

# Clinical Characteristics and Molecular Profiles of Lung Cancer in Ethiopia



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## ABSTRACT

**Introduction:** Lung cancer is the most common cause of cancer deaths worldwide, accounting for 1.8 million deaths each year. Only 20% of lung cancer cases are reported to occur in low- and middle-income countries. An estimated 1.5% of all Ethiopian cancers involved the lung; however, no nationwide cancer registry exists in Ethiopia. Thus, accurate data on clinical history, histopathology, molecular characteristics, and risk factors for lung cancer are not available. The aim of this study was to describe the clinical, radiologic, and pathologic characteristics, including available molecular profiles, for lung cancer at Tikur Anbessa Specialized Hospital (TASH), the main tertiary referral center in Addis Ababa, Ethiopia.

**Methods:** A cross-sectional study was conducted at TASH among 146 patients with pathologically confirmed primary lung cancer, diagnosed from 2015 to 2019 and recorded in the Addis Ababa Cancer Registry at TASH. Clinical data were extracted from patient medical records, entered into a Research Electronic Data Capture database, and analyzed using Statistical Package for the Social Sciences statistical software. Variables collected included sociodemographics, personal exposures, comorbidities, clinical manifestations at presentation, chest imaging results, diagnostic procedures performed, histopathological classification, cancer staging, and type of treatment (if any). A subset of lung biopsies

fixed in formalin for 2 to 7 days, which could be retrieved from the files of the Pathology Department of TASH, were reviewed, and molecular analysis was performed using next-generation sequencing to identify the tumor-oncogenic drivers.

**Results:** Among the 146 patients studied, the mean (SD) age was 54 plus or minus 13 years; 61.6% (n = 90) were male and 25.3% (n = 37) had a history of tobacco use. The most common clinical manifestations included cough (88.4%, n = 129), chest pain (60.3%, n = 88), and dyspnea (53.4%, n = 78). The median duration of any symptoms was 6 months (interquartile range: 3–12 mo). The most common radiologic features were lung mass (84.9%, n = 129) and

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pleural effusion (52.7%, n = 77). Adenocarcinoma accounted for 35.7% of lung cancers (n = 52) and squamous cell carcinoma 19.2% (n = 28) from those specimens was reported. Among patients on whom staging of lung cancer was documented, 92.2% (n = 95) of the subjects presented at advanced stages (stages III and IV). *EGFR* mutation, exons 19 and 20, was found in 7 of 14 tissue blocks analyzed. No specific risk factors were identified, possibly reflecting the relatively small sample size and limited exposures.

**Conclusions:** There are marked differences in the presentation, risk factors, and molecular characteristics of lung cancer in Ethiopia as compared with other African and non-African countries. Adenocarcinoma was the most common histologic type of lung cancer detected in our study, similar to findings from other international studies. Nevertheless, compared with high-income countries, lung cancer in Ethiopia presents at a younger age, a later stage, and without considerable personal tobacco use. The relatively higher prevalence of *EGFR* mutation, from the limited molecular analyses, suggests that factors other than smoking history, such as exposure to biomass fuel, may be a more important risk factor. Country-specific screening guidelines and treatment protocols, in addition to a national tumor registry and greater molecular mutation analyses, are needed to improve prevention and management of lung cancer in Ethiopia.

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**Keywords:** Lung cancer; Staging; Histologic types; Molecular profile; *Epidermal growth factor receptor*

## Introduction

Lung cancer is the most common cause of cancer deaths worldwide, accounting for 11.6% of new cancer cases (2.1 million new cases each year) and 1.8 million annual deaths. Most cases occur in high-income countries (HICs); only 20% occur in low- and middle-income countries. Lung cancer remains the leading cause of cancer mortality among men and women in all areas of the world and has surpassed breast cancer as the leading cause of cancer death in women living in HICs.<sup>1,2</sup> Globally, the greatest risk factor for lung cancer is tobacco consumption, causing 85% of lung cancer in men and 46% in women.<sup>3</sup> Yet, in the past several decades, lung cancer in never smokers has been steadily increasing, now globally ranked seventh among all causes of cancer deaths.<sup>4-6</sup>

