ADDIS ABABA UNIVERSITY

COLLAGE OF HEALTH SCIENCE AND SCHOOL OF MEDICINE

DEPARTMENT OF PATHOLOGY

Histopathologic pattern of neoplastic and non-neoplastic Lung lesions in resected specimens with their clinicoradiologic features in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, over a 5 year period, 2016-2020.

December 25, 2020

Declaration of Principal investigator

I the undersigned, **Amanuel Kassa** agree to accept all responsibilities for the scientific and ethical conduct of this thesis entitled "**Histopathologic pattern of neoplastic and non-neoplastic Lung lesions in resected specimens with their clinicoradiologic features in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, 2016-2020.**

The Thesis is my original work and was not prepared by others. All resources and materials used for this research have been dully acknowledged. I was communicating and providing timely progress report to my advisor and seek the necessary advice, comment and approval in the course of this work.

Amanuel Kassa Tadesse (MD), Final Year Pathology Resident:

_____ _____

Signature Date

Approval of Advisor:

The Student had worked on this research and fulfilled all the requirements and hence hereby can submit the thesis to the Department of Pathology, Tikur Anbessa Specialized Hospital, School Of Medicine, College of Health Sciences, Addis Ababa University.

Dr Wondwossen Ergete (MD), Associate Professor of Pathology:

_____ _____

Signature Date

Thesis submitted to the Department of Pathology, College of Health Sciences, School of medicine Addis Ababa University in Partial fulfillment of the requirements for the Specialty Diploma in Pathology.

Investigator: Amanuel Kassa (MD, Pathology resident)

Advisor: Dr Wondwossen Ergete (MD, Associate professor of pathology)

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Acronyms

AAU: Addis Ababa University

SCC: Squamous Cell Carcinoma

TASH: Tikur Anbessa Specialized Hospital

CCAM: Congenital Cystic Adenomatoid Malformation

TB: Tuberculosis

NSCLC: Non-Small Cell Lung Cancer

CDC: Center for Disease Control

RPMI: Roswell Park Memorial Institute

FOB: Flexible fiberoptic bronchoscopy

OR: Odds ratio

OS: Overall survival

CI: Cumulative Incidence

L1: Level 1 LN status

LN: lymph node

ABSTRACT

Background: List of disease entities affect the lung, with surgically removed masses accounting a large share in proportion. A variety of neoplastic and non-neoplastic lesions are under this category. Results of several studies show neoplastic lesions account for the largest share among resected specimens. From the neoplastic lesions, malignancies are the most common ones; from these primary tumors (carcinomas) are the leading. Benign tumors are very rare compared to the malignant ones, hamartoma being the most common among the benign category. According to the 2018 WHO report, lung cancer is the most cancer (2.09 million cases) and the leading cause of death (1.76 million). According to the Globocan report on the incidence and prevalence of cancer in Ethiopia by 2018, Lung cancer ranks the 7th most common malignancy in Ethiopia. Addis Ababa population-based pattern of cancer therapy, found out that lung cancer ranking as the 5th most common malignant tumor.

Objectives: The aim of this study was to determine the frequency and histopathologic patterns of lung lesions with clinicoradiological features in resected specimens diagnosed in Tikur Anbessa Hospital.

Methods and materials: Retrospective study was conducted on five years biopsy reports of neoplastic and non-neoplastic resected lung lesions submitted from January 01, 2016 to August 30, 2020. Data had been retrieved from the archive of the department of pathology. Clinical presentation and gross description of the lesions was collected from the patient's original biopsy request. Final data analysis was done using latest SPSS version 25.

Results: From a total of 170 cases reviewed 159 cases fulfilled the study criteria and included in the study. From these, 99 (62.3%) of the study subjects were males while the remaining 60 (37.7%) were female. M:F ratio of 1.65:1. The minimum age was 2 month and the maximum age was 73 year. Mean age of patients was 36.8 year. There were 92 (57.9%) non-neoplastic cases and 67 (42.1%) neoplastic cases. The commonest age group for both neoplastic and non-neoplastic lesions were 3rd and 4th decades. Cough and hemoptysis were the commonest clinical presentation (n = 39, 24.5%). The commonest radiologic finding was mass 37 (23.3%). Lobectomy was the most common surgical procedure performed (n=97, 61 %) followed by pneumonectomy 38 (23.9%). Bronchiectasis was the most common non-neoplastic histopathologic entity 18 (11.3%) cases, followed by aspergillosis 16 (10.1%) cases. Out of the 67 neoplastic cases, only 5 (7.5%) cases were benign the rest 62 (92.5%) were malignant. All the benign tumors were hamartoma. The malignant cases had a M:F ratio of 1.06:1. Typical carcinoid was the most common histopathologic type reported (45.2%), followed by adenocarcinoma (25.8%), SCC (9.7%). Majority of the malignant neoplasms were in pathologic stage II (55.2 %). There were 31 (53.4%) cases with known lymph node status. From these, 58.1 % had up to 3 LNs and 25.8 % had up to 4-6 LNs examined with majority had N0 (34.5%) cases and N1 (15.5%) cases.

Conclusion: In this study a higher proportion of non-neoplastic lesions were identified in resection specimens than neoplastic cases. Carcinoid tumor was the most frequent histopathologic subtype.

1. Introduction

1.1 Background

The lungs are pyramidal- shaped, paired organs that are connected to the trachea by the right and left bronchi. It is a major organ of the respiratory system; each lung houses structures of both the conducting and respiratory zones. Grossly the lungs are subdivided in to lobes, three on the right (upper, middle and lower) and two on the left (upper and lower). [1] The bronchial structures normally undergo hierarchal branching culminating at the alveoli. Histologically, the bronchi are lined by respiratory epithelium as that of the trachea and other part of conducting airway. Bronchi can be identified by their cartilage plates and have submucosal glands which as we go down in to the bronchioles will be lost. The lining epithelium also gradually changed to simple cuboidal and then finally to flat alveolar type cells.[2]

There are numerous pathologies that preferentially affects the lungs; infectious, inflammatory, post traumatic, occupational (pneumoconiosis), congenital, neoplastic (both the benign and malignant entities).

From the lists of disease entities affecting the lung, surgically removed mass lesions account a large share with neoplastic and non-neoplastic pathologies sharing their own proportion. From the non-neoplastic categories there are cystic lung diseases; congenital like CCAM, congenital lobar emphysema and from the acquired category emphysema. Infectious categories also are very important pathologies in surgically resected specimens with post TB Bronchiectasis, fungal and parasitic infections being the common ones. Granulomatous inflammatory lesions hold their own share; infectious, non-infectious, vasculitis associated, following aspiration of particulate materials, following certain diffuse interstitial lung diseases.[1]

Another largest share of the resected lung specimens is due to neoplastic lung lesions mostly due to the malignant categories. Primary and secondary malignant processes affect the lung, with the primary being the most common. From the primary malignant processes, carcinomas take the largest share but different mesenchymal as well as lymphohistiocytic tumors also occur in the lung. Since lung is also a common site of hematogenous metastasis so secondary involvement to the lung also occur, still carcinoma is the commonest cause (especially from gastrointestinal and genitourinary and breast), followed by sarcoma, melanoma and germ cell tumors. [3]

Benign lung tumors are very rare compared to the malignant ones, but from the benign ones the most common one being pulmonary hamartoma, bronchial adenoma, Chondroma and other relatively rare entities including papillomas also occur. [3]

1.2 Statement of the problem

Significant morbidity and mortality are undeniably due to the neoplastic specially the malignant ones. This might be due to the frequent late presentationof patients and limited therapeutic and management facilities in the developing countries like Ethiopia.

According to the 2018 WHO report lung cancer is the most common cancer (2.09 million cases) and the leading cause of cancer death (1.76 million deaths) representing close to 1 in 5 (18.5%) cancer death globally. There is a 20 fold variation in lung cancer rates by region which largely reflects the tobacco epidemic and difference in the historic pattern of tobacco exposure. [4]

Among males, lung cancer is the leading cause of death in most countries in Eastern Europe, Western Asia and North Africa and specific countries in Eastern Asia (China) and South-Eastern Asia. The highest incidence rates among men are observed in Eastern Asia (rates are above 40 per 100,000) and in as much of Europe, Eastern Europe (Hungary 77.4 per 100,000 males). [4]

Incidence rate among males remain generally low in Africa, although they range from intermediate to high in several countries in both the Northern and Southern regions, notably in Morocco (31.9 per 100,000) and South Africa (28.2 per 100,000). Among female the highest incidence rates are seen in North America, Northern and Western Europe and Australia with Hungary topping the list. [4]

According to the Globocan report on the incidence and prevalence of cancer in Ethiopia by 2018, 67,573 new cases were found and 47,954 number of deaths due to cancer was found. [5] From this report lung cancer ranks the 7^{th} most common malignancy in Ethiopia. Addis Ababa population-based pattern of cancer therapy, a population-based study by Feuchtner J, et al. (2019) [6] on 588 files found out that lung cancer ranking as the 5^{th} most common malignant tumor with 28 out of 588 files (4.8%).

1.3 Rationale of the Study

As mentioned earlier, data from the literature shows difference in the relative frequencies of the various neoplastic and non-neoplastic lung lesions. Several reports on this topic from different part of the world showed difference in geographic prevalence among the neoplastic and non-neoplastic lesions. Since there is limited information in the literatures about the prevalence of the neoplastic and non-neoplastic lung lesions in Ethiopia, the objective of the current study is to establish the frequency and type of the various neoplastic and non-neoplastic lung lesions diagnosed in resected specimens in Tikur Anbessa Hospital from January 01, 2016 – August 30, 2020 using the 2015 WHO histopathologic classification of Tumors of the Lung, Pleura, Thymus and Heart and to compare the results with those found in similar studies done in different part of the world.

This research will also be important in assessing the geographic differences in the incidence of the lesions and allow clinicians make a realistic judgement in counseling patients before taking biopsy about the probability of diagnosis and the importance of pre-operative diagnostic imaging before any procedures to avoid false positive diagnosis.

2. Literature review

There are many studies done all over the world on the prevalence of different lung lesion in resected specimen. One such study done in Iran at the University Of Medical Science Of YAZD [7], a 7 year descriptive retrospective study on 400 lung resected specimens. The neoplastic and non-neoplastic lesions each account for 50 % each, with 273 cases were male (68.3%) and 127 females (31. 7%). From the 200 cases of Non Neoplastic lesions, TB was 39.9%, pneumoconiosis 27%, pulmonary fibrosis 23%, vasculitis 6%, inflammatory lung disease was 5%. From the rest 200 neoplastic cases, primary lung neoplastic lesions were 56.5 % and lung metastatic lesions 12.5 %. The most common types of neoplastic lesions were SCC (22.5%) and adenocarcinoma (23.5 %). All lesions are more common in male than in female and more common in the age over 60 years (except for vasculitis).

