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CT IMAGING FEATURES AND CLINICOPATHOLOGIC PATTERNS OF LUNG CANCER AT TIKUR ANBESA SPECIALIZED TEACHING HOSPITAL, ADDISA ABABA UNIVERSITY: A DESCRIPTIVE STUDY

BY

MICHAEL GEBREYESUS, MD

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BY: MICHAEL GEBREYESUS, MD

ADVISORS: AZMERA GISSILA, MD

AMIR ALWAN, MD

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ABSTRACT

Background: - Lung cancer is the single most commonly diagnosed cancer and most common cause of cancer deaths worldwide. There are international variations and changing trends in the epidemiology and cell types of lung cancer, which in turn affect the imaging features. CT is the most important imaging modality in lung cancer which is found to have high correlation rate with pathological diagnosis in different studies. In Ethiopia, there is no similar correlative research and this study addresses the deficiency.

Objectives: To assess CT pattern of lung cancer with clinic-pathologic correlation at Tikur Anbessa specialized hospital, Addis Ababa, Ethiopia from June 2015-June 2017.

Methods: Retrospective study was done on a total of 63 patients diagnosed with lung cancer at TASH in a two-year period (from June 2015-June 2017).

Results: Mean age at diagnosis was 50.14 years (SD=11.02), with M:F of 1.33:1; 85.2% of females were housewives. Predominant cell type was adenocarcinoma (47.6%). Most common presenting CT feature was mass (77.8%). History was positive for smoking in 25.4% and TB in 42.4%. Majorities (87.3%) were inoperable (stage IIIB-IV) at time of CT imaging and most frequently reported symptom was cough (91.9%).

Conclusion: Adenocarcinoma is the most common cell type. Pulmonary mass is the frequently encountered presenting imaging feature. Majority of patients present at advanced stage. We observed a narrow gender gap with M:F of 1.33:1 and majority of the female population are housewives. Smoking is not identified as the major risk factor in our study. With the high incidence of pulmonary tuberculosis in the country and presence of history for tuberculosis in 42.4% of the study population, we assume TB as the most important cofounding problem.

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ACRONYMS

AAU	Addis Ababa University
AIDS	Acquired Immune Deficiency Syndrome
COPD	Chronic obstructive pulmonary disease
CT	Computed Tomography
FDRE	Federal Democratic Republic of Ethiopia
FNAC	Fine Needle Aspiration Cytology
GLOBOCAN	Global Burden of Cancer Study
HIV	Human Immune Deficiency virus
LAP	Lymphadenopathy
MDCT	Multidetector computed tomography
MPE	Malignant Pleural Effusion
MPN	Multiple Pulmonary Nodules
MRN	Medical recording number
NSCLC	Non-small cell lung cancer
PFA	Pleural fluid analysis
SCC	Squamous cell carcinoma
SCLC	Small cell lung cancer
SIADH	Syndrome of inappropriate anti-diuretic hormone secretion
SNNP	Southern Nations, Nationalities, and People's region
SPN	Solitary Pulmonary Nodule
SSA	Sub Saharan Africa
SVC	Superior Vena Cava
TASH	TikurAnbesa Specialized Hospital
TB	Tuberculosis
WHO	World Health Organization
WRD	WHO-approved rapid diagnostics

1 INTRODUCTION

1.1 Background

The term *lung cancer* is used to describe tumors arising from the epithelium of the bronchi, bronchioles, and alveoli (1). According to WHO classification, grossly there are two diagnostic categories of epithelial lung cancers with greatest clinical importance, namely small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). The later includes adenocarcinoma, squamous cell carcinoma and large cell carcinoma. These four histologies account for approximately 95% of all epithelial lung cancers. Various rare types of lung cancer make up a small minority of cases including undifferentiated carcinomas, carcinoids, and bronchial gland tumors. Tumors may occur as single or mixed-type histology. This histologic classification of lung cancer is important for staging, treatment, and prognosis(2, 3).

Lung cancer is the most frequently diagnosed cancer and common cause of cancer deaths in the world. An estimated 1.8 million new lung cancer cases occurred in 2012 (12.9% of the total), 58% of which occurred in the less developed regions(4).

The primary risk factor for the development of lung cancer is cigarette smoking, which is estimated to account for approximately 90 percent of all lung cancers(5)**.** Other risk factors include environmental factors like exposure to second-hand smoke, asbestos, radon, metals (arsenic, chromium, and nickel) and polycystic aromatic hydrocarbons(5), radiation therapy(6-8) , HIV infection(9-12), Lung diseases [pulmonary fibrosis(13), pulmonary tuberculosis(14), COPD(15, 16)] and indoor air pollution(17, 18).

The majority of patients with lung cancer have advanced disease at clinical presentation (19). Symptoms and signs can result from local tumor progression (cough, dyspnea, hemoptysis), regional spread (pleuritic chest pain, hoarseness, SVC syndrome, pancoast syndrome, horner syndrome, constrictive pericarditis or cardiac tamponade, dysphagia), or distant metastases (symptoms vary by location). Paraneoplastic syndromes (e.g., hypercalcemia, SIADH secretion) and constitutional symptoms may occur at any stage of the disease. Although symptoms are not specific to the classification or histology of the cancer, certain complications may be more likely

with different types. About 25% of lung cancers are asymptomatic and are detected incidentally with chest imaging(20).

Appropriate treatment for lung cancer is based on whether the tumor is small cell or non-small cell, as well as other tumor characteristics. Based on type and stage of cancer, as well as specific molecular characteristics of cancer cells, treatments can include surgery, radiation therapy, chemotherapy, and/or targeted therapies(3).

Unfortunately, 75 percent of patients with lung cancer present with symptoms due to advanced local or metastatic disease that is not amenable to cure(19). Despite advances in therapy, five-year survival rates average approximately 16 percent for all individuals with lung cancer(21). Therefore, prevention is the most effective strategy for reducing the burden of lung cancer.

1.2 Statement of the Problem

Lung cancer imposes a major global disease burden (22). It has been the most common cancer in the world for several decades. An estimated 1.8 million new cases occurred in 2012, accounting for about 13% of total cancer diagnoses. It is also the most common cause of cancer-related deaths estimated to be responsible for nearly one in five (1.5 million deaths, 19.4% of total)(21). In males, the highest lung cancer incidence rates were in Northern America, Europe, Eastern Asia, and Uruguay. Among females, the highest lung cancer rates were in Northern America, Europe, Australia, New Zealand, North Korea, and China. Both for males and females, the lowest rates were in Sub-Saharan Africa, where Ethiopia is found.

Although the lowest incidence rates were estimated in SSA, there are no actual population based studies and reliable cancer registry system which might contribute to significant underestimation of the incidence (22-24). The GLOBOCAN estimate of lung cancer incidence, mortality and prevalence in Ethiopia is made on basis of extrapolations of data from the Addis Ababa City Cancer Registry, which is the only cancer registry in the country and without considering changes in risk factor prevalence (e.g., smoking, TB, HIV/AIDS, domestic pollution)(22, 23, 25, 26). In Ethiopia, the changing patterns (increasing prevalence) of tobacco smoking (27, 28) with the high TB(29) and HIV/AIDS burden(30, 31) and the fact that more than 90% of the population use solid fuels as a primary source of domestic energy (32) show the presence of significant risk factor for lung cancer in the country. Using smoking prevalence information, Ng

et al(22) estimated lung cancer deaths in SSA to be 44,076 in 2005, which is 2.6 times the most recent WHO estimate in 2003 (17,000 deaths). Their estimate for Ethiopia was 3356 which is about 2.5 times the WHO estimate (1343) and 4.5 times the GLOBOCAN estimate (748). Winkler et al(23) also showed the estimated lung cancer deaths in Ethiopia to be considerably higher than the WHO and GLOBOCAN estimates.

