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"Malignant tumors of the larynx: Risk factors, presentation and clinicopathological analysis of 55 cases "

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ABSTRACT
Introduction: Head and Neck cancer is a major concern among health professionals in developing countries like India. Larynx is the most common site for head and neck malignancy in adults. Tobacco smoking and alcohol are the major risk factors for laryngeal cancer.
Objective: To study the demographic pattern, etiological risk factors, clinical presentation, socioeconomic and occupational differences. To evaluate site of origin and histopathological patterns of laryngeal carcinoma in patients attending the Guntur GGH ENT OPD.
Materials and methods:This is an observational study which was conducted among 55 subjects with laryngeal carcinoma in the Department of Otorhinolaryngology of Government medical college- Guntur.
Results: The most common age group at which maximum number of patients presented to the hospital was 61 – 70years. Majority of the cases were males. The disease was higher among the lower socioeconomic group and smoking was found to be the most common risk factor. The most common chief complaint was hoarseness. Carcinoma of the glottis was more common in this study.
Conclusion: The symptoms of laryngeal cancer can range from mild change of voice to life threatening airway obstruction. Efforts to diagnose laryngeal cancer should be done as quickly as possible. With early diagnosis, effective treatment can be provided which reduces the mortality and morbidity of the diseaseandcan improve and extends the life of laryngeal cancer patients. Prognosis is poor in advanced stages of the disease

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I. Introduction:

Head and Neck cancer is a major concern among health professionals in developing countries [1] like India. Larynx is the most common site for head and neck malignancy in adults [2]. The incidence of laryngeal cancer was 184,615 persons in 2020 worldwide which accounted for 1.1% of all malignant tumours and its one of the major causes of morbidity and mortality in our country. Laryngeal carcinoma has been seen predominately in males but due to changing trend and advanced society where smoking is increasing in females, carcinoma larynx found to be slowly rising among females.

Though various etiological factors have been proposed for incidence of laryngeal carcinomas, the exact cause for cancer larynx is still idiopathic. Various environmental, chemical toxins, Gastro esophageal reflux disease (GERD), malnutrition, HPV (Human papilloma virus) infection especially subtype16 more than subtype18(4) was found to be one of the causative factors for laryngeal malignancy.

Since there are no pathognomic clinical presentations for carcinoma larynx, diagnosis becomes difficult based on clinical symptoms.The larynx is divided into three regions depending upon the anatomical sites: supraglottic region, Glottic region and Subglottic region of larynx [2,3]. Supraglottic laryngeal tumours usually present in later stages so prognosis is not favourable whereas Glottic carcinoma has relatively positive prognosis due to early presentation of symptoms, Subglottic laryngeal carcinoma presentation is not very common and has poor prognosis (2).

Diagnosis is based on direct or indirect visualization of involved site of larynx, supplemented by CT scan and are confirmed by microscopic examination, biopsy and histopathological findings. Direct laryngoscopy and histopathological examination remain the gold standard in diagnosing both benign and malignant lesions of larynx [4,5]. The biopsy material is important for Identification of the type of tumour and the degree of differentiation [6]. All available methods of study should be utilized to make the diagnosis as early as possible [7]. Prevention and early diagnosis of laryngeal carcinoma is the most effective means for increasing cure rates and preserving function.[8]

AIMS AND OBJECTIVES:

 To study the demographic pattern, etiological risk factors and possible mode of spread, socioeconomic and occupational differences.

 To study clinical presentation, site of origin and histopathological patterns of laryngeal carcinoma in patients attending the Guntur GGH ENT OPD.

II. Materials And Methods:

This is an observational study which was conducted among 55 subjects diagnosed with laryngeal carcinoma. This study was conducted in Department of Otorhinolaryngology of Government medical college-Guntur.

