



## CLINICOPATHOLOGICAL STUDY OF CARCINOMA LARYNX

**DR.SHIVKUMAR RAGHUVANSHI<sup>1</sup>, DR.SUNIL KUMAR SINGH BHADOURIYA<sup>\*2</sup>,  
DR.SUSHIL GAUR<sup>3</sup> AND DR.VIVEK KUMAR PATHAK<sup>4</sup>**

<sup>1</sup> Department of ENT and Head & Neck Surgery, L.N.Medical College, Barkatullah University, Bhopal, India

<sup>2</sup> Department of ENT and Head & Neck Surgery, SMS&R, Sharda University, Greater Noida, India

<sup>3</sup> Department of ENT and Head & Neck Surgery, SMS&R, Sharda University, Greater Noida, India

<sup>4</sup> Department of ENT and Head & Neck Surgery, SMS&R, Sharda University, Greater Noida, India

### ABSTRACT

This study was done to determine the risk factors and clinico-pathological pattern of the laryngeal malignancies. Patients were studied with particular importance to the mode of presentation, risk factors, topography and histopathology of the tumour. Out of 100 patients, 96 were males and 4 were females with male to female ratio of 24:1. Maximum number of cases belonged to age group 51-60 years. Tobacco intake in the form of smoking was the major risk factor and present in 76% of cases. Commonest presenting symptom was the dysphagia. Supraglottic area was the commonest site (72%) for laryngeal cancer in this study. Squamous cell carcinoma was found in 98% of patients. Moderately differentiated category seen in 48% of patients. Most of the patients presented in the stage III and IV (30% and 52%). 54 (54%) cases out of 100 cases had cervical lymph node metastasis at the time of presentation. Diagnosis is based on direct or indirect visualization of the larynx, supplemented by CT scan and confirmed by histopathological examination.

**KEYWORDS:** Carcinoma larynx, Histopathological, Clinicopathological, Larynx, Squamous cell carcinoma



**DR.SUNIL KUMAR SINGH BHADOURIYA**

Department of ENT and Head & Neck Surgery, SMS&R, Sharda University,  
Greater Noida, India

\*Corresponding author

## INTRODUCTION

The larynx is a complex organ that serves to protect the lower airways, facilitates respiration and plays a key role in phonation<sup>1</sup>. Based on anatomic location, the larynx is divided into the supraglottic larynx, glottic larynx and the subglottic larynx. Cancer larynx is one of the causes of morbidity and mortality in India. 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<sup>2</sup>. Symptoms of laryngeal cancer vary according to location, size and degree of invasion of tumour. Tumour location and extension pattern within one or more of these regions provide information regarding the progression of disease and unexpected 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 tumour, and the extent of infiltration<sup>3</sup>. Advanced disease has worse prognosis. Supraglottic cancers usually manifest late and have a poorer prognosis. The vast majority of malignant neoplasms of the larynx arise from the surface epithelium and are therefore classified as keratinizing or non-keratinizing squamous cell carcinomas<sup>4</sup>. Other rare malignant forms include verrucous carcinoma, adenocarcinoma, fibrosarcoma and chondrosarcoma<sup>5</sup>. Head and neck cancer, including laryngeal cancer, is associated with exposure to environmental toxins and chemical carcinogens, such as tobacco<sup>6,7</sup> and alcohol<sup>6,8</sup>, asbestos<sup>9</sup>, silica dust<sup>10</sup>, polycyclic aromatic hydrocarbons<sup>11</sup> and therapeutic radiation. Laryngeal cancer risk is substantially higher in people who smoke tobacco and drink alcohol<sup>12</sup>. These risk factors appear to be synergistic, and they result in a multiplicative increase in the risk of developing laryngeal cancer<sup>12,13</sup>. Gastro oesophageal reflux disease<sup>14</sup> (GERD) and nutritional deficiencies (particularly that of vitamins and iron) has been linked with hypo-pharyngeal and laryngeal carcinoma. Human papillomavirus (HPV) is considered as an etiological factor<sup>15</sup>. Laryngeal squamous cell carcinoma (SCC) risk is 5.4

times higher in people with HPV infection<sup>16</sup>. Laryngeal cancer risk is higher for HPV type 16 than HPV type 18. Laryngeal cancer has a high mortality rate if left untreated. Laryngeal cancer is potentially curable if detected early and treated appropriately.

## OBJECTIVE

The aim of the present study was to study the incidence, etiological factor, site of origin, possible spread, clinical aspects, and histopathological patterns of laryngeal carcinoma and to compare and correlate the result of FNAC with Histopathology.