About 60% of the estimated new lung cancer cases in 2012 occurred in the les developed regions of the world. The geographical patterns in mortality likely to follow the patterns in incidence due to the high fatality (ratio of mortality to incidence is 0.87)(4). Majority of patients with lung cancer have advanced disease at diagnosis demonstrating poor prognosis (19, 33). Early detection of suspicious lung lesions and diagnosis of lung cancer is essential in minimizing morbidity and mortality. In this regard, imaging, particularly MDCT plays a major role in screening, early diagnosis, staging, planning surgical approach and post-therapy follow-up. Due to its better spatial resolution CT shows many characteristic morphologic patterns of a suspicious lesion that may strongly suggest the diagnosis. CT is the back bone imaging modality for the TNM staging which is very important for treatment. CT morphological feature also provide potential clues to predict hisological growth pattern, which is another determinant factor of prognosis and therapy selection (33-37). So, it becomes highly imperative to study the CT patterns of lung cancer in correlation with cytopathological diagnosis. To our knowledge, there is no such study done in our hospital or other part of the country.

2 LITERATURE REVIEW

CT is a primary baseline imaging modality in suspected lung cancer cases. According to the National Cancer Institute (INCa) every patient with a clinical suspicion of lung cancer should have a chest CT following chest radiograph even with normal radiographic findings. The major role of imaging, particularly CT is in identifying and characterization of pulmonary lesion which may or may not be seen on the preliminary chest radiograph, in pretreatment staging (in combination with other imaging modalities and histologic studies) and planning of surgical or radiation therapy (38, 39).

Radiological characteristics by cell type

Adenocarcinoma. The incidence of Adenocarcinoma is rising, making it the most common histologic type representing about 50% of lung cancer cases. It is the most frequently diagnosed cell type in women and non-smokers (2, 40, 41). Classically they are peripherally located but may be central in about a quarter of cases (40, 42). Hilar and/or mediastinal involvement is seen in about half of the cases (43). They usually measure <4 cm in diameter and cavitation is seen rarely (4%) (42). On MDCT, three patterns are described: Pure GGN (sub-solid nodules), part solid or mixed GGN (part-solid GGN) and solid nodules (44).

Squamus Cell Carcinoma. Squamous cell carcinoma represents 30% of all lung cancers. Distant metastasis occurs at later stages and have better prognosis than adenocarcinomas. More than two third of cases are centrally located with obstructing endobronchial lesion causing perihilar mass and segmental or lobar atelectasis. Obstructive pneumonitis is also frequently seen distal to the lesion. They are the most likely subtypes to cavitate (82%) and most common causes of superior sulcus tumors. Peripherally located SCC appear as thick walled cavitary nodule /mass which doesn't usually show air-fluid level (41-43).

Superior sulcus tumor is much more commonly seen in older individuals. Imaging appearance include unilateral apical cap of more than 5 mm, asymmetry of bilateral apical caps of more than 5 mm, an apical mass, and bone destruction. It may also invade the chest wall, adjacent vessels (e.g., subclavian vessels), the brachial plexus, mediastinal structures, or vertebral bodies and paravertebral structures (41-43, 45, 46).

Large cell carcinoma. Large cell carcinomas are undifferentiated NSCLC which represents about 5% of all lung cancers. They show rapid growth and metastasis at early stages, hence poor prognosis. They are typically peripherally located and large in size, majority of them (70%) being greater than 4cm at diagnosis. Foci of internal necrosis are also common (41-43).

Small cell lung cancer. SCLC represents 15-20% of all lung cancer cases. It has the strongest association with smoking. SCLC is the most aggressive subtype with the poorest prognosis. It shows very rapid growth and majority of patients have metastases at diagnosis. The usual radiographic feature is hilar or perihilar mass associated with bulky mediastinal lymphadenopathies. In about 10% of the cases, they may present as a peripherally located solitary nodule. The primary tumor may be obscured by bulky adenopathy but noncontiguous parenchymal mass can be identified in up to 41% at CT that may have cavitation rarely (41-43).

There are geographical variations in lung cancer patterns (rates, trends, cell types) which mainly reflect differences in the stage and degree of the tobacco epidemic (21). There are many studies done to assess the trend of lung cancer in their respective locations.

In a prospective study done in India, 30 patients (26 males and 4 females) with strong clinical suspicion and preliminary MDCT diagnosis of lung cancer were included. CT diagnosis had complete correlation in 28 patients (93.3%). The mean age was 59 years (age range between 45 to 80 years) with male predominance (26 males). Out of the 26 male participants, 25 (83.3%) were smokers. The commonest symptom was cough which was noted in 25 cases followed by dyspnea in 24 cases (80%). Two third of the cases showed central hilar mass and peripheral mass lesion was seen in the other one third patients. Contrast enhancement was demonstrated in all of the cases and nodal enlargement in 28 patients (93.3%) with the most common nodal station involvement being the pretracheal and prevascular stations. Although the incidence of adenocarcinoma is increasing and reported to be the most common histologic subtype, in this study SCC was the most frequently seen subtype (16 patients, 53.3%) followed by adenocarcinoma (8 patients, 26.7%). Fifteen out of the 16 cases of the SCC and 7 out of the 8 adenocarcinoma presented as central hilar mass and peripheral mass lesion, respectively. Most of the patients had advanced stage disease at diagnosis (T4N2Mx in 20%) and the bone was the most common site of metastasis seen in 8 patients (26%). Although this study was limited by the

small sample size, it showed MDCT to have an effective role in diagnosis and staging of lung cancer with sensitivity of 100% and accuracy of 93.3% (33).

With the aim of correlating CT diagnosis of pulmonary masses with FNAC, Biswas et al did prospective observational study in 90 patients of Tripura, out of which 71 were pathologically proven primary carcinomas. In this study adenocarcinoma was the most common cell type detected (30 cases) followed by SCC (26 cases). Out of the 30 cases of adenocarcinomas, 22 were located peripherally and 26 patients were smokers. The SCC cases were more common in the central location (16 out of 26) and cavitation was observed in 6 cases. Although this study was not dedicated only for primary lung carcinomas, correlation of CT diagnoses with that of FNAC was 94.5% for malignant lesions, making CT scan study a very useful non-invasive diagnostic modality in lung masses (36).

3 SIGNIFICANCE OF THE STUDY

There is marked epidemiological transition in which the burden of chronic non-communicable and neoplastic diseases is increasing in developing countries like Ethiopia. Out of all the neoplastic conditions, lung cancer is the single most frequently diagnosed and most common cause of cancer-related deaths. Early diagnosis of lung cancer is crucial to reduce mortality and improve patient outcome, for which imaging plays major role. CT is a cornerstone of imaging in lung cancer and has high correlation with pathological diagnosis. Although there is international variation in trends of lung cancer, there is no study done in Ethiopia assessing the epidemiologic and radiopathologic patterns of the disease. Therefore, this study will address this gap. To the best of our knowledge, this study is the first in its kind and will serve as a baseline data for future studies.

4 OBJECTIVES

4.1 General Objectives

- To assess CT features and clinic-pathologic patterns of lung cancer at TikurAnbessa specialized hospital, Addis Ababa, Ethiopia.

4.2 Specific Objectives

1. To describe the CT features of lung cancer.
2. To describe histological pattern of lung cancer.
3. To describe the clinical features of lung cancer.
4. To identify factors associated with lung cancer.

5 METHODS AND MATERIALS

5.1 Study area and period

The study was conducted at Tikur Anbesa specialized hospital (TASH), Radiology department. TASH is one of the largest referral hospitals in the country with 700 beds and give medical service for about 370,000-400,000 patients per year. It has the only oncologic center for the country. This study was conducted from January to August 2017.

5.2 Study design

This is a hospital based retrospective descriptive study.

5.3 Study population

All patients registered as cases of lung cancer and had followup in the oncology unit of TASH since the last two years (June 2015-June 2017).

5.4 Sampling technique

Convenient sampling method was used and all patients with diagnosis of lung cancer are included.

5.5 Eligibility criteria

5.5.1 Inclusion criteria

All patients with a diagnosis of lung cancer and follow up in the oncology unit who have chest CT image or report and pathologic results are included in the study.

5.5.2 Exclusion criteria

Patients with unavailable medical recording chart, chest CT image/report or pathological results were excluded. Those patients with other diagnosis like pulmonary lymphoma, sarcoma or secondary were excluded. Patients who were still on investigation and not started treatment for lung cancer were not included in the study.