INCLUSION CRITERIA:

 Proven cases of laryngeal carcinoma by biopsy or histopathological examination

 Patients who have not undergone any treatment

EXCLUSION CRITERIA:

 Recurrent cases of laryngeal carcinoma

 Benign tumours of larynx

 Patients with associated malignancies in other sites

METHOD OF STUDY:

The present study was undertaken on 55 patients clinically diagnosed as malignant tumours of the larynx. The study was conducted in the department of Ear, Nose and Throat (ENT) of the Government Medical College and General Hospital, Guntur. A proper informed consent was taken from the patients participating in this study after explaining the procedures and method of our study. A complete history regarding age, gender, occupation, family history, socioeconomic background, presenting complaints and site of growth, of each patient was obtained and they were thoroughly examined and investigated. Addiction to smoking, alcohol consumption and tobacco chewing were enquired. Thorough head and neck examination was done. Careful inspection and palpation of neck was done and attention was given to check for the presence of any enlarged lymph nodes. Routine examination of the ear, nose, nasopharynx, oral cavity, and oropharynx was done. Indirect laryngoscope examination was done in the OPD for all clinically suspected malignant lesions. Routine soft tissue x-ray of neck and chest X-ray was routinely done in all cases. Contrast enhanced CT scan of neck was done in all cases. After the clinical diagnosis, these patients were made to undergo direct laryngoscopy under local or general anaesthesia. The findings of indirect laryngoscopy were confirmed, the details regarding extent and type of growth were noted. Biopsy was taken from the growth in the larynx and sent to the department of pathology for histopathological examination. In patients presenting with cervical nodal involvement, FNAC was done. According to AJCC-TNM classification, staging of laryngeal cancer was finally decided.

III. OBSERVATION AND RESULTS

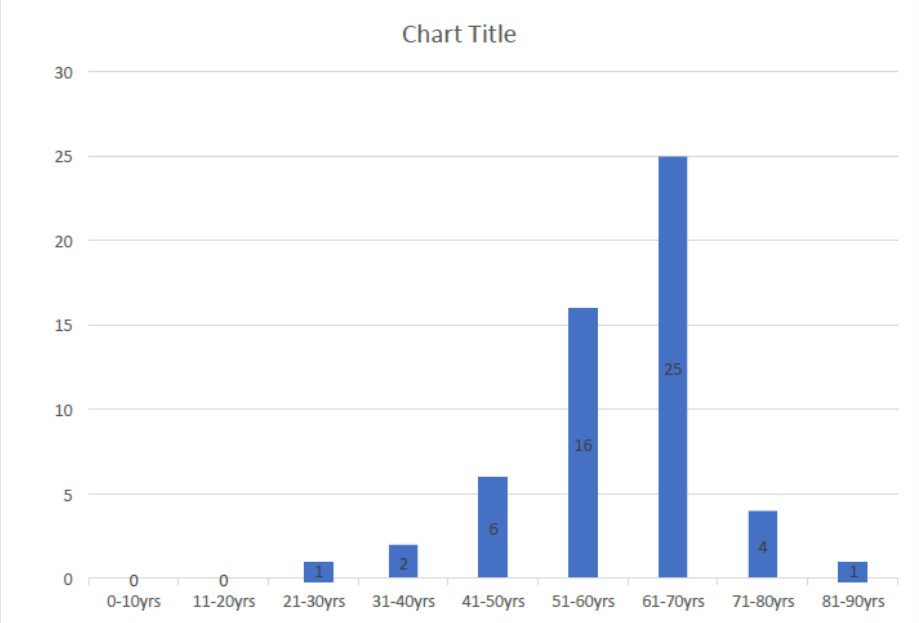
AGE AT PRESENTATION:

Table 1: Distribution of study population according to the age group

AGE	NUMBER OF PATIENTS	PERCENTAGE(%)
0 -10 years	0	0
11-20 years	0	0
21-30 years	1	1.8
31-40 years	2	3.6
41-50 years	6	10.9

51-60 years	16	29.09
61-70 years	25	45.4
71-80 years	4	7.2
81-90 years	1	1.8
TOTAL	55	100%

