

**A STUDY OF CLINICO-PATHOLOGICAL PARAMETERS IN PATIENTS OF CARCINOMA LARYNX**Kartikeya Purohit<sup>1</sup>, Sampan Singh Bist<sup>2</sup>, Vinish Agarwal<sup>3</sup>, Smita Chandra<sup>4</sup><sup>1</sup>Junior Resident, Department of Otorhinolaryngology & Head-Neck Surgery, Himalayan Institute of Medical Sciences, Jollygrant, Dehradun.<sup>2</sup>Professor & HOD, Department of Otorhinolaryngology & Head-Neck Surgery, Himalayan Institute of Medical Sciences, Jollygrant, Dehradun.<sup>3</sup>Assistant Professor, Department of Otorhinolaryngology & Head-Neck Surgery, Himalayan Institute of Medical Sciences, Jollygrant, Dehradun.<sup>4</sup>Associate Professor, Department of Pathology, Himalayan Institute of Medical Sciences, Jollygrant, Dehradun.**ABSTRACT****BACKGROUND**

Incidence of carcinoma larynx in India reported to be 1.3 to 8.8 per 100,000 populations in six different regions of the country. The main risk factors for development of carcinoma larynx are consumption of smoke tobacco and alcohol. The aim of this study was to evaluate clinico-pathological parameters in patients with carcinoma larynx.

**MATERIAL AND METHOD**

A total of 110 patients newly diagnosed with carcinoma larynx were included in this study after taking informed consent from the patient and clearance from the ethics committee. Previously treated larynx cancer patients with recurrence were excluded.

**RESULT**

Pain on swallowing was the commonest presenting symptom present in 101 (91.81%) patients. Smoke tobacco consumption was present in 104 (94.54%) patients, smokeless tobacco consumption was present in 12 (10.90%) patients and alcohol consumption was present in 94 (85.45%) patients with cancer larynx. Most of the patients had inadequate dietary intake as per recommended dietary allowance.

**CONCLUSIONS**

The most common site involved was supraglottis seen in 70 (63.63%) patients. Most of the patients presented with stage III cancer in 43 (39.09%) patients. Squamous cell carcinoma was the histopathological variant seen in all patients in our study. Moderately differentiated squamous cell carcinoma was the most common squamous cell carcinoma variant seen present in 62 (56.36%) patients.

**KEYWORDS**

Larynx, Cancer, Clinico-Pathological.

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**INTRODUCTION**

Carcinoma larynx is quite common in India. Smoking is the most important risk factor for laryngeal cancers. Death from laryngeal cancer is 20 times more likely for heaviest smokers than for non-smokers.<sup>[1]</sup> Smokers of non-filter tip cigarettes have a higher cancer risk than those smoking filter tip cigarettes. With respect to carcinogenesis, alcohol and nicotine consumed together develop a synergistic action and have a multiplicative effect on the cancer risk.<sup>[2]</sup> Tobacco smoke contains multiple classes of established carcinogens including benzopyrenes, polycyclic aromatic hydrocarbons, and tobacco-specific nitrosamines.<sup>[3]</sup> Indians are affected more than westerns. Its current incidence in U.S. is 5 in 100,000 populations.<sup>[4]</sup>

Its current incidence in U.S. is 5 in 100,000 populations.<sup>[4]</sup> Incidence of carcinoma larynx in India reported to be 1.3 to 8.8 per 100,000 populations in six different regions of the country.<sup>[5]</sup> Incidence in females is also increasing as more females are taking to smoking. Patients are mostly in the age group of 40 to 70 years, but younger people may also be affected. Most of carcinoma larynx is squamous cell carcinomas. Most malignancies originate in glottis followed by supraglottis and subglottis. Chronic hoarseness is the most common early symptom.<sup>[6]</sup> Other symptoms of laryngeal cancer include pain in neck, dysphagia, dyspnoea, a lump in the neck and stridor.<sup>[6]</sup>

**MATERIALS AND METHODS**

The present study was carried out in the Department of Otorhinolaryngology, at Himalayan Institute of Medical Sciences, Swami Ram Nagar, Dehradun, over a period of 12 months. A total of 110 patients newly diagnosed with carcinoma larynx were included in this study after taking informed consent from the patient and clearance from the ethics committee. Previously treated larynx cancer patients with recurrence were excluded. The patients selected for this study were subjected to a detailed history and complete Otorhinolaryngology and head and neck clinical examination after detailed informed consent.