5.6 Data collection tools and techniques

Cases of lung cancer registered in the oncology unit of TASH from June 1, 2015 to June 30, 2017 were collected. Using their MRN, the medical recording charts were retrieved to access data regarding socio-demography, clinical history, CT imaging features, pathological results and treatment of the patients. The data were collected and filled in properly designed and pre-tested data collection format. Serial number was given to each patient on the data collection sheet to ensure anonymity. Quality of the data was assured by a properly designed data collection format which was pre-tested, modified and developed before the commencement of the actual data collection. A half-day raining was also given to data collectors about objective of the study, data collection format, on how to extract information from patient files and registers. After data collection, data was checked for consistency and completeness.

5.7 Statistical analysis

The data collected from medical recording charts of the patients were entered, after being encoded and analyzed using SPSS version 20 statistical packages. Data cleaning was performed to check for frequencies, accuracy, and consistencies and missed values and variables. Any logical and consistency error identified during data entry was corrected after revision of the original completed questionnaire. The cleaned and edited data was ready for appropriate statistical analysis. The mean, standard deviation and the frequency of the variables was done and the analyzed data was presented via tables, graphs and texts.

5.8 Ethical consideration

Ethical approval and clearance was obtained ethical review Committee of the Department of Radiology and the Institutional Review Board (IRB) and Research and Publication Committee of the medical faculty of Addis Ababa University. A formal cooperation letter written from the department of Radiology was submitted to the department of Radiotherapy and permission was granted from the head for data collection activities.

There was not any personal identifier in the data collection format. The data was collected, compiled and analyzed by principal investigator and trained data collectors to guarantee privacy of the study participants.

5.9 Dissemination of the Result

The results of this study will be submitted to the Department of Radiology, CHS of Addis Ababa University and will be disclosed to the respective units of the Hospital, health professionals and authorities. We anticipate manuscript submission to a medical journal for publication.

5.10 Definitions

Pulmonary nodules: are focal opacities measuring 3cm or less in diameter, that may be solitary (*Solitary pulmonary nodule)* or multiple (*multiple pulmonary nodules)* (47).

Pulmonary mass: is a focal pulmonary lesion that is greater than 3cm in diameter (47).

Central pulmonary lesions: are those lesions described to be located at hilar region.

Peripheral lesions: are lesions which are not located in the hilar region.

Lymph node involvement: is considered when lymph node size is greater than 1cm in the shortest axis or whenever there is a word “lymphadenopathy” in the report.

Bacteriologically confirmed TB case: is one from whom a biological specimen is positive by smear microscopy, culture or WRD (such as Xpert MTB/RIF) (48).

Clinically diagnosed TB case: is one who does not fulfil the criteria for bacteriological confirmation but has been diagnosed with active TB by a clinician or other medical practitioner who has decided to give the patient a full course of TB treatment. This definition includes cases diagnosed on the basis of X-ray abnormalities or suggestive histology (48).

6 RESULT

6.1 Socio-demographic information

The study population included 36 (57.1%) male and 27 (42.9%) females; M:F of 1.33. The mean age was 50.14 years (range 27-75 years). Majority of the patients (52.4%) were from Addis Ababa followed by patients from the regions of Oromia (20.6%), SNNP (14.3%), Amhara (6.3%), Tigray (3.2%) and Harari (3.2%). House wives comprised higher proportion (42.6%) of the study population (Table 1). Table 7 summarizes socio-demographic, clinical and radiological features in different histologic subtypes.

Table 1: Basic Socio-demographic characteristics of lung cancer patients included in the study, TASH, 2017

Characteristics	No. (Valid %)
Sex	
Male	36 (57.1)
Female	27 (42.9)
Age (mean)	50.14 (SD=11.02)
Address (Region)	
Addis Ababa	33 (52.4)
Oromia	13 (20.6)
SPNN	9 (14.3)
Amhara	4 (6.3)
Tigray	2 (3.2)
Harari	2 (3.2)
Religion	
Orthodox	35 (70)
Muslim	12 (24)
Protestant	3 (6)
Educational level	
Illiterate	6 (18.2)
Primary	8 (24.2)
Secondary	11 (33.3)
Higher	8 (24.2)
Occupation	
House wife	23 (42.6)
Farmer	6 (11.1)
Private	6 (11.1)
Governmental	8 (14.8)
Other	11 (20.4)

SPNN, Southern Nations, Nationalities, and People's region

6.2 Clinical Data

All patients were symptomatic and cough was the most frequently reported symptom at presentation (91.9% cases) followed by chest pain in 59.7%, dyspnea in 38.7%, weight loss in 31.7%, hemoptysis in 19.4% and fever in 11.1%. Neck swelling and discomfort (3.2%), anterior chest wall mass (1.6%) and hoarseness of voice (1.6%) were the least reported complaints at presentation (Figure 1).

There was history of cigarette smoking in 16 patients (25.4%) of the study population. Majority of them (57.1%) smoked for greater than 20 years and 72.7% smoked 10-20 cigarettes per day (Table 2). None of the female patients had smoking history.

In five patients (8.5%) there was a remote history of pulmonary tuberculosis for which they were treated. More than a third of the patients (33.9%) were given anti-tuberculosis treatment for the current illness. In 9 of them the diagnosis was made with chest radiograph and in 2 patients the diagnosis was with PFA. In the rest of the cases given anti-tuberculosis for the current illness, the mode of diagnosis was not mentioned (Table 2).

Table 2: History of smoking and pulmonary tuberculosis in the study population, TASH, 2017

Clinical data	No. (Valid %)
Smoking history	
Absent	47 (74.6)
Present	16 (25.4)
Year[a]	
10-20	6 (42.9)
>20	8 (57.1)
Quantity of cigarette per day[b]	
10-20	8 (72.7)
>20	3 (27.3)
Previous history of pulmonary TB	
Absent	54 (91.5)
Present	5 (8.5)
TB treatment for the current illness	
Absent	41 (66.1)
Present	21 (33.9)
Mode of diagnosis for TB	
CXR	9 (81.8)
PFA	2 (18.2)

[a] duration of smoking in years; [b] amount of cigarette in pieces
TB, tuberculosis; CXR, chest radiograph; PFA, pleural fluid analysis