Another study done by Michael A. Smith, et al. [8] on Prevalence of benign disease in patients undergoing resection for suspected lung cancer, a retrospective analysis was performed on 1,560 patients who underwent resection for focal pulmonary lesions at our institution from January 1995 to December 2002 found 140 cases of benign lesion on pathologic examination of resected specimen. Granulomatous inflammation in 91 patients (65%), hamartoma in 17 patients (12%), pneumonia or pneumonitis in 14 patients (10%), fibrosis in 5 patients (4%), and other include aspergilloma in 13 patients (9%).

Another study done in Brazil on 1056 patients hospitalized for lung cancer treatment over a 10 years period [9], 676 cases underwent resection with definitive diagnosis, Lung neoplasm was found in 622 patients (77.4 % malignant 14.6 % benign) and Non neoplastic disease was confirmed in 54 patients (8%).The most frequent among the Non neoplastic being tuberculosis (n =14) and paracoccidiomycosis (n = 9)

A study by Maiga, A. et al. [10] an 8-year retrospective study on 220 patients (213 male and 7 female) with mean age of 65 years, who underwent pulmonary resection for known or suspected lung cancer, found out that the overall benign rate was 6.8% (i.e. 15 out of 220 patients underwent a non-therapeutic resection of a benign lesion), and the patient information from 178 of 220 patients (81 %) were included as oral presentations at the multidisciplinary conference prior to their planned therapeutic resection. They described it as the lowest non-therapeutic rate reported in the literature.

A retrospective study on pulmonary infection mimicking cancer by Rolston, k. et al. [11] a 3 year review of 2908 consecutive patients with radiologic diagnosis of lung cancer underwent an invasive diagnostic procedure to obtain tissue for histopathologic evaluation. They found out

that 2713 patients (93.3 %) had either a primary or a metastatic pulmonary lesion; 11 patients (0.4%) had a benign process; 37 patients (1.3%) had a documented infection; and 147 patients (5%) had non-specific findings or other pulmonary diseases. Of the 37 patients with infection, 22 were men and 15 were women. The mean age of patients was 10-94 years. Microbiologic details of the 37 patients with pulmonary infections mimicking cancer was given; fungal infection was the commonest 17 (46%), TB 10 (27%), Bacterial 8 (22%), Parasitic 2 (5%).

Another study done in united kingdom by Ben Davies, et al. [12] on Pathologic outcome of 150 consecutively resected lesions found that malignancy was found in 115 patients (77.7 %) : 97 (65.5%) with primary lung pathology ; 18 (12.2 %) had metastatic deposits ; 30 (20.3%) were benign . M:F ratio of(1.15 : 1). From the Primary malignant category adenocarcinoma is the commonest 51 cases (34%), SCC 21 (14%) Carcinoid 11 (7.3%). From the Benign categories; Hamartoma accounts for (n=9), Chondroma (n =2).Non neoplastic TB (n = 8) , Aspergillus (n = 4) , Bronchiectasis (n =1)

Further study done in the United States at Vanderbilt – Ingram Cancer Center at the Department of Thoracic Surgery by Eric L. Grogan, et al. [13] A retrospective study on a 278 thoracic operations performed for a known or suspected cancer between January 1, 2005, and April 1 , 2009 found 65/278 (23 %) patients who underwent surgical resection for a suspicious nodule had a benign pathology : Granulomatous disease (n = 37); Histoplasmosis (n = 15) , Atypical mycobacteria, Blastomycosis and Cryptococcus each had 2 cases , TB (n = 1) , Aspergillus (n = 1).

Another retrospective study by HEIKKI TOOMES, et al. [14] at Rohr Bach Hospital, Heidelberg, West Germany, on 955 coin lesions who underwent resection found that 469 (49 %) were malignant: Primary carcinoma(n =364); SCC (n = 171), Adenocarcinoma (n = 121), Metastasis (n = 89) ; Others including Primary sarcoma (n= 16) . From the benign tumors, Chondroma and others (n = 132). Non neoplastic diseases: Tuberculosis was the commonest (n= 225), Pneumonia / abscess (n = 23), Hydatid cyst (n =22), Bronchogenic cyst (n= 21), Aspergilloma (n= 13).

Several groups of studies done all over the world on the malignant categories have described the proportion and trend of the different histopathologic patterns. One study done in Ibadan, Nigeria by J O Ogunbiyi, [15] a 30 years retrospective study a total of 142 cases were analyzed with a M: F ratio of 1.7 :1. Peak age in females was 2 decades (4th) earlier than for males. SCC was found to be the most common one but adenocarcinoma predominated in females.

A study from Egypt by Amany O., et al. [16] a retrospective study in Assiut University Hospital of 255 patients with primary lung cancer was included in the study. The incidence among males (71.4%) was higher than females (28.6 %) with M: F ratio 2.49:1.00. The highest incidence was in patients above 60 years (48.6%), 66.2 % of patients were smokers. The commonest presenting symptoms were shortness of breath (59.6 %), followed by cough (41.2%) and hemoptysis (31.2 %). The most common radiologic pattern of presentation was mass (71.8 %) followed by effusion (30.6%). NSCLC (83.9 %) is still more frequent than SCLC (16.1 %); however, adenocarcinoma incidence (51.8%) was markedly high and surpassed the squamous

cell carcinoma (22.7 %). The majority of cases were diagnosed at later stages of illness with some of them died before the start of treatment (Stage IIIA 38.8 %, Stage IIIB 29.4 % and Stage IV 12.5 %).

From around the world many studies done in this area, one such study done in Spain [17] a retrospective study on a total of 678 patients diagnosed with lung cancer from January 1998 through December 2002 found out that the most common histologic type were SCC and adenocarcinoma: 605 (89.7 %) were men and 73 (10.3 %) were women with M: F ratio of 8:1, the mean age was 67.1 with a range between 33-94. A cytological or histological diagnosis was obtained for 644 patients (95%). As mentioned above the most common histologic type were SCC 225 (33.2 %) and adenocarcinoma 202 (29.8 %), small cell carcinoma in 89 (13.1%) and large cell carcinoma in 30 (4.4 %). The diagnosis was poorly differentiated carcinoma for 91 patients (13.4 %). Still SCC is the most common type of lung tumor diagnosed in men with a total of 219 cases (36.2 %), adenocarcinoma in 161 patients (26.6 %), small cell carcinoma in 82 patients (13.6%) and poorly differentiated carcinoma in 78 (12.9 %). Among women, adenocarcinoma was the most common malignant tumor. Of the 73 women with lung tumors, 41 (56.2 %) had adenocarcinoma, 13 (17.8%) had poorly differentiated carcinoma, 7 (9.6%) had small cell carcinoma and 6 (8.2%) had SCC.

Earlier studies done on this topic showed a rather change in histologic type of lung cancer over decades, which put factors like increasing incidence of lung cancer among female population who have a propensity for adenocarcinoma. One study done at RPMI found out adenocarcinoma being the most common histologic type for the first time. [18] A retrospective study between 1962 and 1975, on a total of 1682 patients , between the study period there were no significant change in the incidence of other types of histologic type except for adenocarcinoma and SCC. In the study they found out that adenocarcinoma increased progressively from 17.6 % of the total cases in 1962 to 29.8 % by 1975 and SCC which represented 48.6 % of the total cases in 1962 had decreased to only 25.5 % by 1975.They put a remark in the end saying adenocarcinoma will soon become the most prevalent type of lung cancer in the United States.

Studies from other part of the world showed SCC is still the predominant histologic pattern, one such study done in India by Dey A et al. [19] a 4 years retrospective study on 607 patients , 489 male and 118 female found that SCC was the commonest type 213 patients (35.09%) , followed closely by adenocarcinoma 187 patients (30.81%), small cell carcinoma and undifferentiated carcinoma accounting for 100 patients (16.7%) and 71 patients (11.7 %), lastly large cell carcinoma with only 36 patients (5.93%).But the pattern is significantly different in young versus the old (i.e adenocarcinoma and undifferentiated carcinoma are more predominant in the young whereas SCC is more common in older age group irrespective of sex).

Cough is the most common presenting complaint (22% approx.) followed by chest pain, shortness of breath, expectoration, constitutional symptoms, hemoptysis and others. Radiologically upper zone is the most involved zone (40.19%) followed by midzone (34.9%) and

lower zone (22.07%). Mass is the most common lesion of bronchogenic carcinoma (77.3%) followed by pleural effusion (27.8%) and collapse (18.6%).

Further studies done in the United States still go with the progressive increase in incidence of adenocarcinoma, one such large study by Keisha A. Houston et.al. [20] from 2004 to 2009 analyzed incidence data from CDC's National Program of Cancer Registries (NPCR) and a total of 1,096,276 cases were diagnosed and reported in the United States, average annual incidence rate was 73.3 per 100,000 population among men and 49.4 among women. Among those with newly diagnosed lung cancer, 54% were men and 46 % were women. Adenocarcinoma (44%) and SCC (26%) accounted for the largest proportion of cases.

There have been different studies done on carcinoid tumors of the lung, a relatively less common tumors of the lung .One such study done in Norway by Anne Naalsund et al. [21] they included a total of 26,665 lung cancers diagnosed in the period 1993 – 2005, they found out that 265 patients (1%) had carcinoid tumors, of which 11 were diagnosed coincidentally at autopsy. In the remaining 254 patients, Typical carcinoid were found in 188 (74.01%) patients and Atypical carcinoid were found in 59 (23.22%) patients, 7 cases had unclassifiable carcinoid.

Another similar study done on these rare tumor types in China by Zhi Yang et al. [22] between August 1997 and July 2012 surgical resection was done on 4481 patients with bronchopulmonary neoplasm, of these only 44 of which were determined as carcinoid lung tumors (1%). There were female predominance in the patients with carcinoid lung tumors, with M:F ratio of 1: 1.3. Age ranges between 9 and 71 years. In terms of histologic type 32 (72.72%) patients had typical carcinoid while atypical carcinoid was observed in 12 (27.28 %) patients.

Retrospective study was carried out in the Chest Department, Cairo University, by Yosri M. AKL et al. [23] In which four hundred and four confirmed cases of bronchogenic carcinoma were admitted during July 2002 till July 2012. They found that 82.2% of cases were males and 17.8% of cases were females (Male to female ratio was 4.6:1). The highest incidence was in the sixth and seventh decades of life (63.6%). Smoking was found to be the main risk factor in 75.7% of patients.