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Detailed personal history included consumption of smoke tobacco, smokeless tobacco and alcohol intake. As per patient's history, smokeless tobacco consumption was calculated as packets per day and smoke tobacco consumption was calculated in pack years (Number of bidis/cigarettes smoked per day divided by the number of years the person has smoked). Alcohol consumption was calculated in grams per day (Alcohol by volume (%) X volume consumed per day (mL) divided by 1000 and then multiplied by 10). Energy was calculated in Kcal/day, fat in grams/day and proteins in grams/day based on patient's regular diet. General examination and vitals of all patients were recorded.

Systemic examination was done to detect distant metastasis. The oral cavity was examined in detail with help of a tongue depressor using head mirror and bull's eye lamp. Suspected area was evaluated by digital palpation. Detailed examination of larynx and pharynx (Oropharynx/hypopharynx) were done by indirect laryngoscopy mirror (No. 3-7) and by diagnostic laryngeal endoscopy using Karl Storz 70° rigid wide angle laryngeal endoscope (7 mm) to look for second primary and findings were recorded using Imimo software and printed records were obtained. Nasopharynx was examined by posterior rhinoscopy and findings were confirmed by Karl Storz 0° Hopkins rod rigid nasal endoscope (4 mm).

Detailed examination of neck was done including laryngeal framework, laryngeal tenderness, laryngeal crepitus and lymph nodes from level I to level VI. Clinical staging of the tumour was done as per American Joint Committee on Cancer (AJCC) (2012) classification (21). Fine Needle Aspiration Cytology (FNAC) was done by standard technique either using aspiration (Thompson 1982) or without aspiration (Zadela 1987) under all aseptic precautions with a 22-gauge needle for neck swelling. All patients underwent biopsy for histopathological examination under General Anaesthesia (GA) or Local Anaesthesia (LA). Histopathological examination which included type of malignancy, level of differentiation, necrosis, lymphocytic infiltration, mitotic figures and keratinization. Records were maintained.

**OBSERVATION AND RESULTS**

In present study, the age distribution of patients ranged from 24 to 92 years of age with mean age of 51.92±13.06 years. There were 110 patients with cancer larynx in our study, out of which 96 (87.27%) patients were males and 14 (12.72%) patients were females.

Symptoms	Duration	No. of Patients	
Pain on swallowing	0-3 months	68	101
	3-6 months	33	
Change in voice	0-3 months	38	57
	3-6 months	19	
Difficulty in swallowing	0-3 months	45	95
	3-6 months	50	
Swelling in the neck	0-3 months	32	49
	3-6 months	17	
Difficulty in breathing	0-3 months	34	34
Earache	0-3 months	35	57
Per oral bleed	0-3 months	22	

**Table 1: Presenting Symptoms and Duration in Cancer Larynx Patients (n=110)**

Pain on swallowing was the commonest complaint present in 101 (91.81%) patients followed by difficulty in swallowing complaint present in 95 (86.91%) patients. There were 68 (61.81%) patients with pain on swallowing as commonest complaint presented within 3 months of onset of symptoms. (Table 1). Ulceroproliferative growth pattern was seen in 97 (88.18%) patients. There was laryngeal widening present in 16 (14.54%) patients, laryngeal tenderness present in 7 (6.36%) patients and absent laryngeal crepitus in 2 (1.81%) patients.

Type of Addiction	No. of Patients (110)	Percentage
Smoke tobacco	104	94.54%
Smokeless tobacco	12	10.90%
Smoke and smokeless	12	10.90%
Smoke tobacco and alcohol	78	70.9%
Smokeless tobacco and alcohol	6	5.45%
Smoke and smokeless tobacco with alcohol	10	9.09%

**Table 2: Addiction in Cancer Patients (n=110)**

Smoke tobacco consumption was present in 104 (94.54%) patients, smokeless tobacco consumption was present in 12 (10.90%) patients and alcohol consumption was present in 94 (85.45%) patients with cancer larynx. (Table 2). There were 43 (44.79%) male patients and 7 (50%) female patients with less than 100 grams per day protein intake was the commonest, 41 (42.70%) male patients and 9 (64.28%) female patients with 41 to 50 grams per day fat intake was the commonest and 40 (41.66%) male patients with 2001 to 3000 kcal/day energy intake and 5 (35.71%) female patients with less than 2000 kcal/day energy intake was the commonest.

Subsite	No. of Patients	(Percentage)
<b>Supraglottis</b>		
Epiglottis	28	25.45%
Aryepiglottic folds	63	57.27%
Arytenoid area	21	19.09%
False vocal cords	55	50%
<b>Transglottis</b>		
	10	9.09%
<b>Glottis</b>		
True vocal folds	23	20.90%
<b>Subglottis</b>		
Subglottic area	4	3.63%

**Table 3: Subsite Distribution of Patients**

The most common site involved was supraglottis in 70 (63.63%) patients followed by glottis in 23 (20.90%) patients then transglottis in 10 (9.09%) patients and lastly subglottis in 7 (6.36%) patients. Cancer larynx patients in our study had involvement of more than one subsite. (Table 3).

