



CHARACTERISTICS AND SPREAD PATTERN OF LARYNGEAL CARCINOMA : A TERTIARY CARE STUDY

Otorhinolaryngology

Arya Brata Dubey* Institute Of Otorhinolaryngology And Head Neck Surgery, IPGME&R, SSKM Hospital.*Corresponding Author

Arunabha Sengupta Institute Of Otorhinolaryngology And Head Neck Surgery, IPGME&R, SSKM Hospital

Debarshi Jana IPGME&R And SSKM Hospital

ABSTRACT

INTRODUCTION: Laryngeal cancer is the eighteenth most common cancer in the UK. It has strong socioeconomic association, wide geographical variations. This study is highly relevant in India where factors like poor socio-economic conditions, oral consumption of tobacco in its various forms, alcohol, smoking habits in form of beedi and cigarette, lack of awareness about cancer, negligence towards the symptom of voice change and primary treatment from quacks, are highly prevalent. **MATERIALS AND METHODOLOGY:** This prospective cohort study was carried out at Tertiary care Hospital over a period of 1 year 4 months(April 2018 to July 2019). Patients attending at our OPD with symptoms of hoarseness, dysphagia, stridor and other symptoms of Laryngeal Carcinoma were subjected to detailed clinical examination including FOL to confirm the presence of any growth. All patients with growth or vocal cord irregularity or any suspicious lesions underwent biopsy. Socio-demographic, risk factors, characteristics of primary tumor- endoscopic, radiological and histopathological and spread pattern and node status analysed. **RESULTS:** Major bulk of patients belonged to 55-74 years (combined). The mean age of diagnosis is 66.06 years. Males were affected more than females (7.57:1). Majority of patients were farmers (57%) and majority 45(75%) belonged to rural areas. Most patients belonged to low socioeconomic class 30 (50%). Smoke tobacco and smoke tobacco plus alcohol were the major risk factors for laryngeal carcinoma. Majority of patients presented with dysphagia (75%), followed by foreign body sensation (72%), hoarseness (67%), Neck swelling (50%). Cartilage invasion was present among 25% of cases, Both pre-epiglottic and paraglottic space involvement was around 18% and exolaryngeal spread present in 8% of cases. Among them 100% cases delayed symptom recognition was present. 50% cases was attributed due to socio-demographic pattern, 33% due to psychosocial and behavioural (anxiety) and 13% due to delay in practitioner referral. Among Proliferative and Ulceroproliferative N+ is more than N0. Both moderately differentiated and poorly differentiated had more percentage of N+. In Supraglottic tumor Pre-epiglottic space, Paraglottic Space and cartilage invasion was present in equal proportions. In glottic tumor cartilage invasion and exolaryngeal spread was more common. **CONCLUSION:** Supraglottic tumor being common have tendency for lymphatic spread. It mainly presents with dysphagia and hoarseness later. Majority of patients were diagnosed in stage III and stage IV. This is not desirable and causes for delayed diagnosis must be addressed publicly. Early stage tumor have excellent prognosis with advent of radiotherapy and surgical morbidities can be avoided. The HPE reveals high grade of differentiation is associated with low node status. CT features serve as an excellent tool in identifying spread and node involvement and also management protocol.

KEYWORDS

INTRODUCTION

Laryngeal cancer is the eighteenth most common cancer in the UK. It has an incidence of 6.2 per 100 000 males and 1.3 per 100 000 females, resulting in approximately 1800 cases a year¹. Laryngeal cancer incidence also has a strong socioeconomic association, being twice as common in the more deprived groups compared to the more affluent groups. There is also a wide geographic variation, being highest in Scotland and the north of England, mirroring the socioeconomic profiles. According to SEER data, in US Estimated new cases in 2019 is 12,410. The laryngeal carcinoma among all cancer cases is 0.7%. The number of new cases of laryngeal carcinoma was 3 per 1,00,000 men and women per year. The number of deaths was 1 per 1,00,000 men and women per year. The above rates are age-adjusted and based on 2012-2016 data. The percentage Surviving 5 years 60.3% (2009-2015).