The low incidence and mortality of lung cancer in low- and middle-income country is likely due to a lower prevalence of tobacco use (10% in men and <2% in

women) and a shorter life expectancy for the population.<sup>7-9</sup> Nevertheless, limited resources and infrastructure to identify and treat patients with lung cancer may result in lung cancer underreporting. For example, in Ethiopia, there is no nationwide cancer registry, and there is only one oncology referral center in the country, located at Tikur Anbessa Specialized Hospital (TASH) in Addis Ababa, Ethiopia, where incomplete information on patients with lung cancer is available.<sup>10</sup>

Despite these limitations, lung cancer accounted for 2.7% of the total number of all cancers diagnosed at TASH from 2011 to 2017 (n = 12,056) (Tikur Anbessa Specialized Hospital Oncology Center, unpublished data, 2018). An earlier study of the TASH cancer registry found that lung cancer accounted for 1% of all cancers in females and 2% in men.<sup>11</sup> A recent study estimated the true incidence at 1691 new cases each year.<sup>12</sup> These studies likely reflect vast underreporting of lung cancer owing to limited resources to locate, biopsy, and diagnose all patients. As a result, there is very little published information regarding clinical presentations, stage distribution, and histologic subtypes of patients with lung cancer in Ethiopia.

The aim of this study was to link data from the Addis Ababa Cancer Registry with patient information from TASH medical records to determine the broader characteristics of lung cancer in Ethiopia and identify possible risk factors.

## Materials and Methods

### Study Design and Setting

A cross-sectional cohort study was conducted at TASH, the main tertiary referral center in Ethiopia, which has the only oncology center in the country. The oncology center operates three daily outpatient clinics, 5 days per week, and manages 12 inpatient hospital beds. Yearly, more than 12,000 cases of all types of cancers are seen at the oncology center. Staff caring for patients with lung cancer include seven pulmonologists, five thoracic surgeons, and five medical oncologists.

### Population, Tissue Sampling, and Somatic Mutation Analysis

All consecutive patients with pathology confirmed primary lung cancer diagnosed from January 1, 2015, to December 31, 2019, and listed in the Addis Ababa Cancer Registry at TASH were included in the study (n = 237). Histologic subtypes were confirmed mainly by microscopy and histochemical stains in selected cases. The small lung biopsy specimens were fixed in formalin. These tissues were then subsequently stained using hematoxylin and eosin. Microscopic evaluation of the slides was reviewed by experienced pathologists.

Comprehensive medical records were obtained for each patient. We excluded patients less than 18 years of age and those with inconclusive pathology findings, incomplete clinical data, or lung metastasis from other documented primary sites ( $n = 6$ ). Because of inconsistent record retention, patients with untraceable medical records were also excluded ( $n = 85$ ). Thus, 146 records were available for complete review.

In addition, a subset of lung biopsy specimens, fixed in formalin for 2 to 7 days, that could be retrieved from the files of the Department of Pathology at TASH, was reviewed by the Pathology Department of the Columbia University Irving Medical Center, in which the tumor DNA was extracted and targeted next-generation sequencing (NGS) was performed using the 56 oncogenic drivers from the OncoReveal panel (Pillar Biosciences).

### Data Collection

A case report form was used to collect the following information from patient medical records: sociodemographics (i.e., age, sex, region of residence, education level, occupation), risk factors and exposures (i.e., personal smoking history, secondhand smoke exposure, biomass fuel exposure), comorbidities, clinical manifestations at presentation, chest X-ray or computed tomography findings (including location of lesion and metastasis, if applicable), diagnostic procedures performed, histopathological classification, tumor stage, type of treatment (if any), follow-up time from diagnosis, and treatment outcome. At the time of the study, brain imaging and abdominal imaging were performed as part of routine staging of lung cancer in Ethiopia. Nevertheless, positron emission tomography scan was not done as it was not available in Ethiopia. The different chemotherapy regimens used in Ethiopia for the treatment of patients with lung cancer were paclitaxel and carboplatin for adenocarcinoma and large cell carcinoma, cisplatin and gemcitabine for squamous cell carcinoma (SCC), and etoposide and gemcitabine for small cell carcinoma. Nevertheless, none of the patients received any targeted agents or biological therapy as these treatments were not available in Ethiopia.

