

## The Profile of Lung Adenocarcinoma Patients with Positive EGFR Mutation

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### ABSTRACT

**Background:** The high mortality rate in pulmonary carcinoma is a problem encountered in various countries, including Indonesia. According to WHO, there are 2.09 million people affected by lung cancer and 1.76 million deaths due to lung cancer worldwide. This study was aimed to determine the profile of lung adenocarcinoma patients with positive EGFR mutation.

**Methods:** The study was descriptive study with cross-sectional approach using secondary data obtained from medical records of lung adenocarcinoma patients.

**Results:** The present study revealed that lung adenocarcinoma was found higher in patients with age >40 years old (93.9%) compared to those with age <40 years old. It was also higher in male (66.7%) than in female patients. Most patients with lung adenocarcinoma were at the IIIB stage (42.4%). It was also reported that higher cases was found in patients with history of smoking more than 15 years (42.4%). Hemoptoe was the most reported clinical symptoms in patients with lung adenocarcinoma (87.9%). Lung adenocarcinoma was also observed higher in patients without family history of pulmonary adenocarcinoma (81.8%). Seventeen of 33 EGFR mutations (51.5%) were observed in exon 19 and fourteen (48.5%) were in exon 21.

**Conclusion:** The most common EGFR mutation lung adenocarcinoma was observed in exon 19.

**Keywords:** Lung neoplasms; mutation; ErbB receptors; adenocarcinoma of lung

### Introduction

Lung cancer is the leading cause of cancer-related deaths worldwide. In the United States, lung cancer kills 160,000 people each year. The incidence of new cases of lung cancer in the United States ranks second only to breast cancer, which is estimated at 224,390 cases in 2016, or approximately 13% of all cancer diagnoses occur 158,080 deaths in 2016 is about 27% of all cancer deaths.<sup>1,2</sup> The incidence of lung cancer in Indonesia tends to increase. Data and information center of the Ministry of Health showed that the incidence of lung cancer in the Cancer Hospital Dharmais in 2013 ranks third after breast cancer and cervical cancer in the amount of 173 cases or 7% of all cancers and deaths from lung cancer by 65 cases or 12% of of all cancer deaths.<sup>3</sup> The lung cancer is divided into small cell lung cancer (SCLC)/small cell carcinoma. SCLC occurs in 20% of all lung cancers. Although the cancer cells are small, the multiplication of these cells are obviously rapid and form large tumors that spread throughout the body. A typical histological picture is the dominance of small cells that are mostly filled by mucus with a distribution of chromatin without nucleoli. It is also called "oat cell carcinoma" because it looks like the grain of wheat. These small cells tend to congregate around small blood vessels resembling pseudoroset. Mitotic cells that are found in

abundance as well as necrosis. DNA segregation causes a dark color around the blood vessels. Non-small cell lung cancer (NSCLC)/non-small cell carcinoma.<sup>4-7</sup>

## Methods

This was a descriptive study with cross-sectional design depicting lung adenocarcinoma patient profile at Ibnu Sina Hospital Makassar based on secondary data in the medical record. The sampling technique was total sampling, all population of affordable met the inclusion criteria and did not meet the exclusion criteria will be taken into the sample. The inclusion criteria were patients with lung adenocarcinoma treated at Ibnu Sina hospital Makassar from 2017 to 2019. Technique enforcement of diagnosis performed by fine-needle aspiration biopsy (FNAB) and cytology where most of the pathology results found based cytology.

## Result

Data for this study was collected from Ibnu Sina Makassar medical record, from 2017 to 2019 and the total of patients with lung adenocarcinoma was 33 cases, mostly were male with age over 40 years old. Based on a history of smoking, most are up to 15 years smoking history. Most patients had a history of hemoptoe and weight loss meanwhile the patient stage when diagnosed were IIIA stage with WHO PS 1.

