Demographic, clinical, and treatment patterns of non-small cell lung cancer patients seen in Tikur Anbessa Specialized Referral Hospital, Radiotherapy Center; Addis Ababa, Ethiopia, 2017-2020

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ADDIS ABABA UNIVERSITY COLLEGE OF HEALTH SCIENCE

DEPARTMENT OF ONCOLOGY

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Lists of abbreviations:

AACCR ---------- Addis Ababa City Cancer Registry

AAU ---------- Addis Ababa University

AC ---------- Adenocarcinoma

ACS ---------- American Cancer Society

AJCC ---------- American Join Committee on Cancer

ALK---------- Anaplastic lymphoma kinase

CHS---------- College of Health Science

CI ---------- Confidence Interval

Co-60 ---------- Cobalt 60

COPD---------- Chronic obstructive pulmonary disease

CRT ---------- Concurrent Chemo Radiotherapy

CXR ---------- Chest X-Ray

CT ---------- Computed Tomography

DM---------- Diabetics

EBRT ---------- External Beam Radiotherapy

ECOG ---------- Eastern Cooperative Oncology Group

EGFR ---------- Epidermal growth factor receptor

EUBUS-NA ---------- Endobronchial ultrasound and needle aspiration

EUS-NA ---------- Oesophageal ultrasound and needle aspiration

GLOBOCAN ---------- Global Burden of Cancer

Gy ---------- Gray

HR ---------- Hazard Ratio

IAEA ---------- International Atomic Energy Agency

LCNS ---------- Lung cancer in never smokers

MRI ---------- Magnetic Resonance Imaging

NSCLC ---------- Non-small cell lung cancer

OR ---------- Odds Ratio

PD-L1 ---------- Programmed death ligand 1

RR ---------- Relative Risk

RT ---------- Radiotherapy

SCC ---------- Squamous cell carcinoma

SCLC ---------- Small cell lung cancer

SPSS ---------- Statistical Package for Social Science

TASH ---------- Tikur Anbessa Specialized Hospital

TNM ---------- Tumour Size, Nodal involvement, Metastasis

TTNA ---------- Transthoracic needle aspiration

UICC ---------- Union of International Cancer Control

VATS ---------- Video assisted thoracic surgery

WHO ---------- World Health Organization

Contents

Executive summary:

Background: Lung cancer is the most commonly diagnosed cancer and the leading cause of cancer death worldwide. There are two main types of lung cancer, non–small cell lung cancer (NSCLC) and small-cell lung cancer (SCLC). Non–small cell lung cancer (NSCLC) accounts for 80% to 85% of lung cancer. Even though lung carcinoma is the 6th most frequent malignancy in male based on data from Addis Ababa city-based cancer registry, there is lack of published data on demographic, clinical, and treatment patterns of non-small cell lung cancers in Ethiopia.

Objective: To determine the demographic, clinical, and treatment patterns of non-small cell lung cancer patients seen in Tikur Anbessa Specialized Referral Hospital, Radiotherapy Center, Addis Ababa, Ethiopia, 2017-2020

Methodology: A retrospective cross-sectional study design on histopathologically confirmed non-small cell lung cancer patients treated from September 2017 to September 2020. Descriptive statistics (mean, SD, frequency, percentage, graph and table) and chi-square results were generated by using SPSS version 25. P-value of <0.05 was considered as significant.

Result: 126 patients were enrolled in the study. There were 67 (53.2%) males and 59 (46.8%) females giving a male to female ratio of 1.14:1. The mean age at presentation was 52 years, ranged from 24 to 90 years. The majority of the patients presented with cough (103, 81.7%), followed by chest pain (40, 31.7%), haemoptysis (21, 16.7%), shortness of breath (18, 14.3%). According to AJCC staging of lung cancer 43.7% (55) and 32.5% (41) of the patients were diagnosed with stage IVb and IVa diseases, respectively. Ever cigarette smoking was reported in 20 (15.9%) patients. 20(15.9%) patients had associated co-morbid medical illnesses. Mostly the primary lesion was located peripherally in 73% of patients and centrally in 23.8%. The most common histology type was adenocarcinoma in 81(64.3%) patients, followed by squamous cell carcinoma in 34(27%). Metastasis at the time of diagnosis was recorded in 96(76.2%) of cases. Common sites of metastasis were pleura (27.8%) and bone (24.6%), followed by lung, liver, brain and adrenal in 15.9%, 14.3%, 9.5% and 5.6% of patients respectively. Chemotherapy was given in 87.3% of patients. The intent of chemotherapy was palliative in 93.6% patients, neoadjuvant in 3.6% patients and adjuvant in 2.7% patients. Radiotherapy was given in 23.2% of patients with the intent of palliative treatment.

Conclusion and Recommendation: The majority of patients with NSCLC seen at TASH are presented at advanced stage of disease, with adenocarcinoma as the most common histology type and history of smoking in only 16% of the cases. Future studies should examine the causes of lung cancer in the country.

1, Introduction:

1.1, Background:

Lung cancers are tumors arising from the respiratory epithelium in the bronchi, bronchioles, and alveoli. Lung cancer is the most commonly diagnosed cancer and the leading cause of cancer death worldwide (1). About 2.1 million new lung cancer cases are diagnosed each year worldwide (1). Lung cancer incidence varies from one geographic region to another for both sex and it is strongly related to smoking behaviour (2, 3). In the United States, lung cancer is the second most common cancer and the most common cause of cancer-related death in both men and women (4). Gender and racial disparities exist in the incidence and mortality for lung cancer with rates highest in men, particularly those who are African American. Incidence rates among males remain generally low in Africa (1) but the mortality rate is increasing (5).

Smoking tobacco is the main cause of lung cancer, with a latency period between the start of smoking and lung cancer of 15-50 years (6). In addition, the number of pack-years, the tar level of the cigarettes smoked and the age at initiation of smoking are closely related to lung cancer risk (7). The relative risk of smoking is higher for squamous cell carcinoma than for adenocarcinoma (2, 3). Other causes of lung cancer are air pollution, occupational exposure to arsenic, asbestos, radon, chromium, mustard gas and poly-cyclic hydrocarbons, vitamin A deficiency, indoor radon, family history and previous chronic lung diseases, but the effects of smoking are so predominant that trends in other exposure seem unlikely to be largely responsible for the changes in incidence. There are two main types of lung cancer, non–small cell lung cancer (NSCLC) accounting for 80% to 85% and small-cell lung cancer (SCLC) accounting for 15% to 20% (8). NSCLC is further histologically subdivided into adenocarcinoma (AC) and squamous carcinoma (SCC), with large cell carcinoma (including neuroendocrine lung cancers), sarcomatoid carcinoma, and mixed histologic (e.g., Adeno-squamous) subtypes being less common. Prior to the 1990s, squamous cell lung carcinoma was the most common histologic subtype, particularly among men but currently, Adenocarcinoma is the most common histologic subtype of lung cancer in men and women (9).

The management of non-small cell Lung cancer involves many different specialties in multidisciplinary team consisting of a pathologist, radiologist, medical oncology subspecialist, radiation oncology subspecialist, and thoracic surgeon that contribute to the evaluation and management of the patient. Management of NSCLC is based on the stage; extent of disease spread at

the time of diagnosis, performance status, histological cell type and molecular biomarker expression but also must carefully weigh the impact of baseline pulmonary functional status and comorbidities on the patient's ability to tolerate treatment. Surgery, radiotherapy and systemic therapy (including chemotherapy, targeted molecular therapy and immunotherapy) are the three modalities most commonly used to treat patients with NSCLC. They can be used either alone or in combination depending on disease status.

The management of NSCLC in our center was based on the stage of the disease and performance status of the patient. Because of our limited resources,long waiting list for upfront radiotherapy, lack of modern radiotherapy machine, lack of molecular and biomarkers analysis and targeted therapies, majority of our patients received chemotherapy as palliation therapy. To my knowledge, there is no concrete data on the demographic, clinical, and treatment patterns of non-small cell lung cancer in Ethiopia. This retrospective study will try to get objective evidence on demography, risk factor, and clinical stage at diagnosis and management pattern delivered for non-small cell lung cancer in this hospital.

1.2, Statement of the problem:

Non-small cell lung cancer is an aggressive malignancy with great variability in clinical presentation, clinical stages at diagnosis, histological subtypes, and challenging in optimal management. Even though lung carcinoma is the 6th most frequent malignancy in male based on data from Addis Ababa city-based cancer registry(10), there is no a separate comprehensive study to assess the demographic, clinical, and treatment patterns of non-small cell lung cancer.

Ethiopia is home to a growing population of more than 105 million people and is expected to become the ninth most populous country in the world by 2050. The burden of cancer is rising in parallel with the population (11). Cigarette consumption which is the main risk factor of lung cancer is also increasing in Ethiopia. Cigarette consumption was examined in the 6 African countries from which statistics were available. In all of them, it rose steeply between 1967 and 1976 and actually doubled in Libya and Ethiopia. The proportion of tobacco smokers has been increasing since the 1960s (20). Despite the increment of cancer burden, less attention is still given to prevention, early detection and management of cancer. The inadequate attention of governmental organizations, policy makers and non-governmental organizations could be due to low awareness on the scale of burden of cancer in the country.

