



**Addis Ababa University
College of Health Sciences
Department of Radiology**

**Imaging of Patterns of Laryngeal cancer & Correlation with
Laryngoscopy Findings at Tikur Anbessa Specialized Hospital from
2017-2019**

Ilili Amin (MD, 3rd Year Radiology Resident)

**Submitted to Addis Ababa University College of Health Sciences,
Department of Radiology for Partial Fulfillment of Specialty in
Radiology**

December, 2019

Addis Ababa

**Imaging Patterns of Laryngeal Cancer on Cross Sectional Imaging
& Correlation with Laryngoscopy Findings at Tikur Anbessa
Specialized Hospital from 2017-2019**

Ilili Amin (MD, 3rd Year Radiology Resident)

Advisors:

- 1. Amal Saleh, (MD consultant Neuro-Radiologist)**
- 2. Getachew Assefa (MD, consultant Neuro -Radiologist)**

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By: Ilili Amin (MD, 3rd Year Radiology Resident)

THIS THESIS IS ACCEPTED IN ITS PRESENT FORM AS SATISFYING
THESIS REQUIREMENT FOR THE STUDY OF SPECIALITY CERTIFICATE
IN RADIOLOGY

APPROVED BY THE EXAMINING BOARD

Dr. Amal Saleh, Advisor	_____	_____
	Date	Signature
Dr. Getachew Assefa Advisor	_____	_____
	Date	Signature
_____	_____	_____
Examiner	Date	Signature
_____	_____	_____
Examiner	Date	Signature
_____	_____	_____
Chairman	Date	Signature

DECLARATION

I, the undersigned, declare that this paper is my original work and has not been presented for postgraduate study in this or another university and that all sources used for this paper have been fully acknowledged.

Name: Ilili Amin (MD, 3rd Year Radiology Resident)

Signature: _____

Date : _____

Place: Addis Ababa University, college of Health Science, Department of Radiology

This thesis has been submitted with our approval as university advisors

1. Amal Saleh, (MD consultant Neuro-Radiologist)

Signature: _____

Date : _____

Place: Addis Ababa University, college of Health Science, Department of Radiology

2. Getachew Assefa (MD, consultant Neuro -Radiologist)

Signature: _____

Date : _____

Place: Addis Ababa University, college of Health Science, Department of Radiology

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Abstract

Introduction

Head and neck cancer is the commonest cancer among male patients & third commonest cancer in females in a study done at Tikur Anbessa specialized hospital but there is no research done to assess imaging patterns of laryngeal cancer and this is the first study done at Tikur Anbessa specialized hospital as well as in Ethiopia to assess imaging patterns of laryngeal cancer.

Methods

Hospital based descriptive cross-sectional study was used at Tikur Anbessa specialized hospital from 2016-2019. The study participants were all patients with laryngeal mass who came to oncology department & radiology department at TASH. Data was collected from cancer registry in the oncology department as well as by reviewing imaging reports of patients with laryngeal mass who came to radiology and oncology department using structured questionnaire. The data was analyzed using SPSS software version 24.4 and results presented using text, tables and graphs.

Result

The study showed that of the 90 patients who were included in the study had age range from 24 yrs. to a maximum of 85 yrs. with a mean age of 51.5 years with (± 14 SD).

77 (85.6%) presented with hoarseness of voice and Among those 34 cases for which risk factors were specified 23 (67.6%) had cigarette smoking as risk factor while 12 (35.3%) had alcohol as risk factor.

Out of the 79 cases with laryngeal sub sites described, 38 (48.1%) were transglottic, 27 (34.2%) glottic and 12 (15.2%) were supraglottic.

46 (51.1%) patients had extra laryngeal spread, 18 (20%) had no extra laryngeal spread, and for 26 (28.9%) cases it was not specified.

Laryngoscopic cases of glottic location correlates with 46.2% of imaging cases of glottis cancer with the rest 46.2% being transglottic and 7.7% being supraglottic on imaging.

KEY WORDS: CT imaging patterns, laryngeal cancer

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List of Acronyms and Abbreviations

TASH	Tikur Anbessa specialized hospital
ENT	Ear; Nose and Throat
AJCC	American joint committee on cancer staging
AVC	Anterior vocal commissure
RVI	Retroviral infection

1. Introduction

1.1 Background

The commonest causes of morbidity and mortality in Ethiopia are due to communicable diseases such as tuberculosis, HIV/AIDS and malaria. Ethiopia however is successful in reducing deaths related to communicable deaths by 65% but the country's performance in reducing non communicable diseases was minimal making these diseases to join the leading cause of premature mortality in 2010[1, 2]

Cancer cases in Ethiopia have also been steadily rising like many other developing countries which is partly related to lifestyle changes such as increased prevalence of smoking & alcohol, unhealthy high calorie, western diets, environmental exposures, viral infections such as HIV, HPV& chronic infections[2].

Ethiopia has no national cancer registry and there is only one cancer referral center in the country which is located at the Tikur Anbessa specialized hospital in Addis Ababa. On the bases of extrapolations from this only cancer referral center in the country, estimate of cancer incidence, of up to 150,000 cases per year is made. However less attention is given for this dreadful disease which is spreading rapidly due to low awareness of the scale of the cancer burden in Ethiopia among local and international policy makers[3].

A study done to assess pattern of cancer in Tikur Anbessa Specialized Hospital Oncology Center in Ethiopia from 1998 to 2010, head & neck tumors are the commonest malignancy followed by sarcomas in males and third common malignancy in females following gynecologic malignancies & breast cancer[4].

A study done in Nigeria showed that the larynx is the third commonly involved site of all head and neck cancer following nasopharyngeal and sinonasal carcinoma[5]. As to my knowledge there is no published studies done on laryngeal cancer is found in Ethiopia.