## MATERIALS AND METHODS

This study was conducted at Department of Otorhinolaryngology Head and Neck Surgery, Hamidia hospital Gandhi medical college Bhopal. All cases of laryngeal cancer presented from January 2004 to July 2005 were included in this study except recurrent cases after surgery or chemo radiotherapy and cases of benign tumors of the larynx. After obtaining an informed consent, a pre-designed proforma was used to record the data. This study protocol was cleared by institutional ethical committee. All the patients were examined clinically, radiologically and histopathologically. Blood for routine TLC, DLC, ESR, Hb% and blood biochemistry for urea, sugar, cholesterol, SGPT and SGOT were done in all patients. Age, sex, religion, profession, family history of cancer, economic status, nutrition and general hygienic condition were analyzed. Addiction to smoking, tobacco chewing and alcohol were also noticed very carefully. Site of growth and symptoms with duration were noticed. Thorough inspection of neck was done, special attention was paid to the presence of enlarged lymph nodes, size and shape of thyroid gland was noted. Careful examination of the ear, nose, nasopharynx, oral cavity, and oropharynx was done. Indirect mirror examination has been and

still is the most reliable method of making a presumptive diagnosis of carcinoma of larynx and laryngopharynx were done in all patients. Routine soft tissue x-ray of neck both anterior posterior and lateral view were taken in all patients. X-ray chest was routinely taken to detect secondary, and associated pulmonary tuberculosis. CT scan of larynx (from base of skull to root of neck) was routinely done in all patients. Under local or general anaesthesia direct laryngoscopy was done. It was routine procedure applied for all suspected cases of carcinomas larynx and laryngopharynx. In all cases biopsy material was taken for confirmation of diagnosis and for histological grading. Cases presenting with neck nodes, FNAC was done for early diagnosis. Finally staging of carcinoma larynx according to AJCC-TNM classification was decided after clinical examination and imaging studies for treatment planning. Data was entered in Microsoft excel

sheet and data analysis was done by using statistical software SPSS version 17.

## RESULTS

One hundred subjects were recruited for this study; 96 males and 4 females, with a male to female ratio of 24:1. The age ranged from 38-85 years and maximum number of cases belonged to age group 51-60 years. The next common age group was 61 years and above. Most of the patients belonged to rural areas (62%) and low socio-economic class (74%). There were 88 patients with the history of tobacco consumption in the form of cigarette, bidi, hukka, betel leaf and betel nut. Addiction to alcohol was in 26% of cases. In 6 patients no history of any addiction was reported. Potential risk factors are depicted in Table 1.

**Table 1**  
**Risk factors**

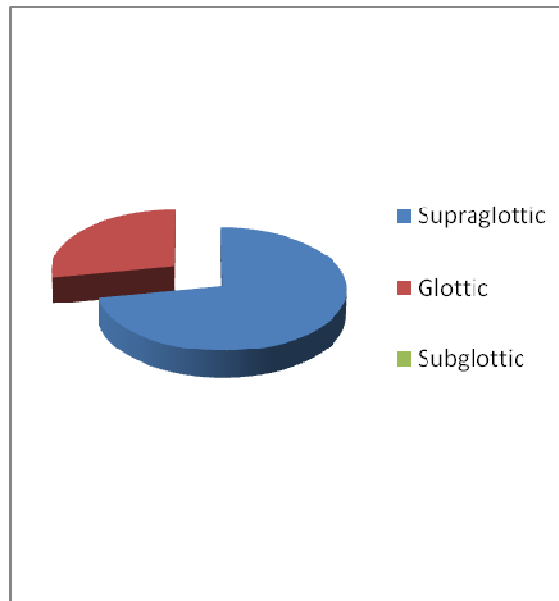
Habit	No. of cases	Percentage
Smoking	76	76
Tobacco Chewing	24	24
Smoking & Tobacco Chewing	12	12
Betel nut / Betel leaf	56	56
Alcohol	26	26
No Addiction	6	6

*The symptoms with which patients presented are shown in Table 2. Difficulty in swallowing was the commonest presentation (61%).*

**Table 2**  
**Symptoms**

	No. of cases	Percentage
Change in voice	42	42
Difficulty in swallowing	61	61
Swelling in neck	43	43
Difficulty in breathing	25	25
Pain in throat	28	28
Pain in ear	20	20
Loss of weight / appetite	56	56
Irritable cough	22	22
Any other	18	18

**Graph 1**  
**Topography of laryngeal cancers**



Cancer stage T1 was found in 9% cases, T2 in 9% cases, T3 in 30% cases and T4 in 52% cases. Table 3 showing distribution of cases in each stage.