1.3, Significance of the study:

This study will provide information on the clinical stages at diagnosis, common presenting clinical feature, histopathological types, and possible associated risk factors of non-small lung cancers among patients treated in TASH. The study will describe the patterns of treatment delivered for these cancers. Moreover, there is lack of awareness on every aspects of cancer in Ethiopia. Due to this, the policy makers didn't give more attention on cancer in general, and lung cancers in particular. So, this study will be used as input to policy makers and concerned bodies to increase awareness on non-small cell lung cancer and to improve prevention and treatment of lung cancer. And finally, this study also mainly used to stimulate further research on non-small cell lung cancers.

2, Literature review:

Cancer incidence and mortality are rapidly growing worldwide. The reasons are complex but reflect both aging and growth of the population, as well as changes in the prevalence and distribution of the main risk factors for cancer, several of which are associated with socioeconomic development (12, 13). Based on GLOBOCAN 2018 estimates there will be an estimated 18.1 million new cancer cases and 9.6 million cancer deaths worldwide in 2018. Throughout the world, lung cancer is the most commonly diagnosed cancer with 2.1 million new lung cancer cases which is 11.6% of the total cases and the leading cause of cancer death with 1.8 million deaths which is 18.4% of the total cancer deaths (1). By sex, lung cancer is the most commonly diagnosed cancer and the leading cause of cancer death in males. Among females, lung cancer is the 3rd commonly diagnosed cancer and the leading cause of cancer death (1).

In the United States, lung cancer is the second most common cancer and the most common cause of cancer-related death in both men and women. The American Cancer Society estimates 155,870 people in the United States died of lung cancer in 2017, including 84,590 men and 71,280 women. The overall ratio of mortality to incidence is high, with the 5-year survival rate in the United States still only 18% (4). Gender and racial disparities exist in the incidence and mortality for lung cancer with rates highest in men, particularly those who are African American. In terms of socioeconomic, lung cancer demonstrates the largest disparity of all cancers, with the death rate in men five times higher for the least educated than for the most educated (4).The highest estimated age-standardized lung cancer incidence rates occur in more developed regions of the world, where smoking is more prevalent (14).

In Ethiopia, Based on GLOBOCAN 2018, the estimated incidence of cancer is 67,573, including 21,200 males and 46,373 females. And the estimated number of cancer deaths is 47,954, including 16,612 males and 31,342 females. Both the incidence and mortality are higher in females. Lung cancer is the 5th most frequent cancer in males with an estimated 1,049 new lung cancer cases (1). Evidence in lung cancer incidence is not available in Ethiopia. But, based on the data from Addis Ababa city-based cancer registry, lung carcinoma was the 6th most frequent malignancy in male (10).

Smoking is the most important modifiable risk factor. More than 50 carcinogens in tobacco smoke have been identified, including tobacco-specific N-nitrosamines (TSNAs) formed by nitrosation of nicotine during smoking, and polycyclic aromatic hydrocarbons (PAHs) (16-18). Both the number of cigarettes smoked per day and the duration of smoking correlate with lung cancer risk, with longer

duration in particular being associated with a much higher risk (19). There is a 20-fold variation in lung cancer rates by region, which largely reflects the maturity of the tobacco epidemic and differentials in the historic patterns of tobacco exposure, including intensity and duration of smoking, type of cigarettes, and degree of inhalation (1). In Africa, cigarette consumption was examined in the 6 African countries from which statistics were available. In all of them, it rose steeply between 1967 and 1976 and actually doubled in Libya and Ethiopia. The proportion of tobacco smokers has been increasing since the 1960s and traditionally only men smoked, but the proportion of female, children, and adolescent smokers has been also increasing (20). In one study done in Addis Abeba, in 125 lung cancer patients, 25.3% had a prior history of smoking (61).

Although the majority of lung cancers are caused by carcinogens present in tobacco smoke, approximately 20% of cases occur in lifetime "never smokers" (<100 cigarettes in their lifetime). Due to the number of lung cancer cases overall, lung cancer in never smokers (LCNS) presents a huge public health problem, comprising the seventh most common cause of cancer death (21). LCNS is more common in women and East Asian ethnicity, has a peak incidence that occurs at a younger age, is usually adenocarcinoma, and targets the distal airways (22). The major causes of LCNS remain unknown, but environmental carcinogens, increased exposures to smoke from burning of charcoal for heating and cooking and second-hand smoke are considered the most likely. second hand or passive smoking is associated with lung cancer with relative risk between 1.14 to 5.20 in people who had never smoked but who lived with a smoker and passive smoking during childhood increased lung cancer risk in adulthood by 3.6-fold (15, 53). It is estimated that approximately 10% of worldwide lung cancer cases are at least in part related to occupational exposures (23).Many workplace materials have been identified as carcinogens, including, among others, arsenic, asbestos, beryllium, cadmium, chromium, nickel, radon, and vinyl chloride. Radon gas was first implicated as increasing lung cancer risk in workers in underground uranium mines. The awareness of radon as a carcinogen has focused attention on domestic radon gas as a common indoor pollutant. Radon is felt to contribute to an estimated 15,000 to 20,000 lung cancer deaths in the United States annually (24).

A slightly greater risk of lung cancer was found among people who consumed at least 30 g/d of alcohol than among those who abstained from alcohol (54). Long-term cumulative exposure to ambient air pollution could result in lung cancer, such as emissions rich in various polycyclic aromatic hydrocarbon compounds, likely through oxidative stress, inflammation, and induction of a procoagulatory state. The proportion of lung cancers attributable to urban air pollution in Europe is estimated to be 11% (55). Approximately 20–30% of smokers develop COPD and 10–15% develops

lung cancer, COPD is by far the most common comorbidity in patients with lung cancer, with a varying prevalence between 30 and 70%. Newly diagnosed lung cancer cases were reported to have a prevalence of COPD as high as six-fold greater than matched smokers without cancer (56). Never-smokers with a history of chronic bronchitis, tuberculosis, or pneumonia were found to have an increased risk of lung cancer (57, 58). First-degree relatives of patients with lung cancer are at increased risk, even after adjusting for smoking habits and individuals with positive family histories found to have a RR of 1.84 (95% CI: 1.64–2.05) for developing lung cancer (59, 60).

There are two main types of lung cancer, non–small cell lung cancer (NSCLC) accounting for 80% to 85% and small-cell lung cancer (SCLC) accounting for 15% to 20%, are identified based on histologic, clinical, and neuroendocrine characteristics (8). NSCLC is further histologically subdivided into adenocarcinoma (AC), squamous carcinoma (SCC), large cell carcinoma (including neuroendocrine lung cancers), adeno-squamous and sarcomatoid carcinoma (includes pleomorphic carcinoma, carcinosarcoma and pulmonary blastoma).Adenocarcinoma is the most common histologic subtype, accounting for 30-40% of all lung cancer in men and women (9, 8, 25). Prior to the 1990s, squamous cell lung carcinoma was the most common histologic subtype, particularly among men. Since then, the incidence of adenocarcinoma rose to be greater than that of squamous cell carcinomas in the US, Canada, many European countries, and Japan (26, 27). In one study done in Addis Ababa University, the most common histopathological classifications were adenocarcinoma in 49 patients (33.6%), and squamous cell carcinoma (SCC) in 28 patients (19.2%) and in 62 patients (42.5%), the histology was not specified (61). The higher rates of adenocarcinoma relative to squamous cell lung cancer are greater in women (28). Adenocarcinoma commonly occurs in the peripheral lung zones, whereas squamous cell carcinoma occurs mainly in central and hilar locations (25).

Approximately a quarter of patients with lung cancer are diagnosed at early stage. These patients are typically symptom-free; their cancers are identified incidentally during evaluation of unrelated issues. And more than half of patients have advanced lung cancer at the time of diagnosis. These patients typically come to attention because of symptoms related to the primary tumour, metastasis to distant sites, or paraneoplastic syndromes (29). In a Surveillance Epidemiology and End Results (SEER) analysis involving all lung cancer histology, 15% of all cases of lung cancer were localized to the primary site at initial diagnosis; 22% had regional lymph node spread and 56% distant metastasis; and the remaining 7% were stage unknown (30). In non–small cell lung cancer (NSCLC),

half the patients present with localized or locally advanced disease and half with advanced disease (31).

Signs and symptoms of lung cancer directly reflect the patient's local, regional, or distant pattern of spread. The most common pulmonary symptoms are cough, haemoptysis, dyspnoea, and chest pain (32). Cough is present in 50% to 75% of lung cancer patients at presentation and occurs most frequently in patients with squamous cell because of their tendency to involve central airways. Tumour eroding into a blood vessel or bleeding from the neo-vasculature supplying the tumour may lead to haemoptysis, which is a presenting symptom in approximately 25% of patients. If tumour blocks airflow through a portion of the lung, shortness of breath may develop and is identified at presentation in approximately 25% of cases. Chest pain is present in approximately 20% of patients presenting with lung cancer. Pain may be attributed to direct extension to the mediastinum, parietal pleura, or chest wall (33). Primary tumours arising within the superior sulcus may produce the classic Pancoast syndrome manifested by shoulder pain, Horner syndrome, and brachial plexopathy. Pancoast syndrome is most commonly caused by NSCLC.