Laryngeal sub site involvement varies amongst many studies. In the USA, glottic carcinomas (59%) are the most common followed by supraglottic (40%) and subglottic (1%)[6].

Most studies in developing countries showed contradictory results regarding the involvement of laryngeal sub sites with laryngeal carcinoma. A Study done in Egypt showed that the glottis is

involved only in (10.8%) of cases while (62.4%) of total patients were affected in the glottic and supraglottic regions, followed by transglottic regions in (20.7%) and Supraglottic tumor occurs in 5.1% of cases[7].A study done in India found out that supraglottic involvement was the commonest (56.9%) followed by the glottis (36.2%) and Trans-glottic tumors(6.89%)[8]. Subglottic sub site is the least to be involved in laryngeal cancer [7, 8].

Laryngeal cancer is predominantly a disease of elderly male. The Egyptian study found out that the mean age at presentation was 57.6 ± 10.5 and Indian study showed that the mean age of 65[7, 8].

There are several risk factors for laryngeal cancer as for many other cancers. These includes alcohol ingestion, cigarette smoking, and dietary factors such as red meat based diet, low vegetable & fruit diets [9]. A study done in Kenya showed that Cigarette smoking & alcohol ingestion are strong risk factors for development of late stage & poorly differentiated laryngeal squamous cell carcinoma [10].

Squamous cell carcinoma is the commonest histologic type accounting for up to 90 % of the cases followed by other types such as Verroucous carcinoma which is a distinct variant of well differentiated carcinoma, adenocarcinoma, adenoid cystic carcinoma, fibro sarcoma & lymphomas [8].

The commonest clinical manifestation of laryngeal cancer is hoarseness of voice while dysphagia, neck swelling and throat pain was commoner among supra glottic cancers while hoarseness of voice was more common in glottic cancers [7].

In addition to imaging request, a patient with suspected laryngeal carcinoma should be investigated with endoscopy which assesses best the mucosal involvement and cord mobility in laryngeal carcinoma[11].

The assessment of sub mucosal extent and invasion of adjacent structures needs cross sectional imaging. Imaging also allows the tumor to be classified according to the relevant T staging by providing important information concerning nodal metastasis, systemic metastasis and the presence of synchronous tumors [11].

Laryngeal cancer is staged according to AJCC which consists, of T defining extent of primary tumor, N defining absence or presence of regional lymph node metastasis and M defines presence or absence of distant metastasis[12]. T stage for laryngeal carcinoma is defined according to each laryngeal sub sites N and M stage is similar for all head and neck tumors except for nasopharyngeal and thyroid carcinoma with different nodal stages[13].

There are many therapeutic options for laryngeal cancer such as surgery, chemotherapy, radiotherapy or in combinations, decisions being made based on evaluation of disease extent and performance status. T1 and T2 classified low volume supraglottic and glottic carcinoma which can be treated with definitive radiotherapy alone. Advanced tumors usually undergo a combination of surgery and radiotherapy, possibly reserving the surgery for radiotherapy failure [11].

The study done on patients with advanced laryngeal cancer showed patients with larynx preservation had a 5-year survival probability of 48%, whereas total laryngectomy patients had a 5-year survival probability of 63% which is not significant statistically. However the study found out that larynx preservation group has more risk for local recurrence. The study also found parameters which have impact on survival such as local recurrence, patient age greater than 70 years, cervical nodal recurrence and disease stage in consecutive orders[14].

There is also several conservative voice preserving surgical options for laryngeal carcinoma such as laser resection with preservation of laryngeal integrity for small epiglottic tumors, partial laryngectomy for larger supra glottic tumors and endoscopic laser resection for small glottic tumor. Any trans glottic tumor, paraglottic tumor or extensive laryngeal cartilage invasion would contraindicate such speech conserving surgery [11].

The role of imaging would be in staging, to guide therapy and also help in assessing postoperative complications such as radio necrosis and recurrence.

On cross sectional imaging of laryngeal cancer one should define the three anatomical sites of involvement as supraglottis, glottis and sub glottis, assess tumor volume, assess relationship of the tumor to the ventricular complex, involvement of sub mucosal spaces and extra laryngeal spread as well as assess cervical lymph node and distant metastasis[11].

CT and MRI have their differences in determining local infiltration and tumor extension. MRI is more accurate than CT scan in T staging compared with CT. Study which compares MRI and CT to assess laryngeal carcinoma in assessing AVC involvement showed that MRI has a higher sensitivity (93-96%) and a higher accuracy (84-86%) in detecting AVC and thyroid cartilage involvement but with reduced sensitivity due to local inflammation caused by the tumor while CT has higher specificity[16].The study concludes choice of imaging modality should be based on specific case scenario as both imaging modality has its own advantage and disadvantages[16].

The choice of imaging for laryngeal cancer is subject to the availability of the CT or MRI scanner and the expertise in interpretation of the scans, as also the ability of the patient to afford the cost of an MRI examination [15].

Imaging also assesses extra laryngeal spread of tumors. An institutional based study which involves 103 laryngectomy specimens with pre-operative contrast enhanced neck CT showed that thyroid cartilage penetration is a common route of extra laryngeal spread of glottic and supraglottic squamous cell carcinoma [17]

The study also showed extra laryngeal spread into surrounding structures without thyroid cartilage penetration occurs in 73% of the cases of extra laryngeal spread, which underwent laryngectomy and 56% of those with pathologically confirmed extra laryngeal spread. The study concludes that the commonest extra laryngeal invasion is anterior (44%) and the least invasion is superior invasion (24%) while posterior and inferior invasion occurs in 33 % of the cases [17].

The lymph node involvement of laryngeal cancers varies according to tumor location and its extent. From all laryngeal sub sites, supraglottic cancers have higher lymph node involvement due to rich lymphatic. Glottis cancers show the lowest lymphatic rate due to the lower lymphatic density in glottic region but since subglottic cancer is rare it is the least sub site to be involved in loco regional metastasis [18].