Graph1: Distribution of age at presentation among study population



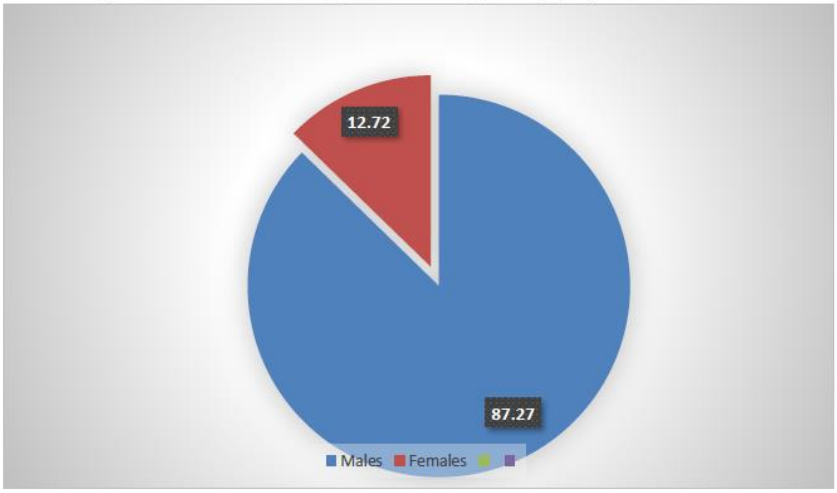
GENDER DISTRIBUTION:

Table 2: Distribution of study population based on gender

GENDER	NUMBER OF PATIENTS	PERCENTAGE(%)
MALE	48	87.27
FEMALE	7	12.72
TOTAL	55	100

The Male to Female ratio was 6.85:1. This indicates that the laryngeal carcinoma is more prevalent in male patients compared to females in our study.

Graph 2: Distribution of gender among study population



OCCUPATION:

Table 3: Distribution of occupation among study population

Occupation	Number	Percentage (%)
Labourer	21	38.2
Farmer	16	29.1
Industry worker	4	7.3
Carpenter / plumber	2	3.6
Mechanic	2	3.6
Lorry/auto drivers	3	5.4
Vendor	3	5.4
Housewives	4	7.3

The above table reveals that risk was highest in men who worked as unskilled or semi-skilled workers [39]. Nearly half of the female patients were homemakers.

SOCIO-ECONOMIC GROUP:

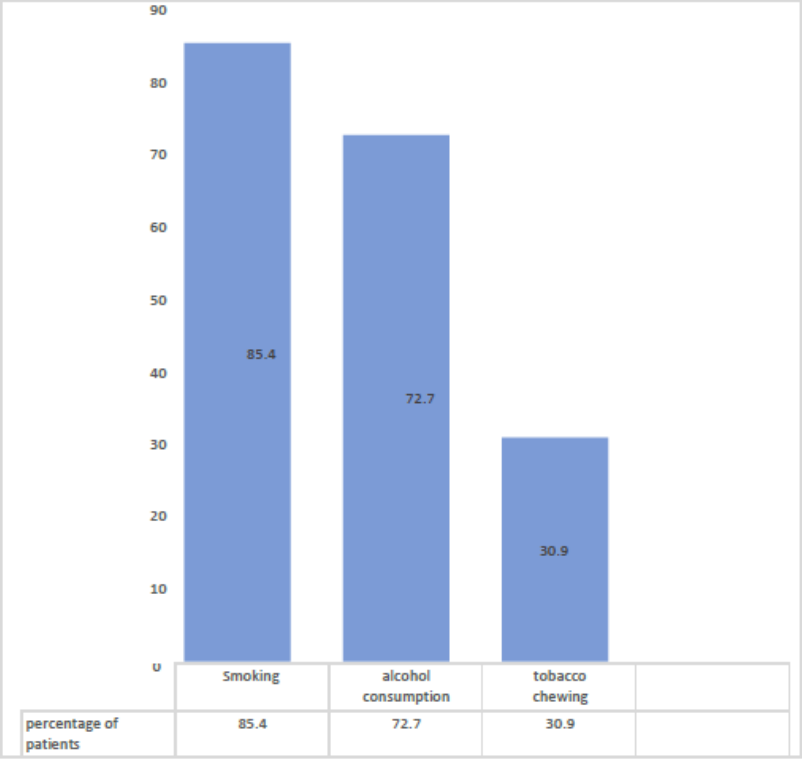
43 patients out of 55, belonged to lower socio-economic group (78.2%). And the rest belonged to lower middle class according to kuppuswamy classification. Malignant lesions of larynx were commonly seen in people residing in rural areas (64.7%) compared to urban (35.3%).

