ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCES

DEPARTMENT OF CLINICAL ONCOLOGY

Demography and Clinico-pathologic Pattern of Laryngeal Cancer at Tikur Anbessa Specialized Hospital: A Retrospective Cross Sectional Study

By: Natenael Eshetu (MD)

April, 2021

Addis Ababa, Ethiopia

ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCES

DEPARTMENT OF CLINICAL ONCOLOGY

Demography and Clinico-pathologic Pattern of Laryngeal Cancer at Tikur Anbessa Specialized Hospital: A Retrospective Cross sectional Study

Principal investigator: Natenael Eshetu (MD)

Advisors: Ayenalem Abreha (MD, Internist, Consultant clinical oncologist)

Ahmedin Jemal (DVM, PhD)

Dr.Eva Johanna Kantelhardt

A Thesis Paper Submitted to the Department of Clinical Oncology of Addis Ababa University in Partial Fulfillment of the Requirements for the Specialization Certificate in Clinical Oncology

April, 2021

Addis Ababa, Ethiopia

Acknowledgments

First of all, I would like to thank the Almighty God, who gave me the commitment and tolerance to pass through various obstacles and come up to the accomplishment of this research work. I am deeply indebted to my advisor, Dr Ayenalem Abreha (MD, Internist, Clinical oncologist), from Addis Ababa University, College of Health Sciences, Department of Clinical Oncology, Ahmedin Jemal (DVM,PhD) and Dr. Eva Johanna Kantelhardt for their understanding, answering my frequent questions without any hesitation, for their countless suggestions, assistance, kindness and invaluable advice.

Abstract

Background: Malignant laryngeal tumors are uncommon, yet invariably fatal neoplasms of the larynx. Late presentation of the disease may worsen management outcomes. Although the incidence of malignant tumors of the larynx is increasing in developing countries, like Ethiopia, there is a lack of evidence regarding the overall profile of laryngeal cancers in Ethiopia.

Objectives: To assess the epidemiologic, clinico-histo-pathologic characteristics of laryngeal patients attending at oncology department of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia.

Methods: A 3-year retrospective cross-sectional review of medical records of patients managed for malignant laryngeal tumors at the oncology department of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, was performed. The demographic, clinical & histopathologic characteristics of participants were computed by using descriptive statistics (mean, percentage, frequencies, and standard deviation). Finally, the study finding was presented using diagrams, tables, and figures.

Results: Most of the laryngeal cancer patients who attended the oncology unit of Tikur Anbessa Specialized Hospital are elderly males, with a male to female ratio of 5.1:1, and the sixth decade being the most affected age stratum. The most common presenting symptom was dysphonia. The majority (88.8%) of patients presented with late stage of the disease and squamous cell carcinoma is by far the most common histopathology, occurring in 98.8% of the patients.

Conclusion: Elderly men are the most affected age group of laryngeal neoplasms. Late disease presentation observed in the patients can lead to poor management outcomes and limited management options. Health education of the community on early features of laryngeal cancer, early symptom detection by clinicians, and policies targeted at reducing cigarette smoking and alcohol consumption is recommended.

Acronyms/Abbreviations

CT	Computed Tomography
ECOG	Eastern Cooperative Oncology Group
GLOBOCAN	Global Burden of Cancer Study
HNC	Head and Neck Cancers
HPV	Human Papillomavirus
LC	Laryngeal cancer
NIAAA	National Institute on Alcohol Abuse and Alcoholism
SCC	Squamous Cell Carcinoma
SNNPR	Southern Nations, Nationalities, and People's Region
TASH	Tikur Anbessa Specialized Hospital
TNM	Tumor, Nodes, Metastasis

Table of Contents

List of tables

List of figures

1. Introduction

1.1 Background

The world is experiencing a rapidly growing burden of cancer-related morbidity and mortality. Worldwide, a sizable portion of the cancer burden is elucidated by head and neck cancers, which encompass a variety of malignant neoplasms occurring in the nasal cavities, paranasal sinuses, nasopharynx, hypopharynx, oropharynx, ear, scalp, oral cavity, and salivary glands [1]. Altogether, they constitute a major public health concern throughout the world in terms of morbidity and mortality [2].Head and neck cancers (HNCs) have been reported to be the tenth most common cancer worldwide [1,2], constituting 5–50 % of all cancers [3,4]. At present, more than 650,000 new cases of head and neck cancer are diagnosed each year worldwide [5], and their incidence appears to be increasing in developing countries [6]. Correspondingly, the incidence, prevalence and mortality of laryngeal cancer (LC) are estimated at 2.76 cases/year per 100,000 inhabitants, 14.33 cases/year per 100,000 inhabitants and 1.66 deaths/year per 100,000 inhabitants, respectively, averaging 3.28 million disability-adjusted life year each year [7]. Additionally, while annual deaths in sub-Saharan Africa resulting from communicable diseases like HIV/AIDS are gradually declining, cancer deaths are projected to increase by 85% between 2008 and 2030 [8].

In simple terms, laryngeal cancers represent those malignant neoplasms that originate from any anatomical site of the larynx, which can metastazsize to any nearby structure. They are five times common in men than in women [9]. A number of risk factors including alcohol consumption and cigarrete smoking have been positively correlated with LC either as a cofactor or as an independent factor [10,11]. These neoplasms assume multiple histopathologic characteristics, with squamous cell carcinoma (SCC) being the most common variant. They are commonly staged as per the tumour–node–metastasis (TNM) system [12]. Regarding prognosis, it was observed that about 60 per cent of patients in affluent countries survive more than than five years and more than 50 per cent survive ten years following a diagnosis of laryngeal cancer[13].

Several studies in resource-poor countries noted late presentations of these neoplasms commonly, resulting in poorer prognosis and compromised health-related quality of life, especially when coupled with host related factors [14-16]. Clinically, although laryngeal cancers oftentimes present with laryngeal symptoms, they can manifest with varying

symptoms, which makes a good knowledge of the disease manifestation and a high degree of suspicion necessary to consider them differential diagnosis [17].

A recent epidemiological review in head and neck squamous cell carcinoma in sub-Saharan Africa revealed that laryngeal SCC alone account for 4.5% of all HNC patients, making it one of the most common cancer in the head and neck [18]. By the same token, although the cancer burden in the country may be significantly underestimated, more than 524 new cases of laryngeal neoplasms were extrapolated to be diagnosed each year in Ethiopia [19] indicating that these neoplasms are among the most common head and neck cancers occurring in the country. Unfortunately, owing to multiple socioeconomic barriers to cancer care such as little awareness, improper understanding of the disease, associated stigma, a sense of hopelessness, and the lengthy process of referral to the country's only specialized center (Tikur Anbessa Specialized Hospital), patients often present with advanced stages of cancer [20].

In the same way, there is no reliable cancer registry and data availability is scanty, particularly given the fact that inaccessible cancers, such as laryngeal cancers, are likely to be under-diagnosed because of their predilection of non-specific presentation and poor availability of necessary imaging technologies in developing countries like Ethiopia [21]. Thus,even though laryngeal malignancies appear to constitute a significant burden of HNC morbidity and mortality, and the fact that the pattern of cancer varies with factors such as geographical location and people's lifestyle, there is no published study that examines the demographic, clinico-histopathologic profile of laryngeal CA patients in the Ethiopian context. Thus, this study is aimed to assess the clinical and epidemiological pattern of laryngeal cancer patients at Tikur Anbessa Specialized Hospital (TASH), Addis Ababa, Ethiopia.