Tobacco smoking and alcohol are the main risk factors for laryngeal cancer, and their effects are synergistic². Smoking is the main risk factor for glottic cancers, whereas alcohol appears to be the bigger risk factor for supraglottic tumours. Within the larynx, tumours may arise from the vocal cords (glottic), superior to the vocal cords (supraglottic), or from below the vocal cords (subglottic). The most common site is glottis (approximately 49 percent) followed by supraglottis (16 per cent). Eighty-five per cent of tumours are squamous carcinomas. The successful management of laryngeal malignancy requires accurate diagnosis, staging, assessment of patient wishes, and selection of the most appropriate treatment for the individual patient with close posttreatment surveillance. In recent decades, major efforts have been made to develop therapeutic strategies to preserve the larynx anatomically and functionally using RT, conservation laryngeal surgery, and chemoradiotherapy (CRT).

This study is highly relevant in India where factors like poor socio-economic conditions, oral consumption of tobacco in its various

forms, alcohol, smoking habits in form of beedi and cigarette, lack of awareness about cancer, negligence towards the symptom of voice change and primary treatment from quacks, are highly prevalent.

The aims and objectives of this study are:

- (i) To determine socio-demographic profile of patients with laryngeal carcinoma
- (ii) To determine symptom and risk factors associated with laryngeal carcinoma.
- (iii) To determine endoscopic, radiological and histopathological parameters
- (iv) To determine stage of diagnosis and causes of delay
- (v) To determine metastatic pattern with respect to characteristics of primary tumour

MATERIALS AND METHODOLOGY

This prospective cohort study was carried out at Tertiary care Hospital over a period of 1 year 4 months(April 2018 to July 2019). Patients attending at our OPD with symptoms of hoarseness, dysphagia, stridor and other symptoms of Laryngeal Carcinoma were subjected to detailed clinical examination including FOL to confirm the presence of any growth. All patients with growth or vocal cord irregularity or any suspicious lesions were counselled for Biopsy.

After Pre-anaesthetic check-up patients underwent Direct Laryngoscopic Biopsy or Microlaryngoscopic Biopsy(MLS). All positive biopsy specimen and matching inclusion criteria were part of sample size.

INCLUSION CRITERIA:

1. Patients with histopathologically proven malignant tumor of larynx.
2. Patients without any systemic debility
3. All patients willing to take part in study through informed written consent

EXCLUSION CRITERIA:

1. Patients who are diagnosed with benign lesion of larynx.
2. Patients with co-existing symptomatic morbidity of ear, nose and throat.
3. Patients with debilitating symptomatic disease

Data would be summarized in form of Tables, Charts including pie chart, clustered chart, bar chart and funnel chart. Our study conform to the principles of the declaration of Helsinki. The proposal was approved by the institutional ethics committee. Written informed consent was obtained from all patients involved in study.

RESULTS

Majority of patients belonged to 65-74 age group (33%), 2% in 20-34 years, 5% in 35-44 years, 10% in 45-54 years, 27% in 55-64 years, 15% in 75-84 years and 8% in more than equal to 85 years. Major bulk of patients belonged to 55-74 years (combined).

The mean age of diagnosis is **66.06 years**. Males patients were 88% of sample size and females were 12%. Among males majority 34% belonged to 65-74 age group followed by 25% in 55-64 years, 15% in 75-84 years 9% in both more than 85 years and 45-54 years, 6% in 35-44 years and 2% in 20-34 years. Among females 43% belonged to 55-64 years, 29% in 65-74 years and 14% in both 75-84 years and 45-54 years. Majority of patients 45 (75%) belonged to rural areas and 15 (25%) patients belonged to urban areas. Most patients belonged to low socioeconomic class 30 (50%), middle class 16 (27%) and high class 14 (23%). Among patients 92% were smokers, 83% were alcoholic, 80% were both smokers and alcoholic, 27% were pan/ Betel nut users, 22% were addicted to tobacco chewing/Zarda/Khaini and in 1 case only we did not find any above risk factor. The spectrum of tobacco and alcohol risk factors is shown in Table 1. Among all types smoke tobacco and smoke tobacco & alcohol are greatest risk factors. Majority of patients presented with dysphagia (75%), followed by foreign body sensation (72%), hoarseness (67%), Neck swelling (50%), cough (40%), dyspnea (33%), otalgia (12%), Blood stained sputum (7%) and aspiration (3%). The duration of symptoms classification has been summarised in Table 2. Symptoms like Foreign body sensation, Cough, Neck swelling, Otagia, Blood stained sputum and aspiration were mainly present for < 1 month duration. Hoarseness was present in majority of patients for 1-3 months. Dysphagia was present in majority of patients for > 1 months.