RISK FACTORS:

Table 4: Distribution of risk factors among laryngeal carcinoma patients

Risk factors	Male	Female	Total no. of patients	Percentage
Smoking	46	1	47	85.4%
Alcohol consumption	40	0	40	72.7%
Tobacco chewing	14	3	17	30.9%
Both smoking and alcohol consumption	39	0	39	70.9%

Graph 3: Distribution of risk factors among study population



PRESENTING COMPLAINTS:

Table 5: Distribution of presenting complaints among study population

Presenting complaints	Total no. of patients	Percentage (%)
Change in voice	33	60
Difficulty in swallowing	19	34.5
Difficulty in breathing	18	32.7
Neck swelling	5	9.1
Stridor	7	12.7

Table 6: Incidence of presenting symptoms against site of the tumour

Site of tumour	Dysphagia	Change of voice	Difficulty in breathing	Neck mass
Supraglottis	17	4	6	5
Glottis	2	29	10	0
Subglottis	0	0	2	0
Total	19	33	18	5

Laryngeal cancers of different subsites produce various symptoms (44). Most of the patients complained more than one symptom during the time of presentation.

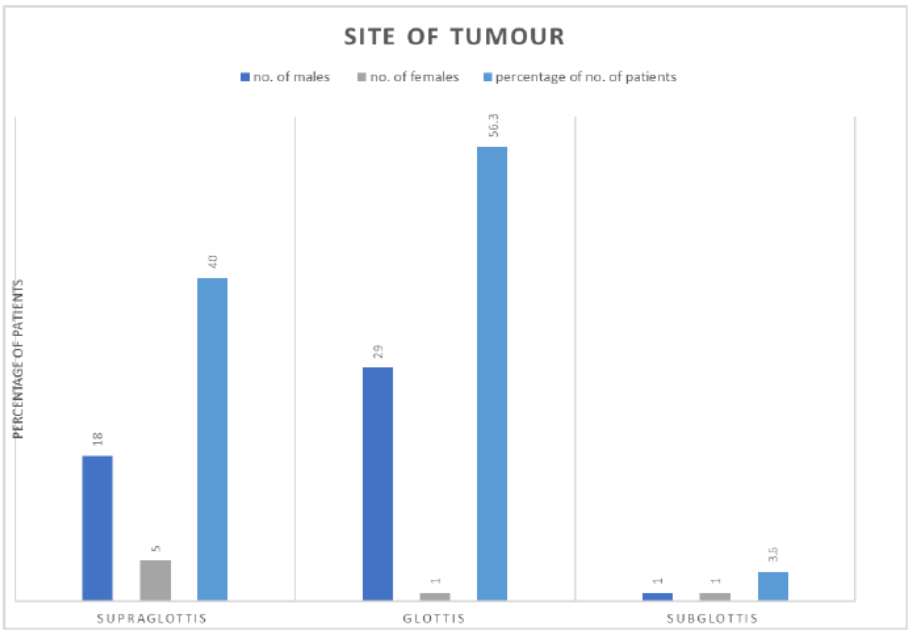
SITE OF TUMOUR:

Table 7: Distribution of site of tumour among study population

Site of tumour	Male	Female	Total	Percentage (%)
Supraglottis	18	4	22	40
Glottis	29	2	31	56.3
Subglottis	1	1	2	3.6
Total	48	7	55	100

The most common site of presentation in our study is Glottis(56.3%) followed by Supraglottis (40%) and the least common presentation is Subglottis which is only among 2 patients (3.6%).

Graph 4: Distribution of site of tumour among study population



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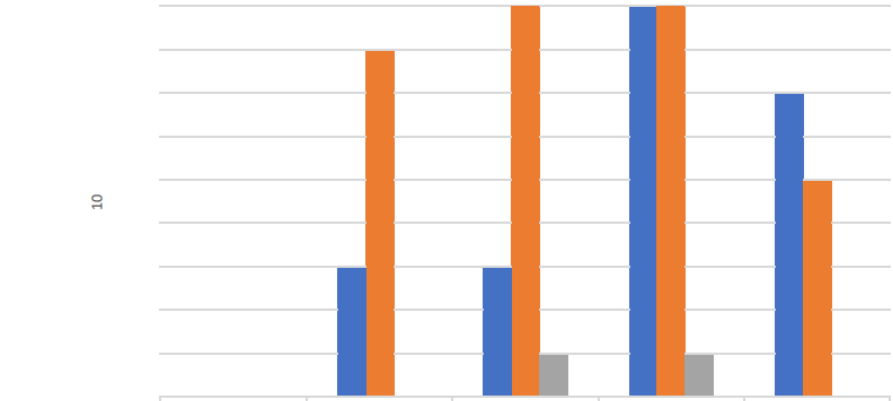
CLINICAL STAGING: We staged the patients according to TNM classification