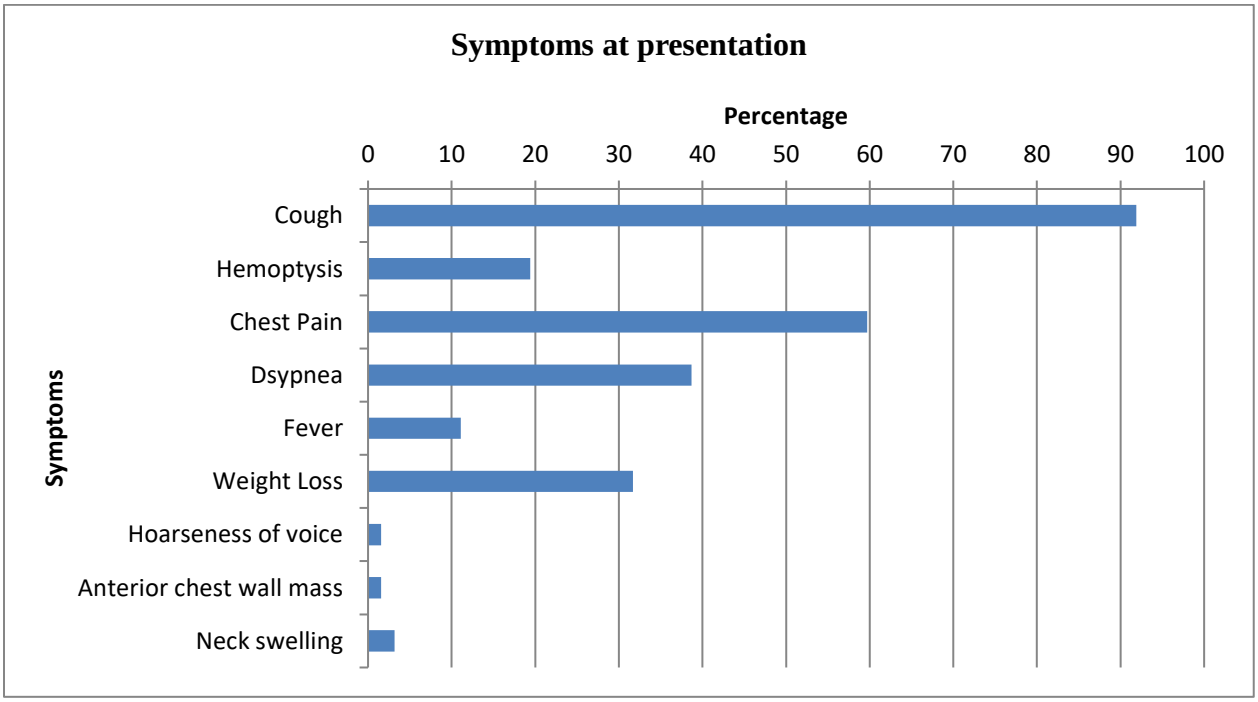

Figure 1: Bar chart showing symptoms of patients at presentation

6.3 Cell type

From the total study population, 56 patients had pre-treatment pathology results out of whom 5 patients also had post-resection (post-operative) pathology examination. The remaining 7 patients had only post-resection pathology examination. The mode of pre-treatment and pre-operative sample taking is summarized in table 3. Bronchoscopic biopsy, either transbronchial or endobronchial biopsy, was the most commonly used modality of sample taking (28.6%) followed by image guided biopsy (25%); imaging modality for guided biopsy was CT in 12 patients and US in 2 patients (Table 3).

Table 3: Mode of pre-treatment sample taking for pathologic examination, TASH, 2017

Sample taking	No. (%)
Image guided biopsy	14 (25)
Bronchoscopic biopsy (TBB/EBB)	16 (28.6)
Bronchoscopic BAL	4 (7.1)
Pleural fluid cytology	8 (14.3)
FNAC from metastatic LAP	6 (10.7)
FNAC from other metastasis	5 (8.9)
Pleural biopsy	3 (5.4)

TBB, Transbronchial biopsy; EBB, Endobronchial biopsy; BAL, Bronchoalveolar lavage; FNAC, Fine needle aspiration cytology; LAP, lymphadenopathy

Adenocarcinoma was the commonest subtype, affecting 30 patients (47.6%). The other histologic subtypes were squamous cell carcinoma (20.6%), small cell carcinoma (1.6%), large cell carcinoma (1.6%), and atypical carcinoid tumor (1.6%). In the rest of the patients no specific cell type diagnosis was made, of which 22.2% was carcinoma and 4.8% was suggestive of malignancy (Table 4).

Table 4: Frequency of histologic subtypes of lung cancer, TASH, 2017

Histologic subtype	No. (%)
Adenocarcinoma	30 (47.6)
Squamous cell carcinoma	13 (20.6)
Small cell carcinoma	1 (1.6)
Large cell carcinoma	1 (1.6)
Atypical carcinoid tumor	1 (1.6)
Carcinoma[a]	14 (22.2)
Malignancy[b]	3 (4.8)

[a] carcinoma cell type not otherwise specified

[b] histopathologic result was suggestive of malignancy

6.4 CT patterns

6.4.1 Features of primary tumor

In this study, pulmonary mass was the most frequently observed parenchymal lesion reported in 49 cases (77.8%) followed by SPN in 5 cases (7.9%) and MPN in 4 case (6.3%). In the remaining 5 cases (7.9%), no pulmonary mass or nodule was reported but they had unilateral malignant pleural effusion with complete (1 case) or partial (4 cases) atelectasis (Table 5).

Table 5: Presenting major CT features of lung cancer in the study population, TASH, 2017

Presenting CT features	No. (Valid %)
Parenchymal lesion	58 (92)
SPN	5 (7.9)
MPN	4 (6.3)
Mass	49 (77.8)
Malignant pleural effusion with no identified pulmonary mass or nodule	5 (7.9)

SPN, solitary pulmonary nodule; MPN, multiple pulmonary nodules.

Taking the cases with pulmonary mass/masses and SPN alone, 66 % of the tumors involved the right lung and 43.4% involved the left lung. Majority of them (83%) were located peripherally and 26.4% were centrally located. The upper lobes were involved more commonly as compared with lower lobes (41.5% and 35.8% respectively). Out of the total 30 adenocarcinoma cases, 70% presented as mass and 10% as SPN, of which 83.3% were located peripherally and 29.2% were central. Squamous cell carcinoma was represented by mass in 84.6% and SPN in 7.7%, majority (66.7%) of which were peripherally located as compared with 41.7% of central location. The small cell carcinoma and atypical carcinoid tumor were located peripherally but the large cell carcinoma was centrally located (Table 10).

Calcification of the tumor was seen in 5.7% of cases of mass and SPN lesions. One case of adenocarcioma had calcification but no calcification was seen in the squamous cell carcinomas. Cavitating lesion was seen in 9.4% cases. Squamous cell carcinoma had more cavitating lesion as compared to adenocarcinoma; 16.7% and 4.1% respectively.

Majority of the tumors had irregular margin (56.8%) and heterogeneous post-contrast enhancement (69.4%).

Out of the total 49 pulmonary mass cases, associated satellite nodules were present in 17 (34.7%). In relation to the primary mass, the satellite nodules involved the same lobe in 6.1%, ipsilateral another lobe in 8.4% and contralateral lung in 20.4%. Satellites nodules were seen in 38.1% of adenocarcioma and 18.2% of squamous cell carcinoma. Associated atelectasis was seen in 36.7% cases of pulmonary masses, which was partial atelectasis in 28.6% and involved the entire lung in 8.2%. Squamous cell carcinoma was associated with atelectasis more than

adenocarcinoma (36.4% and 28.6% respectively). The small cell carcinoma and the atypical carcinoid tumor had partial and complete atelectasis respectively.

Lymphagitic carcinomatosis was present in 20.6% of the study population, majority of which involved the ipsilateral lung. It was seen in 26.7% of adenocarcima and 7.7% of squamous cell carcinoma.

Chest wall invasion was reported in 5(7.9%) patients, 3 of them had adenocarcinoma and 2 had squamous cell carcinoma. Extension to mediastinal structures was seen in 24 (38.7%) cases. Central airway involvement was seen in majority of the cases (79.2%) followed by pulmonary arteries in 58.3%, mediastinal fat in 37.5%, SVC in 29%, aorta in 20.8%, pericardium in 16.7%, pulmonary veins in 12.5% and the heart in 4.2% (Figure 2). Majority of the squamous cell carcinoma (53.8%) and 34.5% of the adenocarcinoma had mediastinal involvement. Both cases of the small cell carcinoma and the carcinoid tumor also had mediastinal invasion.

Table 6: CT features of pulmonary masses and associated findings, TASH, 2017

Characteristics	No. (Valid %)
Site	
RUL	10 (20.8)
RML	2 (4.2)
RLL	8 (16.6)
LUL	10 (20.8)
LLL	9 (18.7)
Rt hilar	11 (22.9)
Lt hilar	3 (6.3)
Size	
(3cm, 5cm]	10 (31.3)
(5cm, 7cm]	13 (40.6)
>7cm	9 (28.1)
Number	
One	44 (89.8)
Multiple	5 (10.2)
Calcification	3 (6.3)
Cavitation	5 (10.4)
Air bronchogram	2 (4.2)
Surrounding GGO	3 (6.3)
Margin	
Smooth	19 (47.5)
Irregular	21 (52.5)
Enhancement	
No enhancement	2 (5.6)
Homogeneous	9 (25)
Heterogeneous	25 (69.4)
Associated satellite nodules	17 (34.7)
Same lobe	3 (6.1)
Ipsilateral another lobe	4 (8.2)
Contralateral to primary tumor	10 (20.4)
Associated atelectasis	18 (36.7)
Partial (segmental/lobar)	14 (28.6)
Entire lung	4 (8.2)

RUL, Right upper lobe; RML, right middle lobe; RLL, right lower lobe; LUL, left upper lobe; LLL, left lower lobe; GGO, ground glass opacity;