**Measurement of Variables.** Tobacco smoking was reported as pack-years (i.e., the number of packs of cigarette smoked per day multiplied by the number of years smoked). There is no standardized measure for biomass fuel exposure; so, we extracted information on whether the patient had exposure to biomass fuel or not. Lung cancer staging was based on the seventh edition of the TNM classification of malignant tumors.<sup>13</sup>

**Data Quality Assurance.** The quality of data was assured by proper design and pretesting of the case

report form on 5% of patient charts. Furthermore, research assistants and medical students from Columbia University Vagelos College of Physicians and Surgeons, who were responsible for extracting data from the medical records, underwent extensive training. Data verification for accuracy was done by the principal investigator on a random sample of patients.

### Statistical Analysis

Data were entered into a Research Electronic Data Capture database<sup>14,15</sup> before it was exported to Statistical Package for the Social Sciences 25 for analysis. Continuous variables were reported as mean, and SD and categorical variables were presented as percentage and simple frequency.

### Ethical Clearance

This study was approved by the Institutional Ethics Review Board of Addis Ababa University, College of Health Sciences, and Columbia University Vagelos College of Physicians and Surgeons.

## Results

### Patient Characteristics

There were 146 histologically confirmed lung cancer of the 239 patients included in the study. The mean ( $\pm$ SD) age of the group was 54 plus or minus 13 years (range of 19–90 y), and 13.7% ( $n = 20$ ) of the patients were less than 40 years of age. Of those studied, 61.6% ( $n = 90$ ) of the patients were men with a male:female ratio of 1.6:1. Most of the subjects were from urban areas, mainly Addis Ababa (76%,  $n = 111$ ). Cigarette smoking was reported by 25.3% ( $n = 37$ ) of patients with a mean of 17.7 plus or minus 10.3 pack-years; 40.0% ( $n = 36$  of 90) of male patients had smoked and 1.8% ( $n = 1$  of 56) of female patients had smoked. Eight subjects (5.5%) had biomass fuel (wood smoke) exposure.

The most common clinical manifestations of lung cancer in our cohort included cough (88.4%,  $n = 129$ ), chest pain (60.3%,  $n = 88$ ), dyspnea (53.4%,  $n = 78$ ), weight loss and decreased appetite (42.5%,  $n = 62$ ), and hemoptysis (34.9%,  $n = 51$ ) in decreasing order of frequency (Table 1). The median duration of symptoms before presentation was 6 months (interquartile range: 3–12 mo). The most common recorded comorbidities included hypertension (14.4%,  $n = 21$ ), diabetes mellitus (14.4%,  $n = 21$ ), history of pneumonia in 11.6%, ( $n = 17$ ), other previous malignancies (8.9%,  $n = 13$ ), and asthma/chronic obstructive pulmonary diseases (4.8%,  $n = 7$ ). A history of tuberculosis treatment was present in 11% of patients ( $n = 16$ ). It is not unusual for lung cancer to be initially misdiagnosed as pneumonia.

**Table 1.** Clinical Manifestations of Patients With Lung Cancer Seen at TASH (n = 146)

Characteristics	Frequency	Percentage (%)
Cough	129	88.4
Chest pain	88	60.3
Dyspnea	78	53.4
Weight loss	62	42.5
Decreased appetite	54	37.0
Hemoptysis	51	34.9
Hoarseness of voice	9	6.2

TASH, Tikur Anbessa Specialized Hospital.

### Radiographic Findings

The most prominent radiologic reported features were lung mass (84.9%, n = 124), pleural effusion (52.7%, n = 77), multiple lung nodules (43.8%, n = 61), extrathoracic metastasis (41.8%, n = 61), atelectasis or consolidation (32.2%, n = 47), and lymphadenopathy (18.5%, n = 27) (Table 2). Most often detected lymph nodes were hilar (16.4%, n = 24) and mediastinal (23.3%, n = 34). A total of 135 patients (92.5%) had more than one finding on their chest imaging results.