**Table 1. Profile of patients with adenocarcinoma**

Characteristics	N	%
<b>Gender</b>		
Men	22	<b>66.7</b>
women	11	<b>33.3</b>
<b>Age</b>		
<40 years	2	6.1
> 40 years	31	93.9
<b>Smoking Status</b>		
Do not smoke	13	39.4
Smoke <15 Years	6	18.2
Smoke > 15 Years	14	42.4
<b>Clinical symptoms</b>		
Cough	23	69.7
Chest pain	19	57.6
Dyspnea	24	72.7
Weight loss	25	75.7
Hemoptoe	29	87.9
<b>Family History</b>		
Negative	6	18.2
Positive	27	81.8
<b>Stadium</b>		
IIA	2	6.1
IIB	2	6.1
IIIA	7	21.2
IIIB	14	42.4
IV	8	24.2

<b>PS WHO</b>		
1	19	57.6
2	14	42.4

**Table 2. Profile of patients with lung adenocarcinoma by pathology**

<b>Characteristics</b>	<b>N</b>	<b>%</b>
<b>How Decision</b>		
FNAB	<b>13</b>	<b>39.4</b>
cytology	<b>20</b>	<b>60.6</b>
<b>EGFR mutations</b>		
ex 19	17	<b>51.5</b>
ex 21	16	<b>48.5</b>
<b>Mutations Ex 21</b>		
L858R	10	<b>58.8</b>
L861Q	7	<b>41.2</b>

The sample profile of this study showed in Table 1. Based on gender, lung adenocarcinoma was more common in men (66.7%) than in women (33.7%). It was also more common in over 15 years smoker (42.4%) than less 15 years of smoker and nonsmoker. The most common clinical symptom was hemoptoe (87.9%), followed by weight loss (75.7%) and dyspnea (72.7%). Mostly, sample age were over 40 years old (31 patients) equal to 93.9% and 57.6% were categorized as Prominent score WHO (WHO PS) 1.

Based on table 2, the diagnosis of lung adenocarcinoma mostly by cytology evaluation (20 cases), equivalent to 60.6% . EGFR Exon 19 mutation was more common than Exon 21 with each percentage were 51.5% and 48.5%. Exon 21 mutations occurred in 17 sample and the L858R type was more than L861Q 10 with ratio 10 cases (58.8%) and 7 cases (41.2%).

## **Discussion**

In the present study using 33 samples obtained based on secondary data from 2017 to 2019 in the RS. Ibnu Sina Makassar. Based on the results of descriptive profiles acquired gender research subjects more than sex males than females. By age, the samples generally aged over 40 years. This is consistent with research in Wulandari, 2017, which is the subject of research in general women and the age range of 50 years.<sup>1,8,9</sup>

This research subject is NSCLC patients who undergo positive EGFR mutation and patients dominate smokers than non-smokers. This is not following the IPASS study found that lung adenocarcinoma predominantly occurs in nonsmokers than smoker. Its study result also has the same with previous research, where a group of nonsmokers patients tends to have positive EGFR mutation.<sup>1,2,10</sup>

Smoking is the cause of 85-90% of all lung cancer cases. A derivative of nicotine in cigarettes is carcinogenic. Lung cancer cells express all histological types of the nicotinic acetylcholine receptor. Nicotine activates signaling pathways in tumor cells and normal cells that inhibits apoptosis, so that the nicotine is involved in the pathogenesis of lung cancer as a mutagen and tumor promoter. Other

materials are associated with lung cancer include asbestos, exposure to radiation, arsenic, nickel, chromium, chloromethyl ether, and air pollutants. Scarring of the lungs is also associated with an increased risk of lung cancer.<sup>5</sup>

Most clinical symptoms are hemoptoe, weight loss and dyspnea. The clinical manifestations of lung cancer depend on the location and extent of the tumor. Clinical symptoms arise signifies have an advanced stage of disease manifestations. Symptoms often appear cough (75%), weight loss (68%), shortness (58-68%), chest pain (45-49%), hemoptoe (29-35%), bone pain (25%), hot (15-20%), SVCS (4%), dysphagia (2%), wheezing and stridor (2%).<sup>1,4,5</sup>

The whole sample of this study are patients with lung adenocarcinoma with EGFR positive mutation, and EGFR exon 19 was the most common type. In EGFR exon 21 type, L858R mutation was predominantly. This study result was similar previous to study done by Wulandari, IPASS and WJTOG3405.<sup>1,2,10</sup>

## **Conclusions**

Lung adenocarcinoma patients in Ibnu Sina hospital Makassar mostly were male gender and smoker with the most common symptom arises is hemoptoe, followed by weight loss and dyspnea. The diagnosed mostly made up by cytology evaluation. Mutation of EGFR Exon 19 was the most common mutation found on this study. Because of its high mortality rate, should be performed the similar studies with a larger population and region. Based on these data it can be concluded that men and smokers have a high risk of becoming pulmonary adenocarcinoma with EGFR exon mutations 19. The data of this study was valuable to strengthen the preventive socialization of lung cancer.

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