The primary nodal drainage of supraglottic region to level II –IV and delphian (prelaryngeal node) for subglottic tumor [11].

Clinico-pathologic study of 50 patients with laryngeal carcinoma to assess nodal metastasis and correlation with tumor characteristics found out that 100 % of glottis tumor, 58.3%of supra

glottic tumor and 51.5% of trans glottic tumors are not associated with loco regional metastasis[19].These also study categorizes lesions as endo laryngeal and extra laryngeal, of which glottis lesions are 100 % endo laryngeal lesions. The study also assess nodal disease in relation with T stage and histologic tumor grade and found out that nodal disease has increased progressively with both T stage and histological grade[19].

Cervical lymph nodes can be assessed by clinical palpation and imaging modalities such as ultrasound scan and post contrast CT in head and neck squamous carcinoma. Imaging criteria's used are size of greater than 15mm in short axis on axial scans(a), Ultrasound findings of longitudinal to short axis ratio of greater than two as oval and less than two as round, CT findings of central nodal necrosis and conglomeration of greater than three lymph nodes are used[20].

There are several criteria's to differentiate malignant from benign lymph nodes in head and neck carcinoma. CT criteria's such as size, central nodal necrosis and ultrasound criteria of longitudinal to short axis ratio (L/S) are used[13].These study correlates clinical and imaging criteria of malignant cervical lymph nodes with histopathologic findings and found out that clinical palpation provided false positive results of about 12.3% and false negative results of about 47.6% with sensitivity of 71.43% and specificity of 75.86%[13].

A study which involves total of one hundred consecutive patients with a histologically proven non-cutaneous Head and Neck Squamous Cell Carcinoma (HNSCC) used a size criteria of 11mm, central nodal necrosis and conglomeration of three or more lymph nodes in the drainage region of the primary tumor on CT as criteria for malignant features and has a sensitivity of 82.9%, a specificity of 89.66%, and an accuracy of 84.85%[13].RECIST 1.1(Response Evaluation Criteria in Solid Tumors) reports lymph nodes of 15mm or more in the short axis on axial images as pathologically enlarged and measurable[20].

The most specific sign in metastatic nodal involvement in the presence of head neck cancer primary tumor is nodal necrosis with specificity of 100%[13].

Ultrasound scanning provided the highest sensitivity (97.1%), specificity (93%), and accuracy (95.96%) for detecting metastatic cervical lymph nodes in this study using L/S of less than two as a cutoff point[13].

The study done in India found out that the commonest cervical lymph node involvement in laryngeal carcinoma is level II followed by level III [8].

Distant metastasis in laryngeal cancer is seen much less frequently. Amongst metastatic sites the lung is the most common site with mediastinum, bone and liver sites can also be involved [11]. The study done in Egypt showed that the liver is the only site that had involved in laryngeal carcinoma patients with metastasis [7].

1.2 Significance of the study

This study will be the first study to be done on laryngeal cancer in Ethiopia as to my knowledge. The study has several variables one of which is that it assesses risk factor which have an implication for the reduction of the burden of this devastatingly growing disease which significantly affects quality of life by impairing swallowing and speech in advanced stage even with treatment. The study will assess imaging reports amongst radiologists in different hospitals as well as correlates it with endoscopic reports in ENT department. This helps to assess any gap that needs to communicate amongst radiologists as well as with ENT department.

The study will also strengthen collaborative works amongst departments to manage patients with laryngeal cancer as the management needs multidisciplinary approach. There are several ways of treatment in patients with advanced laryngeal cancer and larynx sparing surgery is an option even in advanced disease as literature indicates and this should be communicated with the patients.

2. Objectives of the Study

2.1 General Objective

- To determine demographic, endoscopic, imaging patterns and to assess risk factors of laryngeal cancer

2.2 Specific Objectives

- To determine the demographic characteristics of patients with laryngeal cancer
- To assess risk factors for laryngeal carcinoma
- To establish Imaging patterns of laryngeal cancer
- To correlate imaging findings with laryngoscope findings of patients with laryngeal cancer

3. Methods and Materials

3.1 Study Area and Period

The study was conducted at Tikur Anbessa specialized hospital (TASH), college of health science, Addis Ababa University, Addis Ababa Ethiopia. TASH is the largest referral hospital as well as the only oncology center which delivers radiotherapy. The study was done from 2017 – 2019

3.2 Study Design

The study was hospital based descriptive retrospective cross sectional study done at Tikur Anbessa Specialized Hospital. The study includes reviewing of medical records of patients with untreated laryngeal carcinoma from 2016 to 2019 who came to department of radiology and oncology.

3.3 Source Population & Study Population

Source populations are all patients with untreated laryngeal carcinoma sent to radiology and oncology department and study population are all patients with laryngeal carcinoma with imaging reports, medical records for demographic assessment as well as laryngoscopic reports.

3.4 Inclusion and Exclusion Criteria

3.4.1 Inclusion Criteria

- All patients diagnosed with laryngeal cancer imaged at radiology department or sent to oncology center

3.4.2 Exclusion Criteria

- All patients with laryngeal mass other than laryngeal carcinoma, those who did not have Imaging report, biopsy or incomplete medical record were excluded from the study

3.5 Sample Size

All patients with laryngeal carcinoma seen at TASH at oncology department from 2016-2019

3.6 Sampling Technique

Non probability convenience sampling method was used to include all patients with head and neck tumors with laryngeal cancer at radiology department and oncology department.

3.7 Operational Definitions

Supra glottis: extends from tip of epiglottis to the ventricle (involves epiglottis, aryepiglottic folds, arytenoids and false vocal cords).

