ORIGINAL RESEARCH REPORT

Albumin Levels before Therapy and Clinicopathological Parameters of Lung Cancer Patients

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Article Info

Article history:
Received 02-07-2024
Revised 24-09-2024
Accepted 01-10-2024
Published 31-01-2025

Keywords:
Lung Cancer Albumin
Adenocarcinoma
Chronic Respiratory Disease
Human and Mortality

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ABSTRACT

Background: Serum albumin levels provide an objective measure of malnutrition. Albumin plays crucial roles in maintaining intravascular oncotic pressure, facilitating substance transport, and acting as a free radical scavenger. The progression of tumors, including lung cancer, is closely associated with malnutrition and cancer-related inflammation, which suppress albumin synthesis. Therefore, albumin can serve as a biomarker for assessing lung cancer progression. Low albumin levels are linked to poor prognosis. **Objective:** The aim of this study was to examine the relationship between albumin levels and lung cancer. **Material and Method:** This study included 130 lung cancer patients who underwent albumin testing. A cross-sectional study was conducted using medical records of patients diagnosed with lung cancer from January 2023 to December 2023. Data were collected on various factors, including age, gender, smoking status, cancer history, clinical symptoms, histopathological type, cancer stage, EGFR mutation status, ECOG score, clinical pleural effusion, Visual Analog Scale (VAS), and Body Mass Index (BMI). **Result:** The study sample was predominantly male (71.5%), aged over 50 years (76.9%), and active smokers (34.6%). Common symptoms included cough (83.8%) and shortness of breath (72.3%), with pleural effusion present in 53.8%. The majority had a moderate VAS score (46.9%) and were classified as underweight based on BMI (54.6%). Most patients were at stage IVA (63.0%), had an ECOG score of 1 (43.8%), and were diagnosed with adenocarcinoma (73.8%). A significant relationship was found between ECOG scores and albumin levels, with 70.6% of hypoalbuminemic samples having an ECOG score of 3 ($p < 0.005$). **Conclusion:** A significant relationship was observed between albumin levels and ECOG scores in lung cancer patients.

How to cite:
Kusumawardhani, E., Fiayanti, N. 2025. Albumin Levels before Therapy and Clinicopathological Parameters of Lung Cancer Patients. Majalah Biomorfologi-Biomorphology Journal, 35(1):29-39.

***Majalah Biomorfologi* (Biomorphology Journal)** p.ISSN:0215-8833, e.ISSN: 2716-0920
doi: 10.20473/mbiom.v35i1.2025.29-39

Highlights

1. A notable finding was the significant relationship between albumin levels and ECOG scores, emphasizing the potential of albumin as an indicator of functional status in lung cancer patients.

2. The research provided a comprehensive analysis of the correlation between albumin levels and various clinicopathological conditions.

BACKGROUND

Lung cancer is a prominent global health issue, characterized by high incidence and mortality rates. According to GLOBOCAN, an estimated 2.1 million new cases were diagnosed in 2018, rising to 2.2 million in 2020, with 1.8 million deaths (Thandra, et al., 2021). Lung cancer is among the most prevalent cancers in Asia, with incidence rates ranging from 0.06 to 31.5 per 100,000. In Indonesia, lung cancer accounts for 12.6% of cancer deaths, making it the leading cause of cancer mortality, while approximately 8.6% of cancer incidences are attributed to lung cancer. By 2040, the annual number of lung cancer cases is expected to increase from 30,023 in 2018 to 54,983 in 2040 (Pakzad, et al., 2015; Andarini, et al., 2023).

Treatment options for lung cancer depend on the disease stage, the patient's overall health, comorbidities, treatment goals, and available funding. Current treatments include surgery, radiation, chemotherapy, immunotherapy, and targeted therapy. Chemotherapy may be used as a neoadjuvant modality in the early stages or as adjuvant therapy after surgery. Adjuvant therapy is applicable to non-small cell lung cancer (NSCLC) stages IIA, IIB, and IIIA. In advanced stages of NSCLC, chemotherapy may be used for either curative or palliative purposes (Lemjabbar-Alaoui, et al., 2015).