TNM STAGING OF LARYNGEAL CARCINOMA:

Table 8: Distribution of clinical staging (TNM) among study population

TNM staging	Total	Percentage (100%)	Site	Total	Percentage (100%)
Stage0	0	0	-	0	0
StageI	11	20	Supraglottis	3	27.3
			Glottis	8	72.7
			Subglottis	0	0
StageII	13	23.6	Supraglottis	3	23.1
			Glottis	9	69.2
			Subglottis	1	7.69
StageIII	19	34.5	Supraglottis	9	47.3
			Glottis	9	47.3
			Subglottis	1	5.3
StageIV	12	21.8	Supraglottis	7	58.3
			Glottis	5	41.6
			Subglottis	0	0

Graph5: Distribution of clinical staging(TNM) among study population

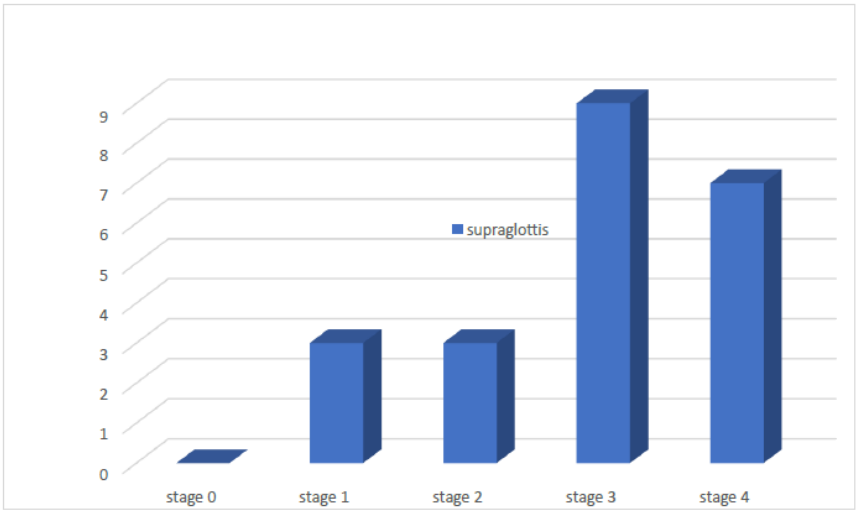


	STAGE 0	STAGE 1	STAGE 2	STAGE 3	STAGE 4
SUPRAGLOTTIS	0	3	3	9	7
GLOTTIS	0	8	9	9	5
SUBGLOTTIS	0	0	1	1	0

The maximum incidence of laryngeal carcinoma was found to be in Stage III (34.5%) followed by Stage II with 13(23.6%),Stage IV with 12(21.8%) and Stage I which is 11(20%) of study population.

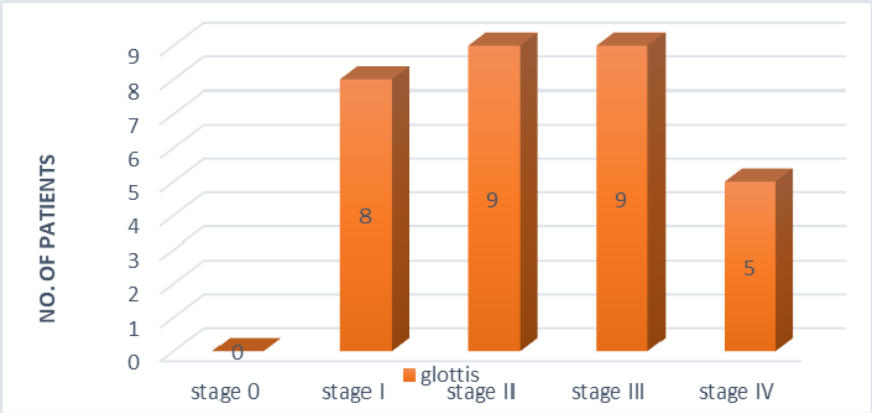
Table 9: Distribution of staging among study population based on the site of the tumour

SITE	STAGEI	STAGEII	STAGEIII	STAGEIV
SUPRAGLOTTIS	**3**	**3**	**9**	**7**
GLOTTIS	**8**	**9**	**9**	**5**
SUBGLOTTIS	**0**	**1**	**1**	**0**
TOTAL	**11**	**13**	**19**	**12**



Graph 6: Distribution of staging among study population involving supraglottis subsite

Among carcinomas involving supraglottic region, almost 16 (72.7%) out of 22 patients presented in advanced stages i.e., stage III in 9 patients (40.9%) and stageIV in 7 patients (31.8%) followed by stage I and II in remaining 6 patients (27.3%) of study population.