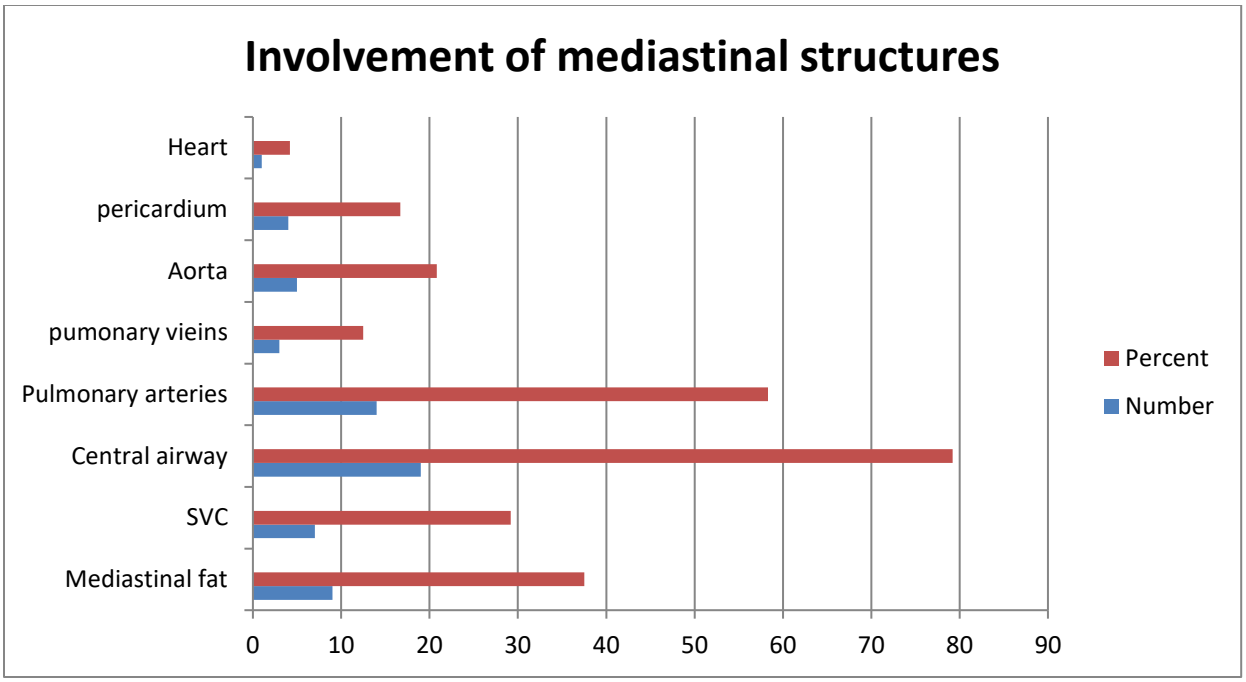

Figure 2: Bar chart showing frequency of involvement of mediastinal structures in the study population

SPN was reported in a total of 5 cases (7.9%); 4 (80%) of them had irregular margin and 1 (20%) had smooth margin. No calcification or cavitation was reported in all the SPN cases. In 4 (6.3%) cases of the study population, the presenting CT feature was MPN with bilateral lung involvement in 3 (75%) cases and unilateral involvement in 1 case (Table 7).

Table 7: CT features of pulmonary nodules in the study population, TASH, 2017

Characteristics	No. (Valid %)
SPN	
Site	
RUL	2 (40)
RML	1 (20)
RLL	1 (20)
LLL	1 (20)
Lobulation	2 (40)
Speculation	4 (80)
Calcification	0
Cavitaion	0
MPN	
Unilateral	1 (25)
Bilateral	3 (75)

SPN, Solitary pulmonary nodule; MPN, Multiple pulmonary nodules; RUL, Right upper lobe; RML, right middle lobe; RLL, right lower lobe; LLL, left lower lobe

6.4.2 Lymph Node Involvement

Out of the total 63 patients, enlargement of the hilar lymph nodes was reported in 13 (20.6%) patients. The most common hilar LAP was ipsilateral to the primary lesion in 7 (11.1%) followed by bilateral involvement in 4 (6.3%) and only contralateral hilar LAP in the remaining 2 (3.2%) patients. Hilar LAP was more frequently seen in adenocarcinoma (16.7%) than in squamous cell carcinoma (7.7%)

Mediastinal lymph nodes were involved in 25 (39.7%) patients. Majority of them (60%) were bilateral and 40% were ipsilateral to the primary tumor. Mediastinal LAP was also more common in adenocarcinoma (53.3%) than in squamous cell carcinoma (30.8%).

Cervical and supraclavicular node involvement was reported only in 2 (3.2%) patients.

6.4.3 Metastasis

Distant metastasis was seen in a total of 42 (66.7%) patients; it was seen in 73% of adenocarcinoma and 38.4% of SCC cases. Out of them, 26 (41.3%) patients had intra-thoracic metastasis (M1a) and 16 (25.4%) patients had extra-thoracic metastasis (M1b). Table 8 summarizes M stages in different histologic subtypes.

Table 8: M stages in different histologic subtypes, TASH, 2017

Cell type	M stage			Total
	M0	M1a	M1b	
Adenocarcinoma	8 (26.7)	14 (46.7)	8 (26.7)	30 (47.6)
SCC	8 (61.5)	4 (30.8)	1 (7.7)	13 (20.6)
Others	5 (25)	8 (40)	7 (35)	20 (31.7)
Total	21 (33.3)	26 (41.3)	16 (25.4)	63

M0, local disease; M1a, intra-thoracic metastasis; M1b, extra-thoracic metastasis

Pleural effusion was found in a total of 31 (49.2%) patients. Majority of them (28 patients) had ipsilateral effusion. Contralateral effusion was seen in 1 case and bilateral effusion in 2 cases. From the 31 cases with pleural effusion, 7 had associated irregular pleural thickening and 4 had smooth pleural thickening. Enhancing pleural nodules were seen in 6 (7.9%) of the study population, 5 of which were associated with effusion. The pleural effusion, pleural thickening and enhancing pleural nodule were noted in adenocarcinoma more frequent than in squamous cell carcinoma.

As described in section 6.3.1, out of the 49 cases presented with pulmonary masses, 10 had associated satellite nodules in the contralateral lung.

Pericardial effusion was described in 3 (4.8%) patients of the total study population, two of whom had adenocarcinoma.

Out of 16 patients with extra-thoracic metastasis, bone metastases were seen in 11 (17.5%) cases of which distant vertebral bone metastases were found in 9 cases. Involvement of the Liver and adrenal gland were seen in 7 (43.8%) and 2 (3.2%) cases respectively. Extra-thoracic metastasis was reported in 26.7% adenocarcinoma with involvement of bone (16.7%), liver (10%) and adrenal gland (3.3%). Only one case of squamous carcinoma had bone metastasis (7.7%) and no liver or adrenal metastasis was seen. No extra-thoracic metastasis was seen in the small cell carcinoma, large cell carcinoma and atypical carcinoid tumor cases (Table 10).

6.4.4 Staging and resection

None of the chest CT reports included stage of the disease. Using the available data from the chest CT reports regarding the tumor, LN involvement and metastasis descriptors, all the cases

were staged retrospectively using the seventh edition of TNM staging system for lung cancer. A total of 55 cases (87.3%) were not operable at the time of CT imaging. Majority of them (66.5%) were stage IV, 11.1% stage IIIA and 9.5% were stage IIIB disease. The remaining five patients (7.9%) had stage IB and three patients (4.8%) had stage IIB disease (Table 10).

A total of 12 (19%) patients were operated. According to the retrospective staging, six of them had potentially resectable tumor while the remaining six patients had advanced and non-operable disease. Table 9 summarizes the pathological and imaging profile of the operated cases and their TNM staging.