Table 1 : Spectrum of Tobacco and alcohol addiction among patients

Type of Addiction	No of patients (59)	Percentage
Smoke tobacco	55	93%
Smokeless tobacco	19	32%
Smoke and smokeless	7	12%
Smoke tobacco and alcohol	38	64%
Smokeless tobacco and alcohol	2	3%
Smoke and smokeless tobacco with alcohol	10	17%

Table 2: Symptoms duration classification

SYMPTOMS	< 1 MONTH	1-3 MONTH	> 3 MONTH
HOARSENESS (40)	12	22	6
DYSPHAGIA (45)	8	17	20
FOREIGN BODY SENSATION (43)	25	8	10
COUGH (24)	14	8	2
DYSPNEA (20)	20	0	0
NECK SWELLING (30)	23	7	0
OTALGIA (7)	5	2	0
BLOOD STAINED SPUTUM (4)	3	1	0
ASPIRATION (2)	1	1	0

Among macroscopic features exophytic and proliferative nature of tumor was in majority. Exophytic group constituted 35%, proliferative group constituted 32%, Ulcero-proliferative constituted 20% and Ulcerative constituted 13%. Majority of patients presented with Stage III(45%), followed by Stage IV (25%), Stage I (15%) and Stage II (10%). Majority of patients were biopsied to have Moderately differentiated Squamous Cell Carcinoma (56%), followed by Well-differentiated Squamous Cell Carcinoma (32%) and Poorly differentiated Squamous Cell carcinoma (12%). Among HPE patterns Majority necrosis was found (77%), Lymphocytic infiltrate (68%),

Mitotic figures- Few (60%), Mitotic figures – Abundant (28%) and keratinisation (18%).

Cartilage invasion was present among 25% of cases, Both pre-epiglottic and paraglottic space involvement was around 18% and exolaryngeal spread present in 8% of cases. Delay in Diagnosis was considered for those patient who presented with hoarseness or dysphagia symptoms for more than 3 months. Total of 24 patients were considered under delayed diagnosis. Among them 100% cases delayed symptom recognition was present.

50% cases was attributed due to socio-demographic pattern, 33% due to psychosocial and behavioural (anxiety) and 13% due to delay in practitioner referral.

Table 3 : Primary characteristics of tumor and association with node status.

MACROSCOPIC FEATURES	N0	N+
EXOPHYTIC	11	10
PROLIFERATIVE	7	12
ULCERO-PROLIFERATIVE	3	9
ULCERATIVE	4	4
DIFFERENTIATION		
WELL DIFFERENTIATED	12 (63%)	7 (37%)
MODERATELY DIFFERENTIATED	13 (38%)	21 (62%)
POORLY DIFFERENTIATED	1 (14%)	6 (86%)

Among exophytic growth both N0 and N+ status are very similar. Among Ulcerative growth both N0 and N+ status are same. Among Proliferative and Ulceroproliferative N+ is more than N0. Both moderately differentiated and poorly differentiated had more percentage of N+. Well differentiated tumor had more of N0 than N+. (Table 3)