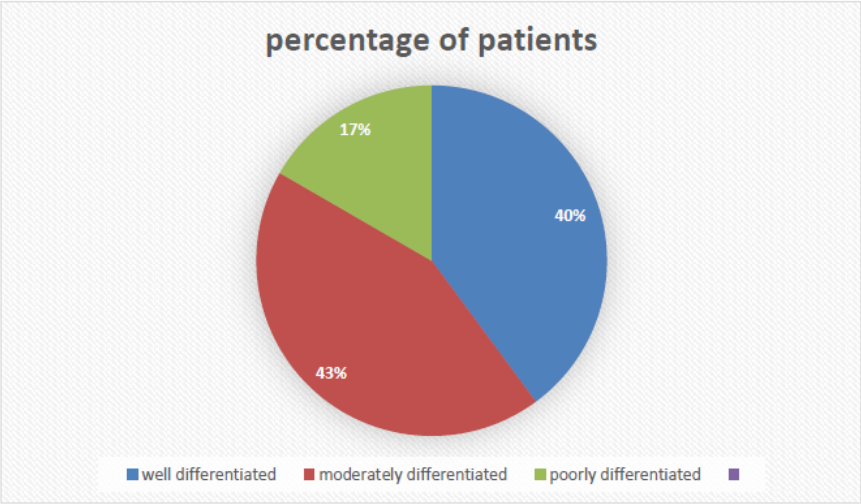
Graph 7: distribution of staging among study population involving glottis subsite

HISTOPATHOLOGICAL FINDING:

Table 10: Distribution of study population based on Histopathological report

Histopathology	Supraglottis	Glottis	Subglottis	Total	Percentage(100%)
Well differentiated SCC	6	15	1	22	40
Moderately differentiated SCC	12	11	1	24	43.6
poorly differentiated SCC	4	3	0	9	16.4
Total	22	31	2	55	100

Moderately differentiated squamous cell carcinoma is the most common histological subtype presented in my study population accounting for 43.6% followed by well differentiated and poorly differentiated squamous cell carcinoma in 22 (40%) and 9 (16.4%) respectively. Broders' histological classification of differentiation in squamous cell carcinoma was used.



Graph 8: distribution of study population based on histopathological report

TREATMENT:

The main modality of treatment offered in our hospital was radiotherapy combined with chemotherapy. Nearly 40% of the patients presented in emergency department with stridor and difficulty in breathing for which emergency tracheostomy was done. For patients who are unable to take oral feeds due to malignant growth, feeding jejunostomy was carried out. As most of the patients presented in stage III, chemoradiotherapy was most offered modality of management. Surgery was not performed in any of our patients. Chemotherapy alone was offered in very few patients who were unfit for surgery and radiotherapy.

Table 11: Emergency tracheostomies done among study population

Total emergency tracheostomies done	Male	Female	percentage
21	18	3	38.18%

IV. DISCUSSION:

The incidence of laryngeal carcinoma differs geographically. Carcinoma larynx is most seen in adults aged 50-75 years and very rare in children and the present study also reported the mean age as 59 years and the age group at which maximum number of patients presented to the hospital was 61 – 70years (45.4%) followed by 51 – 60 years (29.1%) which was consistent with the findings reported by JP Singh Chauhan et al (3) where the mean age group is 58.8 years. In a study by Kumar JS et al (6), the peak incidence of cancer occurred in the 61-70 (36.6%) years. Thompson et al (1999), in his study of malignant tumors of larynx found the mean age as 61 years (the range being from 27–89 years) and incidence of malignant tumors of larynx are more common in 6th decade of life.The youngest age of the presentation is 25 years and the oldest age is 82 years.