Tumour Staging	No. of Patients N=101	Percentage
T1	5	4%
T2	46	42%
T3	48	44%
T4a	11	10%
T4b	0	0

**Table 4: Tumour Staging of Cancer Patients (n=110)**

Node Stage	No. of Patients	Percentage
N0	64	58.18%
N1	26	23.63%
N2a	12	10.90%
N2b	4	3.63%
N2c	2	1.81%
N3	2	1.81%

**Table 5: Nodal Staging in Cancer Larynx Patients (n=110)**

Cervical lymphadenopathy was present in 56 (41.82%) patients and level II cervical lymphadenopathy was the commonest in 42 (63.63%) patients. In cancer larynx patients, most patients presented with T3 stage present in 48 (44%) patients. N1 staging was present in 26 (23.63%) patients; 1 (0.90%) patient had lung metastasis and 1 (0.90%) patient had skeletal metastasis. Most of the patients presented with stage III cancer in 43 (39.09%) patients. (Table 4 and 5).

Level of Differentiation	Cancer Larynx (n=110)
Well differentiated	14 (12.72%)
Moderately differentiated	62 (56.36%)
Poorly differentiated	33 (30.00%)
Basaloid	1 (0.90%)

**Table 6: Level of Differentiation in Squamous Cell Carcinoma Larynx**

Other Parameters	Cancer Larynx (n=110)
Necrosis	80
Mitotic figures-Abundant	36
Mitotic figures-Few	69
Lymphocytic infiltration	75
Keratinisation	47

**Table 7: Other Histopathological Parameters in Cancer Larynx Patients**

Squamous cell carcinoma was the histopathological variant seen in all patients in our study. Moderately differentiated squamous cell carcinoma was the most common squamous cell carcinoma variant seen present in 62 (56.36%) patients, poorly differentiated in 33 (30.00%) patients, well differentiated in 14 (12.72%) patients and basaloid variant seen in 1 (0.90%) patient. Necrosis was the most common histopathological parameter seen in 80 (72.72%) patients. (Table 6 and 7).

## DISCUSSION

The age distribution of patients ranged from 24 to 92 years of age with mean age of  $51.92 \pm 13.06$  years. There were 110 patients with cancer larynx in our study, out of which 96 (87.27%) patients were males and 14 (12.72%) patients were females. It was observed in our study that cancer larynx was more common in males than females with male-to-female ratio was 6.8:1.

Pain on swallowing was the commonest complaint present in 101 (91.81%) patients followed by difficulty in swallowing complaint present in 93 (86.91%) patients. It was found that most of the cancer larynx patients presented to hospital within 3 months of onset of symptoms. There were 68 (61.81%) patients with pain on swallowing as commonest complaint presented within 3 months of onset of symptoms. Yerma A et al.<sup>[7]</sup> found hoarseness of voice (73.92%) as commonest complaint followed by dysphagia (50.95%) and pain in throat (25.59%) in patients with cancer larynx.

It was observed that most patients presented to hospital within 3 months of onset of symptoms or at the most between 3 to 6 months' duration. It was because symptoms of cancer larynx are noticed early by the patients as these symptoms hinder in day-to-day activity of patients, which leads them for early consultation at the hospital.

Smoke tobacco consumption was present in 104 (94.54%) patients, smokeless tobacco consumption was present in 12 (10.90%) patients and alcohol consumption was present in 94 (85.45%) patients with cancer larynx. Prevalence of smokeless tobacco in Middle East in relation to age reflects major changes over the decades in the use of smokeless tobacco.<sup>[8]</sup> In 1970, 2.2% of white male adults aged 18 to 24 years used chewing tobacco or snuff. The prevalence was higher at successively older ages, peaking at 11.8% among men 65 years or older. In 1991, the age trends were reversed with 10.4% of 18-24 year olds using the products and fewer older persons using them: 7.9% of 25-34 year olds, 5.4% of 35-44 year olds, 3.8% of 45-64 year olds and 5.5% of individuals 65 years of age and older.<sup>[9]</sup> A study was conducted by Saedi B et al.<sup>[10]</sup> in which 88.5% patients were tobacco smokers with most of the patients (72.4%) were in the 5th and 6th decades of their life.

In a study by Markou K et al.<sup>[11]</sup> out of 1,088 patients with laryngeal cancer, 86.8% were smokers, 5.6% non-smokers and 7.6% ex-smokers and 70% of patients were at the 6<sup>th</sup> and 7<sup>th</sup> decade of life. Tobacco is an agricultural product processed from the fresh leaves of plants in the genus Nicotiana. The smoke from tobacco elicits carcinogenic effects on the tissues of the body that are exposed to the smoke and consists of 43 carcinogens including polycyclic hydrocarbons and nitrosamines. In a study by Choi SY et al.<sup>[12]</sup> heavy drinkers (Males who consumed 90 grams daily of ethanol) had an approximately 11-fold risk of laryngeal cancer compared with non-drinkers.