Table 9: Pathological and imaging profiles of the operated cases and their staging, TASH, 2017

No.	Cytopathologic diagnosis		Stage	Remark
	Pretreatment	Post-op		
1	-	Adenocarcinoma	IB	
2	Adenocarcinoma	Adenocarcinoma	IB	
3	Adenocarcinoma	Adenocarcinoma	IB	
4	-	Adenocarcinoma	IIB	
5	-	SCC	IIB	
6	-	SCC	IIB	
7	Carcinoma	Adenocarcinoma	IV (T2a, N0, M1a)	- Pleural effusion
8	-	Adenocarcinoma	IV (T2a, N0, M1a)	- Pleural effusion
9	Malignancy	Adenocarcinoma	IV (T4, N0, M1a)	- Pleural effusion - Enhancing pleural nodule
10	-	SCC	IIIA (T4, N0, M0)	- Mediastinal invasion (central airway)
11	Carcinoma	SCC	IIIB (T4, N3, M0)	- Mediastinal invasion (SVC, pericardium, central airway) - Bilateral mediastinal LAP
12	-	SCC	IV (T4, N0, M1a)	- Mediastinal invasion (SVC, pulm.aa, central airway) - Enhancing pleural nodule

SCC, Squamous cell carcinoma; SVC, Superior vena cava; LAP, Lymphadenopathy

7 DISCUSSION

Out of 63 patients 36 were male and 27 were female with a male to female ratio of 1.33:1. This slight male predominance seen in our study is in keeping with most of the studies done worldwide and similar with the findings of Hoque et al (35) and von Groote-Bidlingmaier et al (49) in which the ratios were 1.32:1 and 1.62:1 respectively.

The age range of the patients in this study was from 27 to 75 years with a mean age of 50.14 years (SD=11.02). A retrospective study done in one Indian hospital by Sharma et al (50) showed a mean age of 55.5 years, which is similar to our finding.

According Tsao, about 25% of lung cancer cases are asymptomatic and incidentally detected on chest imaging (20). In contrast, all of the patients in our study were symptomatic at presentation. The most frequently reported symptom is cough (91.9% cases) followed by chest pain in 59.7%, dyspnea in 38.7%, weight loss in 31.7%, hemoptysis in 19.4% and fever in 11.1%. Two patients also reported neck swelling and discomfort on presentation (3.2%), which was explained by metastatic supraclavicular and cervical LAP's. One patient had hoarseness of voice and another one presented with anterior chest wall mass which was later proven to be metastasis to the sternum. In a retrospective study of 8788 patients from 64 hospitals in South Korea, In et al found 6.5% of patient with no subjective symptoms, which is not in line with our finding. However, they found cough to be the most common symptom in the symptomatic population, followed by dyspnea and chest pain which is similar to our finding (51). In the US the reported asymptomatic cases reaching upto 25% is likely due to the already introduced LDCT screening program in a high risk population and better medical checkups. In South Korea, screening is not recommended practice and the 6.5% asymptomatic cases were incidental findings.

Cigarette smoking is the single most important risk factor for lung cancer which accounts for about 90% of all cases (5). According to Behra et al (52), history of active tobacco smoking is present in 87% of male and 85% of female population with lung cancer. Harir et al (53) used database to perform retrospective study with 772 lung cancer cases diagnosed during a 5-year period at University Hospital Center of Oran, West Algeria. Majority of their patient (86%) had history of smoking. Missaoui et al (54) and von Groote-Bidlingmaier et al (49) from Tunisia and South Africa respectively showed similar results. The pattern of smoking we observed in our

study is very different from most of the studies done worldwide as well as the African counterparts. Majority of patients in our study (74.5%) were non-smokers and all of the patients with smoking history are male. None of the female patients included in this study had smoking history. Despite this significant gender difference in smoking history, we didn't find markedly higher male to female ratio as compared to the findings of Harari et al (53) and Yadav et al (33), where the male to female ration was 11.86:1 and 6:1 respectively. The pattern of lung cancer distribution between genders in our study is similar to the findings of Mandal et al (55) in Northeastern India (M:F=1.43:1), however, there was comparable smoking history between male and female in their study. In our study, proportion of lung cancer incidence among the non-smokers is 75.5% which does not correlate with most studies. All of the female patients were non-smokers and 85.2% of them were housewives. Since more than 90% of Ethiopian population use solid fuels as primary source of domestic energy, indoor pollution may contribute to the high proportion of lung cancer in non-smokers particularly females of this region (17, 18, 32).

Various benign pulmonary diseases are associated with increased risk of lung cancer. Although the risk of lung cancer in patients with bronchial asthma, COPD, emphysema and fibrosis are established (13, 15, 16) we found remarkable history only in one patient (1.6%), who was known asthmatic. The risk of lung cancer is also higher in individuals with history of pulmonary tuberculosis (14). In our study, 8.5% had remote history of treatment for pulmonary tuberculosis and another 33.9% were put on anti-tuberculosis treatment for the current illness, some of whom completed the treatment and some discontinued medication after the diagnosis of lung cancer. None of the patients who were initiated on or completed anti-tuberculosis medication for the current presenting illness had bacteriologically confirmed TB, hence difficult to conclude whether tuberculosis was a misdiagnosis or was present with lung cancer as super-infection.

In this study, adenocarcinoma is the commonest subtype, affecting 30 patients (47.6%). It is the most frequently diagnosed cell type both in male and female patients. This is compatible with the current global epidemiology and similar with the findings of von Groote-Bidlingmaier et al in South Africa, where they found adenocarcinoma in 53.9% (2, 40, 41, 49). In contrast, studies done in Tunisia (54), Algeria (53), and India (35) did not show a shift from SCC to adeocarcinoma. In our study, squamous cell carcinoma accounts for 20.6%. In non-smokers, adenocarcinoma is the most frequently encountered cell type (53.2%), however, in individuals

with smoking history we found equal distribution of both adenocarcioma and SCC, 31.3% each. This was against the findings of Yadav et al (33) which showed strong association between smoking and occurrence of SCC. The other histologic subtypes are small cell carcinoma (1.6%), large cell carcinoma (1.6%), and atypical carcinoid tumor (1.6%). In the rest of the patients no specific cell type diagnosis is made (carcinoma in 22.2% and suggestive of malignancy in 4.8%).

In our study, pulmonary mass was the most frequently observed parenchymal lesion (77.8%) followed by SPN (7.9%) and MPN in 4 case (6.3%). Out of the 49 pulmonary masses, size was documented only for 32 cases and 40.6% of them are measured between 5cm and 7cm. The results of von Groote-Bidlingmaier et al (49) were similar to ours; most of the cases in their study population presented as pulmonary mass with a median size of 6.15cm followed by SPN (4.4%). Five (7.9%) of our study population had unilateral malignant pleural effusion with lung collapse and no pulmonary mass or nodule was detected. This may be explained by less conspicuity of parenchymal lesion in a collapsed lung.

The inclination of lung cancer to involve the right lung and the upper lobes has long been reported in previous studies. In a retrospective study of 373 lung cancer cases, Sharma et al (50) found 54.2% of the lesions on the right side and 38.3% on the left side. Similarly, von Groote-Bidlingmaier et al (49) reported 53% of tumors in the right lung and 35% in the left with 55% affecting upper lobes and 22% affecting the lower lobes. Our finding is similar with most of the previous studies showing 66% of the tumors in the right lung and 43.3% in the left with 41.5% involving the upper lobes and 35.8% involving the lower lobe.

Majority (83%) of the tumors in our study are located peripherally and 26.4% centrally. Eighty three percent of the adenocarcima and 66.7% of SCC are peripherally located. In contrast to most of previous studies that show predilection of SCC for central location (41-44, 49), only 41.7% of the SCC in our study were centrally located.

According to previous reports, SCC is the most likely subtype to cavitate (41-43). In a study done by Sharma et al (50), cavitation was found in 13.9% of SCC and 8.3% of adenocarcima. We have similar results with cavitating lesion seen in 16.7% of SCC and 4.1% of adenocarcinoma.

In this study, a total of 42 patients (66.7%) had metastases. Comparing the two dominant cell types, metastases are seen in 73% of adenocarcinoma and 38.4% of SCC. Comparable results were seen in a study by von Groote-Bidlingmaier et al (49), which showed metastases in 63.7% of their study population; 68% of adenocarcima and 51% of SCC had metastases. While studying the changing pattern of bronchogenic carcinoma in 81 patients prospectively over a period of 2 years, Shetty et al (56) observed extrathoracic metastases in 48.1% of the cases; the bone being the most common organ to be involved (19.7%) followed by liver (18.5%) and adrenals (6.1%). Although the proportion of extrathoracic metastases is lower in our study (25.4%) than in the study by Shetty et al (56), we have comparable organ involvement with the bone being the most common organ to be affected (17.5%) followed by liver (11.1%) and adrenals (3.2%). Adenocarcinoma has higher proportion of metastases than SCC which in line with the results of Shetty et al (56) and von Groote-Bidlingmaier et al (49).