1.2. Statement of the problem

In general, cancers are the major cause of death in the majority of the developed countries and many developing countries [22]. In 2018, there were 81 806 male deaths and 12 965 female deaths worldwide from larynx cancer [14]. Recently, reports showed that there is a significant decrease in the incidence of laryngeal cancer in European regions [23] with even better records in mortality rates. In contrast, cancer accounts for about 5.8% of total national mortality in Ethiopia, with an annual mortality estimate of over 51,865. Although meticulous population-based data that accurately depict the situation on the ground do not exist in the country except for Addis Ababa, it is estimated that the annual incidence of cancer is around 77, 352 cases [19]. In 2018, a the available population-based cancer registry in Ethiopia revealed an age-

adjusted incidence of laryngeal cancer of 0.7 in males and 0.1 in females [24]. This undoubtedly poses much suffering and financial loss to the cancer patients, particularly in patients living in countries with such limited therapeutic options.

In reference to the histopathologic features of the tumor, the anatomical site of involvement and stage of the disease appear to play more roles in the prognosis of the disease. Unlike laryngeal tumours involving the glottis, which tend to result in a marked voice change as a result of disruption of the normal functioning of the vocal cords, supra- or subglottic tumours disturb the voice only by the time they have spread to the vocal cords and normally present with hoarseness in advanced stages. Therefore, the latter ones are commonly associated with poorer prognosis if they present with hoarseness of voice [25,26]. Again, in contrast to glottic tumors, supraglottic laryngeal lesions can present with earlier metastatic cervical lymphadenopathy without laryngeal symptoms because of the rich lymphatic supply of the larynx and the vocal cords themselves are poorly supplied by lymphatics.Thus, supraglottic cancers have worse prognosis while the glottic ones have the better prognosis [26].

The rise in cancer burden in head and neck tumors in general and laryngeal cancers in Ethiopian setting, in particular, has been documented and published by the National Cancer Registry, but it is not thought to depict the accurate situation on the ground because cancer diagnosis and notification from health institutions are not as thorough as desirable. This increase has not been captured in local studies especially concerning head and neck cancers in laryngeal carcinomas. Moreover, although a great deal of head and neck cancer patients are usually offered palliative and curative therapy by a handful of clinical oncologists at tertiary hospital, there is no well-established organized approach that focuses on the varying presentations of laryngeal neoplasms.

Low awareness of the scale of the cancer burden among local and international policymakers contributes to the inadequate attention directed towards the disease in Ethiopia and other African countries. As a result, a significant portion of laryngeal cancer patients tends to seek appropriate medical care only by their advanced stages, which makes them more susceptible to death as advanced stages can affect vital functions of life including breathing, mastication, and swallowing [4].

These evidences underline the need to assess the contextual situation and characteristics of patients with laryngeal neoplasms to have insight about the burden of the disease. So, the

purpose of this study is to investigate the overall pattern of laryngeal cancers at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia.

1.3 Significance of the study

The National Health Sector Transformation Plan (HSTP) 2015/16 in line with the country's second growth and transformation plan, has set ambitious goals to improve equity, coverage, and utilization of essential health services, improve quality of healthcare, and enhance the implementation capacity of the health sector at all levels of the system. The plan outlines interventions to reduce the burden of cancer through changes in lifestyle, primary prevention, screening and early diagnosis, appropriate follow-up, treatment, and provision of palliative care. In line with this, cognizance of the prominent characteristics of head and neck cancer (particularly laryngeal cancer) patients will greatly help stakeholders in beating cancer and salvage the overall health cost incurred by these neoplasms. Comprehensive knowledge of laryngeal cancer characteristics will be of irreplaceable help in the early detection of these potentially fatal HNCs and allow oncology practitioners to make better clinical decisions for the best end of clients. More importantly, recognizing the overall pattern of laryngeal cancer will be highly useful for other clinicians such as ENT-otolaryngology physicians in early detection of such tumors during their routine evaluation of patients with head and neck complaints.

Furthermore, it will guide health policymakers and other concerned stakeholders to devise strategic programs on inculcating evidence-based interventional protocol in candidate populations. Hence, the data collected from this study can be a good input to the country's endeavor in handling the several formidable tasks: first, accurately measuring the scale of the national cancer burden and characterizing existing preventive, curative, and palliative care services available at each tier of the health system; second, identifying challenges to the improvement of cancer reporting and specialized oncology services; and finally, designing feasible interventions applicable in a low resource setting.

Finally, the findings obtained from this study will serve as a baseline for other researchers for further in-depth studies.

2. Literature Review

2.1 Demographic characteristics of laryngeal cancer patients

Laryngeal cancer, one of the most common cancers of the aerodigestive track, accounts for 20% of all head and neck cancers. It has varied demographic distribution as a result of different factors. Factors implicated to be associated with the disease. The factors include tobacco smoking, alcohol consumption, radiation, asbestos, and several occupational factors are implicated [27].

In a nation-wide study from 1980 to 2014 done in Denmark, a total of 8748 patients (82% males) were included. The study revealed the median age at diagnosis was 60 years, the range being 18–101 years [23]. A recent study done in Kenya revealed 42 years was the lowest age for laryngeal cancer cases [28]. On the other hand, only a single study from Nigeria reported the larynx to be affected by squamous cell carcinomas in the pediatric population [5], highlighting that laryngeal cancers are too rare in pediatric patients

In 2016, a cross sectional study was carried out in the Regional Cancer Centre, Imphal, Manipur, India to determine the risk factors, clinical symptoms and patterns of spread in laryngeal cancer. This retrospective epidemiological study involved onne hundred and sixteen laryngeal cancer patients showed that the median age at presentation was 65 years. The male to female ratio was 5.4:1. The study added heavy smoking and tobacco chewing were associated in 91.4% and 33.6% of the Indian patients, respectively [29].

In a case control Serbian study that assessed 100 histologically proven laryngeal cancer patients, Arsenijevic S and his colleagues noted that people of lower education level and poor socioeconomic status had an increased risk of getting laryngeal cancer [30]. This study capitalized the previous study of Kleinsasser who stressed that laryngeal cancer is more prevalent among the lower socio-economic class in which it is diagnosed at more advanced stages and the frequency of the disease increased along with age in both sexes [31].

In Sudan, a prospective, cross sectional study involving 82 patients was conducted recently. The study reported that history of smoking was the commonest predisposing factor for laryngeal cancer as it was noted in 75.6% of the patients. Moreover, the study observed the disease was common in people aging older than 60 years, accounting about 56.1% of the studied patients [32].

In 2013, a matched case control study done in Kenya confirmed that cigarette smoking and alcohol ingestion were shown to be strong risk factors for the development of late-stage and poorly differentiated laryngeal squamous cell carcinoma [28]. Additionally, similar to the prior Kenyan study, another prospective study, cross sectional that investigated 82 Sudanese patients who were treated at Khartoum state hospitals noted male preponderance, with around 96% of the cases being males [32].

2.2 Clinical features of laryngeal cancer patients

The clinical manifestation of laryngeal cancers is extremely variable and depends on the anatomic location and size of the primary tumor [12]. Hence, laryngeal cancers can present with a range of symptoms, with significant variation with the site of involvement, stage of the disease, and demographic factors. Among the symptoms, hoarseness of voice is the main presenting feature. Dyspnoea and stridor are late symptoms and usually indicate an advanced tumor. Although not so often encountered, pain in the throat is one of the symptoms experienced by laryngeal cancer patients [27].