Table 4 : Site of tumor and CT spread features

CT FEATURES	SUPRAGLOTTIS	GLOTTIS	SUBGLOTTIS
PRE-EPIGLOTTIC SPACE	11 (27%)	0	0
PARAGLOTTIC SPACE	10 (24%)	1 (6%)	0
CARTILAGE INVASION	10 (24%)	6 (40%)	0
EXOLARYNGEAL SPREAD	0	4 (27%)	1 (25%)

The CT spread features and site of tumor is summarised in Table 4. In Supraglottic tumor Pre-epiglottic space, Paraglottic Space and cartilage invasion was present in equal proportions. In Glottic tumor Cartilage invasion and Exolaryngeal spread was more common

DISCUSSION

Carcinoma of larynx is most common in adults aged 55-75 years and it is rare in children⁷. The mean age of diagnosis was 66.06 years in our study. Results have been observed by Saedi et al (59.92 years) and Lam et al (62 years)^{4,5}.

Shirley stated that malignant laryngeal tumours tend to increase with age, average age of diagnosis being 66 years⁶ and Cocks et al stated that cancer of the larynx can occur at any age with mean presentation at 50-60 years for men and a decade younger for women⁷. In our study 88% were males and 12% females with a ratio of 7.6:1. Chauhan JPS et al⁸ found 60 (92.31%) males and 5 (7.69%) females, with a male to female ratio of 12:1. The male: female ratio in study by Kaur et al was 15.7:1 (47 males & 3 females)⁹. The male to female ratio was 7:3 (i.e. 2.3:1) in case of benign tumours and 29:1 in case of malignant tumours¹⁰. Sharma et al found Malignant tumours were highest (36.6%) amongst labourers, followed by farmers (13.3%) and businessmen (10%)¹⁰. Bakshi et al.¹¹ in their study found that 45% patients were farmers and 39% were labourers. Bakshi et al.¹¹ in their study found that 60% were from the low socioeconomic status, 25% belonged to the middle class and the remaining 15% belonged to the highclass. Bakshi et al.¹¹ found that 78% were rural and the remaining 22% were from urban regions. Chauhan et al⁸ showed incidence of smoking alone was found in 80% cases, 12.30% were addicted to both smoking and chewing tobacco. In this study 17 cases were alcoholic. In alcoholics the risk of hypopharynx cancer was significantly higher than the risk of larynx cancer. These observations are in accordance

with the prior studies. Almadori et al, shows 95% or more have a history of smoking¹². Bakshi et al¹¹ found that smoking was a predisposing factor in 87.8% of the cases and additionally or otherwise alcohol consumption was in 75% of the cases. Maier et al¹³ In a study of 164 cases found that smoking and drinking alcohol increase the dose-dependent risk of laryngeal cancer. Chauhan et al⁸ found difficulty in swallowing was the commonest symptom in 41 (63%) cases and hoarseness was the second commonest presentation (50.76%)⁸. Bakshi et al.¹¹ in their study found that hoarseness was the most common complaint. The most common presenting symptoms in a study¹⁴ were hoarseness (76.66%) and foreign body or pricking sensation of the throat (73.33%). In study by Chauhan et al⁸ 27.69% had glottis, 69.23% had supraglottic and 3.07% had subglottic cancer involvement. Bakshi et al.¹¹ in a study of 690 cases of laryngeal malignancy found that 56% of tumours were supraglottic, 17% glottic, 3.6% subglottic and 13% transglottic tumours. The malignant tumours of the larynx occur more commonly in the supraglottis which is consistent with the studies of Bakshi et al and Datti et al^{11,15}. Chauhan et al⁸ study cervical node metastasis was present in 37 (56.92%) cases at time of presentation. In our case cervical lymph node present in 58% of cases. In the same study patients were mainly of stage of IV (44.62%) and stage III (30.77%) accounting for 71% of all cases. 9 (13.84%) patients belonged to stage II and 7 (10.77%) patients stage I. *Dos Santos CR et al*¹⁶ found that lymph node metastasis was seen in 80 patients with advanced squamous cell carcinoma of larynx, out of which, metastases were concentrated within level II in 59% of cases, level III in 17% of cases, level IV in 11% of cases, and level V in 6% of cases. Most patients presented with T3 stage present in 48 (43.63%) patients. *Markou K et al*¹⁷ observed T3 stage (32%) as the most common presentation in cancer larynx patients. N1 staging was most common presentation in patients with cervical lymphadenopathy present in 26 (23.63%) patients.