Various factors, including albumin levels, influence the success of therapy. Albumin, a protein found in the blood, acts as a carrier for cancer therapies due to its ability to transport substances, undergo natural degradation, accumulate at sites of blood vessel leakage, and be absorbed by rapidly growing cancer cells. As a natural ligand carrier, serum albumin can transport anti-cancer agents. Albumin can extend the circulation half-life of rapidly cleared drugs and enhance their accumulation in tumors. The use of albumin as a carrier for cancer drugs is widespread, including in traditional cancer chemotherapy and therapies involving new biological agents (Moujaess, et al., 2017). Albumin is the most abundant protein in human serum and is synthesized in the liver. Serum albumin levels are often measured in clinical practice to assess the nutritional status of cancer patients. The normal albumin level in healthy adult ranges between 36 and 40 g/L. Low albumin levels are common in inflammation and infection, and hypoalbuminemia is frequently observed in cancer patients. The progression of tumors, including lung cancer, is closely associated with malnutrition and cancer-related inflammation, which suppresses albumin synthesis. Thus, albumin can serve as a biomarker for assessing lung cancer progression. Low albumin levels are associated with poor prognosis and increased mortality (Cordeiro, et al., 2020; Zhang, et al., 2021).

Research has shown that albumin levels independently predict overall survival (OS), with each unit increase in albumin reducing the risk of death by 25%. Albumin can also serve as a prognostic indicator in advanced lung cancer undergoing therapy. However, the role of albumin as a predictive biomarker still requires further investigation (Zhang, et al., 2021; Guven, et al., 2022; Xie, et al., 2023). This study aimed to explore the clinicopathological relationship between albumin levels and lung cancer in order to enhance understanding of albumin’s role as a predictor in lung cancer.

OBJECTIVE

This study aimed to show the relationship between albumin levels and lung cancer.

MATERIAL AND METHOD

This retrospective study utilized medical records to obtain secondary data from 130 lung cancer patients diagnosed at Ulin Hospital, Banjarmasin, Indonesia between January 2023 and December 31, 2023. This was a cross-sectional study that employed a total sampling technique, including only patients diagnosed with primary lung cancer through histopathological examination and with recorded albumin

levels. The exclusion criteria were patients with incomplete medical record data (clinical and laboratory data).

Data collection included age, gender, smoking status, cancer history, clinical symptoms, cytopathological or histopathological type, cancer stage, EGFR mutation status, ECOG score, clinical features of pleural effusion, VAS score, and BMI. Age was grouped into <50 years and >50 years. Gender was categorized as male and female. Smoking history was classified into non-smokers, passive smokers, former smokers, and active smokers. The presence or absence of a family history of cancer was also recorded. Clinical symptoms included chronic cough, shortness of breath, chest pain, and hemoptysis, which are the most common symptoms of lung cancer. EGFR mutation status was classified as wild-type or epidermal growth factor receptor (EGFR) mutation (Ruano-Raviña, et al., 2020; Setyawan, et al., 2022). The ECOG score was divided into five categories: (0) Fully active, able to do all activities without restriction; (1) Unable to perform strenuous physical activities but able to walk and do light or sedentary activities such as light housework or office work; (2) Able to walk and perform self-care but unable to do work activities; up and about >50% of waking hours; (3) Able to perform self-care but spends <50% of waking hours sitting or in bed; (4) Completely disabled, unable to perform self-care, spends all day in a chair or bed; (5) Deceased (Nguyen, et al., 2023). The VAS pain scale was categorized as mild (1–3), moderate (4–6), and severe (7–10). Pleural effusion was classified as present or absent. The cytopathological or histopathological types of lung cancer were divided into small-cell lung carcinoma, adenocarcinoma, large-cell lung carcinoma, and squamous cell carcinoma (Travis, 2020). BMI was categorized as underweight (<18.5 kg/m²), normal (18.5–22.9 kg/m²), and overweight (23.0–24.9 kg/m²) (Haam, et al., 2023). The lung cancer stages studied were stages III and IV. This study also compared clinical characteristics based on albumin levels: hypoalbuminemia (<3.5 g/dL) and normal albumin levels (>3.5 g/dL) (Stares, et al., 2021).