Our study shows high proportion of patients (87.3%) with inoperable tumor at the time of CT imaging. Only eight patients (12.7%) had potentially operable disease, out of whom only 6 (75% of 8) are operated. The reasons for not operating the two patients with stage IB disease could not be found on the medical record; it could be because of comorbidity that was not documented or patient refusal which were the only reasons Imperatori et al (57) found in their study. Another six patients with stages that preclude surgery (stages IIIA-IV) were also operated. Three of those operated patients with advanced stages had pleural effusion which we used as a descriptor of intra-thoracic metastasis; had the effusion been investigated, it might have been negative for malignancy. We may over-staged those three cases while they could have potentially operable disease. However, mediastinal invasion was described in the CT reports of the remaining three advanced cases and it is not clear why they were operated. In our study, the overall resection rate was 19.05%. The proportion of patients who were operated in our study is comparable with that observed in Sweden, Italy and Netherlands with reported resection rates of 17.5%, 24%, and 20% respectively. Much lower rate (4.4%) was reported from South Africa (49). However, we only used data from the initial chest CT reports. If additional modalities (PET-CT, mediastinoscopy) were used like in the other studies mentioned above, many of the patients in our study would be up-staged and not be illegible for surgical resection.

8 STUDY LIMITATION AND STRENGTH

The key limitation of our study is its retrospective design and very small sample size. Many patients in the study were referred to our institution with CT scans done in other governmental/private centers and reported by variable radiologists who may have different level of expertise. Although this may affected the quality of radiologic data collected, we decided to include them in the study since repeat CT is not recommended in such cases with reports of optimal diagnostic value. Moreover, all tissue diagnoses in our study were based only on cytologic or histologic examinations. Therefore, we opted for inclusion of the carcinoma cases with unspecified cell types because none of the pathologic study could be supplemented by ancillary immunochemistry technique, which is not available in the country. Nevertheless, it is unlikely that the predominant cell type (adenocarcinoma) would have been changed if those ancillary techniques were used. In spite of these limitations, this study offers valuable information of lung cancer in our setup for two main reasons. First, the study was undertaken in TASH which is the ultimate referral center and the only cancer site in Ethiopia where patients come from all directions of the country. Data collected from patients who made it to this center can give general picture of the disease. Second, this is the first study of its kind in Ethiopia, which describes the clinical, pathological and imaging (CT) patterns of lung cancer, hence an indispensable base for further future studies.

9 CONCLUSION

In conclusion, we found adenocarcinoma to be the most common cell type of lung cancer. Pulmonary mass is the most common presenting imaging feature. Both adenocarcinoma and SCC most commonly present as peripheral lesions. We observed predilection of lung cancer lesions for the right lung and upper lobes. Majority of the patients present at advanced stage of the diseases with small proportion of potentially resectable lesions. We observed a narrow gender gap with male to female ration of 1.3:1 and majority of the female population are housewives. Smoking is not identified as the major risk factor in our study. With the high incidence of pulmonary tuberculosis in the country and presence of history for tuberculosis in 42.4% of the study population, we assume TB as the most important cofounding problem.

10 RECOMMENDATIONS

Our findings justify the need for awareness creation on the people and health care providers regarding lung cancer and early referral of non-responding TB suspects/cases. We also recommend a facility based prospective study of lung cancer suspects/cases with all the chest CT scans taken on the same CT machine and reported by radiology residents or radiologists of comparable expertise. Causative relations of indoor-pollution, pulmonary TB and other risk factors of lung cancer are also worth studying in our country.

Table 10: Clinical and CT features by cell type, TASH, 2017

Clinical and Radiologic features	Total (n=63)	AD. (n=30)	SCC (n=13)	Small cell (n=1)	Large cell (n=1)	AC (n=1)	Other	
							Ca (n=14)	Ma(n=3)
Sex								
Male	36 (57.1)	16 (53.3)	8 (61.5)	0	1(100)	1 (100)	8 (57.1)	2 (66.7)
Female	27 (42.9)	14 (46.7)	5 (38.5)	1(100)	0	0	6 (42.9)	1 (33.3)
Occupation								
House wife	23 (42.6)	12 (42.9)	5 (50)				5 (50)	1(33.3)
Farmer	6 (11.1)	3 (10.7)	0		1 (100)	1 (100)	1 (10)	
Private	6 (11.1)	6 (21.4)	0				0	
Governmental	8 (14.8)	4 (14.3)	2 (20)	1 (100)			0	1 (33.3)
Other	11 (20.4)	3 (10.7)	3 (30)				4 (40)	1 (33.3)
Smoking history	16 (24.5)	5 (16.7)	5 (38.5)	0	0	0	5 (35.7)	1 (33.3)
Previous history of pulmonary TB	5 (8.5)	2 (7.1)	2 (15.4)	0	0	-	1	0
TB treatment for the current illness	21 (33.9)	12 (40)	2 (15.4)	1(100)	0	1 (100)	5 (35.7)	0
SPN	5 (7.9)	3 (10)	1 (7.7)	0	0	0	1 (7.1)	0
MPN	4 (6.3)	3 (10)	0	0	0	0	1 (7.1)	0
Mass	49 (77.8)	21 (70)	11(84.6)	1(100)	1(100)	1 (100)	11 (78.6)	3 (100)
MPE with collapse	5 (7.9)	3 (10)	1 (7.7)	0	0	0	1 (7.1)	0
General location[a]								
Central	14 (26.4)	7 (29.2)	5 (41.7)	1(100)	0	1(100)	0	0
Periphery	44 (83)	20 (83.3)	8 (66.7)	0	1(100)	0	12 (100)	3(100)
Specific location[a]								
Right lung	35 (66)	16 (66.7)	8 (66.7)	1 (100)	1 (100)	1 (100)	6 (50)	2 (66.7)
RUL	12 (22.6)	6 (25)	2 (16.7)	0	0	0	2 (16.7)	2 (66.7)
RML	3 (5.7)	3 (12.5)	0	0	0	0	0	0
RLL	9 (16.9)	2 (8.3)	2 (16.7)	0	1 (100)	0	4 (33.3)	0
Rt hilar	11 (20.7)	5 (20.8)	4 (33.3)	1 (100)	0	1(100)	0	0
Left lung	23 (43.4)	11 (45.8)	5 (41.7)	0	0	0	6 (50)	1 (33.3)
LUL	10 (18.9)	4 (16.7)	3 (25)	0	0	0	2 (16.7)	1 (33.3)
LLL	10 (18.9)	5 (20.8)	1 (8.3)	0	0	0	4 (33.3)	0
Lt hilar	3 (5.7)	2 (8.3)	1 (8.3)	0	0	0	0	0
Calcification[a]	3 (5.6)	1 (4.1)	0	1(100)	0	0	0	1 (33.3)
Cavitation[a]	5 (9.4)	1 (4.1)	2 (16.7)	0	0	0	1 (8.3)	1 (33.3)
Margin[a]								
Smooth	19 (43.2)	6 (31.6)	5 (50)	1(100)	0	1 (100)	5 (55.6)	1(33.3)
Irregular	25 (56.8)	13 (68.4)	5 (50)	0	1 (100)	0	4 (44.4)	2 (66.7)
Air bronchogram[b]	2 (3.8)	1 (4.1)	1 (8.3)	0	0	0	0	0
Surrounding GGO[b]	3 (5.6)	2 (8.3)	0	0	0	0	1 (8.3)	0
Enhancement[b]								
No	2 (5.6)	2 (12.5)	0	0	-	-	0	0