Our study showed male preponderance with 48 males which is 87.27% of study population and 7 females which is 12.7% which were close to a study conducted by Kumar JS et al. where male patients constituted 90%.This difference may be due to the habit of smoking which is rare in women of this region.The Male to Female ratio was 6.85:1 in our study which is correlated with the studies done by Zeba ahmed et al (9), V Gurunadharaju (10) where the male: female ratio was 8.1:1 and 6.7:1 respectively.

The work population in our study is correlated to study conducted by **DK sharma(7)** where prevalence of malignant tumours was highest among labourers (36.6%) followed by farmers (13.3%).Malignant lesions of larynx were commonly seen in people residing in rural areas (64.7%) compared to urban (35.3%) in our study. Similar results were obtained by DK Sharma et al (7), AB Dubey et al (11) and Chaitanya V et al (2015) and the incidence found to be higher in people from a lower socioeconomic status, poor nutritional diet, and environmental hygiene.

Smoking cigarettes is considered the most common etiologic factor for incidence of laryngeal cancer. In our study, 85.4% of population were smokers, followed by alcohol intake in 72.7% and tobacco chewing in 30.9% of population. Almost 95.8% of males are smokers and only 1 female had a history of smoking. Risk factors in this study were in accordance with other studies. Bakshi et al. [13] found that smoking was a predisposing factor in 87.8% of his study population and alcohol consumption was found in 75% of the cases.Studies conducted by **Gupta et al (18) , Zahir ST et al (14) and JP Singh Chauhan et al (3)** found to have number of smokers as 92%, 87.2% and 80% respectively.

Combined alcohol and tobacco consumption leads to a synergistic effect. Almost 39 patients (70.9%) had both in our study.30.9% had tobacco chewing in our study.Avoidance of alcohol and smoking could prevent laryngeal squamous cell carcinoma.

In our study, majority of the patients (60%) presented with change in voice, being the most common presenting complaint followed by difficulty in swallowing in 34.5% (19) of patients. Change in voice is the most common symptom in **Sathish kumar et al (6)** and **Zeba ahmed et al (9)** in which number of patients presented were 76.66% and 92% respectively. Also in our study, 18 patients (32.7%) presented with difficulty in breathing which is a late symptom and occurs when the growth has considerably increased. Neck swelling is the chief complaint in 9.1% of study population and all patients with neck swelling are associated with supraglottic carcinomas. There were only 2 patients of subglottic cancer who presented with shortness of breath. Difficulty in breathing is present in 30.76% and 30% of patients in a study by JP Singh Chauhan et al (3) and Kumar JS et al (6) as correlated to 32.7% in our study.Among patients of supraglottic cancer, the most common complaint was difficulty in swallowing and in glottis cancer, it was hoarseness of voice.some patients presented with stridor for which we proceeded with emergency tracheostomy followed by direct laryngoscopy and biopsy.

The site of presentation can be supraglottis, glottis or subglottis. Glottis is the most common site of presentation in our study which is almost 56.3% and 40% had supraglottis presentation. The least common presentation is Subglottis which is only among 2 patients.

There is significant difference between site of presentation among males and females. Among females, maximum number of cases involved supraglottis subsite (4 out of 7) whereas 60.4% male patients had glottic presentation.In studies conducted by zeba ahmed et al (9) and Chaitanya V et al, glottis was the commonest site for laryngeal cancer followed by supraglottis. However, JP Singh Chauhan et al, Gupta et al, DK Sharma, Nazim uddin and Bakshi et al showed results with supraglottis as most common site with 54%, 50%, 75%, 56% respectively followed by glottis.

Tumors are staged according to their involvement of the primary location (T), nodal involvement (N) and distant metastasis (M) based on TNM Classification of Cancer Larynx (American Joint Committee on Cancer, 1997).

In our study, maximum number of patients presented with T2 staging which accounts for 38.2% (21 patients) which is followed by T3, T1 and T4 which accounts for 27.3% (15), 23.6% (13) and 10.9% (6) respectively.