Glottis: defined from plane stretching from ventricle to a plane 1cm below the free margin of vocal cord (includes true vocal cords and anterior and posterior commissures)

Sub glottis: extends inferiorly to the caudal aspect of cricoid cartilage.

Tran's glottis: tumors encroaching on both glottis and supraglottic with or without subglottic components and when the site of origin is unclear

Ventricular complex: includes true and false vocal cord with intervening ventricle

Laryngeal Sub mucosal spaces: pre epiglottic and para glottic spaces.

Anterior invasion: thyroid cartilage penetration

Posterior invasion: widening of thyroid, arytenoid space/arytenoid destruction

Superior invasion: base of tongue involvement, thyro-hyoid penetration, thyroid notch penetration

Inferior invasion: Conus elasticus penetration

Anterior vocal commissure (AVC): anterior junctional point of the true vocal cords

DEFINITIONS OF TNM

Primary Tumor (T)

- TX Primary tumor cannot be assessed
- T0 No evidence of primary tumor
- Tis Carcinoma in situ

Supraglottis

- T1 Tumor limited to one subsite of supraglottis with normal vocal cord mobility (Figure 5.3A, B)
- T2 Tumor invades mucosa of more than one adjacent subsite of supraglottis or glottis or region outside the supraglottis (e.g., mucosa of base of tongue, vallecula, medial wall of pyriform sinus) without fixation of the larynx (Figure 5.4A, B)
- T3 Tumor limited to larynx with vocal cord fixation and/or invades any of the following: postcricoid area, preepiglottic space, paraglottic space, and/or inner cortex of thyroid cartilage (Figure 5.5A, B)
- T4a Moderately advanced local disease
Tumor invades through the thyroid cartilage and/or invades tissues beyond the larynx (e.g., trachea, soft tissues of neck including deep extrinsic muscle of the tongue, strap muscles, thyroid, or esophagus) (Figure 5.6)
- T4b Very advanced local disease
Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures (Figure 5.7)

Glottis

- T1 Tumor limited to the vocal cord(s) (may involve anterior or posterior commissure) with normal mobility (Figure 5.8)
- T1a Tumor limited to one vocal cord (Figure 5.8)
- T1b Tumor involves both vocal cords (Figure 5.8)
- T2 Tumor extends to supraglottis and/or subglottis, and/or with impaired vocal cord mobility (Figure 5.9)
- T3 Tumor limited to the larynx with vocal cord fixation and/or invasion of paraglottic space, and/or inner cortex of the thyroid cartilage (Figure 5.10)
- T4a Moderately advanced local disease
Tumor invades through the outer cortex of the thyroid cartilage and/or invades tissues beyond the larynx (e.g., trachea, soft tissues of neck including deep extrinsic muscle of the tongue, strap muscles, thyroid, or esophagus) (Figure 5.11)
- T4b Very advanced local disease
Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures

Subglottis

- T1 Tumor limited to the subglottis (Figure 5.12)
- T2 Tumor extends to vocal cord(s) with normal or impaired mobility (Figure 5.13)
- T3 Tumor limited to larynx with vocal cord fixation (Figure 5.14)

(continued)

Primary Tumor (T) (continued)

T4a	Moderately advanced local disease Tumor invades cricoid or thyroid cartilage and/or invades tissues beyond the larynx (e.g., trachea, soft tissues of neck including deep extrinsic muscles of the tongue, strap muscles, thyroid, or esophagus) (Figure 5.15)
T4b	Very advanced local disease Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures

Regional Lymph Nodes (N)* (See Part II Head and Neck Figures II.1–II.4)

NX	Regional lymph nodes cannot be assessed N0; no regional lymph node metastasis
N1	Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension
N2	Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension, or in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension, or in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension
N2a	Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension
N2b	Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension
N2c	Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension
N3	Metastasis in a lymph node, more than 6 cm in greatest dimension

*Note: Metastases at level VII are considered regional lymph node metastases.

Distant Metastasis (M)

M0	No distant metastasis
M1	Distant metastasis

ANATOMIC STAGE/PROGNOSTIC GROUPS

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1	N1	M0
	T2	N1	M0
	T3	N1	M0
Stage IVA	T4a	N0	M0
	T4a	N1	M0
	T1	N2	M0
	T2	N2	M0
	T3	N2	M0
	T4a	N2	M0
Stage IVB	T4b	Any N	M0
	Any T	N3	M0
Stage IVC	Any T	Any N	M1

3.8 Study Instrument

A well structured questionnaire for data collection was developed from similar studies and utilized for data collection

3.9 Study Variables

The independent variables included in this study were divided into 3 categories based on the source or type of information: patient-level demographics, clinical characteristics, and risk factors.

Patient-level demographic variables are age at diagnosis, sex, and residence area. Clinical characteristics, also captured at the patient level, are overall tumor stage, T category, year of diagnosis, and risk factors for laryngeal cancer includes smoking history, smoking pack years, history of alcohol intake, concomitant history of alcohol & smoking, immune status of patients, dietary habit as red meat based verses vegetable based diet and history of chewing khat.

3.10 Data Collection

Data was collected from cancer registry in the oncology department and patients sent to department of radiology to include all the study variables as well as by reviewing medical records of patients with laryngeal mass in radiology and oncology department.

3.11 Data Analysis

Data was analyzed using the statistical package for the social sciences for windows (SPSS version 24.0) and descriptive statistics such as frequency distribution, mean, standard deviation and percentages. Finally the result was described using text, tables and figures.

3.12 Ethical Considerations

The information obtained from patients medical records as well as imaging reports of the patients was kept confidential & Permission was obtained from research & ethics committee of the department of radiology.

4. Result

4.1 Socio-demographic characteristics

90 patients were included in this study with age ranging from 24 years to 85 years with a mean, mode and median age of 51.5yrs, 60yrs and 53yrs respectively with SD of +/- 14 . 83 (92.2%) were male and remaining 7 (7.8%) were females with male to female ratio of 12:1 as shown in figure 1 below.