### Diagnostic Work-Up

Several modalities were used to establish a tissue diagnosis of lung cancer. The most common were pleural fluid cytology (46.6%, n = 68), fiberoptic bronchoscopy with endobronchial biopsy and bronchoalveolar lavage (39.7%, n = 58), fine-needle aspiration cytology (37.7%, n = 55), chest computed tomography-guided core biopsy (30.8%, n = 45), and surgical biopsy (11.0%, n = 16), in decreasing order. A total of 108 patients (74%) required more than one diagnostic procedure owing to low pathology yield or inadequate specimen.

### Histologic Subtypes

Adenocarcinoma accounted for 35.7% of lung cancers (n = 52), SCC 19.2% (n = 28), large cell carcinoma 1.6% (n = 2), and small cell carcinoma 1.6% (n = 2). In the remaining 42.5% (n = 62), the data on the specific histology subtype could not be retrieved or reported as undifferentiated (Table 3).

### Molecular Analysis of Tumors

Among 23 specimens submitted for molecular testing, NGS was performed on 14 formalin-fixed, paraffin-embedded samples. The tumor area selected for NGS analysis was scored by a pathologist and subsequently macrodissected from the corresponding unstained formalin-fixed, paraffin-embedded tissue sections. The neoplastic content of the selected tumor area varied from 10% to 40%. DNA concentrations of extracted tissue ranged from 0.22 to 2.28 ng/dL. Five

specimens did not meet the quality control metrics for the assay, and two specimens did not harbor any mutations. Of three samples deemed to have too low quality to report, one had no tumor remaining in the tissue block, one was adenoid cystic carcinoma, which was removed from the cohort, and one had mucinous adenocarcinoma. Two samples did not have any histologic evidence of cancer—one primarily necrosis and blood and the other a neuroendocrine tumor favoring carcinoid.

A total of 23 clinically relevant mutations were identified in the remaining 14 samples interrogated by NGS. Mutations in *EGFR* mutations were detected in seven samples, including three exon 19 deletions, three exon 20 insertions, and one single nucleotide substitution. Other hotspot cancer gene mutations detected included *KRAS* (n = 3), *TP53* (n = 5), *PIK3CA* (n = 2), and one mutation each in *APC*, *BRAF*, *CTNNB1*, *HRAS*, *POLE*, and *PTEN* (Fig. 1).

Patients with *EGFR* exon 19 deletion included a 75-year-old woman and a 70-year-old woman, both nonsmokers, with adenocarcinoma and a 42-year-old male smoker with adenocarcinoma histiocytic appearance. Those with *EGFR* exon 20 insertion were a 52-year-old man and a 64-year-old man, both smokers, with adenocarcinoma papillary lepidic and NSCLC solid carcinoma, respectively, and a 62-year-old female nonsmoker with focal mucinous adenocarcinoma. One patient, a 35-year-old woman, nonsmoker with adenocarcinoma histology, had a single nucleotide substitution. *KRAS* was found in a 52-year-old man and 35-year-old man, both smokers, with NSCLC favoring adenocarcinoma and adenocarcinoma, respectively, and a 50-year-old female nonsmoker with adenocarcinoma papillary histology (Table 4).

### Staging and Outcome

For the 100 patients on whom lung cancer staging was documented, 92.2% (n = 92) presented at advanced stages (stages III and IV), whereas only 7.8% (n = 8) were diagnosed at earlier stages (stages I and II). Extrathoracic metastasis was observed in 58.9% (n = 86) of the cases; the most common organs involved were bone (14.4%, n = 21) and liver (14.4%, n = 21); multiple site metastasis was noted in 12.0% (n = 16) of the patients (Table 3).

The median follow-up time was 3 (interquartile range: 1–7.3) months. Most of the subjects were lost to follow-up, 94.5% (n = 138); 1.4% (n = 2) were alive; and 4.1% (n = 6) had died. Treatment mainly consisted of chemotherapy (84.9%, n = 124) and to a much lesser extent surgery (2.7%, n = 4) and radiotherapy (2.1%, n = 3); no information was available on type of treatment for 15 patients (9.1%).