Cough was the most common symptom found in 347 patients (85.9%), followed by dyspnea in 276 patients (68.3%). Most common radiological finding was mass lesion (49.8%) followed by hilar shadow (15.8%), apical opacity (13.1%), and pleural effusion (12.1%).

Distribution of histopathologic cell types according to the radiological findings, showed that 44.4% of cases of squamous cell carcinoma presented with mass lesion followed by 25.2% of cases presented with hilar shadow.In our study, 53.8% of cases of adenocarcinoma presented with mass lesion followed by 21% of cases of adenocarcinoma presented with pleural effusion while hilar shadow incidence was 9.2% of adenocarcinoma cases. Pleural effusion was more frequent with adenocarcinoma, as 51% of cases that presented with pleural effusion were adenocarcinoma and this may be due to that most of adenocarcinoma located peripherally and it can cause pleural invasion. Majority of cases were diagnosed by bronchoscopy (68.1%).

Four types of bronchogenic carcinoma were found: squamous cell carcinoma 37.4% adenocarcinoma 29.5%, small cell carcinoma 14.9%, large cell carcinoma 7.2% and undifferentiated carcinoma 11.1%. In females, adenocarcinoma was the predominant cell type (54.2%) while in males, squamous cell carcinoma was the predominant cell type (42.5%).

Another retrospective study done in Himalayan Institute of Medicine in Uttarakhand, India by Jagdish Rawat et al. [24] on clinicopathologic profile of 203 patients with confirmed cases of lung cancer. They found that Male to female ratio was 8.2:1. The common age group being 40-60 years, 9.86% of the patients were less than 40 years old age. Smoking was found to be the main risk factor in 81.77% patients. The most frequent symptom was cough (72.90%) followed by fever (58.12%).

The most common radiological presentation was mass lesion (46.31%) followed by collapse consolidation with slight predominance of right lung. The adenocarcinoma commonly manifested as peripheral mass or a malignant pleural effusion. Similar finding was also reported in other studies. The SCLC presented commonly as central lesion, which was in agreement with other studies

The most common histopathological type was squamous cell carcinoma (SCC) (44.83%) followed by adenocarcinoma (19.78%) and small cell lung carcinoma (SCLC) (16.75%). The majority patients (73.29%) were diagnosed in the later stages of the disease (III B and IV).

Another study in India department of Pulmonary Medicine in a tertiary medical center [25], studied on the clinicopathologic profile of 266 histopathologically confirmed cases of primary lung carcinoma, found that male to female ratio was 6.6:1. The major age group involved was 41-60 years (52.63%) and the rest were below 40 years group (2.63%). Distribution of age varied from 38 to 85 years. Maximum patients were found in the 41 to 60 years age group (52.63%) followed by 61 to 80 years (39.85%) and least in less than 40 years (2.63%) group.

The commonest clinical symptom was cough (68.42%). The most common radiological finding in the chest was a mass or space occupyinglesion (55.26%). In most cases there was a history of smoking (81.2%). Commonest mode of diagnosiswas made by imaging guided fine needle aspiration cytology in 170 patients (63.91%).

The most common histological type of lung cancer was squamous cell carcinoma (35.34%). Majority of cases were diagnosed in the later stages of diseases (71.8%). It was found that squamous cell carcinoma was the most frequent histological type. History of smoking was found in majority of patients. Major patients were diagnosed at the later stages of disease (Stage 3B or 4).

A case control study done in and analyzed all data of patients with NSCLC, who underwent oncological surgical resections from 01/2007 to 12/2016, retrospectively. The correlation between clinicopathological parameters and lymph node metastasis was investigated by using univariate and binary logistic regression analysis. And included 204 consecutive patients, 142 men (71.7%) and 56 women (28.3%). Lymph node metastases were detected in 38.2% (78/204).

Preoperatively, central tumor localization (OR = 2.6, 95% CI = 1.3–5.1, *P* = 0.005) and tumor size > 3 cm (OR = 2.5, 95% CI = 1.3–4.4, *P* = 0.005) were found to be significant predictive factors for lymph node metastasis. Postoperatively, multivariate analysis showed that intratumoral lymph vessel invasion (L1-status) (OR = 17.3, 95% CI = 5.1–58.4, *P* < 0.001) along with the central tumor localization (OR = 2.8, 95% CI = 1.4–5.8, *P* = 0.004) were significantly associated with lymph node metastasis. In small size tumors (≤3 cm), two predictive factors for lymph node metastasis were found: central tumor localization (OR = 19.4, 95% = 2.1–186.4, *P* = 0.01) and L1-status (OR = 43.9, 95% CI = 3.6–529.4, But histologic tumor type and grading, tumor site and tumor lobe distribution did not prove predictive for lymph node metastasis. (*P* = 0.003). [26]

One study done in the United States by Garaj, A. et al. on the effect of Number of Lymph Nodes Sampled on Outcome in Patients with Stage I Non–Small-Cell Lung Cancer. They 442 patients included on the study, there were 262males and 180 females. Adenocarcinoma was the predominant histology, and the majority of the patients were treated by lobectomy median age at diagnosis was 65years, with a range of 34 to 86years. In the study,0-3 LNs assessed in (26.7 %) 4-6 LNs in (28.1%)7-9 LNs in (21.9%) and more than 9LNs assessed in (23.3 %) of the cases. In these study, the median number of lymph node sassessed was six. They found that a significant increment in the 5 year OS from 47.3 % to 79.1% for those with up to 3 LNs examined to those more than 9 LNs examined, respectively. [27]

3. Objective of the study

3.1 General objective

To determine the frequency and histopathologic patterns of lung lesions with clinicoradiological features in resected specimens diagnosed in Tikur Anbessa Hospital.

3.2 Specific objective

- To show the distribution of neoplastic and non-neoplastic lung lesions by age, gender clinical and image finding and the common surgical procedure done.
- To show frequency of distribution of malignant lung tumors by histopathologic pattern and pathologic stage.
- To assess the number and status of lymph nodes examined in the malignant tumors.

4. Methodology

4.1Study Area

This study was conducted at Tikur Anbessa hospital, pathology department which is found in Addis Ababa, Ethiopia. It is one of the largest tertiary hospitals in the country with the vast majority of the cases investigated at this department being patients who are referred from all over the country.

4.2 Study Design and Period

The study was a cross-sectional retrospective descriptive study where data was retrieved from the archive of the department of pathology that are registered from January 01, 2016 up to August 30, 2020.

4.3 Source Population

All patients whose biopsy specimens were submitted to the department of pathology

4.4 Study population

All patients whose lung resection specimens were submitted to the department in the study period from January 01, 2016 to August 30, 2020

4.4.1.Inclusion criteria

. All resected lung specimens with definitive histopathologic diagnosis

. Complete medical records of patients

. Cases of neoplastic lung lesions under the 2015 WHO Classification of Tumors of Lung will be included in the study

4.4.2.Exclusion criteria

. Incomplete medical record of patients

. Lung resection specimens with descriptive diagnosis

4.5. Sample Size

All resected lung specimens submitted to the department of pathology during the study period with a diagnosis of neoplastic and non-neoplastic tumors and adequate clinical history.

4.6. Data management and Analysis

4.6.1. Data collection procedure

Surgical biopsy request papers were retrieved from the department archives registered fromJanuary 01, 2016 – August 30, 2020 and be subjected for review of the demographic, clinical,gross, microscopic description and final diagnosis.

4.7. Study variables and Data Analysis

In this study, the variables included for analysis are depicted as the following.

- ✓ Age
- ✓ Sex
- ✓ Clinical presentation
- ✓ Radiologic investigation and findings.
- ✓ Type of surgical procedure performed.
- ✓ Histopathologic pattern of the lesion.
- ✓ Behavior of the tumor (benign and malignant).
- ✓ Pathologic T stage at diagnosis.
- ✓ Number and status of lymph nodes examined.

- ➢ Majority of the information were expected to be obtained from the request paper which was sent along with specimens. These variables were subjected for data analysis and the data feeding and analysis was done on computer package SPSS (Statistical Packages of Social Sciences) version 25.

4.8. Ethical considerations

This study was approved by Addis Ababa University, School of medicine, Department of Research Ethics Review Committee (DRERC) and Department of pathology.

5. Results

From a total of 170 cases reviewed, only 159 cases were having complete records suitable for the study. The rest 11 cases were excluded because of incomplete relevant demographic and clinical data and also pathologic reports such as “see description”. From the 159 cases, 99 (62.3%) of the study subjects were males while the remaining 60 (37.7%) were female. (Table 1) M: F ratio of 1.65:1. The minimum age was 2 month and the maximum agewas 73 year. Mean age of patients was 36.8 year. (Table 2)

Demography of the general category

Table 1:Distribution of general category by gender

		Frequency	Percent	Valid Percent	Cumulative Percent
V	Male	99	62.3	62.3	62.3
	Female	60	37.7	37.7	100.0
	Total	159	100.0	100.0	

Table 2: Distribution of general category by age

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
Age	159	.2	73.0	36.808	17.0674
Valid N (listwise)	159				

Distribution of neoplastic and non-neoplastic lesions

There were 92 (57.9%) non-neoplastic cases and 67 (42.1%) neoplastic cases. (Figure 1). The commonest age groups for both neoplastic and non-neoplastic lesions were 3rd and 4th decades. (Figure 2)