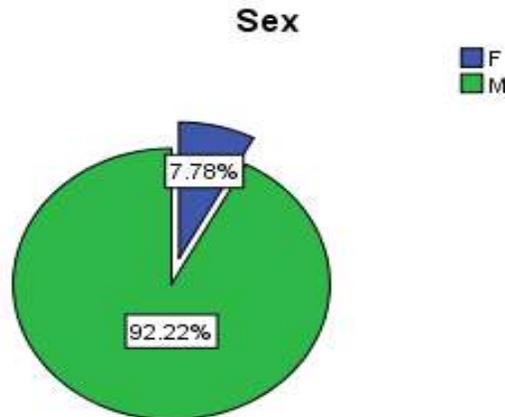


Figure 1: Gender distribution of laryngeal cancer patients at Tikur Anbessa Specialized hospital, 2017-2019

When we see the distribution of cases included in this study by regional states, 27 (30%) were from Oromia region, 19 (21.1%) were from Addis Ababa city administration and 18 (20%) were from Amhara region (See figure 2 below).

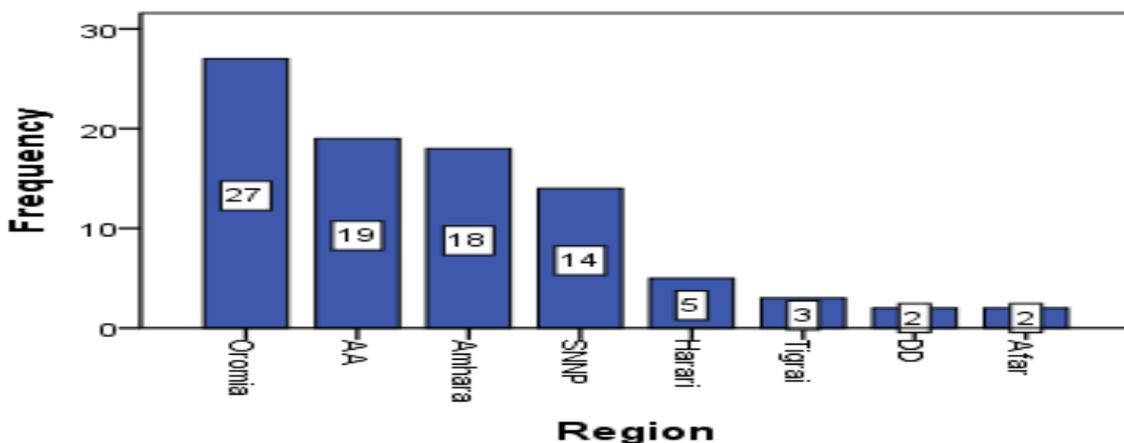


Figure 2: Distribution of laryngeal cancer patients at Tikur Anbessa Specialized hospital by regional states, 2017-2019.

4.2 Clinical features

Among all the study participants 77 (85.6%) had hoarseness of voice, 28 (31.1%) had shortness of breath, 11 (12.2%) had dysphagia and another 11 (12.2%) had neck swelling as indicated in table 1 below.

Table 1: Clinical features of laryngeal cancer patients at Tikur Anbessa Specialized hospital, 2017-2019.

Clinical feature	Frequency	Percentage
Hoarseness of voice	77	85.6
Shortness of breath	28	31.1
Dysphagia	11	12.2
Neck swelling	11	12.2
Cough	4	4.4
Upper airway obstruction	4	4.4
Chocking episode	3	3.3
Difficulty of speaking	2	2.2
Neck pain	1	1.1
Submandibular swelling	1	1.1
Tinnitus	1	1.1

4.3 Risk Factors

Among all the 90 study participants risk factor was not specified for 25 (27.8%) cases whereas for 65 (72.2%) different risk factors were identified. Out of the 65 cases 34 (52.3%) had identifiable risk factors while 31 (47.7%) had no risk factors. Among those 34 cases for which risk factors were specified 23 (67.6%) had cigarette smoking as risk factor while 12 (35.3%) had alcohol as risk factor. See table 2 below.

Table 2: Risk factors of laryngeal cancer among patients at Tikur Anbessa Specialized hospital, 2017-2019

Is there risk factor?	Factors in number and percent	Number & %
Yes-34 (37.8%)	Alcohol-12 (35.3%)	Occasional- 5 (41.7%)
		Heavy- 3 (25%)
		Not specified-4 (33.3%)
	Cigarette-23 (67.6%)	<10 Pack Yr- 9 (39.1%)
		10-20 Pack Yr- 8 (34.8%)
		>20 Pack Yr- 4 (17.4%)
		Not specified-2 (8.7%)
	Chat-9 (26.5%)	
Alcohol & Cigarette-1 (2.9%)		
Immune-RVI +ve-4 (11.8%)		
No-31 (34.4%)		
Not specified-25 (27.8%)		

4.4 Imaging Findings

Laryngeal sub sites involvement

Out of the total 90 study participants, laryngeal sub sites were not specified among 11 cases. Out of the 79 cases with laryngeal sub sites described, 38 (48.1%) were transglottic, 27 (34.2%) glottic and 12 (15.2%) were supraglottic. See table 3 below.

Table 3: Involved laryngeal sub sites of laryngeal cancer patients at Tikur Anbessa Specialized hospital, 2017-2019.

S/N	Anatomic sub sites	Frequency	Percent
1	Transglottic	38	48.1
2	Glottic	27	34.2
3	Supraglottic	12	15.2
4	Hypopharynx	1	1.3
5	Subglottic	1	1.3
	Total	79	100

Of the 38 transglottic sites 17(44.7%) were unilateral right, 9(23.7%) bilateral, 6(15.7%) unilateral left and for 6(15.7%) the site was not specified. Out of the 27 glottic sub sites, 11(40.7%) were unilateral left, 11(40.7%) unilateral right, 4(14.8%) bilateral and for 1(3.7%) the site was not specified. out the 12 supraglottic sub sites, 7(58.3%) were unilateral right, 3(25%) were bilateral, and 2(16.7%) were unilateral left. The only one subglottic is unilateral left.