Tumors of the glottis, for example, typically present at an early stage as they manifest as hoarseness. In contrast to this, tumors affecting the supraglottis are likely to present later with symptoms of pain, hoarseness, or swallowing difficulty [12]. However, it is not uncommon for patients presenting with laryngeal cancer to delay seeking medical advice on developing 'early' symptoms, only to present at a much later stage with symptoms of pain, swallowing difficulty, a palpable neck mass, or even, in extreme cases, with airway compromise [12]. These patients with advanced disease stages usually present with progressive hoarseness and difficulty in breathing, pain, dysphagia, neck swelling, cachexia, and fetor oris as it was noted in Nigerian studies [33]. Dysphagia indicates pharyngeal invasion, and neck swelling indicates extra laryngeal extension or lymph node involvement [27].

In an Iranian study that included 42 cases with laryngeal malignancies, it was observed that the main clinical manifestations were dysphonia, dysphagia, weight loss, dyspnea, laryngalgia, cervical lymphadenitis, stridor, hemoptysis, and coughing [34]. A similar Sudanese study showed that all of the studied patients presented with hoarseness of voice, and only 20% of them presented with stridor[32].

2.3 Histopathologic characteristics of laryngeal cancer patients

Squamous cell carcinomas of the larynx are by far the most common histological type, comprising 95% of laryngeal cancers. The remaining rare types of LCs arise from the other

types of cells within the larynx including adenocarcinoma. For example, in the recent study done in Sudan, 93.9% had a squamous cell carcinoma of the larynx at the glottis region except for one patient who had rare histopathology: botryoid sarcoma of the larynx, an embryonic type of sarcoma normally found in children at age of 3-8 years and rarely can affects adult male and larynx [32].

In an 11-year retrospective review of medical records of patients managed for malignant laryngeal tumor at the University College Hospital, Ibadan, Nigeria , it was found that the most common clinical symptoms patients presented with were hoarseness od voice, cough, and shortness of breath. Transglottis (91.8%) was the most common anatomic tumor location while squamous cell carcinoma was the most commonly identified histologic type, accounting for 96.9% of the cases [35].

A study done in Ghana in 2003 shows that squamous cell carcinoma was the most common histopathology accounting for 88.7%, followed by adenocarcinoma, which constituted 1.7%, and the other types comprise about 9.6% [36]. Similarly, a study from a study done in Tanzania showed that squamous cell carcinoma was the most common histolgy by 98.6% of all cell types compared to adenocarcinoma which was 1.4% [15].

Furthermore, the previous study done in Tanzania revealed that glottis is the most common anatomical site involved by laryngeal cancer (66.7%), while 33.3% had supraglottic tumor involvement and there was no any patient who presented with subglottic tumor [15]. Another report from Iranian population showed that squamous cell carcinoma of larynx affected the supraglottis in 38% of the cases, the glottis in 42.8%, and the remaining 19% being of unknown location [34].

Laryngeal tumours usually metastasize to the upper deep cervical lymph nodes, but supraglottic tumours may cause bilateral nodes, and some subglottic tumours may spread to the upper mediastinal nodes [27]. Owing to poverty-related factors, it was shown that in developing countries such as Kenya, majority of laryngeal cancer patients seek medical help by stage 3 and 4 when the disease has advanced or metastasized to distant parts pf the body [16,28]. Another similar finding was noted by the previous Nigerian study which showed 92.8% patients presented in advanced disease stage [35].

2.4 Assessment and staging

As with all head and neck cancers, diagnosis of laryngeal cancer relies initially on good history taking and clinical examination in the clinic. Laryngeal cancers are, in most cases, obvious following inspection of the larynx with a fibreoptic laryngoscope in the outpatient department. Initial assessment of the tumour stage relies on imaging. Whilst exact protocols vary according to local imaging preferences, it is typical for patients suspected of having laryngeal cancer to undergo either magnetic resonance imaging or computed tomography (CT) of the head and neck and CT scan of the thorax and upper abdomen. The exception to this is in patients presenting with the early stage, T1 lesions of the glottis without anterior commissure involvement, where imaging is unhelpful [27].

Definitive diagnosis is achieved by histological examination of a tissue biopsy, obtained usually at the time of a general anaesthetic endoscopic examination of the larynx, pharynx and upper oesophagus. The examination under anaesthesia is extremely important for staging and should routinely involve inspection with rigid (plane 0° and angled 30° and/or 70°) fibreoptic endoscopes. The aggregate information provided by the imaging and the endoscopic examination facilitates the staging of the tumour according to the tumour–node–metastasis (TNM) system. It is by recourse to the TNM stage of the tumour, in addition to the general fitness of the patient, that treatment decisions are ultimately made [12,27].

Therefore, it can be inferred from the aforementioned review that patient factors such as lifestyle factors, environmental factors and smoking were documented to be predominant risk factors in different settings. And these malignant neoplasms of the larynx are far more common in older men. The clinical presentation of laryngeal cancers is highly variable, mainly depending on the site and size of the primary tumor.

3. Objectives

3.1 General Objective

- To assess the epidemiological and clinical patterns of laryngeal cancer patients attending at oncology department of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia

3.2 Specific objectives

- To describe the demographic characteristics of laryngeal cancer patients attending at oncology department of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia
- To assess the clinical features of patients with laryngeal cancer patients attending at oncology department of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia
- To describe the histopathololologic tumor characteristics of laryngeal cancer patients attending at oncology department of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia

4. Methods and Materials

4.1 Study design

An institution-based cross sectional, retrospective study design was conducted to assess the epidemiological and clinical patterns of laryngeal cancer attending Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia

4.2 Study area and period

The study was conducted at oncology department of Tikur Anbessa Specialized Hospital, starting from October 1st, 2020 to January 31st, 2021. Tikur Anbessa Specialized Hospital (TASH) is a tertiary hospital located in Addis Ababa which is a capital city of the country. It is the largest & oldest public hospital of the country providing high level of clinical care for millions of people and training to health science students from different parts of the country and from the Horn of Africa. The hospital has the leading oncology center in the country, providing tertiary specialist care for a catchment population of approximately 100 million people from different parts of the country with a range of malignancies. It provides palliative and curative therapy for all patients with histopathologically-proven a range of cancers, including head and neck cancers.

The Clinical Oncology Department of TASH is among the most commonly visited units in the hospital. On average, at least 420 head and neck tumors, and more than 50 laryngeal cancer patients are evaluated annually in this facility [37]. The department caters oncologic service to a wide range of population with varying demographic and clinical characteristics, at which this study is focused.

4.3 Source population

The source population for this study was all patients with histologically-confirmed primary laryngeal cancer attending Oncology unit of the hospital for therapeutic reasons.

4.4 Study population

The study population for this study was all eligible laryngeal cancer patients visiting Oncology unit during the study period for therapeutic reasons.