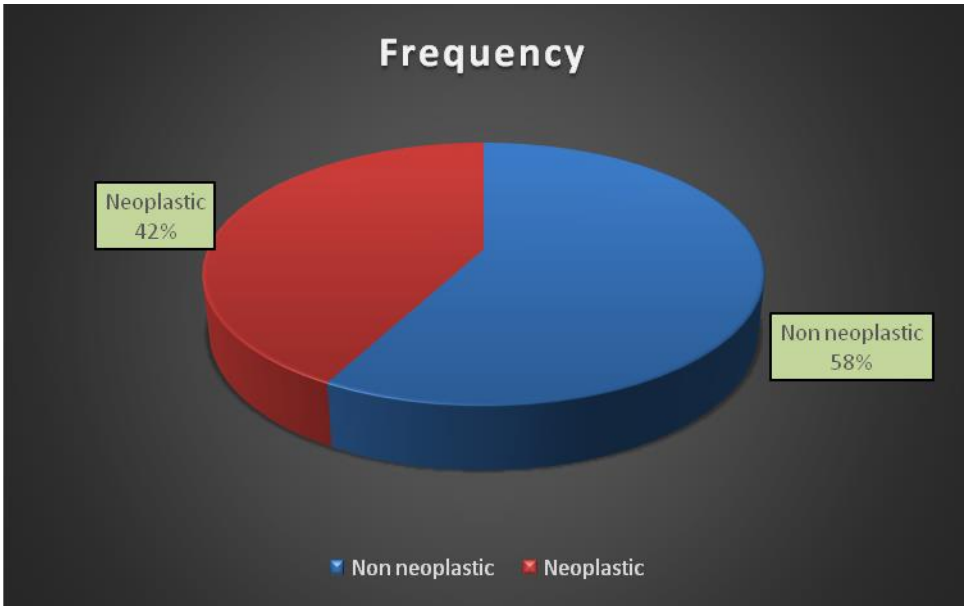

Figure 1:Distribution of neoplastic and non-neoplastic categories

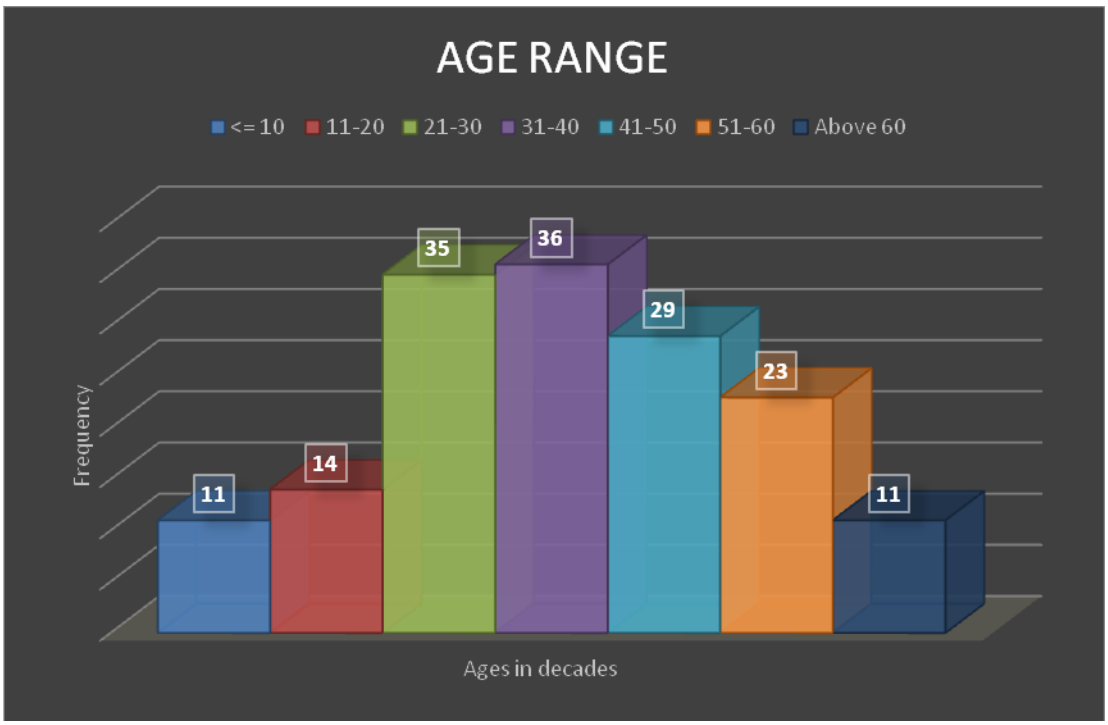

Figure 2: Distribution of general category by age in decades

Clinical presentations and radiologic findings of the general category

Cough and hemoptysis were the commonest clinical presentation (n = 39, 24.5%) followed by cough only (n= 33, 20.8%) and 4 (2.5%) cases were an incidental finding. (Figure 3) Radiologic report was missing in 96 (60.3%) of the request form but present in 63 (39%), from those mentioned almost all were investigated with CT-Scan. (Figure 4). The commonest radiologic finding was mass 37 (23.3%) followed by effusion 5 (3.1%), bronchiectatic change, hyperinflation, cystic and cavitary lesions each account for 4 cases (2.5%). (Figure 5)

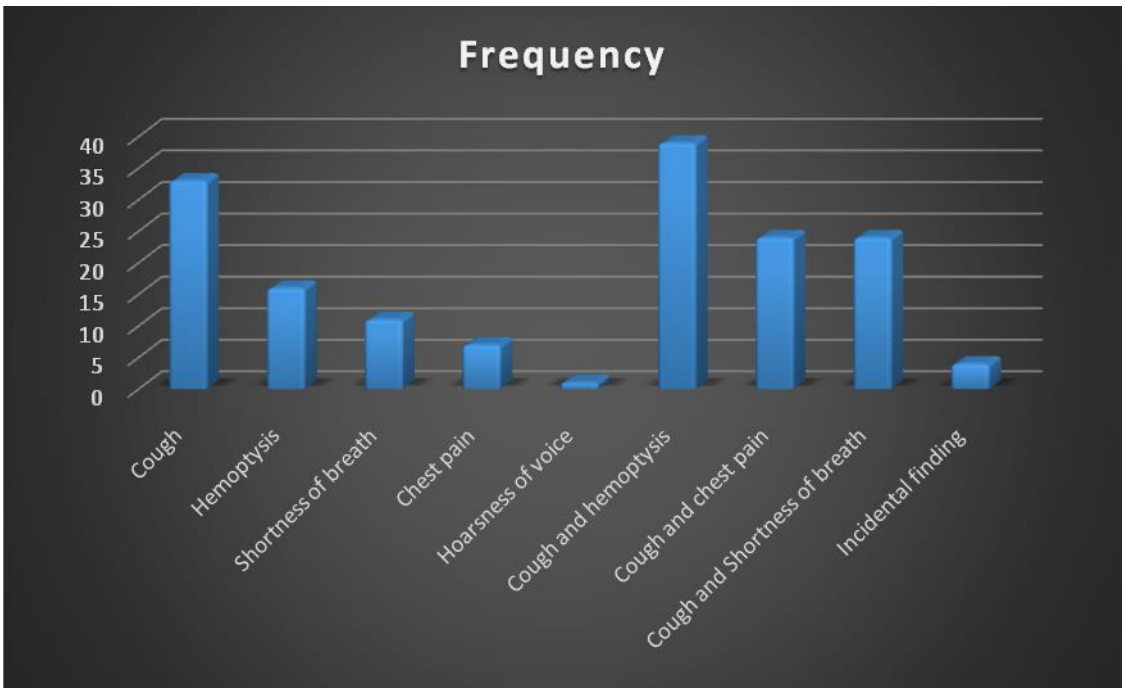

Figure 3: Frequency of clinical presentations of the general category

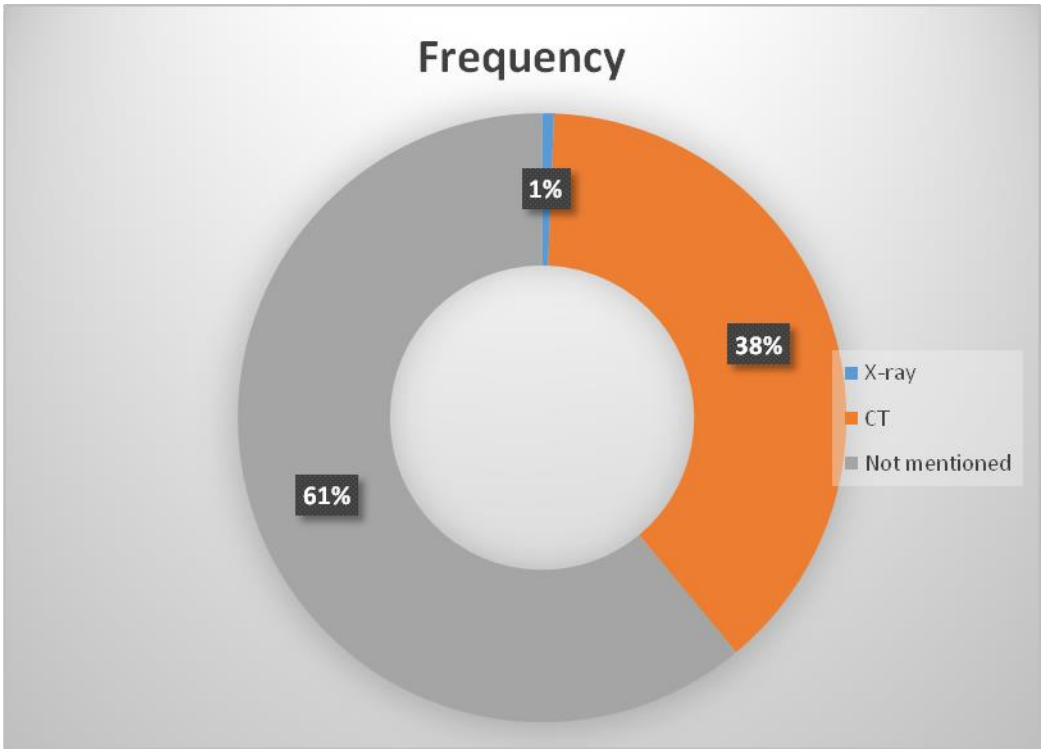

Figure 4: Distribution of radiologic investigation of general category

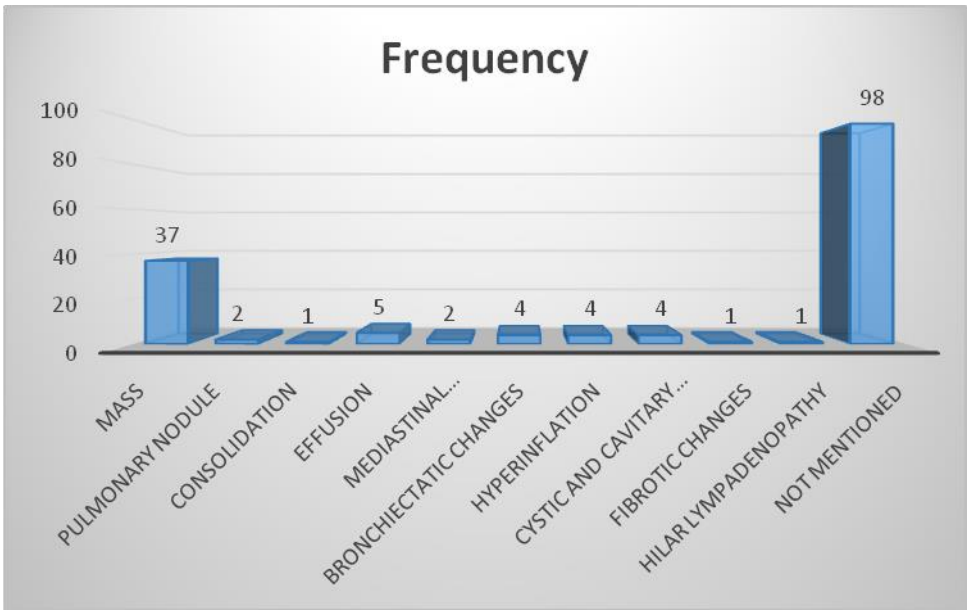

Figure 5: Frequency of radiologic finding in the general category

Frequency distribution of the type of procedure performed

Lobectomy was the most common surgical procedure performed (n=97, 61 %) followed by pneumonectomy 38 (23.9%), wedge resection 22 (13.8%) and Segmentectomy 2 (1.3%).(Figure 6)
Left lung 82 (53%) is more involved than the right lung which accounts for 73 (47%).
The most frequently involved anatomic location beingthe left upper lobe followed by left lower lobe accounting for 42 (27.1%) cases and 21 (13.5%) cases respectively. Bilobe involvement including Right upper and middle 6 (3.9 %); right middle and lower 6 (3.9%) were found. (Table 3)