Out of the 90 study participants 42 (46.7%) had no ventricular complex involvement while 37 (41.1%) had ventricular complex involvement and for 11 (12.2%) involvement of ventricular complex was not specified.

There was no involvement of sub mucosal space among 3 (3.3%) cases. Involvement of sub mucosal space was not specified for 53 (58.9%) cases, but in the remaining 34 (37.8%) cases in which involvement of sub mucosal space was specified 19 (21.1%) were paraglottic, 11 (12.2%) were preglottic and the remaining 4 (4.4%) were both paraglottic and preglottic space.

Anterior vocal commissure was involved in 33 (36.7%) of cases, while in 25 (27.8%) it was not involved and in 32 (35.6%) cases it was not specified.

Out of 90 laryngeal cancer cases included in this study 46 (51.1%) had extra laryngeal spread, 18 (20%) had no extra laryngeal spread, and for 26 (28.9%) cases it was not specified. After excluding those for which laryngeal spread was not specified, there was 71.9% (46 out of total 64 cases) had extra laryngeal spread while 28.1% (18 out of 64) had no extra laryngeal spread.

Among the total 46 cases with extra laryngeal spread, site of extension was described as indicated in table 4 below. 34 (53.1%) had thyroid cartilage penetration, 18 (39.1%) had hypopharyngeal extension while 10 (21.7%) had widening of Thyroid, Arytenoid space/Arytenoid destruction.

Table 4: Site of extra laryngeal spread of laryngeal cancer patients at Tikur Anbessa Specialized hospital, 2017-2019

S/N	Site of extension	Frequency	Percent
1	Thyroid Cartilage Penetration	34	73.9%
2	Hypopharyngeal extension	18	39.1%
3	Widening of Thyroid, Arytenoid space/Arytenoid destruction	10	21.7%
4	Para vertebral, IVB	5	10.9%
5	Base of tongue involvement, thyrohyoid penetration, thyroid notch penetration	3	6.5%
6	Proximal Esophagus Involvement	2	4.3%
7	Conuselasticus penetration	1	2.2%

Out of the 90 laryngeal cancer patients in this study enlargement of cervical lymph nodes were described in 82 (91.1%) patients while in 8 (8.9%) patients it was not specified. Out of those 82 patients, 27(32.9%) had enlarged cervical lymph nodes while 55(67.1%) had no enlarged cervical lymph nodes. Out of the 27 cases with cervical lymph nodes involvement 10(37%) had bilateral involvement, 12(44.4%) had unilateral right, while the remaining 5 (18.5%) had unilateral left cervical lymph node involvement.

Enhancement pattern of enlarged cervical lymph nodes were described in 13 cases. Six (46.2%) had homogenous enhancement, another five (38.5%) cases had heterogeneous enhancement whereas four (30.8%) had heterogeneous enhancement with central necrosis.

When we see level of enlarged lymph nodes, among those with level of enlarged lymph node description 6 were IIA/B (Bilateral), 5 were IA/B (bilateral), 4 were IIA/B (R), 3 were IA/B (R), 2 were III (Bilateral), whereas IA/B (L), IIA/B (L), IV (L), VII (Bilateral) were all one each in number. In general 11 (45.8%) were level II, 9 (37.5%) were level I, 2 (8.3%) were level III, and 1(4.2%) was level IV and another 1(4.2%) was level VII.

The presence or absence of metastasis was specified for 81(90%) of cases while for 9(10%) it was not specified. Out of the 81 cases 2(2.5%) had distance metastasis to the lung) while the remaining 79(97.5%) had no distance metastasis.

From all the study participants, 42 (46.7%) had tracheostomy inserted, 37 (41.1%) had no tracheostomy inserted, in another 11 (12.2%) it was not specified.

4.5 Histopathologic Pattern

The most common histologic type is squamous cell carcinoma 74 (82.2%) followed by carcinoma in situ 6 (6.7%) and dysplasia 3 (3.3%). See table 5 below

Table 5: Histopathologic pattern of laryngeal cancer patients at Tikur Anbessa Specialized hospital, 2017-2019

Histology type		Frequency	Percent
	SCC	81	90.0
	Carcinoma In situ	6	6.7
	adenocarcinoma	1	1.1
	Maltoma	1	1.1
	Undifferentiated cells	1	1.1
	Total	90	100.0

Out of 90 patients 18(20%) patients did not receive radiotherapy at the oncology unit after booked for radiotherapy. Those who took radiotherapy took them longer time to get radiotherapy after get booked.

Table 6: Time interval for radiotherapy

Time interval for radiotherapy	Percentage
5-7months	25(40.9%)
1-4 months	20(32.7%)
7 -10 months	15(24.6%)
1 day	1(1.6%)

Table 7: Number of patients who did not start treatment

Number of patients who did not start treatment	Time interval	Percentage
15	1yr -3yrs	16.6%
3	0.6yr -1yr	3.3%
11	Less than 6 months	12.22%

Out of 90 patients 42 (46.7%) were stage IVA followed by stage III 12 (13.3%) and stage II 9(10%) as seen in table 6 below.

