



## EPIDEMIOLOGY OF SUPRAGLOTTIC CANCER IN OUR REGIONAL INSTITUTE

### Otolaryngology

<b>Manish Verma</b>	Postgraduate resident, Department of Otorhinolaryngology, Pt.BD Sharma Postgraduate Institute of Medical Sciences, Rohtak, Haryana, India
<b>Meena</b>	Postgraduate resident, Department of Pathology, Pt.BD Sharma Postgraduate Institute of Medical Sciences, Rohtak, Haryana, India
<b>Chandni Sharma</b>	Assistant Professor, Department of Otorhinolaryngology, Pt.BD Sharma Postgraduate Institute of Medical Sciences, Rohtak, Haryana, India
<b>Meenakshi Verma*</b>	Postgraduate resident, Department of Anesthesiology, Pt.BD Sharma Postgraduate Institute of Medical Sciences, Rohtak, Haryana, India *Corresponding Author
<b>Keshav Gupta</b>	Postgraduate resident, Department of Otorhinolaryngology, Pt.BD Sharma Postgraduate Institute of Medical Sciences, Rohtak, Haryana, India

### ABSTRACT

Supraglottic cancer is one of the common head and neck cancer (excluding skin). The incidence rates for laryngeal cancer in Central Europe are among the highest in the world. Approximately 87% of laryngeal cancer cases are attributable to tobacco use, of which 75% and 12% are due to current and past smoking, respectively. The occurrence of 12,250 new cases/yr with Male: Female ratio of 4: 1 and it occurs at the peak age of 6th and 7th decades of life. We had conducted a retrospective study on a total of 147 patients of either sex in one year. In these patients, supraglottic cancer was confirmed by histopathological examination of the tissue obtained by direct laryngoscopy and biopsy in the operation theatre. Out of 147 patients, 138 (93.8%) were males and 9 (6.2%) were females. Majority of patients were in the age group of 51-60yrs i.e. 56 patients (38.09%). Smoking was a major risk factor seen in all patients (100%). There was no statistical difference between the two sexes ( $p>0.05$ ).

### KEYWORDS

Supraglottic cancer, Smoking, Histopathological examination, Direct laryngoscopy

#### Introduction:

Laryngeal cancer is the ninth and seventh most common cause of cancer in males in Asia and India respectively. In 2012, an estimated 25,446 new cases were diagnosed, and 17,560 Indians lost their lives from laryngeal cancer.<sup>1</sup> In India, the incidence of laryngeal cancer has been reported to be 1.26-8.18 per 100,000 population, in different regions in the country.<sup>2</sup> Epidemiological studies carried out on laryngeal cancer have highlighted the peculiarities of the disease, like varying risk factors and wide regional variation in incidence and survival.

Supraglottic cancer is one of the common head and neck cancer (excluding skin). The incidence rates for laryngeal cancer in Central Europe are among the highest in the world. Approximately 87% of laryngeal cancer cases are attributable to tobacco use, of which 75% and 12% are due to current and past smoking, respectively. The occurrence of 12,250 new cases/yr with Male: Female ratio of 4: 1 and it occurs at the peak age of 6th and 7th decades of life. More than 90% are squamous cell cancer Glottic Carcinoma (CA) more common in Caucasian (in US). Glottic and Supraglottic CA are equal in African American (US) and accounts for 25% of head and neck cancer and 1% of all cancers.<sup>3</sup>

The most important risk factor for cancer larynx appears to be the tobacco use. National Cancer Registry Program enlists laryngeal cancer as one of the tobacco- related cancer.<sup>4</sup> The IARC monograph also classifies tobacco use as a carcinogenic to humans based on overwhelming on.<sup>5</sup> Apart from tobacco use; alcohol consumption has also been implicated as a risk factor in the development of laryngeal CA. There is a dearth of Indian studies on the association between alcohol and laryngeal cancer, mainly due to social stigma associated with the alcohol habit. Furthermore, women in India do not openly admit to the habit of alcohol consumption.<sup>6</sup> However, a few case-control studies and one cohort study found an almost 2-4 fold increase in the risk of laryngeal cancer due to alcohol consumption.