Also in our study, 61.8% had no lymph nodal metastasis at the time of presentation (N0), since majority of the cases involved glottis which has sparse lymphatic supply. Nodal metastasis is seen in 38.2%, in which 14 had supraglottic, 6 had glottic and 1 had subglottic malignancy representing nodal metastasis is common in supraglottic carcinomas due to rich lymphatics supply and midline location of the supraglottic region. N2 and N3 nodal metastasis occurred in a smaller number of patients. Supraglottic Squamous cell carcinomas usually metastases to levels II, III and IV.Our study corelates with the study done by Nallathambi C et al (5) and JP Singh Chauhan et al [3], where supraglottic cancers had highest nodal involvement with 81.8% and 71% respectively.Distant metastasis is present in none of our study population.

The maximum incidence of laryngeal carcinoma was found to be in Stage III which is 34.5% followed by Stage II which accounts for 23.6% of study population followed by Stage IV (21.8%) and Stage I (20%). The present series signifies that most patients presented in advanced/late stage (56.3%). Our study correlates with the results of Kumar JS et al (6) , Shinde KJ et al who reported a greater incidence of Stage III. Ortega et al. (15) also reported that 64% of larynx tumors were locally advanced stages III and IV cancers.

In our study the most common among supraglottic cancers was Stage III (40.9%) followed by Stage IV (31.8%), whereas in glottic cancers 54.8% patients are diagnosed in stage I and II indicating the early presentation of glottic carcinomas. There were only 2 patients of subglottic cancer and they presented at Stage II and stage III.

All patients underwent direct laryngoscopic examination under general anesthesia for staging, workup and biopsy. Histopathological studies in this series revealed that all patients had squamous cell carcinoma with different degrees of differentiations and none of the other types of carcinomas were found in our study. These findings are consistent with the findings of the studies done by Kumar et al., JP Singh Chauhan et al, Gupta et al and DK sharma et al. stating squamous cell carcinoma was the predominant histologic type.

SCC can be classified according to their degree of differentiation into well, moderately, and poorly differentiated (16). Well differentiated squamous cell carcinoma resembles normal squamous epithelium and contains basal type cells and squamous cells with keratinization and intercellular bridges. Moderately differentiated squamous cell carcinoma has less keratinization, more atypical mitoses, and nuclear pleomorphism. Poorly differentiated squamous cell carcinoma has minimal keratinization and intercellular bridges but many atypical mitoses(17).The highest number of cases in this series were of moderately differentiated carcinoma in 24 patients(43.6%) followed by well differentiated squamous cell carcinoma in 22 patients (40%). These findings corresponds with the results of the studies by JP Singh Chauhan et al (3) Kumar JS et al(6), Lam ky (17), Gupta et al (18) and Chaitanya V et al (12) and Arshi beg et al (4) where maximum percentage of patients had moderately differentiated squamous cell carcinoma followed by well differentiated SCC. Poorly differentiated squamous cell carcinoma was the least common histopathologic type among all Squamous cell carcinomas in our study.

Majority of the patients were from low socioeconomic backgrounds which made it difficult to undergo surgery. As most of the patients presented in stage III, chemoradiotherapy was most offered modality of management. Also, after explaining the sequelae and surgical complications, the patients and relatives preferred conservative treatment with voice preservation in the form of radiotherapy and chemotherapy. Radiotherapy was given as external beam radiotherapy. Patients received a 66-70 Gy dose in 35 divided doses over 6 to 7 weeks. For patients who are unable to take oral feeds due to advanced growth, feeding jejunostomy was carried out (49). In few patients who were unfit for surgery and radiotherapy, chemotherapy was advised.

V. CONCLUSION:

The symptoms of laryngeal cancer can range from mild change of voice to life threatening airway obstruction. The percentage of laryngeal carcinoma is closely related with tobacco use (smoked and unsmoked forms) and alcohol intake. Cancer larynx is highly preventable disease by avoiding the risk factors like tobacco and alcohol. Most cases were diagnosed at an advanced stage (stages III & IV). Efforts to diagnose laryngeal cancer should be done as quickly as possible. CT serves as an excellent tool

in identifying spread and nodal involvement thereby help deciding on treatment modality. With early

diagnosis, effective treatment can be provided which reduces the mortality and morbidity of the disease. Therefore, early identification and management can improve and extends the life of laryngeal cancer patients. Prognosis is poor in advanced stages of the disease.

LIMITATIONS:

- Small sample size
- Difficulty in followup due to COVID pandemic
- A Long term followup of five to ten years could have been more significant to evaluate further.

Conflicts of interest: None
Source of funding: None

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