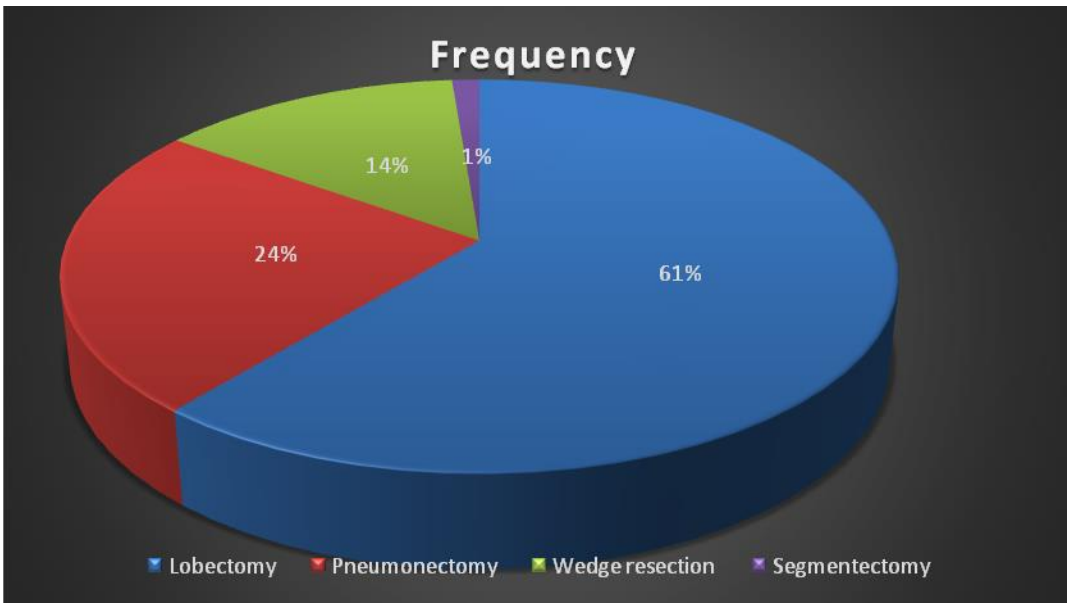

Figure 6: Frequency of surgical procedures in general category

Table 3:Distribution of general category by anatomic location

		Frequency	Valid Percent	Cumulative Percent
Valid	Right Upper lobe	19	12.3	12.3
	Right middle lobe	7	4.5	16.8
	Right lower lobe	18	11.6	28.4
	Left upper lobe	42	27.1	55.5
	Left lower lobe	21	13.5	69.0
	Upper and middle lobes	6	3.9	72.9
	Middle and lower lobes	6	3.9	76.8
	Left pneumonectomy	19	12.3	89.0
	Right pneumonectomy	17	11.0	100.0
	Total	155	100.0	

Demographic distribution of non- neoplastic lesions

Non- neoplastic cases occurred more frequently in males. 64 (69.5%) cases occurred in males and 28 (30.4%) cases occurred in females. Bronchiectasis was the most common non-neoplastic histopathologic entity 18 (11.3%), followed by aspergillosis 16 (10.1%), tuberculosis 11 (6.9%), hydatid cyst 7 (4.4%).(Table 4), (Figure 7) and (Figure 9)

Table 4: Frequency of Non-neoplastic lesions by gender

		Gender		
		Male	Female	Total
Non- neoplastic lesions	Tuberculosis	7	4	**11**
	Bronchiectasis	15	3	**18**
	Aspergillosis	9	7	**16**
	Hydatid cyst	5	2	7
	Congenital lobar emphysema	4	0	4
	CPAM	2	1	3
	Tuberculosis with aspergillosis	1	1	2
	Tuberculosis with bronchiectasis	1	0	1
	Aspergillosis with bronchiectasis	4	2	6
	Chronic fibrosing inflammation	4	2	6
	Intrapulmonary hemorrhage	1	1	2
	Organizing Pneumonia	1	1	2
	Fibrosing Interstitial pneumonia	3	0	3
	End stage fibrotic lung	0	1	1
	Pulmonary alveolar proteinosis	0	1	1
	Cryptogenic organizing pneumonia	1	0	1
	Emphysema	2	1	3
	Lung abscess	1	1	2
	Bronchiolitis obliterans	1	0	1
	Chronic nonspecific inflammation	1	0	1
	Chronic obstructive bronchitis with atelectasis	1	0	1
Total		**64**	**28**	**92**

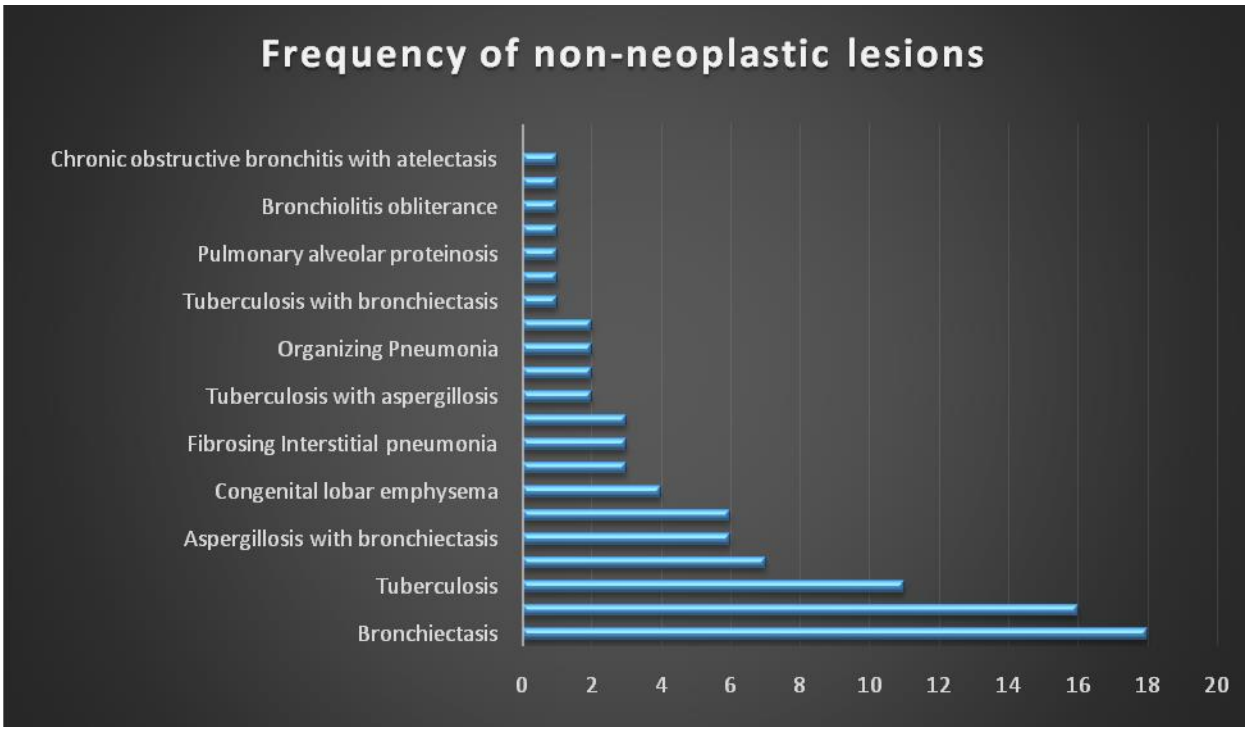

Figure 7: Frequency distribution of non-neoplastic lesions

The commonest age group for the non-neoplastic lesionswere 3rd decades 23 (25%) followed by 4th decades 19 (21%).(Figure 8)

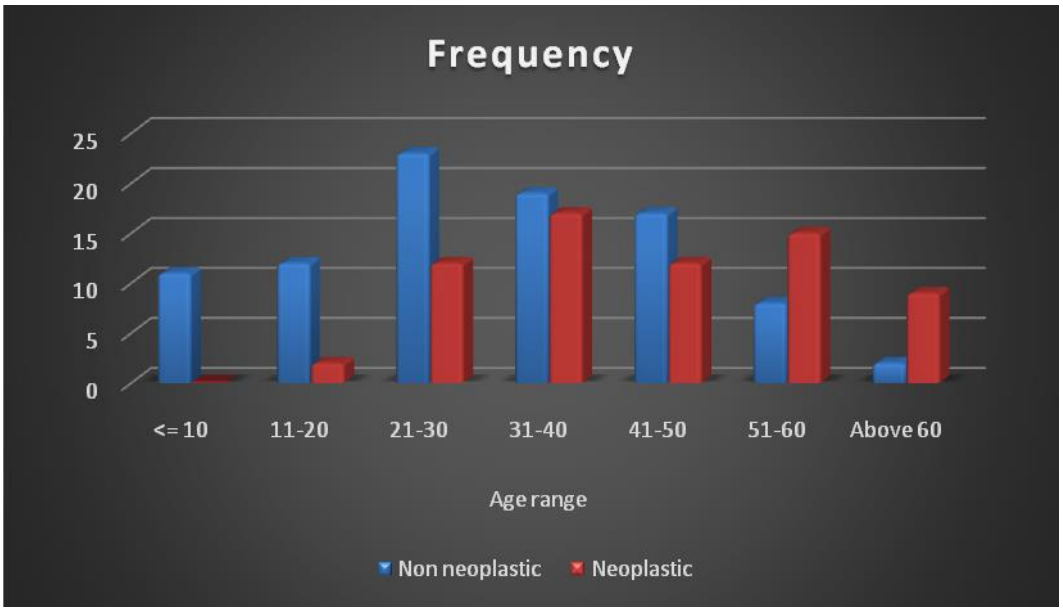

Figure 8: Neoplastic and non-neoplastic lesions with age in decades

Types of procedures done for the non-neoplastic lesions

Lobectomy was performed in 51 (56%) and pneumonectomy 24 (26%), wedge resection in 16 (17%) and segmentectomy in 1 (1%) of the cases. For bronchiectasis 8 lobectomies and 9 pneumonectomies; for aspergillosis 12 lobectomies and 2 pneumonectomies; for tuberculosis 4 lobectomies and 4 pneumonectomies; for hydatid cyst all of them had lobectomies done. (Figure 9)