**Table 3**  
**Distribution of cases in each stage**

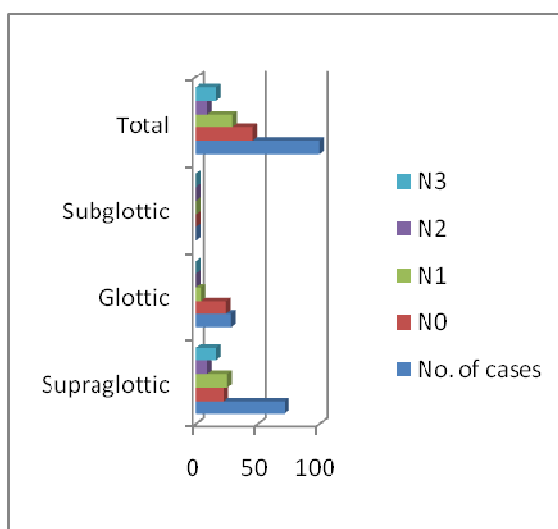
Stage	No. of cases	Percentage
Stage I	9	9
Stage II	9	9
Stage III	30	30
Stage IV	52	52
Total	100	100

Presentation of neck nodes were observed as N0 in 46% cases, N1 in 29% cases, N2 in 9% cases and N3 in 16% of cases. Among these 54% subjects with nodal metastasis, 50 had supraglottic and 4 had glottic malignancy. Table 4 and graph 2 is showing lymph node metastasis.

**Table 4**  
**Lymph node metastasis**

Site	No. of cases	N0		N1		N2		N3	
		No	%	No.	%	No.	%	No	%
Supraglottic	72	22	31	25	33	9	12	16	22
Glottic	28	24	85	4	15	-	-	-	-
Subglottic	-	-	-	-	-	-	-	-	-
Total	100	46		29		9		16	

**Graph 2**  
**Lymph node metastasis**



CT scan was found to be well informative and cost effective for evaluating the larynx prior to treatment for staging. Case presented with cervical metastasis (54) underwent FNAC study. On fine needle cytology report 45 cases (i.e. 83%) show positive finding (i.e. metastatic carcinoma) while 9 cases (i.e. 17%) were negative (i.e. Haemorrhagic smear). Table 5 is showing FNAC findings.

**Table 5**  
**Fine Needle Aspiration Cytology**

FNAC Finding	No. of Cases	Percentage
Metastatic Carcinoma	45	83%
Haemorrhagic Smear	9	17%
Total	54	100%

Histopathological evaluation by punch biopsies via direct laryngoscopy revealed that Squamous cell carcinoma (SCC) was present in 98% of patients – well differentiated type in 30%, moderately differentiated in 48%, and poorly differentiated in 20% patients, while adenocarcinoma found only in 2% patients.

**Table 6**  
**Histology**

Histological type	No. of cases	Percentage
Well differentiated squamous cell carcinoma	30	30
Moderately differentiated squamous cell carcinoma	48	48
Poorly differentiated squamous cell carcinoma	20	20
Adenocarcinoma	2	2
Total	100	100

## DISCUSSION

Laryngeal carcinoma accounts for a small fraction of all human malignancies (less than 2%), but the incidence varies geographically<sup>5</sup>. The American Cancer Society estimates that about 12,250 new cases of laryngeal cancer were diagnosed in 2008<sup>17</sup>. Carcinoma of larynx is most common in adults aged 55-75 years; it is rare in children<sup>18</sup>. In present study the age ranged from 38-85 years. Similar results have

also been observed by Mattick and Mancini (1954), Dutta Chowdhury et al. (1959) and Adeyemo in Nigeria<sup>19</sup>. Nasir Iqbal et al. (2005) has shown peak incidence to be 50–60 years. In contrast to international studies done by Johansen LV et al<sup>20</sup> (Denmark) and studies conducted at Greenebaum Cancer Center 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, with women smoking more in recent years. In present study males to females rate was 24:1, the obvious difference seems to relate to the social habit of smoking which is rare in women in this region. These results were close to the studies by Adeyemo in Nigeria and Dedivitis in Brazil<sup>21</sup>. Shroff<sup>22</sup> in his study found that 96.4% were males. Putney and Chapman found male to female percentage as 96% and 4% respectively. 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<sup>17,23</sup>. In present study, majority of the patients belonged to low socioeconomic class of rural areas, with a strong history of tobacco use. These observations are in conformity with the prior studies. Almadori et al<sup>24</sup>, shows 95% or more have a history of smoking, which increases risk in a dose-dependent way. In the present study incidence of smoking alone was found in 76% cases, 12% were addicted to both smoking and chewing tobacco. In this series majority (52%) patients have smoking index "300 or above". Majority of patient smoked between 10-20 bidis per day for 20-30 years. In this study 26 cases were in both smoking and alcoholic group and only 2 cases were purely alcoholic. It was reported that in alcoholics the risk of hypopharynx cancer was significantly higher than the risk of larynx cancer<sup>25</sup>. Avoiding cigarettes and alcohol could prevent about 90% of laryngeal squamous cell carcinoma. 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<sup>26</sup>. In current study change of voice especially hoarseness was the third commonest presentation (42%). Thekdi et al 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 hemoptysis. Difficulty in swallowing was found to be the commonest symptom (61% cases). It was mainly for solids. Pain in throat was present