**Table 2.** Radiologic Features of Patients With Lung Cancer Seen at TASH (n = 146)

Radiologic Findings	Frequency	Percentage (%)
Lung mass	124	84.9
Pleural effusion	77	52.7
Lung nodules	64	43.8
Metastasis to other sites	61	41.8
Collapse consolidation	52	35.6
Lymphadenopathy	47	32.2
Lung opacity <sup>a</sup>	27	18.5
Lymphangitic carcinomatosis	13	8.9
Pleural thickening	12	8.2
Erosion of rib	5	3.4
Cavity	4	2.7
Calcification	4	2.7
Pancoast tumor	2	1.4

<sup>a</sup>Lung opacity includes opacity other than mass or nodule, such as ground-glass opacity, fibrosis.

TASH, Tikur Anbessa Specialized Hospital.

## Discussion

In our study of 146 patients with histologically confirmed lung cancer, we found that most presented at a relatively young age (median 54 years) and with late-stage disease. Adenocarcinoma was the most frequently detected histologic type of lung cancer in our cohort, and

**Table 3.** Histopathology, Stage, and Metastatic Site of Patients With Lung Cancer Seen at TASH (n = 146)

Characteristics	Frequency	Percentage (%)
Histopathology		
Adenocarcinoma	52	35.7
Squamous cell carcinoma	28	19.2
Bronchogenic carcinoma	20	13.7
Other	16	11.0
Unknown	14	9.6
Undifferentiated	11	7.5
Small cell carcinoma	2	1.4
Large cell carcinoma	2	1.4
Nonsmall cell carcinoma	1	0.7
Stage		
Stage IV	81	57.9
Staging not documented	37	25.3
Stage III	14	10.0
Missing variable	6	4.1
Stage I	5	3.5
Stage II	3	2.1
Site of metastasis		
Bone	21	14.4
Liver	21	14.4
Multiple sites	16	12.8
Other site in lung	15	10.3
Other, unspecified	12	8.2
Brain	10	6.8
Adrenals	7	4.8

TASH, Tikur Anbessa Specialized Hospital.

*EGFR* mutations, which are more common in non-smokers and women,<sup>16,17</sup> were found in half of the specimens subjected for molecular analysis. In addition, the most common universal risk factor, cigarette smoking, was absent in most patients in our cohort.

The mutational landscape of the 14 samples sequenced seemed to be different from that reported in the literature.<sup>18,19</sup> We saw a larger number of *EGFR* mutations (30.4%) compared with *KRAS* mutations (13.1%). Notably, the number of *EGFR* exon 19 deletion mutations (three of seven) detected was similar to the *EGFR* exon 20 insertion mutations (three of seven). The latter group of mutations, known to confer resistance to first- and second-generation tyrosine kinase inhibitors, is reported to have a prevalence of 2% to 3%.<sup>20</sup> Nevertheless, our small cohort of samples tested revealed an overabundance of these mutations, up to 13%. Interestingly, there are new small molecule tyrosine kinase inhibitors (mobocertinib) and monoclonal antibodies (amivantamab) that have found to be promising in patients with *EGFR* exon 20 insertion mutations.<sup>21</sup>

Compared with other countries in Africa, our patients were significantly younger at presentation (median = 54 y). A study from Johannesburg, South Africa, found that the median age for their white patients with lung cancer was 66 years,<sup>22</sup> and one from Cairo, Egypt, reported that the highest incidence of lung cancer was in the sixth and seventh decades of life.<sup>23</sup> In a study from central Tunisia, the median age of lung cancer was 64 years for males and 61 years for females.<sup>24</sup> Our mean age was similar to a study from South Africa of black patients wherein the median age was reported at 57 years.<sup>22</sup>

Our patients presented with late-stage disease, limiting treatment options and portending a poor outcome. There are several factors that may account for this finding. Lack of access to health care, patient reluctance to seek medical attention, and limited specialized diagnostic and treatment centers probably all played a role. It is also possible that lung cancer in Ethiopia may be more aggressive in its course, mediated by risk factors other than personal tobacco use.