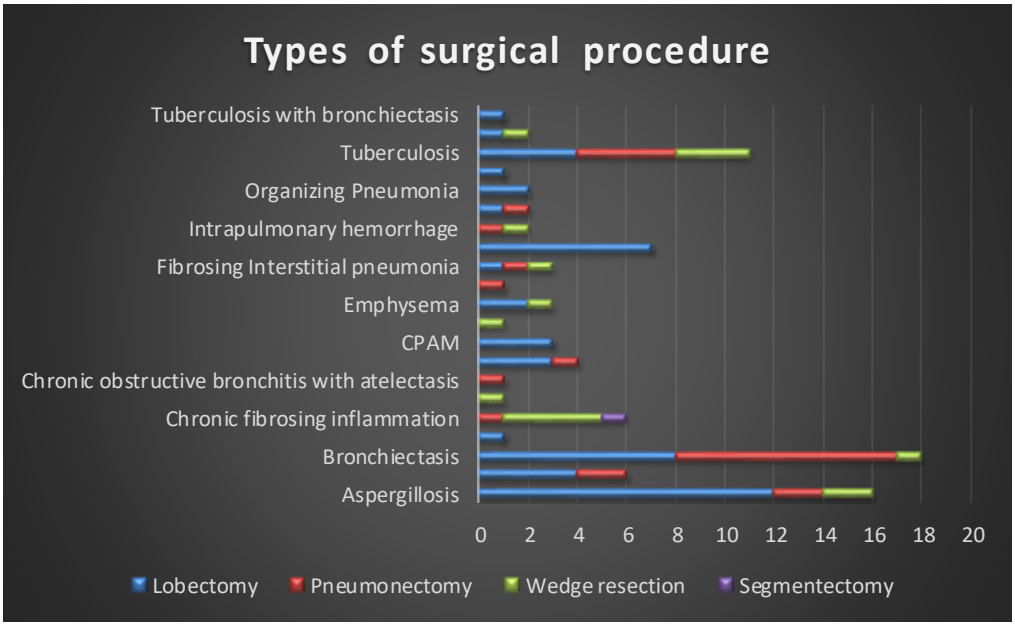

Figure 9:Types of procedure for non-neoplastic lesions

Neoplastic tumors

Out of the 67 neoplastic cases, only 5 (7.5%) cases were benign the rest 62 (92.5%) were malignant.(Table 5)

Table 5: Frequency of neoplastic lesions

		Frequency	Valid Percent	Cumulative Percent
Valid	Benign	5	7.5	7.5
	Malignant	62	92.5	100.00
	Total	67	100.0	

Benign tumors

For the benign lesions M: F ratio is 1.5:1, commonest age group of occurrence is 5th decades 3 (60%). All the benign cases have histopathologic diagnosis of Hamartoma. (Table 6)

Table 6: Benign lesions with age range

		Age range			
		31-40	41-50	51-60	Total
Benign lesions	Pulmonary hamartoma	1	3	1	5
Total		1	3	1	5

Demographic distribution of malignant tumors

From the malignant cases, male and female show almost equal incidences; 32 (51.6%) were males and 30 (48.4%) females with M:F ratio of 1.06:1.(Table 7)

Table 7: Malignant lesions with gender

		Gender		
		Male	Female	Total
Malignant lesions	Adenocarcinoma	9	7	16
	Squamous cell carcinoma	4	2	6
	Large cell Neuroendocrine carcinoma	1	0	1
	Typical carcinoid	11	17	28
	Atypical carcinoid	2	2	4
	Adenosquamous carcinoma	2	0	2
	Undifferentiated carcinoma	2	0	2
	Monophasic synovial sarcoma	1	1	2
	Solitary fibrous tumor	0	1	1
Total		32	30	62

The age distribution of malignant lesions shows minimum age was 20 and maximum age was 73 with a mean age of 44 years.

For typical carcinoid the minimum age was 20 year and the maximum age was 60 year with mean age of 35. For adenocarcinoma the minimum age was 34 year and the maximum age was 73 year with the mean age being 55.8 year. For SCC the minimum age was 24 year the maximum age was 64 year with the mean age being 39.5 years.

The mean age for adenocarcinoma was older 55.75 year when compared with the other two common histopathologic types, typical carcinoid the mean age was 35 years and for SCC the mean age was 39.5 years. (Table 8). The commonest age group was 4th decades 16 (26%) and 6th decades 14 (23%).

Table 8:Age of malignant tumors

Malignant lesions	Mean	Maximum	Minimum
Adenocarcinoma	55.750	73.0	34.0
Squamous cell carcinoma	39.500	64.0	24.0
Large cell Neuroendocrine carcinoma	68.000	68.0	68.0
Typical carcinoid	35.214	60.0	20.0
Atypical carcinoid	55.000	68.0	45.0
Adenosquamous carcinoma	51.000	60.0	42.0
Undifferentiated carcinoma	58.500	62.0	55.0
Monophasic synovial sarcoma	24.000	28.0	20.0
Solitary fibrous tumor	55.000	55.0	55.0
Total	43.952	73.0	20.0

Radiologic finding and procedures done for malignant tumors

From those with documented radiologic findings, mass was the commonest finding 24 (80%), followed by mediastinal lymphadenopathy 2 (6.7%), pulmonary nodules, effusion cystic and cavitary lesions and hilar lymphadenopathy each accounting for 1 (3.3%). (Table 9)

Table 9: Malignant lesions with radiologic findings

Histopathologic type	Mass	Pulmonary nodule	Effusion	Mediastinal LAP	Cystic & Cavitary	Hilar LAP	Not mentioned	Total
Adenocarcinoma	5	1	1	1	0	0	8	16
SCC	3	0	0	0	0	0	3	6
Large cell NEC	1	0	0	0	0	0	0	1
Typical carcinoid	12	0	0	0	0	1	15	28
Atypical carcinoid	2	0	0	0	0	0	2	4
Adenosquamous	0	0	0	0	0	0	2	2
Undifferentiated	0	0	0	1	0	0	1	2
Monophasic SS	1	0	0	0	1	0	0	2
SFT	0	0	0	0	0	0	1	1
Total	24	1	1	1	2	1	1	62

Lobectomy was the commonest procedure done with 43 (69.4%) cases had lobectomies; 14 (22.6%) of the cases had pneumonectomies; 4 (6.4%) of the cases had wedge resection and only 1 (1.6%) of cases had segmentectomy done (Table 10)

Table 10: Malignant tumors with types of surgical procedures

Type of surgical procedure	Total

		Lobectomy	Pneumonectomy	Wedge resection	Segmentectomy	
Malignant lesions	Adenocarcinoma	11	5	0	0	16
	Squamous cell carcinoma	5	0	1	0	6
	Large cell Neuroendocrine carcinoma	1	0	0	0	1
	Typical carcinoid	19	8	1	0	28
	Atypical carcinoid	4	0	0	0	4
	Adenosquamous carcinoma	1	1	0	0	2
	Undifferentiated carcinoma	1	0	0	1	2
	Monophasic synovial sarcoma	1	0	1	0	2
	Solitary fibrous tumor	0	0	1	0	1
Total		43	14	4	1	62

Distribution of malignant tumors with histopathologic pattern

Frequency of the malignant neoplasms with histopathologic type; typical carcinoid is the most common type reported 28 (45.2%), followed by adenocarcinoma 16 (25.8%), SCC 6 (9.7%), atypical carcinoid 4 (6.5%), adenosquamous carcinoma 2 (3.2%), undifferentiated carcinoma 2 (3.2%), monophasic synovial sarcoma 2 (3.2%), large cell neuroendocrine carcinoma 1 (1.6%), solitary fibrous tumor 1 (1.6%). (Table 11) and (Figure 10)

Table 11:Histopathologic pattern of malignant tumors

		Frequency	Valid Percent	Cumulative Percent
Valid	Adenocarcinoma	16	25.8	25.8

	Squamous cell carcinoma	6	9.7	35.5
	Large cell Neuroendocrine carcinoma	1	1.6	37.1
	Typical carcinoid	28	45.2	82.3
	Atypical carcinoid	4	6.5	88.7
	Adenosquamous carcinoma	2	3.2	91.9
	Undifferentiated carcinoma	2	3.2	95.2
	Monophasic synovial sarcoma	2	3.2	98.4
	Solitary fibrous tumor	1	1.6	100.0
	Total	62	100.0	

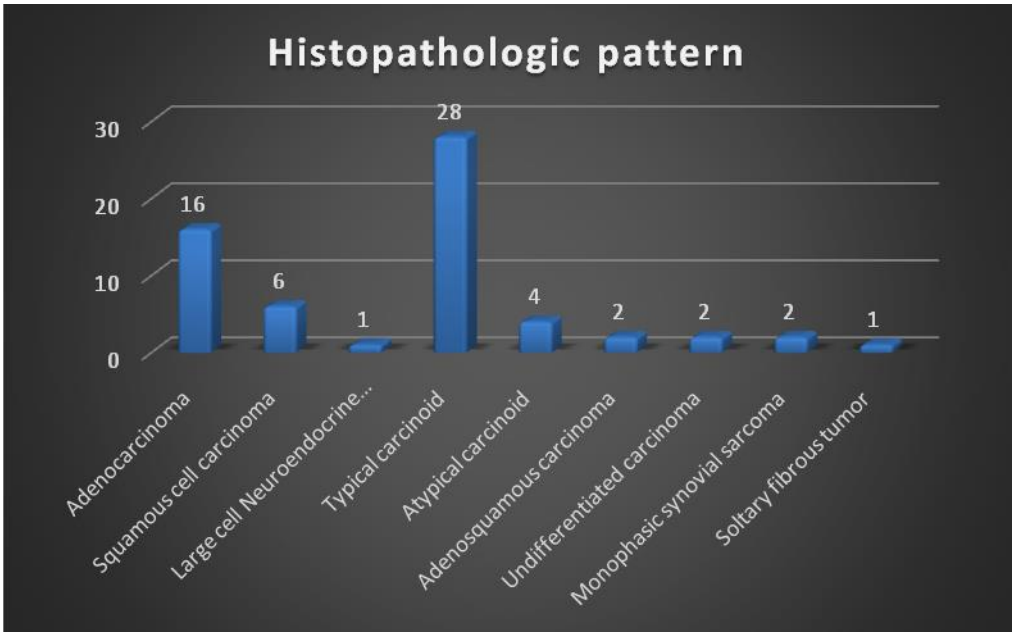

Figure 10: Malignant tumors with histopathologic pattern

Malignant tumor with pathologic T stage

Majority of the malignant neoplasms were in pathologic stage 2, 32 (55.2 %), with stage 1 and 3 have equal frequency of 12 (20.7%) cases.Typical carcinoid [7 (26%) cases are at stage 1 and 13 (48%) are stage 2], Adenocarcinoma [4 (25%) cases are at stage 1 and 8(50%) cases are at stage 2]. (Table 12) and (Figure 11)