4.5 Inclusion and exclusion criteria

4.5.1 Inclusion criteria

- All patients with histologically-confirmed laryngeal cancer regardless of their stage and those who have complete medical record

4.5.2 Exclusion criteria

- Patient who have preceding other symptomatic oropharyngeal or laryngeal anomaly

- Reports with a doubtful or controversial diagnosis

- Medical charts that can't be retrieved

- Incomplete medical records

4.6 Sample size determination

All medical records of laryngeal cancer patients were reviewed

4.7 Variables in the study

- Demographic characteristics such as sex, age, residence, smoking and alcohol ingestion history
- Clinical profile of laryngeal cancer patients
- Tumor characteristics and stage of the disease

4.8 Operational definition

- **ECOG performance status** – it is scale used to assess how patient's disease is progressing, assess how the disease affects the daily living abilities of the patient and determine appropriate treatment and prognosis and is developed by Eastern Cooperative Oncology Group
- **Cancer stage** – the extent or severity of spread of the cancer based on the American Joint Committee on Cancer (AJCC) TNM system. T describes size of the tumor and spread to nearby tissue, N describes spread of cancer to nearby lymph nodes, M explains the distant spread to other parts of the body
- **Supraglottic** – anatomic region of the larynx that includes posterior surface of the epiglottis, arytenoid (right and left), ventricular bands (right and left), and Ventricular cavities (right arid left), aryepiglotic folds.
- **Glottic** – anatomic region of the larynx that includes true vocal cords (right and left) & anterior commissure.
- **Subglottic** – anatomic region of the larynx that includes right and left wall of the subglottis which is located below the vocal cord.
- **Tumor grade** – a system used to classify cancer cells in terms of how abnormal they look under the microscope and how quickly the tumor is likely to grow and spread.

4.9 Data collection tools and techniques

Data was collected from Oncology unit of TASH using a structured checklist containing closed and open ended questions specifically designed for the study. The tool was prepared by reviewing related literatures done in other areas [19]. The data was collected from the medical chart of each participant by two trained health professionals, under close supervision and facilitation by the principal investigator. Each day, the collected data was checked for accuracy and completeness.

4.10 Data quality management

An English version of the checklist was used to collect data. Brief training for the data collectors (two health professionals) about the process of data collection was given before the process of data collection. Close supervision was maintained during data collection and filled checklists were double-checked daily for consistency and completeness by the data collectors and principal investigator.

4.11 Methods of data analysis

Data entering, coding and clearing was performed using Epi-info version 7.0 and the analysis was done using SPSS version 26. Frequency and cross tabulation was used to check for missed value and variables. The demographic, clinical & histopathologic characteristics of patients were computed by using descriptive statistics such as mean, percentage, frequencies, and standard deviation. Finally, the study finding was presented using diagrams, tables and figures.

4.12 Ethical Considerations

Ethical clearance was obtained from Ethical Review Committee of Clinical Oncology Department of the college. Permission letter was submitted to the medical record unit from the Clinical Oncology Department & Research Directorate to retrieve and review the charts. After this, introduction & familiarization of the data collectors with team unit was secured. The questionnaires were kept anonymous and confidential.

4.13 Dissemination of the study findings

The findings of this study will be submitted to Department of Clinical Oncology of College of Health Sciences, Addis Ababa University as a partial fulfillment of specialty degree in Clinical Oncology. The outcome of this study will be presented at annual oncologic conference. Furthermore, as the results are assumed to be inputs for the health policy makers, effort will be exerted to notify the Federal Ministry of Health (FMoH) on the gross picture of the study

findings. Finally, the manuscript will be submitted to reputable scientific journals for possible publication.

5. Results

5.1 Socio-demographic characteristics of patients

This study included data derived from 116 laryngeal cancer patients who attended Oncologic clinic of TASH, after excluding 8 patients who didn't fulfill the inclusion criteria. Among the studied patients, most (97) were males and the remaining 19 were females. And participants' age ranged from 17 to 85 with a mean age of 53.7 ±13.6 years and nearly one-third (36) of them being in their sixth decade of life. Majority (98; 84.5%) of the patients were documented to be married while the remaining ones were reported to be either single, divorced or widowed (Table 1).

With regard to religious affiliation, a little more than half (66) of the subjects were Orthodox Christians while Islam and Protestant Christianity were documented in 34 (13.8%) and 16 (29.3%) of the patients, respectively. Concerning the residence, nearly one-third (38) of the patients claimed to be dwellers of Oromia region while one-fourth (30) of all patients reported to be residents of the capital, Addis Ababa. The remaining more than one-fourth of the patients came from different regions of the country, as detailed in Table 1.

Regarding occupation, close to two-fifths (45) of the patients were self-employed, whereas 34.5% (40) were employed and 26.7% (31) claimed not to be employed by the time of visiting the clinic for medical care.

With respect to history of substance use, a little less than half of the patients (51) were cigarette smokers before being diagnosed to have laryngeal cancer, all of whom reported to be active smokers while the rest 65(56%) of the patient denied history of any form of cigarette smoking upon questioning by their respective clinicians. Similarly, among all the studied patients, a little less than two-thirds (75) of the patients claimed not to take alcoholic beverages regularly while the rest 41 (35.2%) classified themselves as alcohol drinkers.

Table 1: Socio-demographic characteristics of laryngeal cancer patients attending Oncology clinic of TASH, AA, Ethiopia, from Sep 1st, 2017 to Aug 31st, 2020

Variable (n=116)		Frequency	Percent (%)
Sex	Male	97	83.6
	Female	19	16.4
Age strata	<40 years	16	13.8
	40-49 years	21	18.1
	50-59 years	36	31
	60-69 years	28	24.2
	≥70 years	15	12.9
Marital status	Married	98	84.5
	Single	11	9.5
	Widowed	4	3.4
	Divorced	3	2.6
Religion	Orthodox	66	56.9
	Muslim	34	13.8
	Protestant	16	29.3
Residence	Oromia	38	32.8
	Addis Ababa	30	25.9
	Amhara	22	19.0
	SNNPR	15	12.9
	Harari	4	3.4
	Tigrai	3	2.6
	Afar	2	1.7
	Somali	1	0.9
	Gambella	1	0.9
Occupation	Self-employed	45	38.8
	Employed	40	34.5
	Unemployed	31	26.7
Smoking	Yes*	51	44
	No	65	56
Alcohol	Yes	41	35.3
	No	75	64.7

*all of them mentioned to be active smokers and no any passive smoker.