Table 8: Stages of laryngeal cancer patients at Tikur Anbessa Specialized hospital, 2017-2019

		Frequency	Percent
Stages	0	3	3.3
	I	6	6.7
	II	9	10.0
	III	12	13.3
	IVA	42	46.7
	IVB	5	5.6
	IVC	2	2.2
	Not given	11	12.2
	Total	90	100.0

4.6 Laryngoscope findings and correlation with imaging findings

Out of 90 patients who had laryngeal carcinoma 57(57.8%) had do laryngoscopic findings seen on the medical record .out of 38(42.2%) patients who had laryngoscopic findings34(89.5%) had specified site of involvement as 16(47.1%) was glottis laryngeal cancer,10(29.4%) was transglottic,7(20.6%) was supraglottic cancer,1(2.9%) patient had subglottic laryngeal cancer.

Table 9: Laryngoscope findings of the patients with laryngeal cancer

		N	%
Diagnosis	laryngeal ca	38	42.2%
	No finding	52	57.8%
Anatomic site mentioned		34/38	89.5%
Anatomic site	Glottis	16	47.1%
	Supra	7	20.6%
	Trans	10	29.4%
	Sub	1	2.9%
Anterior commissure		5	5.6%
Extra-laryngeal spread		8	8.9%

There is no description on laryngoscope as to the submucosal or ventricular complex involvement. There was only 5 (5.6%) patients with laryngeal cancer described to have anterior commissure involvement and 8 (8.9%) had extra-laryngeal spread described as hypo pharyngeal extension.

Table 10: Comparison of the findings of imaging with that of laryngoscope in patients with laryngeal cancer

	Imaging		Laryngoscopy	
	N	%	N	%
Laryngeal cancer	90	100%	38	42.2%
Site of cancer identified	79	93.4%	34	89.5%
Involvement of anterior commissure	33	36.7%	5	5.6%
Extra-laryngeal spread	46	51%	8	8.9%

Out of 90 patients only 38(42.2%) of patients have laryngoscopic findings while all patients have imaging finding. Imaging also described site of involvement in 79(93.4%) patients and laryngoscope describes site in 34(89.9%) out of 38 patients who had laryngoscope findings.

Table. 11: Comparison of location of the cancer in laryngoscopy verses imaging

			Imaging			Total	
			Glottis	Supraglottic	Transglottic		
Laryngoscopy	Glottis	N	6	1	6	13	
		%	46.2%	7.7%	46.2%	100.0%	
	Supraglottic	N	0	2	4	6	
		%	0.0%	33.3%	66.7%	100.0%	
	Transglottic	N	5	0	5	10	
		%	50.0%	0.0%	50.0%	100.0%	
	Subglottic	N	0	0	1	1	
		%	0.0%	0.0%	100.0%	100.0%	
	Total		N	11	3	16	30
			%	36.7%	10.0%	53.3%	100.0%

Table.12: Accuracy of laryngoscopy in identifying tumor location

		Imaging		Laryngoscopy	
		N1		N2	% of N1
Location	glotic	27		16	59.3%
	supra	12		7	58.3%
	trans	38		10	26.3%
	sub	1		1	-

Laryngoscopic cases of glottic location correlates with 46.2% of imaging cases of glottis cancer with the rest 46.2% being transglottic and 7.7% being supraglottic on imaging. Among the cases in whom the location was supra-glottic on laryngoscopy, 33.3% were also supra-glottic on imaging but 66.7% were transglottic on imaging. Of the transglottic tumors on laryngoscopy,

50% were on the same site on imaging but the rest 50% were glottis on imaging. Comparison for subglottic tumors was impossible due to low event rate of subglottic cancers due to its rarity. Among the 38 cases of transglottic cancers on imaging, only 26.3% were identified as transglottic by laryngoscopy. The agreement of laryngoscopy with imaging on glottic and supraglottic locations of the cancer were 59.3% and 58.3% which are better than the one observed in transglottic cancers.

5. Discussion

In this study, it was found that the majority of laryngeal cancer patients were male adult with age ranging 24yrs to 85yrs. Risk factors were also assessed in this study and found out that smoking was the commonest risk factor followed by alcohol. Majority of patients who had cigarette smoking as risk factor were less than 10 pack year's history of smoking followed by 10-20 pack years.

Transglottic laryngeal subsite was the most frequently involved site. Submucosal involvement as well as anterior commissure was commonly involved. Extra laryngeal spread was also assessed in this study and found out that thyroid cartilage penetration was the most common extra laryngeal site involved. In these study majority had no enlarged cervical lymph node and similarly majority had no distance metastasis.

The study showed that the majority of laryngeal cancer patients in this study were male (92.2%) and their mean age 51.5 yrs which was similar with other studies that laryngeal cancer is a disease of elderly men (7,8). The mean age of patients in this study was less than other studies such as those done in India (65yrs) and in Egypt (57.6 yrs) (7, 9).

Hoarseness of voice which was the commonest clinical feature in this study is similar with clinical presentation of laryngeal cancer patients studied in Egypt. These study also showed that shortness of breath was the common clinical manifestations following hoarseness of voice which is a different finding when compared with other studies even though dysphagia and neck swelling is common manifestations in both studies (7).

The study showed that cigarette smoking and alcohol consumption were strongly associated risk factors among laryngeal cancer patients which is similar with other studies done in Kenya and India which indicated that cigarette and alcohol as a strong risk factors among laryngeal cancer patients (9, 10).

The order of magnitude of laryngeal subsite involvement which was transglottic followed by Glottic and supraglottic is different from study done in USA in which glottis subsite was the commonest site followed by supraglottic cancer (6) rather the study matches with other studies done in developing countries where transglottic is commonly involved rather than one site (7).

The extra laryngeal site of spread in this study is thyroid cartilage penetration (73.9%) which is similar with study done by Chen; S.A et al which also states that thyroid cartilage penetration is the most common site of extra laryngeal spread (17).