Symptoms related to metastatic disease may be constitutional or organ related. The most common sites of NSCLC metastases are the brain, bone, liver, adrenals, and lung, although any organ can be affected (34). Focal neurologic symptoms, persistent headache, bony pain, unexplained weight loss, anorexia, or fatigue should raise the suspicion for metastatic disease. Likewise, laboratory abnormalities such as anaemia, liver function test abnormalities, or hypercalcemia should raise concern for distant spread (29).

In most patients, an experienced clinician can make a clinical diagnosis of lung cancer with a high degree of reliability (>95%).The main factors that contribute to this are the risk factors for development of lung cancer e.g., age, smoking history, family history, presence of significant COPD, the clinical presentation, and the radiographic appearance of the lesion on CT (35).In patients with a high suspicion of lung cancer, a biopsy can confirm the diagnosis, but in this situation, the false negative rate of a nonspecific diagnosis is approximately 20% (36); therefore, a surgical biopsy should be pursued unless the patient is too high risk (37). When doing a tissue biopsy, it is crucial to obtain enough tissue for histologic and molecular characterization (36).

Assessing the tumour stage is a critical aspect of the evaluation of all patients known or suspected of having lung cancer. Clinical stage is determined by all information available before any definitive

treatment. This involve history and physical examination, imaging studies or may involve invasive biopsies or surgical procedures with sampling the primary tumour, intrathoracic lymph nodes, pleural fluid, or extra thoracic sites (38). Pathologic stage is determined only if surgical resection with intent to cure is performed. Clinical stage drives the initial treatment decisions, and thus, it is imperative that the process of defining the clinical stage be performed rigorously.

If the clinical evaluation is negative for distant metastasis, the incidence of finding occult distant metastases detectable by imaging varies according to the clinical intrathoracic stage. For clinical stage I by CT with a negative clinical evaluation, the incidence of finding true distant metastases is approximately 5% (35, 39-42), and the incidence of detecting a false-positive finding of a distant metastasis is actually higher. In patients with clinical stage III (N2), the incidence of finding occult disease is 25% to 30% (35, 39-42). For clinical stage II, there is less data but the incidence appears to be 15% to 20% (35, 40). Therefore, in clinical stage II or III patients imaging for distant metastases: PET and brain MRI with and without contrast should be done, although an abdominal/pelvic CT, bone scan, and brain CT with contrast is reasonable if PET is not available or brain MRI is not possible.

If there are no distant metastases, the status of the mediastinal nodes becomes critical in determining the right treatment strategy. Much information is already available from the CT scan. There are multiple techniques to invasively confirm the presence or absence of N2, 3 involvement. These include traditional mediastinoscopy, video mediastinoscopy, endobronchial ultrasound and needle aspiration (EBUS-NA), oesophageal ultrasound and needle aspiration (EUS-NA), simple “blind” transbronchial needle aspiration (TBNA) and video-assisted thoracic surgery (VATS).The technique and thoroughness of how the procedure is done probably has a major impact on the reliability of the results (43).

Molecular testing on tumour specimens should be performed on all non-squamous tumours and squamous tumour samples from patients who were never-smokers, had small biopsies, or mixed histology. Mutational testing should include assays for EGFR, ALK, ROS1, and BRAF, as these all currently have therapeutic indications (44). Additionally, all NSCLC should be assessed for tumour expression of PD-L1 (45).

Lung cancer management involves many different specialties in multidisciplinary team consisting of a pulmonology subspecialist, medical oncology subspecialist, radiation oncology subspecialist, and

thoracic surgeon that contribute to the evaluation and management of the patient.management of NSCLC is based on the stage, extent of disease spread at the time of diagnosis, performance status, histological cell type and molecular biomarker expression but also must carefully weigh the impact of baseline pulmonary functional status and comorbidities on the patient's ability to tolerate treatment. Surgery, radiotherapy and systemic therapy are the three modalities most commonly used to treat patients with NSCLC. They can be used either alone or in combination depending on disease status.

The standard of care for operable patients with stage I and stage II disease are complete surgical resection with the possible addition of adjuvant chemotherapy (46). The type of surgery could be lobectomy, pneumonectomy, wedge resection or segmentectomy.

For medically inoperable patients, stereotactic body radiation therapy (SBRT) is an excellent treatment option (47). For stage III patients, a significant amount of controversy exists regarding optimal management. For select patients with stage IIIA disease at diagnosis who are candidates for surgical resection, neoadjuvant chemotherapy or chemoradiotherapy is often used (48). For patients with unresectable stage III disease, the standard approach is concurrent chemoradiotherapy for fit patients or sequential chemotherapy and radiotherapy for patients who cannot tolerate concurrent treatment (49).

For stage IV patients without significant local presenting symptoms or need for urgent radiation, systemic therapy is the standard initial treatment approach. For stage IV patients with significant local presenting symptoms requiring urgent radiotherapy, such as SVC obstruction, haemoptysis, or cord compression, palliative radiotherapy followed by systemic therapy is the preferred treatment approach. Systemic therapy includes chemotherapy, targeted therapy and immunotherapy. Molecular targeted therapy is the standard first-line treatment for patients with these identified driver mutations (50, 51), whereas systemic platinum-based cytotoxic chemotherapy is the standard treatment for patients without EGFR mutations or ALK rearrangement or those with unknown mutation status (52). For patients with stage IV disease, owing to the poor prognosis, a detailed discussion of the goals of care with consideration of early referral to hospice is part of the initial treatment approach.

3, Objectives

3.1, General objective:

- To determine the demographic, clinical, and treatment patterns of non-small cell lung cancer patients seen in Tikur Anbessa Specialized Referral Hospital, Radiotherapy Center, Addis Ababa, Ethiopia from September 2017 to September 2020

3.2, Specific objectives

- To assess the demographic characteristic of non-small cell lung cancer
- To assess the common risk factors of non-small cell lung cancer
- To assess the histologic subtypes and primary location of non-small cell lung cancer
- To assess the clinical stage at initial presentation
- To determine the patterns of treatment delivered to non-small cell lung cancer

4, Methodology

4.1, Study Area:

The study was conducted in Tikur Anbessa Specialized Hospital Radiotherapy center. It was established 26 years back with the help of International Atomic Energy Agency (IAEA) and currently has two Cobalt 60 teletherapy units; one Linac accelerated teletherapy installed recently and one HDR Brachytherapy unit mainly used for gynecologic malignancy.

In the center, eight consultant oncologists, three medical physicists, and eight radiotherapists are currently working. The center has started speciality training in clinical oncology since 2013 and currently forty-two residents are under training. Activities include inpatient admission for chemotherapy and outpatient clinic for new patient evaluation, radiotherapy planning and treatment and follow up.

Black Lion Hospital, Addis Ababa, houses Ethiopia's only cancer referral centre

4.2, Study design:

Institution based Retrospective cross-sectional study design was used.

4.3, Sources of data:

Data was collected from patient charts and log books.

4.4, Source population:

All cancer cases treated at TASH, Radiotherapy center between September 2017 and September 2020.

4.5. Study population:

All cases of histopathologically confirmed non-small cell lung cancer patients whose charts were found between September 2017 and September 2020.

4.6, Inclusion criteria:

Patients with pathologically confirmed non-small cell lung cancer

4.7, Exclusion criteria:

- ✓ Inadequate data
- ✓ Diagnosis not confirmed by histopathology
- ✓ Cancer of two or more primary site

4.8, Variables:

Independent variables

- Age
- Sex
- Place of living
- Risk factors (cigarette smoking, family history, previous RT to chest, other)
- Comorbidity (DM, HTN, COPD, HIV)
- Pathologic subtype
- Performance status
- Laterality (right, left, other)
- Tumour location
- Tumour size
- TNM stage
- Molecular status (positive, negative, unknown)

Dependent variables

- Type of surgery
- Type of chemotherapy
- Type of radiotherapy
- Type of targeted therapy

4.9, Sample size determination and sampling procedure:

All cases of histopathologically confirmed non-small cell lung cancer patients that fulfil the inclusion criteria whose charts were found between September 2017 and September 2020 were included in the study.

4.10, Data collection tools and procedures:

Two days training was given on the purpose of the study and data extraction techniques for data collectors. Data was collected by the data collectors using a pretested and structured questionnaire from the patient medical record chart. The collecting team was consisted of two chart finders from chart room; two oncology residents and one supervisor. The chart was collected based on the HMIS record and all the cards that lack the inclusion criteria and fulfil the exclusion criteria were returned. Data collection process was supervised by the advisor.

4.11, Data management and Quality assurance:

The collected data were checked daily for completeness and accuracy. The completed questionnaires were placed in a protected place.

4.12, Data processing and analysis:

Data was coded and analyzed using SPSS version 25. Basic descriptive analyses like frequency, proportion mean and median was done. Results are presented by tables, figures and statements. Association between variables have been done by the Chi-Square Test of association and P-value of <0.05 was considered as significant.

4.13, Ethical consideration:

Ethical approval was obtained from the ethical review board off Addis Ababa University College of health science. Confidentiality of the information was maintained throughout the study by excluding names as identification in the data extraction form and the data was used only for the purpose of the proposed study. In addition, health care professionals from the cancer treatment centre extract the data from medical records respecting the confidentiality.

4.14, Dissemination of results:

The study finding will be submitted to the department of oncology, AAU-CHS. Publication of the result on scientific journals will be considered through peer review and presentations on different meetings and conferences.