International Agency for Research on Cancer monograph on indoor air pollution classifies indoor air pollution from coal usage as a known human carcinogen (IARC Group1), while that from biomass (primarily wood) as a probable human carcinogen (IARC Group 2A).<sup>7</sup>  
<sup>8</sup> In a developing country like India where as much as 74% of the total

population uses solid fuels for cooking,<sup>9</sup> it has been estimated that indoor air pollution may account for up to 4-6% of the national burden of disease.<sup>10</sup> A multicentric case-control study conducted in India between 2001 and 2004, found no increased risk of laryngeal cancer among ever-users of solid fuels compared to lifelong users of modern fuel. However, long duration (>50 years) of coal usage was found to be a risk with duration-dependent increase in risk for laryngeal cancer.<sup>11</sup>

Supraglottic cancer is seen less frequently than glottic cancer and is treated differently from tumors of the glottic and subglottis. Due to its location, the disease and its treatment can affect the function of the larynx, including speech, swallowing, and breathing. 85-95% of laryngeal tumors are squamous cell CA. Characterized by epithelial nests surrounded by inflammatory stroma and keratin pearls, these features are pathognomonic of CA. Verrucous CA, Fibrosarcoma, Chondrosarcoma, Minor salivary CA, Adenocarcinoma, Oat cell CA, Giant cell and Spindle cell CA.<sup>12</sup> The incidence of laryngeal CA by site includes Glottic- 59%, Supraglottic-40%, and Subglottic- 1%. Supraglottic cancer involves epiglottis, aryepiglottic folds, arytenoids, false vocal cords & ventricles. These tumors more aggressive due to their direct extension into pre-epiglottic space, lymph node metastasis, direct extension into lateral hypopharynx and glossoepiglottic fold and tongue base. Risk factors include prolonged use of tobacco and excessive alcohol intake is the primary risk factors. The two substances together have a synergistic effect on laryngeal tissues. 90% of patients with laryngeal cancer have a history of both. Other risk factors are Human papilloma virus 16 & 18, chronic gastric reflux, occupational exposures, prior history of head and neck irradiation.<sup>13</sup> (Fig. 1)

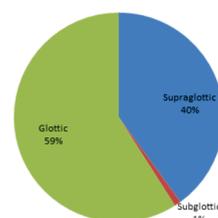


Fig.1. The incidence of laryngeal carcinoma by the site.

### Material and methods:

The present retrospective study was conducted in the Department of Otorhinolaryngology and Pathology PGIMS, Rohtak on a total of 147 patients either sex in two years. In these patients, supraglottic cancer was confirmed by histopathological examination of the tissue obtained by direct laryngoscopy and biopsy in the operation theatre.

The evaluation of the varied clinical presentation of supraglottic cancer as well as the risk factors associated with it was carried through physical examination, complete head and neck examination, palpation for nodes, laryngeal crepitus, and quality of voice (breathy voice-cord paralysis, muffled voice-supraglottic lesion). Direct laryngoscopy was done in all the patients and tissue taken for biopsy was sent for histopathological examination.

### Technique of Direct Laryngoscopy and Biopsy:

Direct Laryngoscopy is a diagnostic and therapeutic procedure for examination and removal of a foreign body, cyst nodule, polyp or tumor. It also is a way to improve vocal quality by injecting biocompatible agents that amplify one's voice. Among the few complications that may occur are the injuries to teeth, risks of general anesthesia, bleeding after biopsy, and failure of a vocal cord to heal after the biopsy. Voice change or hoarseness is possible after vocal cord surgery. Direct laryngoscopy is the most common procedure performed on the larynx requiring general anesthesia. This procedure is used to visualize and biopsy diseases in and around the larynx. The procedure is performed under general or local anesthesia. The patient is positioned in a way that allows extension of the head and neck. The teeth and gums are protected, and the laryngoscope is introduced into the mouth and throat. The laryngoscope has a rigid, hollow barrel through which the larynx and pharynx are visualized and the biopsy taken from the respected site. Fiberoptic light cables are used for illumination. Most procedures on the larynx are relatively short, usually less than one hour. Patients are observed for a few hours post-operatively and then are sent home if they meet certain criteria.<sup>14</sup>