Homogen	9 (25)	3(18.7)	4 (40)	1 (100)	-	-	1(12.5)	0
Heterogen	25 (69.4)	11 (68.7)	6 (60)	0	-	-	7 (87.5)	1 (100)
Satellite nodule[b]	17 (34.7)	8 (38.1)	2 (18.2)	1 (100)	0	0	4 (36.4)	2 (66.7)
T3	3 (6.1)	0	1 (9.1)	0	0	0	1 (9.1)	1 (33.3)
T4	4 (8.2)	3 (14.3)	1 (9.1)	0	0	0	0	0
M1a	10 (20.4)	5 (23.8)	0	1 (100)	0	0	3 (27.3)	1(33.3)
Atelectasis[b]	18 (36.7)	6 (28.6)	4 (36.4)	1 (100)	0	1 (100)	5 (45.5)	1 (33.3)
Partial	14 (28.6)	3 (14.3)	4 (36.4)	1 (100)	0	0	5 (45.5)	1 (33.3)
Complete	4 (8.2)	3 (14.3)	0	0	0	1 (100)	0	0
Lymphangitic carcinomatosis	13 (20.6)	8 (26.7)	1 (7.7)	1 (100)	0	0	3 (21.4)	0
Ipsilateral	9 (14.3)	6 (20)	1 (7.7)	1 (100)	0	0	1 (7.1)	0
Bilateral	4 (6.3)	2 (6.7)	0	0	0	0	2 (14.3)	0
LAP								
Hilar	13 (20.6)	5 (16.7)	1 (7.7)	1 (100)	1 (100)	0	5 (35.7)	0
Mediastinal	25 (39.7)	16 (53.3)	4 (30.8)	1 (100)	1 (100)	0	3 (21.4)	0
Cervical/supraclav.	2 (3.2)	0	0	0	0	0	2 (14.3)	0
Mediast. invasion	24 (38.7)	10 (34.5)	7 (53.8)	1 (100)	0	1 (100)	4 (28.6)	1 (33.3)
Pleural effusion	31 (49.2)	18 (60)	3 (23.1)	1 (100)	0	0	8 (57.1)	1 (33.3)
Ipsilateral	28 (44.4)	16 (53.3)	3 (23.1)	1 (100)	0	0	8 (57.1)	0
Contralateral	1 (1.6)	0	0	0	0	0	0	1 (33.3)
Bilateral	2 (3.2)	2 (6.7)	0	0	0	0	0	0
Pleural thickening	15 (23.8)	9 (30)	3 (23.1)	1 (100)	0	0	2 (14.3)	0
Smooth	6 (9.5)	5 (16.7)	1 (7.7)	0	0	0	0	0
Nodular/irregular	9 (14.3)	4 (13.3)	2 (15.4)	1 (100)	0	0	2 (14.3)	0
Enhancing pleural nodule	6 (9.7)	3 (10)	1 (7.7)	1 (100)	0	0	1 (7.7)	0
Pericardial effusion	3 (4.8)	2 (6.7)	0	0	0	0	1 (7.1)	0
Chest wall invasion	5 (7.9)	3 (10)	2 (15.4)	0	0	0	0	0
Vertebral body involvement	9 (14.3)	4 (13.3)	0	0	0	0	4 (28.6)	1 (33.3)
Metastasis (extrathoracic/M1b)[c]	16 (25.4)	8 (26.7)	1 (7.7)	0	0	0	6 (42.9)	1 (33.3)
Bone	11 (17.5)	5 (16.7)	1 (7.7)	0	0	0	4 (28.6)	1 (33.3)
Liver	7 (11.1)	3 (10)	0	0	0	0	4 (28.6)	0
Adrenal	2 (3.2)	1 (3.3)	0	0	0	0	1 (7.1)	0
Staging								
IB	5 (7.9)	4 (13.3)	0	0	0	0	1 (7.1)	0
IIB	3 (4.8)	1 (3.3)	2 (15.4)	0	0	0	0	0
IIIA	7 (11.1)	1 (3.3)	3 (23.1)	0	1 (100)	1 (100)	0	1 (33.3)
IIIB	6 (9.5)	2 (6.7)	3 (23.1)	0	0	0	1 (7.1)	0

IV	42 (66.5)	22 (73.3)	5 (38.5)	1 (100)	0	0	12 (85.7)	2 (66.7)

Data are present as number of patients with percentage of total valid cases

[a] Applies only for the cases with SPN and pulmonary masses (n=54). One patient can have multiple masses.

[b] For pulmonary masses only

[c] Metastases to more than one organ may be present in one patient

T3, satellite nodules on same lobe; T4, satellite nodules in ipsilateral another lobe; M1a, involving contralateral lung

AD, Adenocarcinoma; AC, Atypical carcinoid; SCC, Squamous cell carcinoma; Ca, carcinoma with no specified cell type; Ma, pathologic result was suggestive of malignancy

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12 APPENDIX 1. DATA COLLECTION FORMAT

Code No_____

Part I. Demographic Data		
SN	**Questions**	**Response category**
1	Sex	1. Male 2. Female
2	Age	
3	Adress/Location	1. Urban 2. Rural
Part II. Smoking History		
4	History of smoking	1. Absent 2. Present
5	If present	Years
		1. <10 yr 2. 10-20 yr 1. >20 yr
		Quantity of cigarette
		1. <10 cigarette 2. 10-20 3. >20
Part III. Clinical Data		
6	Presentation	1. Symptomatic 2. Incidental

7	If reply for question 6 is 1	1. Cough 2. Hemoptysis 3. Chest pain 4. Dyspnea 5. Fever 6. Weight loss
8	Previous history of pulmonary TB	1. Absent 2. Present
9	If reply for the above question is 2	1. Not treated 2. treated
10	History of TB treatment for current illness	1. Absent 2. Present
11	HIV status	1. Non reactive 2. Reactive
12	Known history of ILD	1. Absent 2. Present
Part IV. Pretreatment pathological data		
13	Diagnosis (cell type)	
14	Sample taking	1. Image guided 2. Bronchoscopy 3. BAL

Part V. Treatment		
15	Modality	1. Surgery 2. Chemotherapy 3. Radiotheraphy 4. Combination_____
16	If operated	1. Surgical staging?_____ 2. Post op pathological diagnosis_____
Part VI. CT features		
17	Solitary pulmonary nodule	1. Site/location a. RUL b. RML c. RLL d. LUL e. LLL 2. Lobulation 3. Speculation 4. Density a. GGO b. Mixed c. Solid 5. Calcification 6. Cavitation 7. Enhancement a. No b. Homogeneous

		c. Heterogenous 8. Fissure attachement 9. Pleural attachement 10. Pleural retraction toward nodule 11. Vascular convergence 12. Peripheral fibrosis 13. Vascular involvement
18	Multiple pulmonary nodules	1. Size of largest 2. Number 3. Both lung 4. One lung 5. Single lobe
19	Pulmonary mass	1. Location 2. Size 3. Number 4. Calcification 5. Cavitation 6. Air bronchogram 7. Surrounding GGO
20	Lymphangitic carcinomatosis	1. Absent 2. Unilateral 3. bilateral
21	Hilar LAP- lymph nodes with short axis >1 cm	1. Absent 2. Unilateral 3. Contralateral 4. Bilateral
22	Mediastinal LAP-lymph nodes with short axis >1 cm	1. Absent 2. Unilateral 3. Contralateral

		4. Bilateral
23	Cervical and supraclavicular lymph nodes	1. Absent 2. Present
24	Mediastinal invasion	1. Mediastinal fat 2. Superior vena cava 3. The central airways 4. Pulmonary arteries 5. Pulmonary veins 6. Aorta 7. Heart 8. Pericardium
25	Diaphragmatic elevation	1. Absent 2. Present
26	Diaphragmatic invasion	1. Absent 2. Present
27	Pleural effusion	1. Absent 2. Present
28	Pleural thickening	1. Enhancing 2. Non enhancing 3. Costal 4. Mediastinal 5. Diaphragmatic
29	Enhancing pleural nodules/masses	1. Absent 2. Present

30	Pleural calcification	1. Absent 2. Present
31	Pericardial effusion	1. Absent 2. Present
32	Chest wall invasion	1. Absent 2. Present
33	Vertebral body invasion	1. Absent 2. Present
34	Extra-thoracic metastasis	1. Liver 2. Adrenal 3. Bone