5, Results:

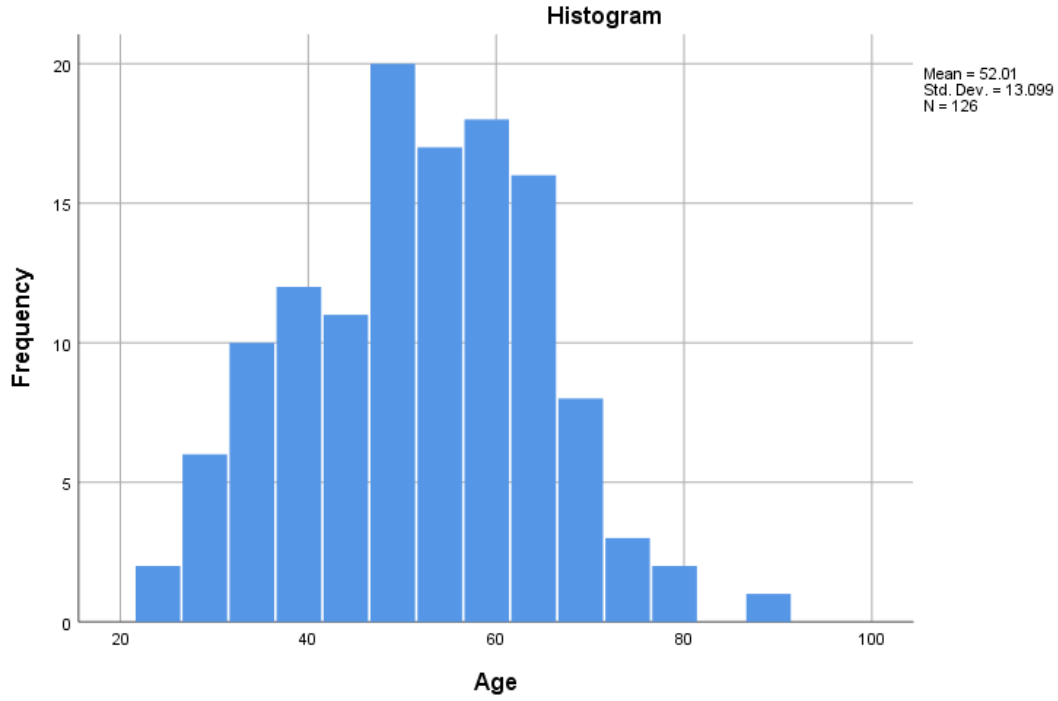
5.1, Socio-demographic pattern of patients, clinical presentation, stage, risk factors, and co-morbid medical conditions

A total of 168 patients were treated as NSCLC in our radiotherapy center during the study period. 42 patients were excluded from the study due to incomplete data in 4 patients, 2 because of associated secondary primary and 36 patients because of no pathology report. Thus, 126 patients were enrolled in the study representing 75% of the cases. There were 67 (53.2%) males and 59(46.8%) females giving a male to female ratio of 1.14:1 (table 1). The mean age at presentation was 52 (SD=13.1, ranged from 24 to 90 years) (histogram 1). 99 (83.2%) of the patients were married and 11(9.2%) were widow at the time of the study (table 2). 40 (42.6%) were housewives and 22(23.4%) were farmers in occupation (table 3) and 22(17.5%) came from the rural part of the country (table 1). The majority of the patients 58(46%) came from Addis Ababa and the remaining 33(26.2%), 16(12.7%) and 14(11.1%) came from Oromia, Amhara and SNNPR region respectively (bar chart 1). The majority of patients presented 44 (34.9%) between 3-6 months compliant (bar chart 2). The majority of the patients 103(81.7%) presented with cough followed by chest pain 40(31.7%), haemoptysis 21(16.7%), shortness of breath 18(14.3%). Asymptomatic presentation was recorded in 1(0.8%) patient (table 4). ECOG performance status of I and II was recorded in 81(64.3%) and 37(29.4%) of the patients respectively (table 1). According to AJCC staging of lung Cancer the majority of patients, 55 (43.7%) and 41(32.5%) was stage 4b and 4a respectively (bar chart 3).

Ever cigarette smoking was reported in 20(15.9%) patients (table 1) and 50% of smokers took >= 30 packs a year. 20(15.9%) patients had associated co-morbid medical illnesses, such as hypertension in 11 patients, diabetic Mellitus in 8 patient and HIV infection in 1 patients (table 1). 28(22.2%) of patients were treated for pulmonary TB before they were diagnosed as non-small cell lung cancer (table 1)

Table 1- Distribution of NSCLC patients treated in Tikur Anbessa referal hospital from 2017-2020 in term of gender, address, PS, risk factor and comorbidity status.

Variable	Catagory	Frequency	Percentage
Sex(n=126)	Female	59	46.8
	Male	67	53.2
Residency(n=126)	Urban	104	82.5
	Rural	22	17.5
ECOG-PS(n=126)	PS-1	81	64.3
	PS-2	37	29.4
	PS-3	4	3.2
	PS-4	4	3.2
Comorbidity(n=126)	DM	8	6.4
	HTN	11	8.7
	HIV	1	0.8
	None	106	84.1
Smoking histroy	yes	20	16
	no	106	84
Pulmonary TB treatment(n=126)	yes	28	22.2
	no	98	77.8



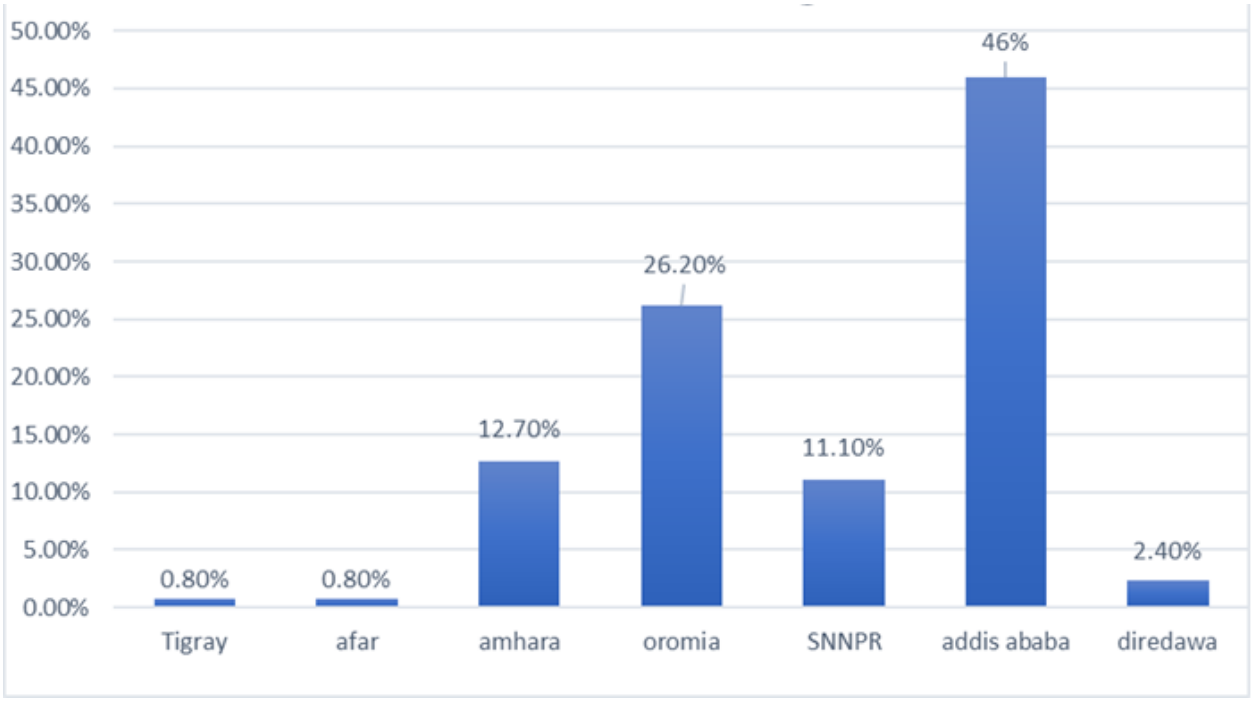
Histogram 1 – Age distribution of NSCLC patients treated in Tikur Anbessa referal hospital from 2017-2020.

Table 2- Marital status of NSCLC patients treated in Tikur Anbessa referal hospital from 2017-2020.