Chauhan et al⁸ in this series revealed that (98.46%) patients had squamous cell carcinoma and only 1 (1.54%) case had adeno carcinoma. Wang et al concluded that SCC accounts for 99% of all primary laryngeal carcinomas¹⁸. Wiligen et al stated that 95% of laryngeal carcinomas were typically squamous cell carcinoma and adenocarcinoma was rarely seen¹⁹. Amongst squamous cell carcinoma the highest number of cases in this series were of moderately differentiated carcinoma (56%) which corresponds to findings of Lam et al and Shetty et al^{5,20}. Kaufman and Burke²¹ stated that SCC of the larynx accounts for over 90% of laryngeal cancers. Kumar et al.²² stated that 95% of all laryngeal carcinomas are typical SCC. Jaiswal and Hoang²³ stated that out of all primary laryngeal carcinomas, 99% are SCC.

Bakshi et al.¹¹ found that 69% were non-keratinizing SCC and 27% were keratinizing SCC.

Kaufman and Burke²¹ stated that SCC of the larynx accounts for over 90% of laryngeal cancers. Kumar et al.²² stated that 95% of all laryngeal carcinomas are typical SCC. Jaiswal and Hoang²³ stated that out of all primary laryngeal carcinomas, 99% are SCC.

Bakshi et al.¹¹ found that 69% were non-keratinizing SCC and 27% were keratinizing SCC.

CONCLUSION

Laryngeal cancer being common around 5th to 6th decade a higher element of suspicion should be present among these age group and relatives. Even though incidence among males is still high , there is a uprising trend among females due to increasing trend of smoking and alcohol. Higher incidence among low socioeconomic class and rural areas points towards lack of awareness or lack of motivation. The tendency to ignore symptoms is very common among rural areas and Low class. The contribution of smoke tobacco and alcohol combined is very important risk factor. Even though there has been major awareness against these , society has not fully understood or accepted the consequences. An innovative measure is required to deal with this dilemma. Difficulty swallowing or voice change should alert physician and appropriate referral to ENT should be done. Campaign regarding symptoms recognition should be undertaken at rural health centre. Supraglottic tumor being common have tendency for lymphatic spread. It mainly presents with dysphagia and hoarseness later. Majority of patients were diagnosed in stage III and stage IV. This is

not desirable and causes for delayed diagnosis must be addressed publicly. Early stage tumor have excellent prognosis with advent of radiotherapy and surgical morbidities can be avoided. The HPE reveals high grade of differentiation is associated with low node status. CT features serve as an excellent tool in identifying spread and node involvement and also management protocol.