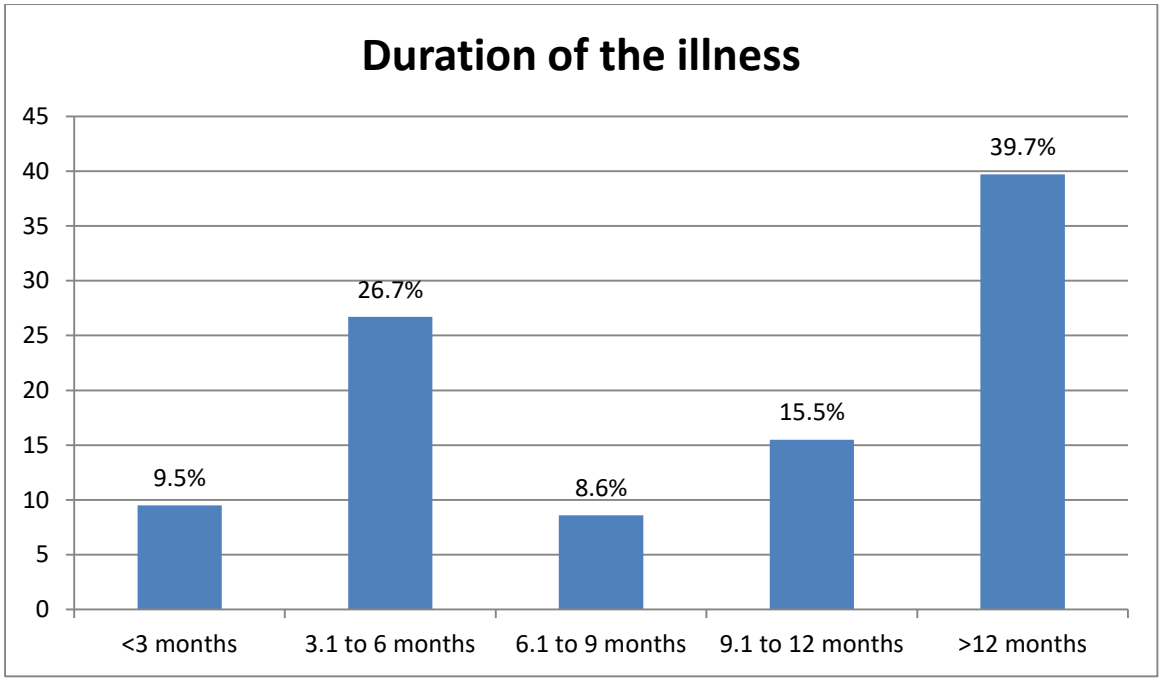

Figure 1: Duration of illness of laryngeal cancer patients attending Oncology clinic of TASH, AA, Ethiopia, from Sep 1st, 2017 to Aug 31st, 2020

Finally, considering the duration of the illness as reported by the patients, nearly two-fifths (46) of the patients stated to suffer from the clinical complaints for more than a year by the time they were clerked at the oncology clinic. Likewise, 26.7% (31) of the patients reported their duration of illness to be in the range of 3.1 to 6 months while 15.5% (18) had been described to be ill for 9.1 to 12 months, by the time of their first visit to the oncology OPD (Fig. 1).

5.2 Clinical profile of patients

Clinical data of the studied subjects' medical records reveals that hoarseness of voice is the most common presenting symptom in patients with laryngeal cancer as it was documented in 112 (96.6%) of the patients. The next most common symptoms of laryngeal malignancy in the studied patients were shortness of breath (69.8%), neck swelling (36.2%), dysphagia (28.4%), cough (19%) and throat pain (6). On the other hand, referred otalgia, choking, significant weight loss, and halitosis (fetor oris) were mentioned in less than 10% of all the studied patients. Lastly, a little more than half (61) of the studied patients were noted to have undergo tracheostomy at some point as a result of progressive shortness of breath to establish the airway (Table 2).

Table 2: Clinical profile of laryngeal cancer patients attending Oncology clinic of TASH, AA, Ethiopia, from Sep 1st, 2017 to Aug 31st, 2020

Clinical feature	Frequency	Percent
Hoarseness	112	96.6
Dyspnea	81	69.8
Neck swelling	42	36.2
Dysphagia	33	28.4
Cough	22	19
Throat soreness	7	6
Otalgia	2	1.7
Choking	2	1.7
Unplanned, significant weight loss	2	1.7
Halitosis	0	0
Tracheostomy	61	52.6

Moreover, with respect to ECOG performance status, the current study showed that majority (87; 75%) of the patients belonged the ECOG performance category 1. Besides, a little more than one-fifth (25) of the patients were classified as ECOG performance category 2 while the remaining 4 were categorized to either ECOG 0 or 3 category (Fig 2).

5.3 Histo-pathologic tumor characteristics

Among all the reviewed medical records of the 116 studied patients, squamous cell carcinoma was by far the most common histologic variant as it was noted in 114 (98.8%) of the studied patients whereas each adenocarcinoma and lymphoepithelioma accounted for 0.9% of the cases. With regard to the anatomical site of the lesion, glottic was the most common site (44.8%), followed by transglottic and supraglottic, which were documented in 30.2% and19.8 % of the studied patients. Subglottic laryngeal cancer was observed in only 6 (5.2%) of the patients, as summarized in Table 3.

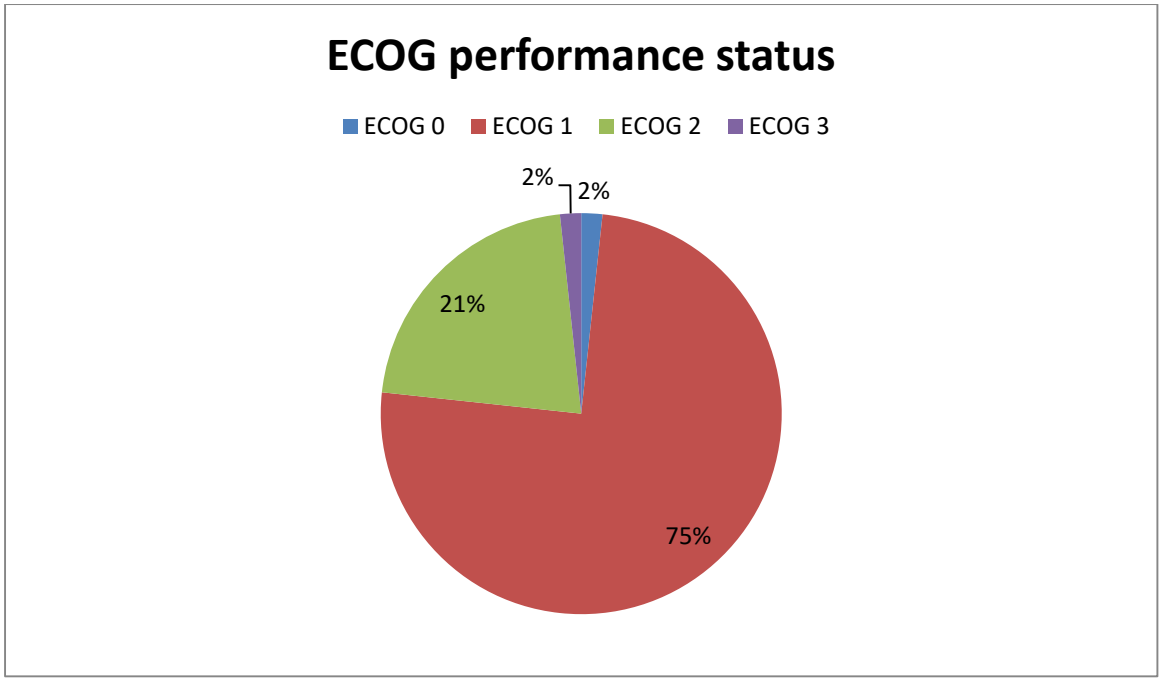

Figure 2: ECOG performance status of laryngeal cancer patients attending Oncology clinic of TASH, AA, Ethiopia, from Sep 1st, 2017 to Aug 31st, 2020

Table 3: Histo-pathologic characteristics of laryngeal cancer patients attending Oncology clinic of TASH, AA, Ethiopia, from Sep 1st, 2017 to Aug 31st, 2020