Table 12: Malignant tumors with pathologic T stage

	Frequency	Valid Percent
Stage 1	12	20.7
Stage 2	32	55.2
Stage 3	12	20.7

	Stage 4	2	3.4
	Total	58	100.0

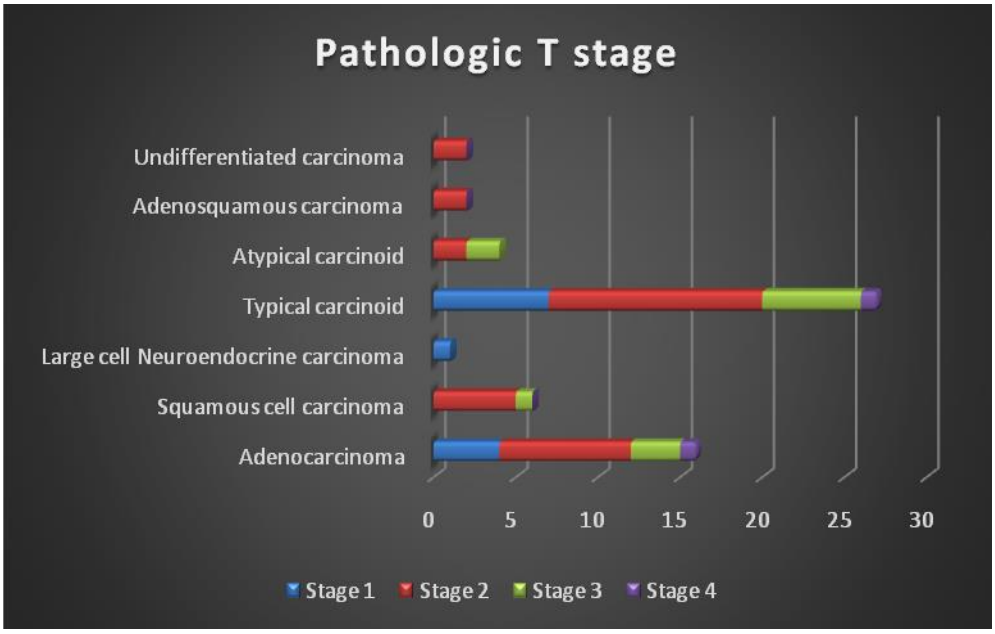

Figure 11: Pathologic T stage of malignant tumors

Number and status of lymph node examined in malignant tumors

There were 31 (53.4%) cases with known lymph node status and 27 (46.6%) cases with unknown lymph node status. From those 20 (34.5%) had N0, 9 (15.5%) had N1 and 2 (3.4%) had N2. (Figure 12) SCC and adenocarcinoma had the highest lymph node positivity,33% and 25% respectively. (Table 16) and (Figure 15) From those examined lymph nodes; 18 (58.1 %) had up to 3 LNs examined, 8 (25.8 %) 4-6 LNs, 3 (9.7 %) had 7-9 LNs and 2 (6.5 %) cases had more than 9 LNs examined. (Table 13)

Table 13: Number of lymph nodes examined

	Frequency	Valid Percent
1-3	18	58.1
4-6	8	25.8

	7-9	3	9.7
	10 and above	2	6.5
	Total	31	100.0

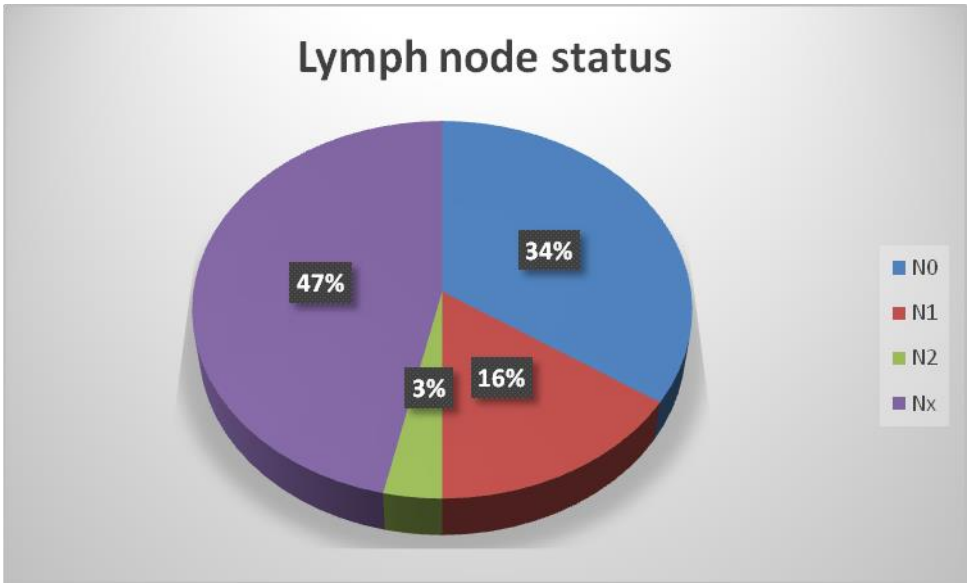

Figure 12: Frequency of lymph node status

Table 14:Lymph node status with histopathologic pattern

		Lymph node status				
		N0	N1	N2	Nx	Total
Malignant lesions	Adenocarcinoma	5	3	1	7	16
	Squamous cell carcinoma	0	2	0	4	6
	Large cell Neuroendocrine carcinoma	0	1	0	0	1

	Typical carcinoid	12	2	1	12	27
	Atypical carcinoid	2	1	0	1	4
	Adenosquamous carcinoma	0	0	0	2	2
	Undifferentiated carcinoma	1	0	0	1	2
Total		20	9	2	27	58

6. DISCUSSION

According to the 2018 WHO report lung cancer is the most common cancer (2.09 million cases) and the leading cause of cancer death (1.76 million deaths) representing close to 1 in 5 (18.5%)

cancer death globally. The male to female ratio globally is 1.89:1. [4] Closely put twice more commonly occur in males than in females. According to Globocan report on the incidence and prevalence of cancer in Ethiopia by 2018, lung cancer ranks the 7th most common malignancy in Ethiopia. Addis Ababa population-based pattern of cancer therapy, a population-based study by Feuchtner J, et al. (2019) [6] on 588 files found out that lung cancer ranking as the 5th most common malignant tumor with 28 out of 588 files (4.8%).

In the present study 159 cases were evaluated totally. 99 (62.3%) of the study subjects were males while the remaining 60 (37.7%) were female. (Table 1) M: F ratio of 1.65:1 which is similar to one study done in Ibadan Nigeria with M: F ratio (1.7:1) [15], but another study in Iran showed a slightly higher M: F ratio (2.15:1) [12] and a lower than the present study was found in United Kingdom (1.15:1) [12].

There were 92 (57.9%) non-neoplastic cases and 67 (42.1%) neoplastic cases. (Figure 1) The commonest age groups for both neoplastic and non-neoplastic lesions were 3rd and 4th decades. Slightly closer distribution of neoplastic and non-neoplastic lesions was found in one study done in Iran (50 % each) [7]. Another study done in Heidelberg, West Germany found that 64 % of neoplastic and 36 % non-neoplastic lesions [14]. Study done in the United States at Vanderbilt – Ingram Cancer Center found an even lower non-neoplastic rate 65/278 (23 %) patients who underwent surgical resection for a suspicious nodule had a benign pathology [13]. Lowest rates of benign and non-neoplastic lesions by Rolston et al., (6.7 %) [11], Smith et al., (9%) [8] and Maiga et al., (7 %) [10].

The most common clinical presentation in the present study was cough and hemoptysis. Study by Rolston et al., [11] and many others cough was the commonest presentation.

From the non-neoplastic lesions bronchiectasis was the most common non-neoplastic histopathologic entity 18 (11.3%), followed by aspergillosis 16 (10.1%), tuberculosis 11 (6.9%). But several studies have found that tuberculosis is the commonest 39 % Yazd et al., [7], One study in Brazil tuberculosis accounts for 46.7% [9], Eric L. Grogan, et al. [13] tuberculosis 57% followed by histoplasmosis 23%.

The mean age for non-neoplastic lesions in the present study is 2 decades earlier than two other studies done by smith et al., (58.2) [8] and Eric L. Grogan, et al [13]. The male to female ratio for the non-neoplastic lesions was 2.3:1 (64 male and 28 female) which is slightly higher than found by Smith et al., M:F ratio of 1.37:1 [8] but lower than that found by Eric L. Grogan, et al., 3.5:1 [13]. The most common procedure done for non-neoplastic lesions in the present study were lobectomy which was performed in 51 (56%) and pneumonectomy 24 (26%), wedge resection in 16 (17%) (figure 11)similar to study done in United Kingdom by Ben Davies, et al.[12] found that lobectomy was the commonest procedure performed 58% followed by limited resections including wedge resections 34% but a significantly lower rate of pneumonectomies (0.6%) [12] and another study by HEIKKI TOOMES, et al. lobectomy was still the commonest procedure but at a lower rate (34.9%) and pneumonectomy rate was 1.5%. [14]

In a study conducted in North America, Smith et al. [8] found that 9% of benign diseases mimic primary lung cancer. Rolston et al., observed a 6.7% prevalence of benign diseases mimicking primary lung cancer. [11] These findings are very similar to study done by Homirch, G. K., et al, which showed an 8% prevalence. [9]. Their studies include the benign (neoplastic) with the non-neoplastic lesions with a logic that both conditions have a good prognosis post-operatively. Comparing these to the present study benign disease rate; adding benign diagnosis to the non-neoplastic was found to be n= 97 (61%), which is a very significant number one explanation is related to factors associated with national epidemiology such as high incidence of granulomatous infectious diseases like tuberculosis that present with findings indicative of neoplasm. Post TB Complications like bronchiectasis and cavitary aspergillosis are indirect reflection of the infectious disease burden in resource limited countries like Ethiopia.