REFERENCES

1. Cancer Research UK website, 2009. <http://info.cancerresearchuk.org/cancerstats/types/larynx/> accessed October 5, 2009
2. Tuyns AJ, Audigier JC. Double wave cohort increase for oesophageal and laryngeal cancer in France in relation to reduced alcohol consumption during the second world war. *Digestion* 1976; 14: 197-208.
3. Parsad KC, Abraham P, Peter R. Malignancy of the larynx in a child. *ENT Ear Nose Throat J*. 2001;80(8):508-11
4. Saedi B, Razmpa E, Sadeghi M, Mojtahed M, Mojtahed A. The epidemiology of laryngeal cancer in a country on the esophageal cancer belt. *Indian J Otolaryngol Head Neck Surg*. 2009;61(3):213-7.
5. Lam KY, Yuen AP. Cancer of the larynx in Hong Kong: a clinico-pathological study. *Eur J Surg Oncol*. 1996;22(2):166-70.
6. Shirley D (1997) Cartilaginous lesions of the larynx. Grand rounds archives BCM. Bobby R Alford Department of Otolaryngology: Head and Neck Surgery
7. Cocks H, Quraishi M, Morgan D, Bradley P (1999) Leiomyosarcoma of the larynx. *Otolaryngol Head Neck Surg* 121:643-646
8. Jitendra Pratap Singh Chauhan, Bhartendu Bharti, Sunil Singh Bhadouriya, Abhay Kumar, Prem Narain, Jaypal Singh. Laryngeal cancer: a clinicopathological study of 65 cases. *Int J Otorhinolaryngol Head Neck Surg*. 2018 Jan;4(1):163-168
9. Kaur K, Sonkhya N, Bapna A.S., Nodal metastasis from laryngeal carcinoma and their correlation with certain characteristics of Primary Tumor. *Indian Journal of Otorhinolaryngology and Head Neck Surgery*, Vol 54, N.o.- 4
10. Sharma DK., Sohal B.S., Bal M.S., Aggarwal S, Clinico-Pathological Study of 50 Cases of Tumours of Larynx, *Indian J Otolaryngol Head Neck Surg* (July 2013) 65(Suppl 1):S29-S35.
11. Bakshi J, Panda NK, Sharma S, Gupta AK, Mann SBS. Survival pattern in treated cases of carcinoma larynx in north India: a 10 year follow up study. *Ind J Otolaryngology Head Neck Surg*. 2004;56(2):99-103.
12. Almadori G, Bussu F, Gadoni G, Galli J, Paludetti G, Maurizi M. Molecular markers in laryngeal Squamous cell carcinoma: Towards an integrated clinicobiological approach. *Eur J Cancer*. 2005;41:683-93
13. Maier H, Gewelke U, Dietz A, Heller W (1992) Risk factors of cancer of the larynx: results of the Heidelberg case-control study. *Otolaryngol Head Neck Surg* 107(4):577-582
14. J Sathish Kumar♦, Nim Narboo Bhutia, Tenzing Jigme Bhutia, Pradip Malik, Madhumangol Singh, H Priyoshakhi Devi, Malignant Tumors of the Larynx: A Clinico-pathological Study of 30 Cases, *Middle East Journal of Cancer*; April 2015; 6(2): 71-78.
15. Datti PV, Patel CB, Sayed BA. The incidence of laryngeal cancer in Baroda. *Indian J Otolaryngology*. 1971;23:152-62.
16. Dos Santos CR, Goncalves Filho J, Margrin J, Johnson LF, Fertilo A, Kowalski LP. Involvement of level I neck lymph nodes in advanced squamous carcinoma of the larynx. *Ann Otol Rhinol Laryngol*. 2001 Oct; 110(10): 982-4.
17. Markou K, Christoforidou A, Karasmanis I, Tsiropoulos, Triaridis S, Constantinidis I. Laryngeal cancer: epidemiological data from Northern Greece and review of the literature. *Hippokratia*. 2013 Oct-Dec; 17(4): 313-318.
18. Wang M, Liu C, Li W, Chang S, Chu P. Salivary gland carcinoma of the larynx. *J Chin Med Assoc*. 2006;69(7):322-5.
19. Wiligen M, Kumar V. Head and neck. In: Kumar V, Abbas AK, Fausta N, editors. *Robbins and Cotran pathologic basis of diseases*. 7th ed. Philadelphia, USA: Lippincott; 2005: 786-788
20. Shetty R, Kali A. Prognostic significance of serum L-fucose level in head and neck malignancy. *Int J Pharma Bio Sci*. 2014;5(1):210-6.
21. Kaufman JA, Burke AJ (1997) The etiology and pathogenesis of laryngeal carcinoma. In: *The otolaryngologic clinics of North America, Current Concepts in Laryngeal Cancer* 130(1):1-13
22. Kumar V, Abbas AK, Fausto N (2004) *Robbins and Cotran's pathologic basis of disease*, 7th edn. Saunders, India, pp 786-787
23. Jaiswal VR, Hoang MP (2004) Primary combined squamous and small cell carcinoma of the larynx. *Arch Pathol Lab Med* 128: 1279-1281