Data were presented in tabulated form in Microsoft Office Excel for Mac, Version 16.89.1 (24091630) and analyzed using the IBM SPSS Statistics for Windows, version 21.0 (IBM Corp., Armonk, N.Y., USA). Age, smoking status, gender, and also family history of cancer were presented in the form of numbers (n) and percentages (%) calculated using descriptive statistical analysis. This study presented a tabular clinicopathological comparison based on the number of patients who had albumin levels <3.5 g/dL and >3.5 g/dL. Statistical analysis using the chi-square test was conducted, with p-value <0.05 considered statistically significant.

RESULT

Table 1 shows that 130 patients with concordant results were diagnosed with lung cancer. Ninety-three patients (71.5%) were male, 100 patients (76.9%) were over 50 years old, 45 patients (34.6%) had a history of smoking, and 127 patients (97.7%) had no family history of cancer. The main clinical complaints were chronic cough (83.8%) and shortness of breath (73.2%), and the majority of patients (63%) were at stage IVA. Among the patients, 96 (73.8%) had adenocarcinoma, and 40 (52.6%) had wild-type EGFR mutation status. The ECOG scores of the research sample at diagnosis were 1 and 2 for 43.8% and 43.1% of the patients, respectively. Additionally, 53.8% of the patients had pleural effusion, and 46.9% had a moderate VAS score.

In Table 2, there was no significant relationship between albumin levels and gender, age, smoking history, family history, clinical symptoms, cell type, stage, EGFR mutation, presence of pleural effusion, VAS, or BMI ($p>0.005$). However, a significant relationship was found between albumin levels and ECOG score in lung cancer patients, with a p value of 0.004 ($p< 0.005$).

DISCUSSION

This study found that most lung cancer patients were over 50 years old (76.9%). Lung cancer rarely occurs in individuals under 45 years old and is more common in older people because exposure to risk factors has accumulated over time (Pakzad, et al., 2015). This finding was consistent with a nationwide study in Spain in 2020, which revealed that the mean age of lung cancer patients was 64 years (Ruano-Raviña, et al., 2020). A study conducted in Surabaya also found that most inpatient lung cancer patients were over 50 years old (Chairudin, et al., 2020).

Table 1. Clinical characteristics of research samples.

Parameters		n	Percentage (%)
Gender	Male	93.0	71.5
	Female	37.0	28.5
Age group (years)	<50	30.0	23.1
	>50	100.0	76.9
Smoking history	Non-smokers	38.0	29.2
	Active smokers	45.0	34.6
	Passive smokers	24.0	28.5
	Former smokers	23.0	17.1
Family history of cancer	Yes	3.0	2.3
	No	127.0	97.7
Clinical Symptom	Chronic cough	109.0	83.8
	Shortness of breath	94.0	72.3
	Chest pain	74.0	56.9
	Bleeding caught	19.0	14.6
Histopathological types	Small cell lung carcinoma	1.0	0.8
	Adenocarcinoma	96.0	73.8
	Large cell lung carcinoma	1.0	0.8
	Squamous cell carcinoma	32.0	24.6
Stage	III	24.0	18.5
	IVA	82.0	63.0
	IVB	24.0	18.5
Egfr mutation	Wild type	40.0	52.6
	Egfr mutation	36.0	47.4
Ecog	1	57.0	43.8
	2	56.0	43.1
	3	17.0	13.1
Pleural effusion	Yes	70.0	53.8
	No	60.0	46.2
VAS	Mild (1-3)	49.0	37.7
	Moderate (4-6)	61.0	46.9
	Severe (7-10)	20.0	15.4
BMI	Overweight	9.0	6.9
	Underweight	71.0	54.6
	Normal	50.0	38.5

