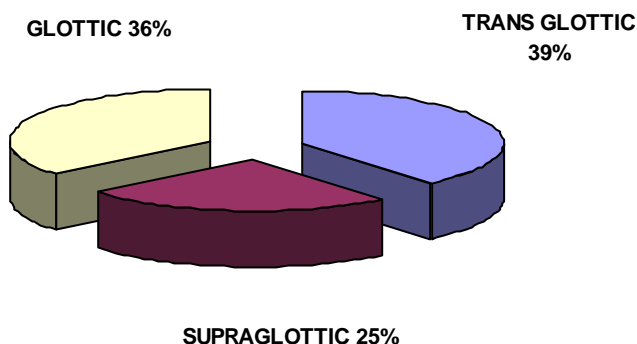
**TABLE I:
RISK FACTORS (n=100)**

Risk factors	Percentage
Cigarette	34
Cigarette + pan	24
Pan+Tobacco	19
Berri	7
Hukka	4
Niswar +cigarette	3

**TABLE II:
PRESENTING SYMPTOMS OF LARYNGEAL
CANCER (n=100)**

Symptoms	Percentage
Change of voice / Hoarseness	92
Odynophagia	58
Sore throat	28
Dysphagia	18
Dyspnoea /Stridor	17
Neck mass	9
Weight loss	8
Anorexia	6
Ear ache	4

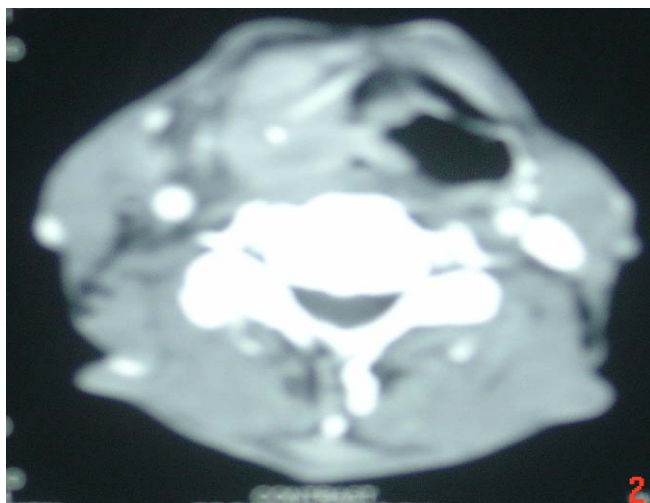
**FIGURE I:
TOPOGRAPHY OF LARYNGEAL CANCER**



**FIGURE II:
CERVICAL NODAL METASTASIS IN
SUPAGLOTTIC TUMOUR**



**FIGURE III:
CT SCAN (AXIAL VIEW) SHOWING THYROID
CARTILAGE INVOLVEMENT**



DISCUSSION

Laryngeal cancer accounts for 40% of all head and neck malignancies⁴. The American Cancer Society estimates that about 12,250 new cases of laryngeal cancer were diagnosed in 2008.⁹ Carcinoma of larynx is most common in adults aged 55-75 years; it is rare in children.¹⁰ In present study the age ranged from 35-67 years (mean 54 ± 7.9). Similar results have also been observed by Hasan S et al,¹¹ Aslam MJ et al,¹² Iqbal² and Adeyemo in Nigeria.¹³ In contrast to international studies done by Johansen LV et al¹⁴ (Denmark), Jin C⁴ and studies conducted at Greenebaum Cancer Center⁸ found most patient in the sixth and seventh decade.

In the 1950s, the male-to-female ratio in patients with laryngeal cancer was 15:1. This ratio had changed to 5:1 by the year 2000, and the proportion of women afflicted by the disease is projected to increase in years to come. These changes are likely a reflection of shifts of tobacco use (smoked and unsmoked), with women smoking more in recent years.² In present study males to females rate was 8.1:1, the obvious difference seems to relate to the social habit of smoking which is rare in our women folk.³ These results were close to the studies by Adeyemo in Nigeria¹³ and Dedivitis in Brazil.¹⁵