Variable (n=116)		Frequency	Percent (%)
Type	SCC	114	98.3
	Adenocarcinoma	1	0.9
	Lymphoepithelioma	1	0.9
Site	Supraglottic	23	19.8
	Glottic	52	44.8
	Subglottic	6	5.2
	Transglottic	35	30.2
Clinical stage	I	4	3.4
	II	9	7.8
	III	28	24.1
	IVA	59	50.9
	IVB	11	9.5
	IVC	5	4.3
Histologic grade	Grade cannot be assessed (GX)	56	48.3
	Well differentiated (G1)	43	37.1
	Moderately differentiated (G2)	9	7.8
	Poorly differentiated (G3)	6	5.2
	Undifferentiated (G4)	2	1.7

Furthermore, stage-wise analysis shows that nearly two-thirds (75) of the studied patients were diagnosed to have laryngeal cancer by the time the cancer reached an advanced clinical stage with stage IVA, IVB, and IVC accounting for 59 (50.9%), 11 (9.5%) and 5 (4.3%), respectively. Besides, about one-fourth (28) of the patients were diagnosed at clinical stage of III while only 13 (11.2%) of the patients were staged to either stage I or II based on the American Joint Committee on Cancer (AJCC) TNM system by the time of diagnosis. Additionally, the most common histologic grading report was GX (56; 49.3%), which was followed by well differentiated (G1), which was documented in in 43 (37.1%) of the patients. And the histologic grade of 17 (14.7%) patients ranged from moderately differentiated to totally undifferentiated, as detailed in Table 3.

6. Discussion

In this study 116 laryngeal cancer patients were studied and it was found that 83.6% were males, making a male to female ratio of 5.1:1, suggesting that laryngeal cancer has a noticeable propensity of attacking male population. This corresponds to the study done by Menach and colleagues to assess the demographic and histology pattern of laryngeal squamous cell carcinoma at Kenyatta National Hospital, Kenya, who recorded that 96% of all patients were males while only 4% were females [28]. A similar five-year review of laryngeal cancer patients that aimed to determine the risk factors, clinical symptoms and patterns of spread of the disease in Northeastern India demonstrated a male to female ratio of 5.4:1 [29]. Another 10 year-review Nigerian study showed a male to female ratio of 5.2:1 [16]. This can be explained partly by the fact that males tend to experience more risky behaviors like excessive alcohol consumption and cigarette smoking which lead to laryngeal cancer development compared to females.

In this study, the youngest patient aged 17 years while the oldest one was 85 years with mean age of 53.7±13.6 years: the sixth decade being the most affected age group. This in concordance with the finding by the previous Indian study where the median age at presentation was 65 years, the range was 37 – 85 years, and the seventh decade being the most affected age group [29]. Another retrospective carried out among black African patients with laryngeal carcinomas visiting hospitals of Nigeria observed constituted a mean age of 56 ±6.8 years [16]. The results obtained confirm that laryngeal cancer is more common in elderly population compared to other age groups and this can be explained by the fact that with aging, it is likely for the immune system and genetic repair mechanism to weaken.

In the current study, a little less than half of the patients were active cigarette smokers before development of the disease although no record of passive smoking was noted. Also, a little more than one-third of the patients were observed to be alcoholics. This is in line with multiple previous studies including the one done in Kenya which observed that 66% of patients with laryngeal cancer were cigarette smokers [28]. Although these findings per se cannot confirm the strong dose–response and time-response correlation between smoking and laryngeal cancer noted in certain studies [38], they may imply that longer duration and greater intensity of cigarette smoking portend a great risk for laryngeal SCC as shown in studies performed worldwide [39].

Moreover, a little more than one-fourth of the patients confessed both to ingest alcoholic beverages and smoke cigarette. These results were consistent with the results of the large scale

analysis done by Hashibe and others in 2009 to determine the interaction between tobacco and alcohol ingestion as risk factors for head and neck cancer which demonstrated a greater than multiplicative joint effect (synergistic effect) of tobacco smoking and alcohol consumption for head and neck cancer risk [40].

The present study revealed that hoarseness of voice was the most common presenting symptom in patients with laryngeal cancer, and followed by shortness of breath, neck swelling, dysphagia, cough and throat pain. These results were agreement with the results of the study done by Latifi and others in 2012 on Iranian patients with laryngeal cancer, which documented that dysphonia was the most common clinical symptom, and the other major clinical manifestations of the patients were dysphagia, weight loss, dyspnea, soreness, stridor, hemoptysis, and coughing [34]. A similar pattern was also documented in the prior Kenyan and Ghanaian studies [28,36]. At this juncture, it should be pointed out that some constitutional symptoms such as weight loss and depressed appetite might have been left undocumented in patients' medical charts.

However, this study found that majority of the patients was seen after 6 months of onset of first symptoms. The delayed reporting may probably be due to lack of awareness by patients and the fact that significant portion of the studied population were out of the capital where Oncologic services are scarce, making them prone to the long waiting list. Moreover, it can be due to the evidence that some primary care physicians may lack the knowledge that hoarseness of voice which does not resolve after a couple of weeks of treatment may signify a possible neoplasm of the larynx. The late reporting may also be due to alternative local medical therapy for hoarseness which is well supported by patients; these patients only report to the hospital when there is difficulty in breathing (a sign of advanced laryngeal cancer)[36]. Moreover, the delay can result from the impression that smokers may even conceive that the change in voice is merely due to their long standing history of smoking. This situation is unfortunate as most laryngeal cancers are curable when detected early.

Regarding the anatomical site of the lesion, this study has found that glottic and transglottic was the most common site, both accounting for three fourths of all patients while the remaining were accounted by supraglottic (19.8%) and suglottic (5.2%) tumors. This is in contrast to the previous study done in India in which supraglottis was the commonest (56.9%) followed by glottis (36.2%), trans-glottic tumors (6.9%) and carcinoma of the subglottis being never observed [29]. Another differing pattern was observed in the Nigerian study which noted that

transglottic carcinoma was the commonest with 43.0%, followed by supraglottic 37.6% [16]. These variations can be explained by difference in time of presentation. For example, the Nigerian patients were observed to have late presentation in most of the patients with loco-regional involvement [16].

Squamous cell carcinoma was by far the commonest histological type among the studied participants. A similar pattern was documented by numerous authors such as Sandabe [14] and Menach long with his colleagues [28] who observed SCC to be the commonest in Nigerian and Kenyan population, respectively. A closest finding was recorded in Ear Nose and Throat (ENT) unit of Ghanian hospital where 88.7% of the laryngeal cancer patients were found to have SCC [36].

Besides, almost half of the laryngeal cancer patients were categorized to have GX (grade cannot be determined) while more than a third of the patients had been labelled to have well differentiated (G1) in their histologic grade report. The large number of undetermined grading noted in this study is of great concern as histologic grading are important prognosticating parameters along with other host and tumor related factors [35] and need to be assessed for better prognosis profile of the patients. A recent review by Bradford and other members of the International Head and Neck Scientific Group posits that poorly differentiated cancers usually have a higher rate of metastatic disease when compared with well-differentiated cancers [14]. By a similar token, Ferlito and associates stress that a histological classification of neoplasms is extremely important for a reliable prognosis to be established and it provides the basis for clinical management of patients [41]. Hence, this may be a good reminder for pathologists to take due amount of time for assessment of histologic grade and other tumor-specific features although it is understandable that GX histologic reports can result from compromised quality of sampling technique such as failure to resect the primary tumor and surgical resection after giving neoadjuvant therapy (post-therapy grade).