Globally, cigarette smoking is the most common risk factor for lung cancer. In similar studies from South Africa and Egypt, cigarette smoking was found to be a major risk factor for lung cancer.<sup>22,23</sup> Most of our patients with lung cancer were never smokers and predominantly women. This finding is in keeping with the overall low smoking rate of only 3.9% in Ethiopia (7.1% men and 0.8% women).<sup>25</sup>

In our small number of cigarette smokers, the average pack-years was generally low (17 pack-years). This is close to the mean pack-years of smoking in African patients in a study from South Africa, 21.7 plus or minus 14.3, which was in marked contrast to the white

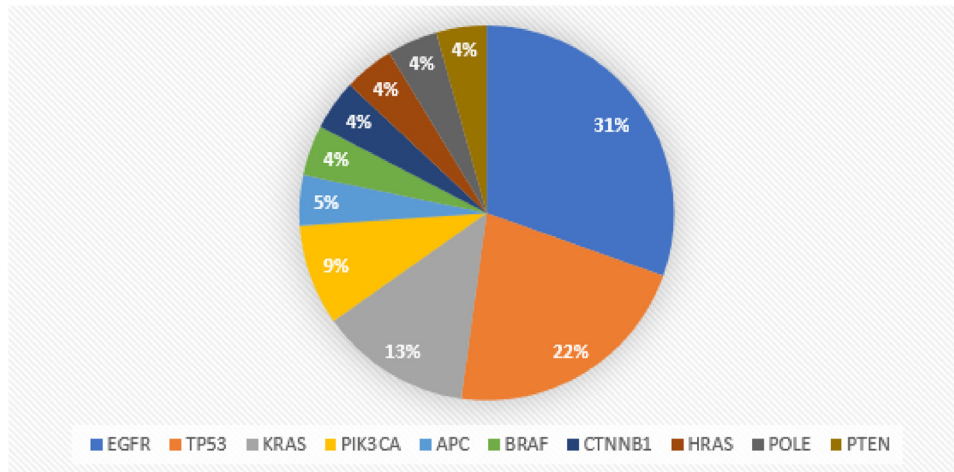


Figure 1. Mutations detected among 14 samples sequenced.

patients with pack-years of 52.7 plus or minus 21.7.<sup>18</sup> These findings support previous observations that African patients tend to develop lung cancer at a lower dose of smoking,<sup>26,27</sup> a possible explanation for the lung cancer found in our predominantly male smokers. This also underscores the hypothesis that there may be biological differences in response to tobacco smoke between Africans and Caucasians.<sup>28</sup>

A number of factors have been implicated in the pathogenesis of lung cancer in never smokers, such as exposure to secondhand smoke, use of solid fuels and indoor cooking in poorly ventilated households (mainly in low-income countries), particulate matter inhalation, radon gas exposure, and genetic predisposition.<sup>29,30</sup>

These factors have been supported in studies from other African countries, such as Nigeria and Morocco.<sup>31,32</sup> We were unable to clearly identify specific risk factors for lung cancer in our population. This may reflect patient selection, missing data, low cigarette use, and few reports of biomass exposure, which is unusual because the rate of biomass fuel use for cooking in Ethiopia is known to be very high.<sup>33</sup>

Adenocarcinoma was the predominant cancer in our cohort. This finding is in concert with global reports that adenocarcinoma is the most common histologic type of lung cancer in both men and women, and in smokers and nonsmokers.<sup>34</sup> Our results differ from those of previous studies done in South Africa,<sup>22</sup> Egypt,<sup>23</sup> Tunisia,<sup>24</sup> Iran,<sup>35</sup>

Table 4. Molecular Analysis of Specimens With Lung Cancer Fixed in Formalin

Number	Diagnosis	Molecular Analysis (Gene) and Variant	Comment	Age	Gender	Ever Smoker
1	NSCLC, favor adenocarcinoma	HRAS G12S	Lower coverage (low confidence)	41	Male	No
2	Adenocarcinoma, papillary	KRAS G12D and CTNNB1 S37F	—	50	Female	No
3	Adenocarcinoma, acinar and solid	TP53 G244D	—	24	Female	No
4	Adenocarcinoma, papillary/lepidic	EGFR exon 20 insertion and APC D556V	—	52	Male	Yes
5	NSCLC (solid carcinoma)	EGFR exon 20 insertion	—	64	Male	Yes
6	Adenocarcinoma, histiocytic appearance	EGFR exon 19 deletion	TP53 p R175H, POLE pL272LX	42	Male	Yes
7	Adenocarcinoma with focal mucinous/signet ring cell features	EGFR exon 20 insertion	TP53 pQ331X	62	Female	No
8	NSCLC	PTEN D301fs PIK3CA E542K	—	65	Male	Yes
9	Adenocarcinoma	BRAF V600E PIK3CA E545K	—	65	Male	Yes
10	Adenocarcinoma	EGFR exon 19 L747P	TP53 D281G	35	Female	No
11	Adenocarcinoma	EGFR exon 19 del E746_750del	—	70	Female	No
12	NSCLC, favors adenocarcinoma	KRAS G12V	—	52	Male	Yes
13	Adenocarcinoma	KRAS G13D	—	35	Male	Yes
14	Adenocarcinoma	EGFR exon 19 del E746_750del	TP53 137_138del	75	Female	No

del, deletion.