### Result:

The supraglottis is embryologically derived from the buccopharyngeal anlage in the region of the third and fourth branchial arches. Despite the theoretical separation of the supraglottis from the rest of the larynx, no anatomical or histological barrier has been identified. Furthermore, supraglottic tumors invading the paraglottic space have access to the glottis via the medial surface of the thyroid cartilage. Lymphatic vascularity in the supraglottis is much denser than in the glottis and subglottis. This is important in the development of supraglottic cancer and leads to a significantly higher incidence of cervical lymph node metastases in tumors of this subsite.<sup>13</sup>

Out of 147 patients, 138 (93.8%) were males and 9 (6.2%) were females. Majority of patients were in the age group of 51-60yrs i.e. 56 patients (38.09%), Smoking was a major risk factor seen in all patients (100%). Dysphagia (100 pts.), Odynophagia (86pts) and neck swelling (81pts) were major clinical features observed. Level 2 nodes were more frequently involved (40 pts.). In the majority of patients epiglottis was involved (46.9%). Histopathological evaluation revealed all supraglottic cancers to be of squamous cell type (moderately differentiated type 96.59%). Squamous cell CA characterized by hyperplasia, dysplasia, CIS (carcinoma in situ), invasive CA. Invasive CA characterized by: well, moderately, or poorly differentiated Nest of malignant epithelial cells, desmoplastic & inflammatory stroma, keratin pearls (in well and moderately differentiated CA). There was no statistical difference between the two sexes ( $p > 0.05$ ). (Fig.2)



Fig.2. Clinical features in carcinoma Supraglottic

### Discussion:

The analysis of our retrospective study in 147 patients showed that supraglottic cancer had male predominance. Majorities are the squamous cell with moderately differentiated type and epiglottis was mainly involved (46.9%). Smoking was found to be a major risk factor in almost all the patients.

Rao et al. (1999) found that bidi and cigarette smoking to be associated with cancer of the larynx, however, the risk of laryngeal cancer was found to be much more for bidi than for cigarette. Chewing of tobacco in the form of Khaini, Zarda, Mawa, Paan, etc. is also prevalent in India. Many studies including a large multicentric case-control study of 511 laryngeal cancer cases have not found tobacco chewing as a risk factor for laryngeal ca.<sup>6</sup>

Kapil et al. (2005) studied 305 laryngeal cancer patients and found that chewing of betel leaf with tobacco increases the risk for laryngeal cancer by 2.37 fold but like other studies, it failed to find any association between cancer larynx and tobacco chewing. Similar results were found in our study, smoking was a major risk factor in almost all the patients but no correlation was found between smoking and chewing of betel leaf in patients.<sup>15</sup>

Hernandez BY et al. (2014) studied the influence of human papilloma virus on laryngeal cancer and they found its association, most frequently with subtypes 16 and 18. It has been detected in 21% of advanced laryngeal cancers, most commonly detected in women compared to men. Whereas, we had not studied such correlation through our retrospective data.<sup>16</sup>

Jones TM et al. (2016) studied that the presentation of laryngeal cancer is highly variable and depends on the location and size of the tumor. Tumors of the glottis, typically presents as hoarseness in early stages. Supraglottic tumors are more common with late symptoms of pain, hoarseness or difficulty swallowing,<sup>17</sup> while, in our study maximum patients presented with dysphagia rather than neck swelling or pain.

### CONCLUSIONS

Carcinoma larynx has a varying distribution in different regions of India. The chief complaints of difficulty in swallowing and the appearance of neck swelling in supraglottic CA make its diagnosis earlier, as seen in the above retrospective study conducted in northern part of India (Haryana). The female smokers in the families especially in the rural areas representing only the "tip of the iceberg" should be screened to find out all the hidden cases not reporting to hospitals due to social stigma among villagers and to accurately normalize the data and prevent the risk rises with increasing levels of smoking and alcohol drinking in India.