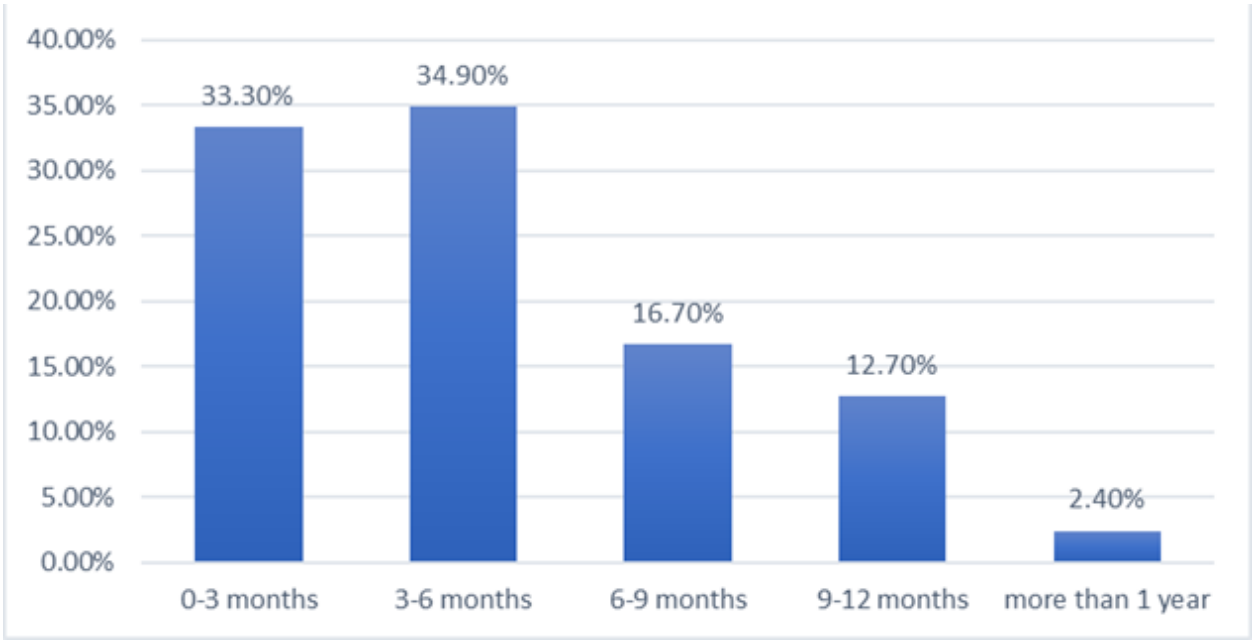
Marital Status	Number of patients	Percentage
married	99	83.2
single	6	5.0
widow	11	9.2
divorced	3	2.5
Total	119	100.0

Table 3 – Occupational status of NSCLC patients treated in Tikur Anbessa referal hospital from 2017-2020.

Occupational status	Number of patients	Percentage
house wife	40	42.6
farmer	22	23.4
merchant	7	7.4
nurse	3	3.2
student	1	1.1
office work	4	4.3
driver	3	3.2
pension	1	1.1
police	2	2.1
teacher	2	2.1
journalist	1	1.1
Construction	1	1.1
judge	1	1.1
sugar factory	2	2.1
cleaner	1	1.1
metal factory	1	1.1
arm industry	1	1.1
wood craft	1	1.1
Total	94	100.0



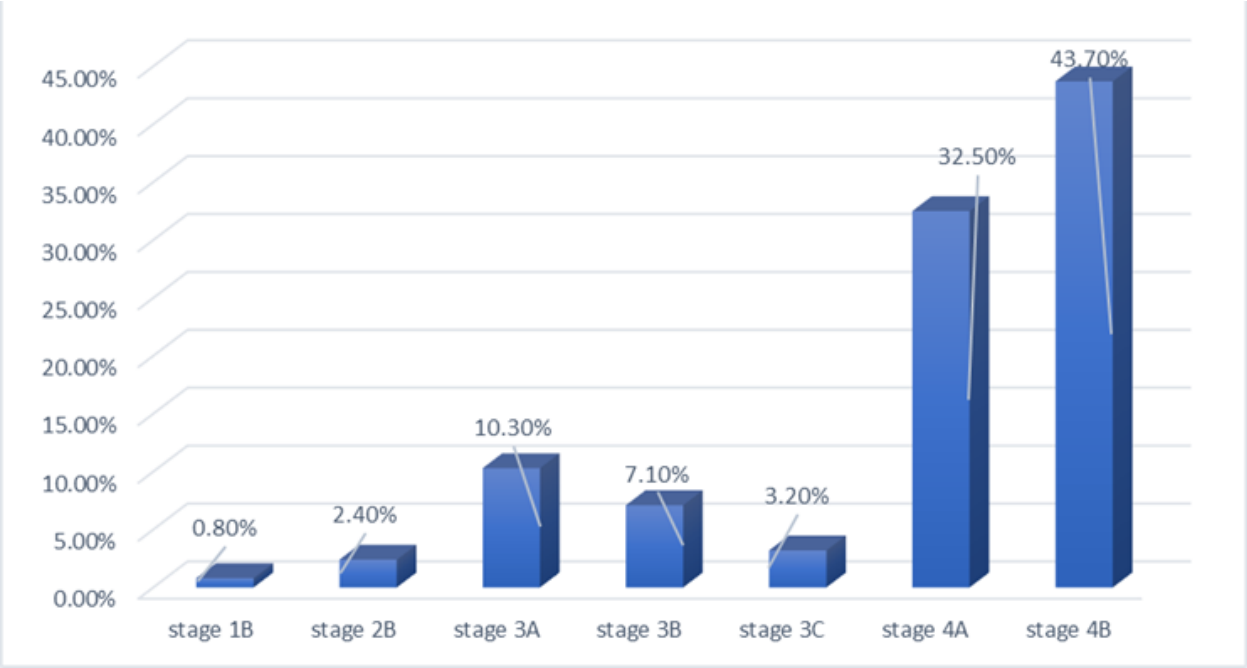
Bar Chart 1- Regional distribution of NSCLC patients treated in Tikur Anbesa referral hospital from 2017-2020



Bar chart 2- Duration of symptoms of NSCLC at initial presentation in patients treated at Tikur Anbesa referral hospital from 2017-2020

Table 4 - Initial clinical presentation of NSCLC patients treated in Tikur Anbessa referal hospital from 2017-2020.

Initial clinical presentation	Number of patients	percentage
History of cough at presentation(n=126)	103	81.7
History of hemoptysis at presentation(n=126)	21	16.7
asymptomatic at presentation(n=126)	1	0.8
History of dyspnea at presentation(n=126)	18	14.3
other manifestation at presentation(n=126)	13	10.3
History of chest pain at presentation(n=126)	40	31.7



Bar chart 3- TNM group staging at initial diagnosis in NSCLC patients treated at Tikur Anbesa referral hospital from 2017-2020

5.2, Pathological pattern

The primary tumor size was >7cm in 49(44.5%) of patients, followed by 5-7cm and 3-5cm in 27(24.5%) and 27(24.5%) of patients respectively (table 5). Mostly the primary lesion was located peripherally in 92(73%) of patients and in 30(23.8%) centrally (chart 1). Left lung and right lung involvement was occurred in 59(46.8%) and 58(46%) respectively (chart 2). Based on lung lobe involvement by the tumor; left lower lobe, left upper lobe, right upper lobe and right lower lobe were involved in 30(23.8%), 29(23%), 21(16.7%) and 21(16.7%) respectively (table 6). The most common histology type was adenocarcinoma in 81(64.3%) patients, followed by squamous cell carcinoma in 34(27%) patients (table 7). Only in 17 patients was histology sub-type reported and out of these 5 patients have papillary sub-type, 2 acinar, 2 solid and 2 keratinizing SCC (table 8). Most of the tumors 114(90.5%) had unknown grade status on the pathological report (table 9).

Metastasis at the time of diagnosis was recorded in 96(76.2%) of cases (chart 3). common sites of metastasis were pleura (27.8%) and bone (24.6%), followed by lung, liver, brain and adrenal in 15.9%, 14.3%, 9.5% and 5.6% of patients respectively (table 10).

Table 5- Primary tumour size of NSCLC at initial presentation in patients treated at Tikur Anbesa referral hospital from 2017-2020

Tumour size	Number of patients	Percentage
0-2 cm	1	0.9
2-3 cm	6	5.5
3-5 cm	27	24.5
5-7 cm	27	24.5
>7 cm	49	44.5
Total	110	100.0

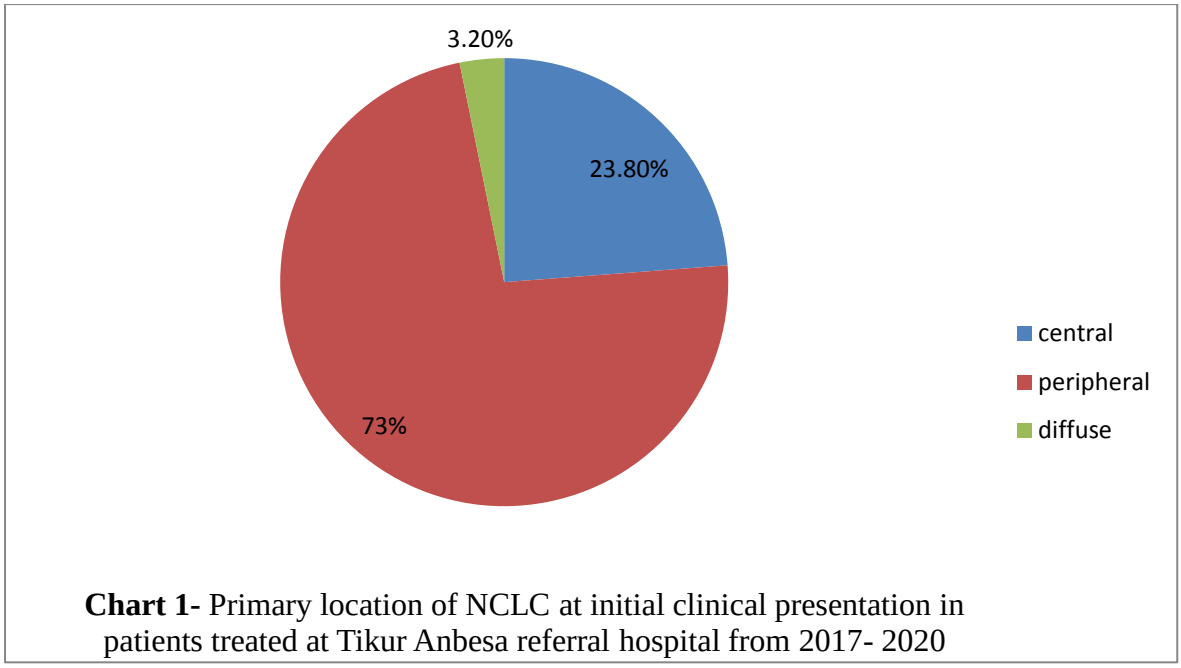


Chart 1- Primary location of NCLC at initial clinical presentation in patients treated at Tikur Anbesa referral hospital from 2017- 2020