Based on this research, the majority of lung cancer patients (71.5%) were male. Globally, men are twice as likely to be diagnosed with and die from lung cancer, which is thought to be due to the higher prevalence of smoking among men (Thandra, et al., 2021). Despite being more common among men, there is currently a trend of increasing lung cancer rates in developing countries, with rising death rates among women globally (Thandra, et al., 2021; Fan, et al., 2023). A study conducted at Ulin Hospital, Banjarmasin in 2013 also found that most lung cancer patients (73.13%) were male (Thandra, et al., 2021). In Indonesia, lung cancer is more commonly found in men (Gondhowiardjo, et al., 2021; Thandra, et al., 2021). The results of this study were similar to those conducted in Asia, where approximately 71.13% of lung cancer patients were male (Pakzad, et al., 2015). A national study in Spain also showed that 74.3% of lung cancer patients were male (Ruano-Raviña, et al., 2020).

In Indonesia, the majority of lung cancer cases (85%) are related to smoking. This high number may be due to smoking being culturally accepted (Kristina, et al., 2016). The chemicals in cigarette smoke are toxic and produce free radicals, which can trigger gene mutations and DNA damage, both of which are associated with cancer (Tang, et al., 2022).

Interestingly, this study found that most primary lung cancer patients did not have a family history of cancer. This finding contradicts the literature, which states that a family history of lung cancer increases the risk of developing lung cancer by up to threefold compared to individuals without a family history (Kanwal, et al., 2017). The impact of family history on lung cancer is not well-understood because genetic factors are often masked by environmental factors such as smoking, air pollution, and biomass burning, which have a significant impact on lung cancer risk. A study also showed that Asian populations with a family history of lung cancer are more susceptible to developing the disease

compared to Western populations (Ang, et al., 2020). The analysis revealed no significant relationship between albumin levels and factors such as gender (p=1), age (p=1), smoking history (p=0.764), or family history (p=0.573).

Table 2. Clinicopathology comparison based on albumin levels.

Parameters	Albumin< 3.5 g/dL	Albumin> 3.5 g/dL	p-value
Gender			
- Male	39(41.9%)	54(58.1%)	1
- Female	16(43.2%)	21(56.8%)	
- >50	42(42.0%)	58(58.0%)	1
- < 50	13(43.3%)	17(56.7%)	
Smoking History			
- Non-smokers	8 (34.8%)	15(65.2%)	
- Active smokers	18(40.0%)	27(60.0%)	0.764
- Passive smokers	11(45.8%)	13(54.2%)	
- Former smokers	18(47.4%)	20(53.6%)	
Family History of cancer			
- Yes	2 (66.7%)	1 (33.3%)	0.573
- No	53(41.7%)	74(58.2%)	
Clinical Symptom			
- Chronic Cough	47(43.1%)	62 (56.9%)	0.853
- Shortness Of Breath	38(40.4%)	56 (59.6%)	0.615
- Chest Pain	35(47.3%)	39 (52.7%)	0.252
- Bleeding Caught	9 (47.4%)	10 (52.6%)	0.817
Histopathological types			
- Adenocarcinoma	35 (36.5%)	61 (63.5%)	
- Large cell	1 (100%)	0 (0%)	
- Squamous cell carcinoma	18 (56.3%)	14 (43.8%)	0.085
- Small cell carcinoma	1 (100%)	0 (0%)	
Stage			
- III	8 (33.3%)	16 (66.7%)	0.449
- IVA	33 (40.2%)	49 (59.8%)	
- IVB	14 (58.3%)	10 (41.7%)	
EGFR Mutation			
- Mutation (+)	14 (38.9%)	22 (61.1%)	0.566
- Wild type	12 (30%)	28 (70%)	
ECOG			
- 1	16 (28.1%)	41 (71.9%)	
- 2	27 (48.2%)	29 (51.8%)	0.004*
- 3	12 (70.6%)	5 (29.4%)	
Pleural Effusion			
- Yes	31 (44.3%)	39 (55.7%)	
- No	24 (40.0%)	36 (60.0%)	0.753
VAS			
- 0	2 (15.4%)	11 (84.6%)	
- Mild (1 – 3)	13 (36.1%)	23 (63.9%)	0.093
- Moderate (4 – 6)	29 (47.5%)	32 (52.5%)	
- Severe (7 – 10)	11 (55.0%)	9 (45.0%)	
IMT			
- Underweight	33 (45.8%)	39 (54.2%)	
- Normal	19 (38%)	31 (62%)	0.372
- Overweight	3 (37.5%)	5 (62.5%)	