Lastly, most (88.8%) of the patients in this study presented with stage 3 and 4 of laryngeal cancer. This is in line with certain scholars that state that tumors that are causally linked to cigarette smoking and alcohol ingestion have been shown to progress rapidly and present in advanced stages [42]. Contributing factors to the late presentation can be the relatively low health seeking behavior, ignorance and poverty, and lack of adequate health facilities and personnel as well as high cost of health care.

7. Strength and limitations

7.1 Strength

- The study was done at the leading Oncology unit of the country where the highest numbers of oncologic patients (including head and neck ones) with varying socio-demographic characteristics are expected to be represented.

- The author was involved in the data quality management personally in order to assure authenticity and completeness of data collected as well as the results obtained.

- The fact that the study was retrospective chart review in its nature, there was no concern of COVID-19 transmission in the process of data collection.

7.2 Limitations

- This study design was a cross-sectional, and hence it is challenging to make causal inferences and alternative explanations of the findings.

- Being a hospital based retrospective study, some important information in patients' clinical records were missing due to improper filling of patients' particulars. Moreover, the exclusion of incomplete medical records has resulted in smaller sample size which may compromise the statistical power.

8. Conclusion and Recommendations

Most of the laryngeal cancer patients who attended Oncology unit of Tikur Anbessa Specialized Hospital are males in their sixth decade of life. They present with late stage of the disease and squamous cell carcinoma is the most common histopathology. Late disease presentation observed in our patients can lead to decreased complete disease remission following treatment in our set up, with limited management options As the dysphonia is the most common early sign of the laryngeal cancer, clinicians at all levels should continue to examine thoroughly any voice changes for more than two weeks, especially in elderly men. Besides that, surgical pathologists should provide a sufficiently comprehensive diagnosis (with emphasis on tumor grading) to enable clinicians develop an optimal plan of management and to the extent possible, estimate prognosis.

It would be prudent for the government and other stakeholders to formulate policies that are targeted at reducing cigarette smoking and alcohol consumption that will reduce the prevalence and incidence of laryngeal cancer in the coming generations. Moreover, health education and improvement of health infrastructures are necessary in order to overcome late disease presentation. Outreach services should also be considered as significant portion of the patients are out of the capital.

Further nation-wide studies to assess incidence and prevalence of laryngeal cancer with consideration of a wide range of potential risk factors, such as economic status, detailed smoking and alcohol consumption history, radiation history, and a number of occupational factors, nutritional status, and their management should be projected.

References

1. Pai SI, Westra WH. Molecular pathology of head and neck cancer: implications for diagnosis, prognosis, and treatment. Annual Review of Pathological Mechanical Disease. 2009 Feb 28;4:49-70.
2. Fan CY. Epigenetic alterations in head and neck cancer: prevalence, clinical significance, and implications. Curr Oncol Rep. 2004;6:152–61
3. Garfinkel L. Perspective on cancer prevention. Cancer J Clin. 1995;45:5–9.
4. Gilyoma JM, Rambau PF, Masalu N, Kayange NM, Chalya PL. Head and neck cancers: a clinico-pathological profile and management challenges in a resource-limited setting. BMC research notes. 2015 Dec 12;8(1):772.
5. Otoh EC, Johnson NW, Danfillo IS, Adeleke OA, Olasoji HA. Primary head and neck cancer in North Eastern Nigeria. West Afr J Med. 2004;23:305–13.
6. Ringström E, Peters E, Hasegawa M, Posner M, Liu M, Kelsey KT. Molecular oncology, markers, clinical correlates. Human papillomavirus type 16 and squamous cell carcinoma of the head and neck. Clin Cancer Res. 2002;8:3187–92.
7. Nocini R, Molteni G, Mattiuzzi C, Lippi G. Updates on larynx cancer epidemiology. Updates on larynx cancer epidemiology. Chinese Journal of Cancer Research. 2020(32):1.
8. Bray F, Ren JS, Masuyer E, Ferlay J. Global estimates of cancer prevalence for 27 sites in the adult population in 2008. Int J Cancer. 2013 Mar 1;132(5):1133-45.
9. Curado MP, Edwards B, Shin HR. Cancer incidence in five continents IARC scientific publication, Lyon. France UK cancer charity Centre.2008.
10. Zeka A, Gore R, Kriebel D. Effects of alcohol and tobacco on aerodigestive cancer risks: a meta-regression analysis. Cancer Causes and Control. 2003;14(9): 897–906.
11. P¨oschl G, Seitz HK. "Alcohol and cancer," Alcohol and Alcoholism. 2004;39(3):155–165.
12. Jones TM, De M, Foran B, Harrington K, Mortimore S. Laryngeal cancer: United Kingdom National Multidisciplinary guidelines. J Laryngol Otol. 2016 May; 130(Suppl 2): S75–S82.
13. Cancer Research UK. Laryngeal cancer statistics. www.cancerresearchuk.org/ cancer-info/cancerstats/types/larynx/
14. Bradford CR, Ferlito A, Devaney KO, Rinaldo A. Prognostic factors in laryngeal squamous cell carcinoma. Laryngoscope: Investigative otolaryngology.2020.

15. Peter M, Mathew D, Mrema A. Profile and treatment outcome of laryngeal cancer patients attended at Orci from 2008 to 2011. Canc Therapy & Oncol Int J. 2017; 5(4).
16. Sandabe MB, Garandawa H, Isa A. Laryngeal cancers in sub-Saharan Africa. Head and Neck Cancer. InTech. 2012.
17. da Lilly-Tariah OB, Somefun AO, Adeyemo WL. Current evidence on the burden of head and neck cancers in Nigeria. *Head & Neck Oncology.* 2009;1:14.
18. Faggons CE, Mabedi C, Shores CG, Gopal S. Review: Head and neck squamous cell carcinoma in sub-Saharan Africa. Malawi Medical Journal. 2015;27(3): 79-87
19. GLOBOCAN (IACR) 2020
20. Federal Ministry of Health Ethiopia. National cancer control plan 2016-2020.october 2015.
21. Musner N. Childhood cancer is a neglected disease: quality of care and survival rates have lagged in poorer countries. Nature. 2013.
22. WHO. Global Status Report on Noncommunicable Diseases. World Health Organization. 2014.
23. Nahavandipoura A, Jakobsena KK, Grønhøja C, Jensena DH, Karnova KKS, Aganderb TK. Incidence and survival of laryngeal cancer in Denmark: a nation-wide study from 1980 to 2014. Acta Oncologica. 2019; 58(7):977–982.
24. Timotewosa G, Solomona A, Mathewosb A, Addissiec A, Bogaleb S, Wondemagegnehu T. First data from a population based cancer registry in Ethiopia. Cancer Epidemiology. 2018;53:93–98.
25. Flint PW, Cummings CW. Cummings otolaryngology: head and neck surgery, 5th edn. St Louis, Mo; London: Mosby, 2010.
26. Williamson JS, Biggs TC, Ingrams D. Laryngeal cancer: an overview. Trends in Urology & Men's Health. November 2012.
27. Roland NJ, McRae RDR, McCombe AW. Key Topics in otolaryngology and head and neck surgery,2nd ed.2001.
28. Menach OP, Patel A, Oburra HO. Demography and histologic pattern of laryngeal squamous cell carcinoma in Kenya. Journal of Otolaryngology.2014.
29. Nallathambi C, Yumkhaibam SD, Singh LJ, Singh TT, Singh IY, Daniel N. Clinico-Epidemiologic Patterns of Laryngeal Cancer: 5-year Results from a Regional Cancer Centre in Northeastern India. Asian Pacific Journal of Cancer Prevention. 2016;17.