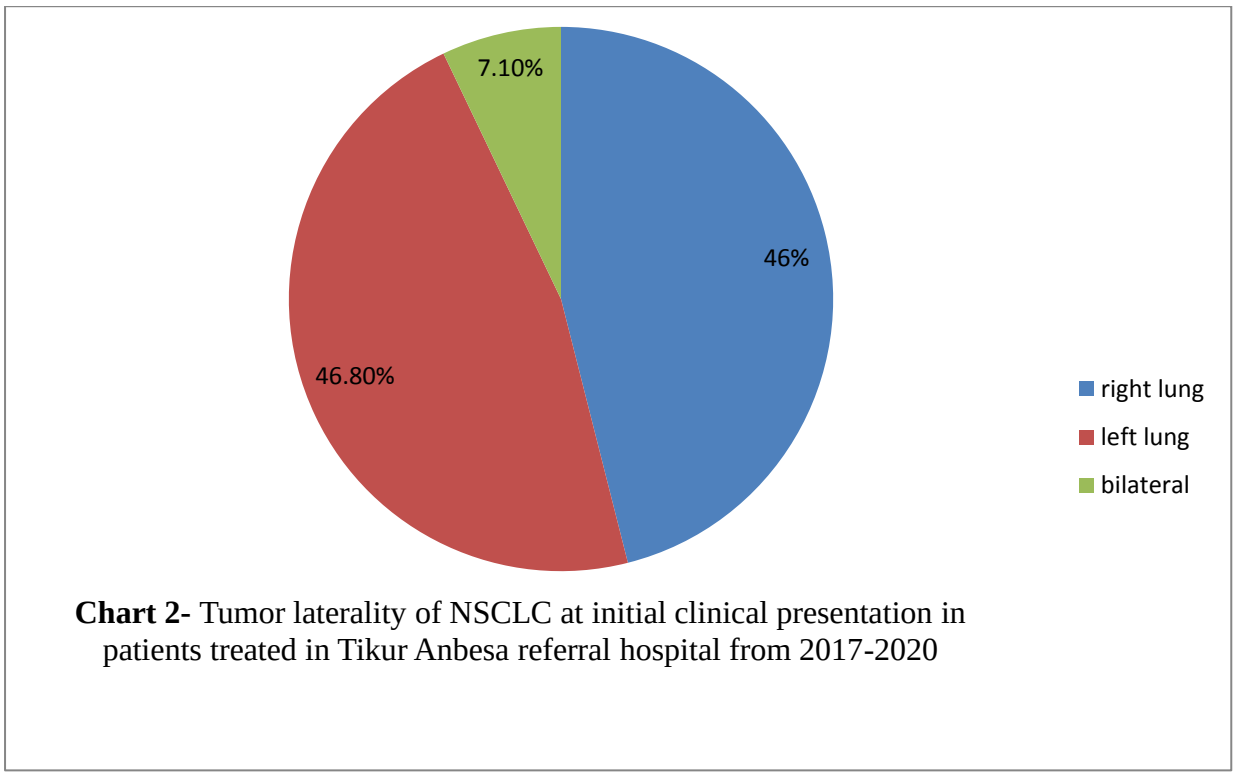


Chart 2- Tumor laterality of NSCLC at initial clinical presentation in patients treated in Tikur Anbesa referral hospital from 2017-2020

Table 6- Distribution of lung lobes involvement by NSCLC in patients treated at Tikur Anbesa Referral Hospital from 2017-2020

Lunge lobes	Number of patients	Percent
left lower lobe	30	23.8
left upper lobe	29	23.0
right lower lobe	21	16.7
right mid lobe	15	11.9
right upper lobe	21	16.7
diffuse	10	7.9
Total	126	100.0

Table 7- Common histologic types of NSCLC patients treated in Tikur Anbesa Referral Hospital from 2017-2020

Histologic types	Number of patients	Percentage
Adenocarcinoma	81	64.3
Squamous cell carcinoma	34	27.0
Large cell carcinoma	6	4.8
Adenosquamous	3	2.4
Pleomorphic carcinoma	2	1.6
Total	126	100.0

Table 8 - Histologic sub type of NSCLC in patients treated at Tikur Anbesa Referral Hospital from 2017-2020

Histologic subtype	Frequency	Percentage
mucinous	1	5.9
mixed	1	5.9
lipidic	1	5.9
papillary	5	29.4
acinar	2	11.8

keratinizing	2	11.8
micropapillary	1	5.9
bronchioalveolar	1	5.9
solid	2	11.8
non-keratinizing	1	5.9
Total	17	100.0

Table 9 - Histology grade of NSCLC in patients treated at Tikur Anbesa Referral Hospital from 2017-2020

Histology grade	Frequency	Percent
well differentiated	4	3.2
moderately differentiated	4	3.2
poorly differentiated	4	3.2
not mentioned	114	90.5
Total	126	100.0

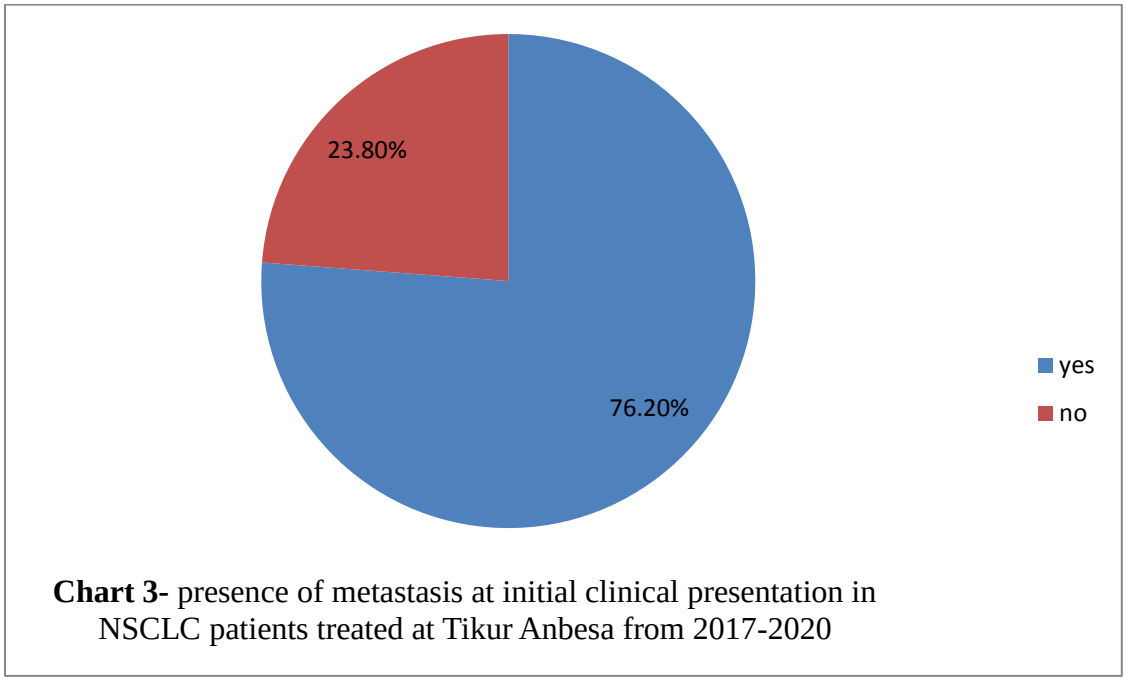


Chart 3- presence of metastasis at initial clinical presentation in NSCLC patients treated at Tikur Anbesa from 2017-2020

Table 10 – Common metastatic sites of NSCLC in patients treated at Tikur Anbesa Referral Hospital from 2017-2020

Site of Metastasis	Number of patients	Percentage
presence of metastasis to plueral	35	27.8
presence of metastasis to lung	20	15.9
presence of metastasis to liver	18	14.3
presence of metastasis to bone	31	24.6
presence of metastasis to brain	12	9.5
presence of metastasis to adrenal	7	5.6

5.3, Pattern of diagnosis and clinical care

5.3.1 Diagnosis

The diagnosis of non-small cell lung cancer was commonly confirmed pathologically by image guided core needle biopsy in 47(37.3%), FNAC in 25(19.8%) and broncoscopic biopsy in 23(18.3%) of Patients (table 10). The tissue diagnosis was acquired from the primary tumour site in 109(86.5%) and from metastatic site in 17(13.5%) of patients (table 11). Initial diagnostic workup including CXR, chest CT-Scan, Abdominal U/S, Abdominal CT scan, Brain CT-Scan and Brain MRI were recorded in 23.8%, 100%, 91.3%, 11.1%, 3.2%, and 8.7% of the patients respectively (table 12). No molecular biomarker like EGFR mutation, ALK rearrangement, ROS-1 rearrangement, BRAF V600E mutation or PD-L1expression was done in any of patients.