In this study, shortness of breath and chronic cough were the most common symptoms. This finding is consistent with a prospective cohort study, which revealed that chronic cough and dyspnea are the two most common symptoms (Walter, et al., 2015). However, these findings differed from national guidelines for lung cancer, which state that coughing is the most frequently encountered symptom (60–70%) in lung cancer cases (Ministry of Health of The Republic of Indonesia, 2023). According to a national study in Spain, coughing and shortness of breath are the two most commonly reported symptoms in lung cancer cases (Ruano-Raviña, et al., 2020). The percentage of lung cancer patients with cough and shortness of breath tends to increase, whereas the percentage of patients coughing up blood tends to decrease (Chowienczyk, et al., 2020). The analysis showed no significant relationship

between the clinical symptoms of chronic cough (p=0.853), shortness of breath (p=0.615), chest pain (p=0.252), or coughing up blood (p=0.817) and albumin levels.

A study conducted in Surabaya showed that around 81.5% of lung cancer cases were adenocarcinoma (Chairudin, et al., 2020). According to the literature, adenocarcinoma is the most frequent subtype of lung cancer, accounting for about 60% of NSCLC cases in both men and women. Squamous cell carcinoma is the second most common subtype, accounting for about 20% of cases. Squamous cell carcinoma is closely related to smoking, while adenocarcinoma is less associated with smoking (Zheng, 2016; Nur I, et al., 2023). Based on the analysis, there was no significant relationship between lung cancer cell type and albumin levels (p=0.085). However, most lung cancer patients, based on cell type, experienced hypoalbuminemia, except for those with adenocarcinoma. This finding differed from other studies, where most lung cancer patients experienced hypoalbuminemia, with small-cell carcinoma and large-cell carcinoma showing the highest percentage of hypoalbuminemia. This may be because these two types of cancer are more aggressive than adenocarcinoma (Rajdev, et al., 2018; Singh & Rao, 2022).

All participants in this study had stage III-IV lung cancer, with a predominance of stage IVA cases. This finding was consistent with a study in China, where the majority of lung cancer patients were diagnosed at stage IVA. Data from Persahabatan Hospital Jakarta similarly indicates that most lung cancer cases are identified at a late stage (III or IV). Delayed medical consultation often leads to late-stage diagnoses, as symptoms may not initially suggest lung cancer. Therefore, early screening and detection are crucial, especially in high-risk populations (Zhang, et al., 2021; Ministry of Health of The Republic of Indonesia, 2023).

In addition, most stage III and IV lung cancer patients did not experience hypoalbuminemia. This finding was in contrast with a study in India, where the majority of stage IV cancer patients experienced hypoalbuminemia. However, that study used a lower cut-off value, defining hypoalbuminemia as albumin levels <3.4 g/dL, whereas in this study, hypoalbuminemia was defined as albumin levels <3.5 g/dL (Singh & Rao, 2022). Based on the analysis, no significant relationship was found between lung cancer stage and albumin levels (p=0.449). However, the incidence of hypoalbuminemia in this study increased with the advancing stage of lung cancer. In stage IVB, hypoalbuminemia was observed in 58% of the samples, a higher incidence than in stages III and IVA, where the incidences were 33% and 40%, respectively. Patients with stage III tend to have better albumin levels than those with stage IVA and IVB, with the percentage of normal albumin values being higher at 66.7% for stage III, 59.8% for stage IVA, and 41.7% for stage IVB. Hypoalbuminemia indicates an elevated catabolic state caused by cytokines produced by the tumor and tumor progression itself. Cachexia is another mechanism of hypoalbuminemia in cancer patients. Hypoalbuminemia (albumin <35 g/L) combined with impaired nutritional status in geriatric cancer patients is a strong predictor of poor outcomes and mortality (Moujaess, et al., 2017).