30. Arsenijevic S, Pantovic V, Gledovic Z, Stojanovic J, Belic B Demographic characteristics of patients with Laryngeal cancer and their socioeconomic status 2010;15 (1): 131- 135.
31. Kleinsasser 0. Tumors of the larynx and hypopharynx. Stuttgart: Georg Thieme Verlag, 1988: 1-24.
32. Ahmed S, Abdelrhman S, Taha M, Malik M, El Naseh W. Etiology and clinical presentation of laryngeal cancer in Sudanese patients. Inter J Otorhinolaryngology. 2018;5(1).
33. Iseh KR, Abdullahi M, Aliyu D. Laryngeal tumours: Clinical pattern in Sokoto, Northwestern, Nigeria, Nig journal of medicine. 2011;20(1).
34. Latifi H, Mikaili P, Latifi K, Torbati H. Squamous cell carcinoma of larynx in Northwest Iran. European Journal of Experimental Biology. 2012; 2 (1):242-246.
35. Fasunla AJ, Ogundoyin OA, Onakoya PA, Nwaorgu OG. Malignant tumors of the larynx: Clinicopathologic profile and implication for late disease presentation. Niger Med J. 2016;57(5): 280–285.
36. Kitcher ED, Yarney J, Gyasi RK, Cheyuo C. Laryngeal Cancer at the Korle Bu Teaching Hospital Accra Ghana. Ghana Med J. 2006;40(2): 45-49.
37. Fekadu A. Clinicopathology and treatment patterns of head and neck cancers at Tikur Anbessa Specialized Hospital, Radiotherapy center, Addis Ababa, Ethiopia. 2019. Thesis. AAU. [unpublished]
38. Zuo JJ, Tao ZZ, Chen C, et al. Characteristics of cigarette smoking without alcohol consumption and laryngeal cancer: overall and time-risk relation. A meta-analysis of observational studies. Eur Arch Otorhinolaryngol. 2017;274:1617–1631.
39. Bosetti C, Gallus S, Peto R, Negri E, Talamini R, Tavani A, et al. Tobacco smoking, smoking cessation, and cumulative risk of upper aerodigestive tract cancers. American Journal of Epidemiol. 2008;167(4):468–473.
40. Hashibe M, Brennan P, Chuang SC, Boccia S, Castellsague X, Chen C, et al. Interaction between tobacco and alcohol use and the risk of head and neck cancer: pooled analysis in the International Head and Neck Cancer Epidemiology Consortium. Cancer Epidemiol Biomarkers Prev. 2009 Feb;18(2):541-50.
41. Ferlito A, Thompson LDR, Cardesa A, Gnepp DR, Devaney KO, Rodrigo JP, Hunt JL, Rinaldo A, Takes RP. The importance of histological types for treatment and prognosis in laryngeal cancer. Eur Arch Otorhinolaryngol. 2013.

42. Trigg DJ, Lait M, Wenig BL. Influence of tobacco and alcohol on the stage of laryngeal cancer at diagnosis. Laryngoscope. 2000;110(3):408–411.

Annex

Annex I

Information sheet to medical director of the Hospital

Addis Ababa University, College of Health Sciences, Department of Clinical Oncology,

This sheet was read for medical director of the hospital before collecting any information from the medical charts.

Greetings. My name is Dr. Natenael Eshetu and I am a postgraduate student in Clinical Oncology at AAU.

This governmental hospital was selected to conduct the proposed study “Demography and Clinico-pathologic Pattern of Laryngeal Cancer at TASH: A Retrospective Study" as it is the largest government hospitals in the country with well-functioning onclogic center.

I am humbly requesting your esteemed office to give me permission to conduct the stated study in this hospital. Please read the following information for further understanding:

What the study is about: The purpose of this study is to assess Demography and Clinico-pathologic Pattern of Laryngeal Cancer at TASH. The study is designed to be retrospective study on laryngeal cancer patients.

What I will ask you to do: If you agree to facilitate the undertaking of this study; I will be using a checklist to collect necessary data from the medical records of patients. The checklist will include questions about socio-demographic and clinical data of the adult cardiac patient. I would very much appreciate your cooperation in this study.

Risks and benefits: The result of the study is believed to help responsible body to advance oncologic center’s care by creating an insight to integrate evidence based oncologic practice.

Confidentiality: All information gathered from the log book and patient medical record will be kept confidential. Any of patients’ personal information will not be registered. The records of this study will be kept private. In any sort of public report, we will not be including any information that will be making it possible to identify the patient. Research records will be kept in a locked file; only the researcher will have access to the records.

Contact Address of the Principal Investigator

Name**:** Natenael Eshetu

Mobile Phone**:** +251911005134 Email: natenaeleshetu@gmail.com

Annex II

English Version Questionnaire

Questionnaire ID: _____ MRN: _____

Section 1: Demographic data				
S.N.	**Question item**	**Possible answer**		
101	Age in years			
102	Sex	1. Male ☐	2. Female ☐	
	Marital status	1. Married 2. Single 3. Divorced 4. Widowed		
103	Educational level			
104	Religion	1. Orthodox 2. Protestant 3. Muslim 4. Other _____ (specify)		
105	Region	1. Addis Ababa 2. Dire Dawa 3. Oromia 4. Amhara 5. Tigray 6. Somalia 7. SNNPR 8. Gambela 9. Benshangul gumuz 10. Harari 11. Afar		
106	Occupation	Employed ☐	Unemployed ☐	Self-employed ☐
107	Smoking History	1. Yes	2. No	
108	If positive history of smoking	1. Active smoker	2. Passive smoker	
109	Alcohol Consumption	1. Yes	2. No	
Section 2: Clinical data of the patient				
201	Hoarseness of voice	1. Yes	2. No	
202	Dysphagia/odynophagia	1. Yes	2. No	
203	Referred otalgia	1. Yes	2. No	

204	Sore throat	1. Yes	2. No	
205	Cough	1. Yes	2. No	
206	Difficulty with breathing	1. Yes	2. No	
207	Frequent choking	1. Yes	2. No	
208	Unplanned, significant weight loss	1. Yes	2. No	
209	Persistent halitosis	1.Yes	2.No	
210	Neck mass	1.Yes	2.No	
211	Tracheostomy done	1.Yes	2.No	
212	Duration of initial symptom	1. 0-3 months 2. 3.1-6 months 3. 6.1-9 months 4. 9.1-12 months 5. More than 01 year		
213	ECOG performance status	1. 0 2. 1 3. 2 4. 3 5. 4		
Section 3: Histo-pathologic findings at diagnosis				
301	Type of laryngeal CA	SCC ☐ Adenocarcinoma ☐ Lymphoepithelioma ☐ Spindle cell carcinoma ☐ Undifferentiated ☐		
302	Site of lesion	Supraglottic ☐ Glottic ☐ Subglottic ☐ Transglottic ☐		
303	Staging	I ☐ II ☐ III ☐ IVA ☐ IVB ☐ IVC ☐		
304	Histologic findings	Grade cannot be assessed(GX) ☐ Well differentiated (G1) ☐		

		Moderately differentiated (G2) ☐ Poorly differentiated (G3) ☐ Undifferentiated (G4) ☐