India,<sup>32,36,37</sup> Nepal,<sup>38</sup> Malaysia,<sup>39</sup> Nigeria,<sup>31</sup> and Senegal,<sup>40</sup> where SCC was the most common lung cancer cell type. These older studies may not reflect current rising trends of adenocarcinoma than SCC in most regions of the world, possibly owing to diagnostic advances, use of low tar-filtered cigarettes, and changes in smoking patterns.<sup>39</sup>

*EGFR* mutations, found in most specimens undergoing molecular analysis, have been revealed to be an oncogenic driver among Asian and non-Asian never smokers.<sup>41</sup> Furthermore, *EGFR* mutations have been associated with biomass fuel exposure, particularly wood smoke exposure, as a risk factor for lung cancer.<sup>42,43</sup> It is possible that our *EGFR* findings support biomass exposure as a risk factor for lung cancer found in our nonsmokers. Larger, specific studies are needed to confirm this likelihood. The other common molecular findings were *KRAS* mutations, which pertain almost exclusively to lung cancer in smokers as found in our population.

This study has several limitations including its retrospective design, incomplete documentation, and missing data or tissue availability on many patients. In addition, the study was done at one center, which limited generalizability for the country at large. Finally, the retrospective nature of the study together with a small sample size made the identification of risk factors for lung cancer in our cohort not feasible.

In conclusion, we presented for the first time, specific demographic, clinical, radiographic, and pathologic characteristics and molecular alterations of lung cancer in Ethiopia. Adenocarcinoma was the most common histologic subtype of lung cancer detected in our study, a finding similar to that from other international studies. Nevertheless, compared with HICs, lung cancer in Ethiopia presents at a younger age and without significant personal tobacco use. The relatively higher prevalence of *EGFR* mutations, from the limited molecular analyses, suggests that factors other than smoking, such as exposure to biomass fuel, may be a more important risk factor. As most patients were from Addis Ababa, the location of the referral hospital, our study may not fully reflect lung cancer in greater Ethiopia.

Country-specific prevention strategies, screening guidelines, and treatment protocols, in addition to a national tumor registry and a greater molecular mutation analysis, are urgently needed to improve the outcome of lung cancer in Ethiopia.

## Availability of Data and Materials

All data generated or analyzed during this study are included in this published article.

## CRedit Authorship Contribution Statement

**Tewodros H. Gebremariam:** Conceptualization, Methodology, Formal analysis, Investigation, Writing—original draft, Visualization, Project administration.

**Deborah A. Haisch:** Software, Data curation, Resources, Writing—review and editing.

**Helen Fernandes:** Visualization, Resources, Writing—review and editing.

**Dawit K. Huluka, Amsalu B. Binegdie, Aschalew Worku:** Methodology, Investigation.

**Mathewos A. Woldegeorgis, Wondwosen Ergetie:** Data curation, Resources.

**Lillian M. Zerihun, Matthew Cohen:** Investigation, Data curation.

**Pierre P. Massion:** Writing—review and editing.

**Charles B. Sherman:** Conceptualization, Methodology, Writing—review and editing, Supervision, Funding acquisition.

**Anjali Saqi:** Resources, Writing—review and editing.

**Neil W. Schluger:** Conceptualization, Methodology, Formal analysis, Resources, Writing—review and editing, Supervision, Funding acquisition.

## Ethics Declarations

The institutional review board of Addis Ababa University College of Health Sciences approved the study protocol.

## Informed Consent

All subjects signed informed consent. College institutional review board approved the study protocol on November 27, 2017, with protocol number 080/17/IM and renewed on March 3, 2019.

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