### REFERENCES:

1. Ferlay J, Soerjomataram I, Ervik M, Forman D, Bray F, Dikshit R, et al. GLOBOCAN 2012, Cancer Incidence and Mortality Worldwide in 2012. Lyon, France: International Agency for Research on Cancer; 2012.
2. ICMR. Individual registry-wise annexure. In: Three-year Report of Population- Based Cancer Registries 2009-2011. Bangalore: National Cancer Registry Program (ICMR); 2013.p. 92-150.
3. Hashibe M, Boffetta P, Zaridze D, Shagina O, Szeszenia-Dabrowska N, Mates D, et al. Contribution of tobacco and alcohol to the high rates of squamous cell carcinoma of the supraglottis and glottis in Central. Europe. Am J Epidemiology. 2007; 165(7):814-20.
4. ICMR. Sites of cancer associated with use of tobacco. In: Three-year Report of Population Based Cancer Registries 2009-2011. Bangalore: National Cancer Registry Program (ICMR); 2013. p. 23-6.
5. International Agency for Research on Cancer. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Tobacco Smoke and Involuntary Smoking. Vol. 83. Lyon, France: International Agency for Research on Cancer; 2004.
6. Rao DN, Desai PB, Ganesh B. Alcohol as an additional risk factor in laryngopharyngeal cancer in Mumbai. A case- control study. Cancer Detect Prev 1999; 23:37-44.
7. Baan R, Straif K, Grosse Y, Secretan B, El Ghissassi F, Bouvard V, et al. Carcinogenicity of alcoholic beverages. Lancet Oncol 2007;8:292-3.
8. Straif K, Baan R, Grosse Y, Secretan B, El Ghissassi F, Coglianov V, WHO International Agency for Research on Cancer Monograph Working Group. Carcinogenicity of household solid fuel combustion and of high-temperature frying. Lancet Oncol 2006; 7:977-8.
9. Office of the Registrar General of India Ministry of Home Affairs. Census of India. New Delhi, India; 2001.
10. Smith KR. National burden of disease in India from indoor air pollution. Proc Natl Acad Sci USA 2000; 97:13286-93.
11. Sapkota A, Gajalakshmi V, Jetly DH, Roychowdhury S, Dikshit RP, Brennan P, et al. Indoor air pollution from solid fuels and risk of hypopharyngeal/laryngeal and lung cancers: A multicentric case-control study from India. Int J Epidemiol 2008; 37:321-8.
12. Mastronikolis NS, Papadas TA, Goumas PD, Triantaphyllidou IE, Theocharis DA, Papageorgakopoulou N, Vynios DH. Head, neck, Laryngeal tumors: an overview Atlas Genet Cytogenet Oncol Haematol. 2009; 13(11):888-893.
13. Armstrong WB, Vokes DE, Maisel RH. Malignant tumors of the larynx. In: Flint PW,

- Haughey BH, Lund VJ, Niparko JK, Nager GT, Richardson MA, Robbins KT, Thomas JR, editors. Cummings otolaryngology-head & neck surgery. 5th ed. Philadelphia, PA: Mosby; 2010. P1482–511.
14. KIRSTEINA. Direct laryngoscopy. *Lancet* 1895; 1:1132.
  15. Kapil U, Singh P, Bahadur S, Dwivedi SN, Singh R, Shukla N. Assessment of risk factors in laryngeal cancer in India: A case-control study. *Asian Pac J Cancer Prev* 2005; 6:2027.
  16. Hernandez BY, Goodman MT, Lynch CF, Cozen W, Unger ER, Steinau M, et al. Human Papillomavirus Prevalence in Invasive Laryngeal Cancer in the United States. 2014; 9: e115931.
  17. Jones TM, De M, Foran B, Harrington K, Mortimore S. Laryngeal cancer: United Kingdom National Multidisciplinary guidelines. *J Laryngol Otol*. 2016; 130: S75-S82.