Based on EGFR mutation status, 36 of the 130 samples had EGFR mutations. This figure is similar to research at Ulin Hospital in 2015, where 13 of 38 samples had EGFR mutations (Khasanah, et al., 2019). According to the literature, stage IV adenocarcinoma-type lung cancer patients with wild-type mutations have a shorter survival rate. Meanwhile, patients with EGFR mutations who receive EGFR-tyrosine kinase inhibitor (EGFR-TKI) therapy have better survival rates. EGFR gene mutation is a predictive factor for response to EGFR-TKI therapy, leading to longer progression-free survival (RPS) (Zheng, 2016). Although EGFR mutation status and albumin levels did not show a significant relationship in this study, research suggests that albumin levels can predict the effectiveness of afatinib therapy in NSCLC patients with EGFR mutations (Kwok, et al., 2022).

Based on the ECOG score, most patients had scores of 1 and 2. This finding is consistent with the literature, which states that 40% of patients have an ECOG score of at least 2 (Sehgal, et al., 2021). The ECOG score was developed to assess the functional capacity and prognosis of cancer patients. It is crucial for clinicians to frequently evaluate the performance status of lung cancer patients using the ECOG score to determine their current functional capacity and adjust treatment plans accordingly. The ECOG score can also predict prognosis (Nguyen & Byeon, 2023). Cancer patients with an ECOG score of at least 2 have a worse prognosis. Therapeutic decisions for lung cancer patients with poor performance status still require further investigation to optimize clinical outcomes. In this study, the higher the ECOG score, the more severe the hypoalbuminemia. A similar study showed that 18 of 24 patients with an ECOG score of 3 experienced hypoalbuminemia, which was comparable to this study, where 12 of 17 patients with an ECOG score of 3 had hypoalbuminemia (Singh & Rao, 2022). Based

on the analysis, there was a significant relationship between albumin levels and ECOG scores, with a p-value of 0.004. This was expected, as higher ECOG scores and low albumin levels are poor prognostic factors for lung cancer. Additionally, ECOG scores and hypoalbuminemia are often found together, especially in patients with advanced lung cancer (Sehgal, et al., 2021; Zhang, et al., 2021).

Most of the samples in this study experienced pleural effusion, a condition often caused by lung cancer and a major cause of malignant pleural effusion (MPE) in men (Psallidas, et al., 2016). According to the literature, MPE is predominantly observed in advanced-stage lung cancer, which aligns with the results of this study, as the samples consisted of stage III and IV lung cancer patients. Pleural effusion in lung cancer is associated with higher morbidity and mortality rates (Divisi, et al., 2020). A retrospective study also found that albumin levels are one of the predictors of survival for NSCLC patients with MPE, where low albumin levels are associated with lower survival (Zhang, et al., 2021).

Based on the analysis, pleural effusion was unrelated to albumin levels (p=0.753). Pleural effusion is a common complication in various diseases, particularly cancer. It occurs when the pleura is involved in a malignancy, either locally or through a metastatic process in the pleural cavity. This involvement increases the permeability of blood vessels, leading to the production of more fluid than the lymphatic system can absorb or impairing the lymphatic system's ability to drain the fluid. Pleural effusion in cancer often indicates advanced disease. In lung cancer, the presence of pleural effusion is typically associated with stage IV and correlates with lower life expectancy in non-small cell lung cancer (NSCLC). In patients with lung cancer and pleural effusion, factors such as advanced age, male sex, smoking status, advanced cancer stage, and metastasis cannot be used as reliable prognostic factors. However, low albumin levels serve as a prognostic indicator and reflect poorer overall survival (OS) (Peng, et al., 2022).