The Majority of patients with laryngeal cancer in this study did not have lymph node enlargement 55 (67.1%) while only of 22(32.9%) had lymph node enlargement. These could be due to lymph node involvement is related to primary laryngeal supraglottic subsite involvement. These study had similar findings to study done in India that glottis cancer has less involvement of lymph node than supraglottic cancer (19).Considering the level of cervical lymph node involved in this study, level II (45.8%) was the most involved level of cervical lymph node which is similar with study done in India. The second most involved level of cervical lymph node is level I (37.5%) in this study, which is different from the study done in India which states that the second most involved level of cervical lymph node is level III (8).

The enhancement pattern of lymph nodes was only described in 13 cases out of 90 patients in these study and of the described cases a total of 69.3% have heterogeneous enhancement with 30.8% have specifically described as heterogeneous enhancement with central necrosis which is the most specific sign of the metastatic nodal involvement in head and neck cancer according to Saafan, M., et al.

Majority of laryngeal cancer patients had no distance metastasis in this study which could be due to suboptimal imaging modalities used to screen all patients in Ethiopia with cancer as they are screened only with chest X-ray and abdominal US. The patients usually not screened with cross sectional imaging and no nuclear medicine imaging in Ethiopia. With its limitation these study showed that the most involved organ mentioned is lung, which is similar with other studies (11), but it is different from the study done in Egypt, which indicated that liver is the only site of distance metastasis(7).

The most common histologic type identified was squamous cell carcinoma (88.0%) which is similar to the study in India (8).Carcinoma in situ, adenocarcinoma, lymphoma were other histologic types identified in decreasing order their prevalence in this study which are different from the study done in India which indicated verrucous carcinoma, adenocarcinoma, adenoid cystic carcinoma listed from second to fifth by their prevalence (8).

This study assessed the mean time interval between diagnosis to treatment of laryngeal cancer at TASH which is the only center for radiotherapy in Ethiopia and found out that it takes about 7.03 months in average to get radiotherapy .The study also found out 20% of patients did not get radiotherapy which emphasizes that along cue for radiotherapy.

In these study most patients had no laryngoscopic findings documented on the medical record as most of the patients were referred from other hospitals to the only oncology center at TASH but Most patients who had laryngoscopic findings have specified anatomic site of involvement by the laryngeal cancer but submucosal involvement as well as ventricular complex involvement was not reported on laryngoscope. There was only anterior commissure and hypopharyngeal spread was reported in the minority of the cases.

There was poor correlation between laryngoscopy and imaging on the anatomic location of the tumor within the larynx. Most of patients with supraglottic and glottic site involvement on laryngoscope had transglottic site involvement on imaging. The highest rate of misidentification of location of the tumor on laryngoscopy occurred in cases of transglottic laryngeal cancers. Among the 38 cases of transglottic cancers on imaging, only 26.3% were identified as transglottic by laryngoscopy.

6. CONCLUSIONS

- The mean age of presentation in laryngeal cancer 51.5 yrs
- Cigarette smoking and alcohol intake was the two most common risk factors among patients with laryngeal carcinoma
- Transglottic sub-site - the commonest sub-site which was involved and strongly associated with extra laryngeal spread
- Imaging reports were complete and provided detailed additional diagnostic information to stage laryngeal cancer.
- Laryngoscope findings were incomplete

Limitations of the Study

- Lack of mentioning of important risk factor for all study participants
- Lack of laryngoscopic findings on the medical record
- This a retrospective study which didn't follow patients to assess time interval,treatment outcome and survival rate.

Recommendations

- Clinicians should assess important risk factors for all laryngeal cancer patients.
- Standardized imaging and laryngoscope reporting formats and kept on file for all institutions.
- Establish additional oncology center where the patient would get timely management
- Large Scale prospective study should be done to assess treatment out come and survival rate

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Annexes

Annex 1: Written Questionnaire form

1) Age of the patient

2) Sex

1)M

2)F

3) Residence area

1) oromia

2) amhara

3)tigrari

4) SNNP

5) gambella

6)afar

7)Somali

8)benishangul-gumuz

9)harari

10) addisababa&diredawa

4) Any risk factors

1)yes

2)No

if yes

1) Alcohol ingestion,

1) Heavy

2)occasional.....

2) Cigarette smoking

1) none 2) < 10 pack years 3) 10-20 pack years 4) > 20 pack years

3) Chewing chat

4) Concomitant hx of alcohol ingestion and smoking

5) Immune status

1)R VI POS

2) RVI NEG.....

6) Any dietary data available

1)yes

2) No

If yes

1) Red meat based diet

2)vegetable based diet

5 Clinical presentations

1)Hoarseness of voice,

2) Dysphagia,

3) Neck swelling,

4) Neck pain,

5) others, please specify

Imaging findings

5) Anatomical sites of involvement

- 1) glottic,
- 2) supraglottic,
- 3) subglottic,
- 4) transglottic

site of involvement

1) unilateral if yes 1) R 2) L

2) bilateral

6) Involvement of ventricular complex,

- 1) yes
- 2) no

7) Involvement of sub mucosal space, if yes

- 1) preglottic space
- 2) paraglottic space

8) Anterior vocal commissure involvement

- 1) yes
- 2) No

9) extra laryngeal spread, site of extension

- 1) Thyroid cartilage penetration
- 2) Widening of thyroid , arytenoid space/ arytenoid destruction
- 3) Base of tongue involvement, thyrohyoid penetration, thyroid notch penetration
- 4) Conuselasticus penetration
- 5) hypopharyngeal extension
- 6) proximal esophagus involvement

- 13) Endoscopic findings
- 14) Endoscopic diagnosis
- 15) Endoscopic differential diagnosis if given
- 16) Imaging diagnosis
 - 16.1) imaging DDX if any given
- 17) Staging at the time of diagnosis
 - 17.1) TNM
 - 17.2) stage
 - 1) I 2) II 3) III 4) IV A 5) IVB 6) IVC
- 18) Histopathologic result
 - 18.1) Histopathologic diagnosis
- 19) Time interval for the treatment after diagnosis is made