There were 43 (44.79%) male patients and 7 (50%) female patients with less than 100 grams per day protein intake was the commonest, 41 (42.70%) male patients and 9 (64.28%) female patients with 41 to 50 grams per day fat intake was the commonest and 40 (41.66%) male patients with 2001 to 3000 kcal/day energy intake and 5 (35.71%) female patients with less than 2000 kcal/day energy intake was the commonest. In a study by Farhangfar A et al.<sup>[13]</sup> loss of appetite, difficulty chewing, dry mouth, thick saliva and pain were individual symptoms that significantly associated with reduced dietary intake in a cohort of head and neck cancer patients.

The most common site involved was supraglottis in 70 (63.63%) patients followed by glottis in 23 (20.90%) patients than transglottis in 10 (9.09%) patients and lastly subglottis in 7 (6.36%) patients. Trigg et al.<sup>[14]</sup> observed that the commonest subsite involved was supraglottis (53%) followed by glottis (39%), transglottis (7%) and subglottis (1%).

Ulceroproliferative growth pattern was seen in 97 (88.18%) patients. Rousseau A et al.<sup>[15]</sup> observed that cancer larynx usually presents as ulceroproliferative lesion. Ulceroproliferative pattern was seen commonly in cancer larynx, which could be due to friction of mucosal surfaces while eating and swallowing.

There was laryngeal widening present in 16 (14.54%) patients, laryngeal tenderness present in 7 (6.36%) patients and absent laryngeal crepitus in 2 (1.81%) patients.

In a study by Chen SA et al<sup>[16]</sup>, 63 cases of laryngeal cancer with extralaryngeal spread were identified, out of which anterior spread by thyroid cartilage penetration occurred in 44% cases, followed by thyroid widening seen in 33% cases.

Cervical lymphadenopathy was present in 56 (41.82%) patients and level II cervical lymphadenopathy was the commonest in 42 (63.63%) patients. Dos Santos CR et al<sup>[17]</sup> 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<sup>[11]</sup> 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. In a study by Markou K et al<sup>[11]</sup> on laryngeal cancer, N1 stage was commonest presentation present in 26 (23.63%) patients; 1 (0.90%) patient had lung metastasis and 1 (0.90%) patient had skeletal metastasis.

Papac RJ<sup>[18]</sup> observed that 75% of patients with distant metastases had pulmonary deposits. Patients with distant metastasis usually present in late stage of disease as most of them belonged to rural area with poor medical facility, transportation and belief in religious ritual and traditional medicines. Most of the patients presented with stage III cancer in 43 (39.09%) patients. Similar findings were seen in a study by Markou K et al.<sup>[11]</sup> It was observed in our study that patients usually presented with late stage disease which was because of self-neglect, failure to seek medical care early in the course of disease and few of them were taking different forms of Indian medicine for long duration. Squamous cell carcinoma was the histopathological variant seen in all patients in our study.

Moderately differentiated squamous cell carcinoma was the most common squamous cell carcinoma variant seen present in 62 (56.36%) patients, poorly differentiated in 33 (30%) patients, well differentiated in 14 (12.72%) patients and basaloid variant seen in 1 (0.90%) patient. In a study by Thakur S et al<sup>[19]</sup>, squamous cell carcinoma was the commonest histological type seen in 98.6% cases with laryngeal cancer. Busquets JM et al<sup>[20]</sup> conducted a study on head and neck squamous cell carcinoma and concluded that most of the patients (55.5%) had moderately-differentiated squamous cell carcinoma. Necrosis was the most common histopathological parameter seen in 80 (72.72%) patients. Necrosis in histopathological reporting is associated with high T classification and high N classification and thus poor prognosis of disease.<sup>[21]</sup>

## CONCLUSION

- Majority of patients of carcinoma larynx had presenting symptom of pain on swallowing.
- Chronic tobacco and alcohol consumption was the most common aetiological factor in our study.
- Majority of patients had inadequate dietary intake as per recommended dietary allowance.
- Supraglottis was the most common subsite involved.
- The most common clinical presentation was ulceroproliferative growth pattern.

- More than half of the patients presented with cervical lymphadenopathy.
- Most of the patients were diagnosed at stage III of cancer.
- Squamous cell carcinoma was the most common histopathological type seen and moderately differentiated squamous cell carcinoma was the most common differentiation variant observed.

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