Table 10 - Procedures used to confirm histopathology of NSCLC in patients treated at Tikur Anbesa Referral Hospital from 2017-2020

Biopsy procedure	Frequency	Percentage
FNAC	25	19.8
Thoracentesis	10	7.9
Open biopsy	19	15.1
Broncoscopic biopsy	23	18.3
Image guided core needle biopsy	47	37.3
BAL	2	1.6
Total	126	100.0

Table 11 – Sites where tissue diagnosis acquired from to diagnose NSCLC in patients treated at Tikur Anbesa Referral Hospital from 2017-2020

Tumour sites	Frequency	Percentage
primary tumor site	109	86.5
metastatic site	17	13.5
Total	126	100.0

Table 12 - Initial Workup done to diagnose NSCLC in patients treated at Tikur Anbesa Referral Hospital from 2017-2020

Imaging modality	Frequency	percentage
Chest x-ray	30	23.8%
Chest CT-Scan	126	100%
Abdominal CT-Scan	14	11.1%
Abdominal U/S	115	91.3%
Brain CT-Scan	4	3.2%
Brain MRI	11	8.7%

5.3.1 Clinical care

Surgery was done in 16(12.8%) of patients with the intent of curative treatment (table 13). The type of surgery done was; lobectomy, pneumonectomy, wedge resection and other type of surgery in 6(37.5%), 5(31.3%), 3(18.8%) and 2(12.5%) respectively (table 13). Chemotherapy was given in 110(87.3%) of patients (table 13). The intent of chemotherapy was palliative in 103(93.6%) patients, neoadjuvant in 4(3.6%) patients and adjuvant in 3(2.7%) patients (table 13). The commonly used chemotherapy regimens are cisplatin with paclitaxol in 54(49.1%) patients, carboplatin with paclitaxol in 42(38.2%) patients and gemicitabine with cisplatin in 11(10%) patients (table 14). Radiotherapy was given in 29(23.2%) of patients with the intent of palliative treatment (table 13). The dose of radiotherapy was different based on the site and indication of radiotherapy. Supportive care as primary treatment was decided in 15 (11.9%) of patients with pain management using morphine, dexamethasone and therapeutic thoracentesis (table 13). No targeted therapy was used in any of the patients.

Table 13 –Type of treatment given and the intent of the treatment in NSCLC patients treated in Tikur Anbesa referral hospital from 2017-2020

Type of primary treatment	**Category of treatment**	**Number of patients treated**	**Percent of treated patients**
Surgery done(n=125)	yes	16	12.8
Type of surgery done(n=16)	Lobectomy	6	37.5
	Pneumonectomy	5	31.2
	Wedge resection	3	18.8
	Others	2	12.5
Chemotherapy given(n=126)	yes	110	87.3
Intent of chemotherapy (n=110)	Adjuvant chemotherapy	3	2.7
	Neoadjuvant chemotherapy	4	3.6
	Palliative chemotherapy	103	93.6
Radiotherapy given (n=125)	yes	29	23.2
Supportive care(n=126)	yes	15	11.9

Table 14 – Commonly prescribed chemotherapy regimen for NSCLC patients in Tikur Anbesa referral hospital from 2017-2020

Chemotherapy	Frequency	Percentage
cisplatin	1	0.9
gemicitabin/carboplatin	1	0.9
5-FU/cisplatin	1	0.9
gemicitabine/cisplatin	11	10.0
carboplatin/paclitaxel	42	38.2
cisplatin/paclitaxel	54	49.1
Total	110	100.0

5.5, Association analysis

There is strong evidence of relationship between cigarette smoking and sex (chi-square=20.935, df=1, $p<0.001$). This study also indicated a strong evidence of relationship between histology type (SCC and Adenocarcinoma) and primary location of the lesion (central or peripheral) (chi-square =20.328, df=1, $p<0.001$). This study also indicated a strong evidence of relationship between the primary tumour size >3cm and metastatic presence (chi-square=11.452, df=2, $p<0.003$).

6, Discussion:

Throughout the world, lung cancer is the most commonly diagnosed cancer with 2.1 million new lung cancer cases which is 11.6% of the total cases and the leading cause of cancer death with 1.8 million deaths which is 18.4% of the total cancer deaths (1). By sex, lung cancer is the most commonly diagnosed cancer and the leading cause of cancer death in males. Among females, lung cancer is the 3rd commonly diagnosed cancer and the leading cause of cancer death in the world (1).In Ethiopia, lung cancer is the 5th most frequent cancer in males with an estimated 1,049 new lung cancer cases (1). And based on the data from Addis Ababa city-based cancer registry, lung carcinoma was the 6th most frequent malignancy in male (10).

In our study, the majority of the patients were in a relatively younger age group, the ages ranged from 24 to 90 years. The median and mean age at presentation was 53 and 52 respectively. The male to female ratio was 1.14:1, which is different from United State where the incidence is higher for males because smoking is more prevalent (4). In our study, ever cigarette smoking was reported in only 20(15.9%) patients and all of them where male. This was lower than the study done in Addis Ababa University where history of cigarette smoking in lung cancer patients was 25.3% (61). The causes of LCNS could be increased exposures to smoke from burning of charcoal for heating and cooking, environmental carcinogens and second-hand smoke. Since 40 (42.6%) were housewives and 22(23.4%) were farmers in occupation and 22(17.5%) came from the rural part of the country where burning charcoal for heating and cooking is common.

Both the number of cigarettes smoked per day and the duration of smoking correlate with lung cancer risk, with longer duration in particular being associated with a much higher risk (19). Approximately 10% of worldwide lung cancer cases are at least in part related to occupational exposures (23). In this study, we could not determine the association between NSCLC and smoking and occupational exposure. Newly diagnosed lung cancer cases were reported to have a prevalence of COPD as high as six-fold greater than matched smokers without cancer and COPD is by far the most common comorbidity in patients with lung cancer, with a varying prevalence between 30 and 70% (56). In our study, 20(15.9%) patients had associated co-morbid medical illnesses, such as hypertension in 11 patients, diabetic Mellitus in 8 patient and HIV infection in 1 patients. 28(22.2%) of patients were treated for pulmonary TB before they were diagnosed as non-small cell lung cancer. No patient was diagnosed to have COPD as a comorbidity, which could be related to the low incidence of cigarette smoking.

In our study, The most common histology type of NSCLC was adenocarcinoma in 81(64.3%) patients, followed by squamous cell carcinoma in 34(27%) patients, which is consistent with the finding in US, Canada, many European countries, and Japan, where, the incidence of adenocarcinoma rose to be greater than that of squamous cell carcinomas (26, 27). There is strong evidence of relationship between histology type (SCC and Adenocarcinoma) and primary location of the lesion (central or peripheral) (chi-square =20.328, df=1, $p<0.001$). Adenocarcinoma commonly occurs in the peripheral lung zones, whereas squamous cell carcinoma occurs mainly in central locations.

Based on SEER analysis involving all lung cancer histology, 15% of all cases of lung cancer were localized to the primary site at initial diagnosis; 22% had regional lymph node spread and 56% distant metastasis; and the remaining 7% were stage unknown (30). In non–small cell lung cancer (NSCLC), half the patients present with localized or locally advanced disease and half with advanced disease (31). In our study, metastasis at the time of diagnosis was recorded in 96(76.2%) of cases. According to AJCC staging of lung Cancer the majority of patients, 55 (43.7%) and 41(32.5%) was stage 4b and 4a respectively. The majority of the patients 103(81.7%) presented with cough followed by chest pain 40(31.7%), haemoptysis 21(16.7%), shortness of breath 18(14.3%).

In patients with a high suspicion of lung cancer, a biopsy can confirm the diagnosis, but in this situation, the false negative rate of a nonspecific diagnosis is approximately 20% (36); therefore, a surgical biopsy should be pursued unless the patient is too high risk (37). When doing a tissue biopsy, it is crucial to obtain enough tissue for histology and molecular characterization (36). In our study, most of our patients presented with distance metastasis. The diagnosis of non-small cell lung cancer was commonly confirmed pathologically by image guided core needle biopsies in 47(37.3%), FNAC in 25(19.8%) and broncoscopic biopsy in 23(18.3%) of Patients and the tissue diagnosis was acquired from the primary tumour site in 109(86.5%) and from metastatic site in 17(13.5%) of patients. Molecular characterization was not done in any of the patients because such investigation modalities are not available in Ethiopia.