Most of the samples in this study experienced moderate pain, based on the Visual Analog Scale (VAS). This finding aligns with research in China, where the majority (72.4%) of participants reported moderate pain, with some even having stage IV lung cancer, although no statistically significant relationship was found (p = 0.093). Pain is a common symptom in cancer patients and significantly impacts their quality of life. Between 60% and 80% of patients with advanced cancer experience chronic pain, with around a third of them experiencing severe pain (Wang, et al., 2014). Among the study participants, those with severe pain had a higher incidence of hypoalbuminemia (55%) compared to those with mild and moderate pain (13% and 29%, respectively). Hypoalbuminemia in these cases may be linked to decreased appetite. A study found that lower appetite was significantly associated with both low albumin levels and higher pain scores in advanced cancer patients (Goodrose-Flores, et al., 2022).

Most of the samples in this study had an underweight nutritional status based on BMI, and no statistically significant relationship was found. Overweight status is a known risk factor for many malignancies. However, the incidence of lung cancer is inversely proportional to BMI. Additionally, a higher BMI is associated with a better prognosis in lung cancer patients, especially those with early-stage NSCLC and those undergoing chemotherapy. A meta-analysis showed that overweight or obese patients have a lower mortality rate, with this relationship being more pronounced in Asians (Chen, et al., 2021).

Since BMI is thought to be closely related to cancer risk, analyses were performed based on this factor. Individuals with normal body weight exhibit an inverse relationship with the risk of lung cancer. In this study, BMI was not related to albumin levels (p = 0.372), but 45.8% of samples with underweight status experienced hypoalbuminemia. The incidence of hypoalbuminemia was higher in underweight individuals compared to those with normal or overweight BMI. Research on BMI and cancer risk suggests that obesity may have a protective effect against lung cancer. Although few studies have examined the relationship between BMI and albumin levels in lung cancer patients, these two factors can be used to assess nutritional status. Liu, et al., (2022) and Zhang et al., (2021) found that individuals with albumin levels >3.5 g/dL and BMI >25 kg/m² had longer progression-free survival (PFS).

Lower albumin levels not only reflect poor nutrition but also indicate systemic inflammation. Systemic inflammation and poor nutritional status can impair immune cell infiltration into tumors, which may serve as protective factors against lung cancer. Additionally, BMI can be directly correlated with the number of mature dendritic cells within tumors, a positive prognostic factor for lung cancer. Inflammatory states can develop before or simultaneously with lung cancer, contributing to increased energy consumption, malnutrition, and catabolic processes (Alifano, et al., 2021).

Albumin levels are one of the prognostic factors in lung cancer. A meta-analysis showed that low albumin levels increased the risk of death by 1.52–1.8 times compared to patients with higher albumin

levels. Additionally, low albumin levels were negatively correlated with overall survival (OS). Furthermore, there was a negative correlation between low albumin levels and progression-free survival (PFS). However, several studies have found no statistically significant relationship between albumin levels and PFS. In early-stage cancer, preoperative hypoalbuminemia is linked to larger tumor size and invasion of the visceral pleura. Hypoalbuminemia is a negative prognostic factor for tumor recurrence and survival in patients who have undergone NSCLC surgery (Zhang, et al., 2021; Guven, et al., 2022).

Hypoalbuminemia is an important factor for patients with NSCLC, affecting those with localized disease treated surgically and patients with metastases undergoing cytotoxic chemotherapy. A study revealed that patients with albumin levels less than 3.5 g/dL who received first-line targeted therapy and immunotherapy were at a higher risk of death within 12 weeks of initiating treatment. Albumin levels can help identify patients who may not benefit from therapy, allowing for more appropriate treatment options (Stares, et al., 2021). This is consistent with the findings of this study, where the higher the stage of lung cancer, the greater the proportion of patients experiencing hypoalbuminemia. In stage IV lung cancer, patients often receive palliative therapy (Gupta & Lis, 2010).