in 28% cases. Verma et al. reported 50.95% complaining of dysphagia and 25.59% pain in throat. Swelling in neck in all cases was due to secondary metastasis, found in 43% cases which correspond to the figure of 44.16% in Verma's series<sup>27</sup>. Cervical metastasis was found to be more frequent in supraglottic than in glottic cancer. Difficulty in breathing is a late symptom and occurs when the growth has considerably increased. In cases of glottic cancer, the growth reduces the chink to mere opening causing dyspnoea. In this series dyspnoea was present in 25% cases whereas it was present in 47.38% cases in Verma's series and 35% cases in Deka's series<sup>28</sup> and 12.1% cases in Das's series. In present study 28% had glottis, 72% had supraglottic and no subglottic cancer involvement observed. Dutta Chowdhury et al. found 88.6% as supraglottic in origin. Datti et al. reported 81.5% as supraglottic, 15.5% as glottic and 3% as subglottic involvement<sup>29</sup>. Taskinen (1969) found that 67% had supraglottic origin<sup>30</sup>. In North America 60% of laryngeal neoplasm are glottic and in UK it comprises 50%. Supraglottic comprises above 40% of all laryngeal cancer in UK and 30% in North America. Subglottic carcinoma accounted for < 5% cases<sup>31</sup>. The incidence of lymph gland metastasis varies with the location of primary tumour. The high incidence of metastasis in supraglottic tumour is due to rich lymphatics supply in the supraglottic portion of larynx. Low incidence in glottic cancer is due to paucity of lymphatics in vocal cord. In present study cervical node metastasis was present in 54% of cases at time of presentation. Highest percentage of cervical metastasis was found in supraglottic carcinoma. Out of 72 cases of supraglottic carcinoma, 50 case (69%) were present with lymph node metastasis in which 25 case (50%) was N1 group 9 cases (8%) was N2 group and 16 cases (32%) was N3 group present with Lymph node metastasis. Only 4% glottic case present with lymph node metastasis. Ledermann found the incidence as follows – supraglottic 40%, glottic 3%, subglottic 13%, transglottic cancer 13%<sup>32</sup>. Datti et al. showed the incidence as follows – glottic 4%, subglottic 6.6%, supraglottic 23.3%. Patient in this series were mainly of stage of IV (52%) and stage III (30%)

accounting for 82% of all cases. 9% patients belonged each to stage I and II. McNeil (1985) in his study noted that 91.3% of his cases were in stage I whereas in our series only 9% cases could be graded as stage I. The findings in this series correspond to findings in the series of Verma et al. in which 60.4% cases were of stage IV, 21.3% of stage III, 11.78% of stage II and 6.43% of stage I. In contrast Matsuo JM et al (New York), shows 60% early stage and 40% late stage<sup>33</sup>. Metastasis rate is more common in supraglottic tumours, and in tumours with larger surface dimension. Approximately 95% of all laryngeal and hypo pharyngeal malignant tumors are Squamous cell carcinoma. Carcinoma of the supra- and subglottic larynx are more likely to be nonkeratinizing and poorly differentiated. These are often large at the time of diagnosis, more aggressive in behavior, and tend to metastasize early. 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. In this present series FNAC study show 83% positive finding (i.e., metastatic carcinoma) while 17 were negative finding (i.e., Haemorrhagic smear). Histopathological studies in this series revealed that (98%) patients had squamous cell carcinoma and only 2 cases had adeno carcinoma. Amongst squamous cell carcinoma the highest number of cases in this series were of moderately differentiated carcinoma (48%) which corresponds to findings of Datti et al (1971) in which more of moderately

differentiated cases were seen. This is in contrast to series of Shaw in which more of well differentiated cases were seen<sup>34</sup>. Rathan Shetty et al. in their study of 50 patients of head and neck cancers most commonly found moderately differentiated squamous cell carcinoma<sup>35</sup>. In the present series, the incidence of distant metastasis is 4% whereas Extell et al. (1976) reported from United States that 15% of patients with laryngeal carcinoma have distant metastasis at time of presentation.

## CONCLUSION

This study has been done to improve understanding and care of patients with laryngeal carcinoma. The symptoms of laryngeal tumours can vary from mild hoarseness of voice to life threatening respiratory distress. Laryngeal cancer should be considered major public health problem in developing country. All available methods of study should be utilized to make the diagnosis as early as possible. With early diagnosis and treatment, it is possible to reduce the incidence and mortality of this problem. Early detection can improve and prolong the life of these patients.

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