NSCLC management involves many different specialties in multidisciplinary team. Management is based on the stage; extent of disease spread at the time of diagnosis, performance status, histological cell type and molecular biomarker expression but also must carefully weigh the impact of baseline pulmonary functional status and comorbidity on the patient's ability to tolerate treatment. Surgery, radiotherapy and systemic therapy are the three modalities most commonly used to treat patients with NSCLC. They can be used either alone or in combination depending on disease status. The standard

of care for operable patients with stage I and stage II disease are complete surgical resection with the possible addition of adjuvant chemotherapy (46). However, most of the patients we see in our environment present late with advanced disease at the time of diagnosis. In this study, Surgery was done in 16(12.8%) of patients with the intent of curative treatment. The type of surgery done was; lobectomy, pneumonectomy, wedge resection and other type of surgery in 6(37.5%), 5(31.3%), 3(18.8%) and 2(12.5%) respectively. Chemotherapy was given in 110(87.3%) of patients. The intent of chemotherapy was palliative in 103(93.6%) patients. Radiotherapy was given in 29(23.2%) patients, all of them with the intent of palliative treatment. For stage IV patients with significant local presenting symptoms requiring urgent radiotherapy, such as SVC obstruction, haemoptysis, or cord compression, palliative radiotherapy followed by systemic therapy is the preferred treatment approach. Lack of accessibility to radiotherapy and other targeted therapies, such as drugs that act on EGFR, ALK, ROS1, and BRAF may have resulted most of our patients to be treated with the intent of sub optimal palliative treatment. For patients with stage IV disease, owing to the poor prognosis, a detailed discussion of the goals of care with consideration of early referral to hospice is part of the initial treatment approach. In this study, supportive care as primary treatment was decided in 15 (11.9%) of patients with pain management using morphine, dexametasone, therapeutic thoracentesis and others.

7, Conclusions and Recommendations:

7.1, Conclusion

The study has shown non-small cell lung cancer affects a diverse group of patients in terms of age, sex, place of living, marital status and occupation. Cigarette smoking history was found in 16% of NSCLC patients. Being 46.8% of patient females and 42.6% house wife the risk of charcoal indoor smoking could be entertained. Adenocarcinoma was most common histology type of NSCLC followed by SCC. There is also a strong relationship between cigarette smoking and sex, between histology type and primary location of the lesion and between primary tumour size greater than 3cm and presence of metastasis. The majority of the patients had an advanced stage of illness which required palliative care with combination of chemotherapy, radiotherapy and supportive care to improve quality of life.

7.2, Recommendation

The principal investigators recommend that public and health provider awareness programs on environmental and cigarette smoking as a major risk factors for NSCLC have to be done. Future studies should be done to examine the causes of lung cancer in the country. Awareness creation on early detection and treatment should be done. In addition to the available treatment modality, additional medications like targeted therapy and immunotherapy drugs should be available since most of our patients present at late stage.

7.3, Limitation of study

- ✓ The cases registered on logbooks and patient charts were discordant for many patients resulting in many patients to be discarded.
- ✓ Incomplete data on histopathology subtype and grades and treatment given were seen in the majority of the cases.
- ✓ This is a retrospective study which is less powerful than a prospective study

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Annexes;

Data extraction tools:

Serial. No	Variable	Category
1	MRN	----------
2	Sex	A, male B, female
3	Age in years	----------
4	Occupation	----------
5	Marital status	A, Married B, Single C, Divorced D, Widow
6	Region	A, Tigray B, Afar C, Amhara D, Oromia E, Somalia F, Benishangul Gumuz G, SNNPR H, Gambelia I, Harari J, Addis Ababa K, Dire Dawa
7	Residency	A, Urban B, Rural C, Not documented
8	**Comorbid Medical Condition**	
8.1	Diabetic mellitus	A, Yes B, No
8.2	Chronic hypertension	A, Yes B, No
8.3	HIV infection	A, Yes B. No C, Unknown
8.4	Previous diagnosis with COPD	A, Yes B, No
8.5	Previous history of treatment for pulmonary tuberculosis	A, Yes B, No
9	**Risk Factors**	
9.1	Smoking history	A, Yes B, No
9.2	If question no 9 is "yes" how many packs a year?	----------
9.3	Family history of lung	A, Yes

	cancer	B, No
9.4	Previous history of radiation therapy to the chest	A, Yes B, No
10	**Clinical presentation and**	**diagnostic workup**
10.1	ECOG Performance status	A, 0 B, 1 C, 2 D, 3 E, 4
10.2	Initial clinical presentation	A, Cough B, Haemoptysis C, Dyspnoea D, Chest pain E, Asymptomatic (incidental finding) F, Other (specify) ----------
10.3	Duration of initial symptom	A, 0 – 3 months B, 3 – 6 months C, 6 – 9 months D, 9 -12 months E, More than 1 year
11	Imaging modalities used for initial diagnosis and staging	A, Chest CT-Scan B, Chest X-Ray C, PET-CT Scan D, Abdominal CT-Scan E, Abdominal U/S F, Abdominal MRI G, Bone scan H, Brain MRI I, Brain CT-Scan
12	Primary location of the lesion on the lung	A, Central B, Peripheral
13	Which lobe	----------
14	Tumour laterality	A, Right lung B, Left lung C, Other
15	Primary Tumour size	A, 0 - 2cm B, 2 - 3cm C, 3 – 5cm D, 5 – 7cm E, > 7cm
16	Tissue diagnosis acquired from	A, Primary tumour site B, Metastatic site
17	procedure used to confirm histopathology of Non-small cell lung cancer	A, EBUS Biopsy B, EUS Biopsy C, VATS D, FNAC

		E, Thoracentesis F, Sputum Cytology G, Mediastinoscopy H, Open Biopsy I, Bronchoscopy J, image guided core needle biopsy
18	Histological type of NSCLC	A, Adenocarcinoma B, Squamous cell carcinoma C, Large cell carcinoma D, Adeno-squamous E, Pleomorphic carcinoma F, Carcinosarcoma G, Pulmonary blastoma
19	Histologic subtype	----------
20	Histologic grade	A, Well-differentiated B, moderately differentiated C, poorly differentiated D, Undifferentiated E, not mentioned
21	Initial TNM group stage of NSCLC	A, IA1 B, IA2 C, IA3 D, IB E, IIA F, IIB G, IIIA H, IIIB J, IIIC K, IVA L, IVB
22	What was the distance metastatic site (if stage IV)	----------
23	Is molecular biomarker done	A, Yes B, No
24	If question no 23 is “yes”, which biomarker was positive	A, EGFR mutation B, ALK rearrangement C, ROS-1 rearrangement D, BRAF V600E mutation
25	Is PD-L1 expression test done	A, Yes B, No
26	**Treatment**	
27.1	Is surgery done	A, Yes B, No
27.2	If question no 27.1 is “yes”, what type of surgery is done	A, Segmentectomy B, Wedge resection C, Lobectomy D, Pneumonectomy

		E, Other----------
27.3	Is chemotherapy given	A, Yes B, No
27.4	If question no 27.3 is "yes", what was the intent of chemotherapy	A, Adjuvant chemotherapy alone B, Adjuvant Concurrent chemoradiotherapy C, Neoadjuvant chemotherapy alone D, Neoadjuvant concurrent chemoradiotherapy E, Palliative chemotherapy
27.5	If question no 27.3 is "yes", what was the chemotherapy regimen	----------
27.6	Is radiotherapy given	A, Yes B, No
27.7	If question no 27.6 is "yes", what was the intent of radiotherapy	A, Definitive CCRT B, Adjuvant CCRT C, Neoadjuvant CCRT D, Palliative RT
27.8	If question no 27.6 is "yes", what was the site, dose and fractionation of radiotherapy	----------
27.9	Is targeted therapy used	A, Yes B, No
27.10	If question no 27.9 is "yes", what type of targeted therapy was used	A, EGFR targeted therapy B, ALK targeted therapy C, ROS-1 targeted therapy D, BRAF V600E targeted therapy E, PD-L1 targeted therapy
27.11	Targeted therapy was given as	A, 1st line B, 2nd line C, 3rd line
27.12	Is on supportive care	A, Yes B, No

Patient information sheet (English version):

This patient information collection sheet is intended to determine the demographic, clinical, and treatment patterns of non-small cell lung cancers at Tikur Anbessa Specialized Hospital (TASH), Addis Ababa, Ethiopia. The study will be conducted through reviewing secondary data. The study will give some evidence and information for governmental and non -governmental organizations which work in the area of non-communicable disease specifically on NSCLC at national, regional and district level by providing basic information on the clinical, pathology and treatments on NSCLCs. Information which is necessary for the study will be taken from patient chart, log book and radiotherapy treatment sheet. As the study will be conducted through review of medical records alone, the individual patients will not be subjected to any harm as far as the confidentiality is kept. To preserve the confidentiality, residents working in cancer treatment center of Tikur Anbessa specialized hospital will extract the data from the medical records. Moreover, no personal identifiers will be used on data collection form.

Date of review----------

Day---------- month---------- year----------

Name of reviewer---------- Signature----------

Time started---------- Time ended----------

Total number of records reviewed----------

Result; (A) complete (B) incomplete (C) excluded

Action taken for incomplete data----------

Name of supervisor----------

Signature----------

Principal investigator address: 0930927931

Assurance of primary investigator:

I, the undersigned Clinical Oncology Resident agree to accept responsibility for the scientific, ethical and technical conduct of the research project and for provision of required progress reports as per terms and conditions of the research and publications office of the Addis Ababa University.

Name of the Investigator: Dr. Amanuel Asefa (4th Year Clinical Oncology Resident)

Signature_____ Date_____/_____/_____

APPROVAL OF THE PRIMARY ADVISOR

Advisor Name: Dr. Wondimagegnehu Tigeneh (MD, MPH, Consultant Oncologist)

Signature_____ Date _____/_____/_____