In addition to being a prognostic factor, decreasing albumin levels during treatment can help clinicians predict patients who may develop treatment resistance. If this occurs, the clinician must immediately consider alternative therapy. This approach can reduce treatment-related risks, allow patients to receive appropriate palliative care, and enable them to make informed decisions (Zhang, et al., 2021). Cohort studies have shown that albumin levels can predict lung cancer risk, with increases in albumin levels being inversely proportional to cancer risk. Albumin acts as a scavenger and antioxidant (Yoon, et al., 2022).

The precise cause of low albumin levels in cancer patients remains unclear, though several mechanisms have been proposed. Cancer cells can produce cytokines, such as interleukin-6 (IL-6), which influence albumin production. Micrometastases in the liver may also cause Kupffer cells to produce cytokines such as IL-1β, IL-6, and tumor necrosis factor, which can affect albumin production. Increased vascular permeability in cancer patients, caused by the release of tumor necrosis factor, allows more albumin to pass through the capillary wall and into the extravascular space, exacerbating hypoalbuminemia (Nazha, et al., 2015). However, advanced cancer patients with hypoalbuminemia show only minor changes in the rate of transcapillary albumin loss, which has little correlation with serum albumin levels. Lastly, hypoalbuminemia can occur when there is an imbalance between albumin degradation and synthesis. This has been demonstrated in sarcoma-bearing mouse models compared to controls. Nutritional status, as reflected by albumin levels, can also help predict survival outcomes in patients receiving anti-cancer therapy. Albumin is a widely available and inexpensive parameter that can indicate the nutritional status of cancer patients (Nazha, et al., 2015). However, albumin still has limitations. In anaplastic lymphoma kinase (ALK)-positive NSCLC cancer patients, albumin levels are not sufficient to predict survival outcomes. Therefore, there is a need for better prognostic markers that integrate albumin levels with other factors (Guven, et al., 2022).

Strength and limitations

This study provides a detailed examination of various clinicopathological parameters, including clinical symptoms, histopathological types, cancer stages, EGFR mutation status, ECOG scores, pleural effusion, VAS scores, and BMI. The comprehensive data collection allows for an in-depth analysis of the relationships between these parameters and albumin levels in lung cancer patients. The study also highlights the role of albumin levels as a prognostic factor in lung cancer, particularly in relation to ECOG scores and other clinical characteristics. Focusing on a widely available and cost-effective parameter, this research can aid in the early detection of high-risk patients and guide treatment decisions, especially in resource-limited settings.

However, the study has several limitations. These include incomplete medical record data, lack of information on nutritional intake (which could serve as a confounding factor), and the diverse socioeconomic backgrounds and comorbidities of the study sample. Additionally, there are only a few studies that compare the clinicopathological features of lung cancer patients with their albumin levels. Future studies should include direct interviews with patients to obtain more comprehensive data and be conducted in various locations to allow for broader generalization of the findings.

CONCLUSION

This study showed no significant relationship between EGFR mutation status, clinical symptoms, pleural effusion, VAS scores, BMI, or cancer stage and albumin levels. However, a significant association was found between albumin levels and ECOG scores. Further research with a larger sample size is needed to explore the relationship between albumin levels and ECOG scores in greater detail.

Acknowledgment
The authors would like to express their sincere gratitude to Ulin Hospital for providing the facilities and resources necessary for this study. We particularly thank the Department of Pulmonology at Lambung Mangkurat University for their support and assistance throughout the research process. Access to advanced equipment and the collaborative environment were instrumental in the successful completion of this project. We also acknowledge the administrative and technical staff for their invaluable assistance and cooperation. Without their dedication and support, this research would not have been possible.

Conflict of Interest
All authors have no conflict of interest.

Ethic Consideration
This study has been approved by the Ethics Committee of Ulin Regional General Hospital, Banjarmasin, with approval number 75/VI-Reg Riset/RSUDU/24, on 05-06-2024.

Funding Disclosure
There was no funding for this research.

Author Contribution
EK contributes to conception and design, drafting of the article, critical revision of the article for important intellectual content, and final approval of the article. NFH contibutes to conception and design, analysis and interpretation of the data, provision of study materials or patients, statistical expertise, administrative, technical, or logistic support and collection and assembly of data.

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