In Ethiopia, TB is still a major public health problem. The country is still among the 22 high TB burden countries with high number of missed and infectious TB cases in the community. The prevalence and incidence of TB in Ethiopia in 2014 were 211 and 214 per 100,000 populations respectively.

With regard to diagnostic methods, we highlighted the importance of investigative modalities like fibrobronchoscopy in the assessment of suspected lung cancer lesions. This minimally invasive method was used for the diagnosis of more than half of the patients studied (55.6%). The need for surgical samples, for diseases mimicking cancer, was relatively high in the study done by Homirch, G. K., et al (33.4%).[9] However, studies published prior to the use of computerized tomography, have described up to 64% of samples from surgical material. This reduction is probably a result of the improvement and dissemination of less invasive methods with excellent diagnostic yield such as computerized tomography or ultrasound-guided core lung biopsy.

A multidisciplinary review may lead to the comprehensive implementation of diagnostic modalities that better identify patients most likely to benefit from therapeutic resection. Recent data suggest that the engagement of surgical oncologists in tumor boards results in higher rates of curative intent surgery for patients with early-stage non–small cell lung cancer ,Maiga, A. et al. [10] Since it needs a careful balance between attempting to identify and resect early stage lung cancer and minimizing the rate of resection of benign pulmonary lesions. [8]

Out of the 67 neoplastic cases, only 5 (7.5%) cases were benign the rest 62 (92.5%) were malignant. (Table 7). This very low prevalence of benign neoplastic lesion in the present study was similar to study done by Ben Davies, et al. which found a prevalence of 7.3%. [12]. In the present study all cases with benign diagnosis were found to be hamartoma but other study showed hamartoma and chondroma.[12]

In the present study the malignancy rate among the neoplastic lesions was 92.5 % which is closer to study done by Rolston, k. et al. which showed a rate of 93.3 %. [11] But a lower rate of malignancy was found in study done by Ben Davies, et al. (77.7%). [12]

From the malignant cases, in the present study male and female show almost equal incidences ;32 (51.6%) were males and 30 (48.4%) females with M:F ratio of 1.06:1. (Table 10) This result showed a higher incidence of malignancies in females when compared to the 2018 WHO report where the male to female ratio globally was 1.89:1. [4] One large study by Keisha A. Houston et.al [20] among those with newly diagnosed lung cancer found a similar result compared to result of the present study, an M:F ratio to be 1.17:1 Another study done in Ibadan, Nigeria by J O Ogunbiyi, [15] found a M: F ratio of 1.7 :1. Amany O., et al. (2.49:1). [16].
But different several studies across the world still show a predominance of lung carcinoma among males; Yosri M. AKL et al. found M:F ratio 4.6:1 [23] Dey A et al. Male female ratio 4.14:1 [19].

In the present study the age distribution of malignant lesions shows minimum age was 20 and maximum age was 73 with a mean age of 44 years. (Table 11) The commonest age group was 4^{th} decades (26%) and 6^{th} decades (23%). (Figure 10). This showed a significant proportion of cases were seen at an earlier age group when compared to study done in Egypt by Amany O., et al. [16] where the highest incidence was in patients above 60 years (48.6%).

The relation between age groups and histological cell type The mean age for adenocarcinoma was older 55.75 year when compared with the other two common histopathologic types, typical carcinoid the mean age was 35 years and for SCC the mean age was 39.5 years. (Table 11). But study by Yosri M. AKL et al. [23] shows that the squamous cell carcinoma was common after the age of 50 years (84.1%) while the small cell carcinoma was common in the age period between 40 and 60 years (70%) and also adenocarcinoma cell type was common in the age period between 40 and 60years (63.9%).

Cough and hemoptysis were the most common clinical presentation in the present study. The most common presenting symptom was cough (68.42%) followed by breathlessness (63.15%) Bhattacharyya S. Kumar et al. [25] Cough was the most common symptom found in (72.90%) patients, followed by fever (58.12%) Rawat J. [24] Another study by Yosri M. AKL et al. [23], cough was the most common symptom (85.9%) and was followed by dyspnea (68.3%), expectoration (66.8%), chest pain (59.7%), hemoptysis (35.1%). Another study by Amany O., et al. [16], the commonest presenting symptoms was shortness of breath (59.6 %), followed by cough (41.2%) and hemoptysis (31.2 %). Generally, the variation in the types of symptoms and its incidence is usually dependent on the behavior of histopathologic subtype, tumor location and the presenting stage at the time of diagnosis. [23]

In the radiologic finding of the present study mass was the commonest radiologic finding 80 %. This is in accordance with study by Amany O., et al. [16], where the most common radiologic pattern of presentation was mass (71.8 %) followed by effusion (30.6%). Higher percentage of effusion at presentation is attributed to the late presentation (Stage IIIA 38.8%, Stage IIIB 29.4% and Stage IV 12.5) Lung mass was the commonest radiological picture, as it occurred in (49.8%) by Yosri M. AKL et al. [23] near to that percentage (46.31%) that was reported by Rawat et al. [24]

Regarding the histopathologic subtype, typical carcinoid was the most common type reported 28 (45.2%), followed by adenocarcinoma 16 (25.8%), SCC 6 (9.7%), atypical carcinoid 4 (6.5%). (Table 14). These results were against most studies done in various parts of the world. One such study done in Norway by Anne Naalsund et al. [21] they included a total of 26,665 lung cancers diagnosed in the period 1993 – 2005, they found out that 265 patients (1%) had carcinoid tumors. 11 were diagnosed coincidentally at autopsy. In the remaining 254 patients, Typical carcinoid were (74.01%) and Atypical carcinoid were (23.22%).

Other study by Santos- Martinez et al. [17] found that the most common histologic types were SCC 225 patient (33.2 %) and adenocarcinoma 202 patients (29.8 %). The most common histologic types were SCC (33.2 %) and adenocarcinoma (29.8 %) according to Dey A et al. [19]. In another study by Rawat et al., [24] they reported that 44.8% of cases were squamous cell carcinoma followed by adenocarcinoma (19.7%) Yosri M. AKL et al. [23]. The commonest were SCC (37.4%) and adenocarcinoma (29.5 %).
Recent studies show an increase in the trends of adenocarcinoma; adenocarcinoma incidence (51.8%) was markedly high and surpassed the squamous cell carcinoma (22.7 %). Amany O., et al. [16]. Adenocarcinoma was the commonest (34%), SCC (14%), carcinoid (7.3%) according to study by Ben Davies, et al. [12].
The higher incidence of carcinoids (typical and atypical) in the present study could be explained by higher proportion of earlier presentation at an operable stage, this fact is supported by Anne Naalsund et al. [21] where the majority of cases were classified as Stage I (82 %). Another factor could be due to the frequent central anatomic location of the tumor; approximately 80% of pulmonary carcinoids occur centrally, and 20% are peripheral [28], so earlier presentation with the common manifestations like cough and hemoptysis and these were the commonest presentation in the present study.
The present study only includes cases obtained from resection procedures, this will exclude majority of cases that present at an inoperable stage (those with effusion, metastasis and others). Since most of our lung carcinoma patients came in late inoperable stages, they were not represented in this study.
On one study by Yosri M. AKL et al. [23], there were 90.2% of the cases present at inoperable stage whereas those at operable stage were 9.8 %. Another study by Jagdish Rawat et al. [24] found similar result where the majority patients (73.29%) were diagnosed in the later stages of the disease (III B and IV). In all these studies they used FOB, thoracic US guided, CT guided biopsies so the inoperable cases would be included. The majority of cases were diagnosed at later stages of illness with some of them died before the start of treatment (Stage IIIA 38.8 %, Stage IIIB 29.4 % and Stage IV 12.5 %) according to Amany O., et al. [16].

Majority of the malignant neoplasms were in pathologic stage 2, 32 (55.2 %), with stage 1 and 3 have equal frequency of 12 (20.7%) cases. This had slight difference from one case control study which showed pathologic stage 1 was the commonest (45.1%) with stage 2 and stage 3 had frequencies 26.5 % and 17.2 %. [26]. In the present study typical carcinoid [(26%) cases were at stage 1 and (48%) were stage 2]. (Table 15) A study by Anne Naalsund et al. [21]

showed 86.1% of pathologic stage 1 and 12.1 % of stage 2, giving a higher proportion of early stage (a tumor not exceeding 5 cm) cases in both.

A case control study showed that histologic tumor type and grading, tumor site and tumor lobe distribution did not prove predictive for lymph node metastasis. [26] So different histopathologic subtype of malignant lesions had range of positive lymph node status.

With regard to the number of lymph nodes examined, in the present study few numbers of lymph nodes were examined for patients; a higher percentage (83.9 %) had 1-6 LNs and 17.1 % had more than 6 LNs examined (Table 16). But one study done in the United States by Garaj, A. et al [27] 45.2 % had more than 6 LNs examined. When adequate lymph node sampling is not performed, the true N stage remains unrecognized because all the lymph nodes are not dissected and pathologically examined, which may result in a spurious downstaging of such patients.[26] So adequate sampling of lymph node is mandatory; these tasks may be shared by the pathologist specially in sampling Station 11-14 LNs (intrapulmonary). The rest Station 10 (hilar) and lower Stations (Mediastinal) will be the task of the surgeons to Sample and label accurately for optimal patient management.

7. CONCLUSION

- In this study a higher proportion of non-neoplastic lesions were identified in resection specimens than neoplastic cases. This signifies the need for different preoperative imaging and non-invasive diagnostic procedures be implemented. The commonest age group for both neoplastic and non-neoplastic cases was a decade earlier than other studies around the world. The commonest clinical presentation, radiologic investigative modality and radiological finding were similar with other studies around the world. A higher proportion of malignancy and a lower benign tumor was similar with other studies around the world. Carcinoid tumor was the most frequent histopathologic subtype. A lower number of LNs were examined per patient in this study.

8. RECOMMENDATION

- It will be wise to have a multidisciplinary team approach; this will help to identify and resect an early stage lung carcinoma and at the same time minimize the rate of unnecessary resection for benign pulmonary lesions.
- In this study there were cases with inadequate pathologic reporting. So preparing and following a standard grossing and reporting dataset is recommended so as to minimize

inadequate grossing and incomplete pathologic reporting which will have a direct adverse impact on subsequent patient management.

- Most of the data sent to the pathologist are incomplete, especially clinical information regarding the sample labeling (LN station). This will make it difficult to assess the N category since it is dependent on the station of the respective LNs examined. So Interdepartmental communications is advised between pathologist, clinicians and radiologist.
- Further study inclusive of image guided and fluid cytologic samples should be undertaken to understand the true prevalence of malignant histopathologic subtypes.

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