The exact etiology of laryngeal carcinoma is not well known, but exposure of the mucosa to a wide variety of ingested and inhaled exogenous carcinogenic agents greatly increase the risk of developing these tumors.^{3,9,11} In present study, majority of the patients belonged to low socioeconomic class of urban areas, with a strong history of tobacco use. These observations are in conformity with the prior studies.^{1,2,8} Abdul Hadi et al¹⁶ (Lahore) identified smoking 90% and 5% each alcohol and pan as a risk factors. Almadori G et al¹⁷ (Italy), shows 95% or more have a history of smoking, which increases risk in a dose-dependent way, however alcohol was not used by any of our patients whereas in many other studies it played a major role as carcinogens. It was reported that in alcoholics the risk of hypopharynx cancer was significantly higher than the risk of larynx cancer, which may be explained by the fact that hypopharynx enters in contact with the bolus (alcohol) and the air (tobacco smoke) while air pass is through larynx but not the bolus.¹⁸ In addition to tobacco consumption most of the patients had history of tea consumption but in the literature this has not emerged as an important risk factor. However, Eduardo observed that the habit of drinking a local tea called mate was associated with a three fold increase in risk of laryngeal cancer, after controlling for the effects of age, tobacco and alcohol consumption⁶. Avoiding cigarettes and alcohol could prevent about 90% of laryngeal SCC.^{4,8}

Most of the laryngeal cancers arise in the glottic region and are symptomatic at early stages as a result of hoarseness and changes in the voice.^{2,19} In current study change of voice especially hoarseness was the commonest presentation (92%). Similar findings were observed by Udaipurwala¹ in 90.9% patients and Adeyemo in 87% patients.¹³ Raitiola H et al (Finland),²⁰ Thekdi AA et al¹⁹ (USA) reveal glottic cancer patients present with hoarseness in early stages while in late stages other symptoms like dysphagia, dyspnoea or stridor, neck swelling, loss of weight and haemoptysis may develop. In present study 39% patients had transglottic, 36% had glottic and 25% had supraglottic tumours. The fact that most of the tumours turn out to be transglottic is not a dilemma. It is the mere neglect on the part of these patients that makes them presented with more advanced pathology. These results are very close to the studies done by Udaipurwala and a randomized study at Jinnah Postgraduate Medical Centre (JPMC) where glottic cancer was found to be common (37.8%) followed by the transglottic site (36.2%).¹ Glottis 56%, supraglottis 36%, transglottic tumours 8% and no subglottis tumour involvement observed by Aslam M J et al¹² (Islamabad). Raitiola H et al,²¹ revealed glottis 57%, supraglottis 43% and no sub-glottis tumour.

Most (80%) of the patients were in T3/T4 stage and only 8% in T1 stage. Abdul Hadi et al¹⁶ (Lahore), reported 91.66% at late stage and only 8.33% at early stage. Adeyemo in Nigeria¹³ found 82.9% patients with T3/T4 lesions at presentation and only 6.4% with T1 lesions. In contrast Matsuo JM et al (New York), shows 60% early stage and 40% late stage.²²

Metastasis rate is more common in supraglottic than glottic or subglottic tumours and in tumours with larger surface dimension.⁴ In present study neck nodes were present in 16% of patients out of which 8% were supraglottic tumours. Iqbal N² reported that supraglottic carcinomas are associated with clinically positive lymph nodes in 55% at initial diagnosis with a 16% incidence of bilateral involvement. In contrast, lesions of the true vocal cords are rarely metastasize, having 2% to 5% risk of nodal metastasis. This fact is consistent with the result in the present study.

Approximately 95% of all laryngeal and hypopharyngeal malignant tumors are SCC.² Carcinoma of the supra- and subglottic larynx are more likely to be non-keratinizing and poorly differentiated. These are often large at the time of diagnosis, more aggressive in behavior, and tend to metastasize early (20-40% of the cases). In contrast, lesions of the true vocal cords are typically small when detected, and more often moderately to well differentiated, rarely metastasize, and tend to be associated with a better prognosis.^{2,4} In this study 98% patients had Squamous cell carcinoma and

only 2% had chondrosarcoma. Well differentiated SCC was more commonly found variety (85%) as compared to poorly differentiated. Identical results were also present in a study conducted at JPMC.¹

In conclusion approximately 98% of all laryngeal malignant tumors are squamous cell cancers. The incidence of laryngeal carcinoma is closely correlated with tobacco use (smoked and unsmoked forms). Majority of the patient presented in the advanced stages. Change of voice – especially hoarseness is the commonest presenting complaint. The clinician has a much great responsibility regarding the disease as careful evaluation and early treatment bring a probability of cure while the failure may be followed by a relatively uncomfortable and unsavoury death.

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