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Prevalence Of EGFR Mutations in Stage III–IV Non-Small Cell Lung Cancer: A Single-Center Study from Vietnam

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Abstract

Background: Lung cancer is one of the most common malignancies in Vietnam, with non-small cell lung cancer (NSCLC) accounting for approximately 80% of all cases. Targeted therapies using epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs) have demonstrated significant clinical benefits in patients harboring EGFR mutations. However, treatment response and resistance patterns vary depending on the specific EGFR mutation type. Therefore, identifying EGFR mutations is essential for prognosis and treatment selection in advanced NSCLC.

Objective: To determine the prevalence of EGFR gene mutations in stage III–IV NSCLC patients and to evaluate the relationship between selected clinical characteristics and EGFR mutation status.

Methods: A descriptive study was conducted on 56 patients diagnosed with stage III–IV NSCLC who underwent EGFR mutation testing and received treatment at Gia Lai General Hospital between January 2023 and November 2025. Clinical characteristics and EGFR mutation profiles were analyzed to assess mutation frequency and associated factors.

Results: The overall EGFR mutation rate was 37.5%. The most frequently detected mutations were exon 19 deletions (Del19) and exon 21 L858R substitutions. EGFR mutations were more common in females than in males and were observed more frequently in non-smokers compared with smokers.

Conclusions: The EGFR mutation prevalence observed in this study is comparable to rates reported in other Vietnamese studies. The associations between EGFR mutation status and clinical characteristics identified at Gia Lai General Hospital are consistent with findings reported in both national and international literature.

Keywords: Non-small cell lung cancer (NSCLC), molecular biomarkers, histopathology, EGFR mutation

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Introduction

Cancer is one of the leading causes of mortality worldwide. Among all malignancies, lung cancer accounts for a high proportion of both new cases and cancer-related deaths, particularly in developing countries [1,2]. In Vietnam, lung cancer consistently ranks among the five most common cancers, with an increasing incidence trend [3]. Non–small cell lung cancer (NSCLC) accounts for approximately 80-85% of all lung cancer cases, and the majority of patients are diagnosed at an advanced or metastatic stag [1,3]. Advances in molecular biology have ushered in a new era in the treatment of lung cancer, particularly with the development of targeted therapies [4]. Tyrosine kinase inhibitors (TKIs) have been used effectively in patients with non–small cell lung cancer (NSCLC) harboring EGFR gene mutations, significantly improving progression-free survival and enhancing patients' quality of life [5]. However, the therapeutic efficacy of this class of agents largely depends on the presence and specific type of EGFR gene mutation.

Studies have shown that the prevalence of EGFR mutations varies considerably across geographic regions and populations. In Asian countries, particularly in East Asia, the proportion of patients with non–small cell lung cancer (NSCLC) harboring EGFR mutations ranges from 30% to 50%, which is substantially higher than that reported in Western countries [1,5]. The most common mutations are exon 19 deletions (Del19) and the L858R point mutation in exon 21 [6]. Additionally, certain clinical factors, such as female sex, never-smoking status, and adenocarcinoma histology, have been shown to be closely associated with a higher prevalence of EGFR mutations [3,5]. In Vietnam, EGFR gene testing has gradually been implemented in several major healthcare institutions. However, at the provincial level and in regional hospitals, access to this testing remains limited [3,5]. Furthermore, epidemiological data regarding the distribution of EGFR mutations within local populations are still incomplete, posing challenges to the development of appropriate personalized treatment strategies.

Recent advances in molecular oncology have further emphasized the role of epidermal growth factor receptor (EGFR) mutations as one of the most important predictive biomarkers in non–small cell lung cancer. EGFR is a transmembrane receptor tyrosine kinase that regulates cellular proliferation, differentiation, and survival through downstream signaling pathways such as PI3K/AKT and RAS/RAF/MEK/ERK. Activating mutations within the tyrosine kinase domain lead to constitutive activation of these signaling pathways, promoting tumor growth and progression. The identification of these mutations has transformed the therapeutic landscape of NSCLC by enabling the use of targeted therapies such as EGFR tyrosine kinase inhibitors (TKIs), which have demonstrated superior response rates and progression-free survival compared with conventional chemotherapy in selected patients. Consequently, international clinical guidelines now recommend routine EGFR mutation testing for patients with advanced NSCLC, particularly those with adenocarcinoma histology, to guide individualized treatment strategies and optimize clinical outcomes [6, 7].

At Gia Lai General Hospital, targeted therapy has initially been introduced into clinical practice for patients with lung cancer. However, no systematic study has yet been conducted to evaluate the prevalence of EGFR gene mutations or to investigate the association between mutation status and clinical characteristics in the local population. Based on the above considerations, we conducted this study with the aim of providing real-world data and establishing a scientific basis for the more effective and appropriate implementation of targeted therapy for patients in the local setting.

Methods

Study population: The study included 56 patients with stage III–IV non–small cell lung cancer (NSCLC) who underwent EGFR mutation testing and received lung cancer treatment from January 2023 to November 2025.

Inclusion criteria:

- Histologically or cytologically confirmed diagnosis of stage III or IV NSCLC.
- No prior treatment with tyrosine kinase inhibitors (TKIs).
- Availability of adequate tumor specimens for EGFR mutation testing (for cases in which testing had not yet been performed).
- Complete administrative and clinical data available for research purposes.

Exclusion criteria:

- Patients or their families who declined to participate in the study.

Study Design: A retrospective cross-sectional descriptive study.

Study Procedure: Patients were selected according to the predefined inclusion criteria. Data were collected using standardized case report forms and analyzed using SPSS version 22 and Microsoft Excel 2016.

Ethical considerations: This retrospective cross-sectional descriptive study was reviewed and approved by the Ethics Committee of Gia Lai General Hospital.

Results

A total of 56 patients with stage III–IV non–small cell lung cancer (NSCLC) who underwent EGFR mutation testing and were treated at the Department of Oncology, Gia Lai General Hospital were included in the study. The following results were obtained. General characteristics of the study population is shown in the table below.

Table 1. Characteristics of the Study Population

Characteristics		Number of cases	Percentage
Age	≤60	13	23,2%
	>60	43	76,8%
Sex	Male	34	60,7%
	Female	22	39,3%
Smoking status	Smoker	31	55.4%
	Non-smoker	25	44,6%
Stage	III	3	5,3%
	IV	53	94,7%
Histopathology	Squamous cell carcinoma	6	10,7%
	Adenocarcinoma	50	89,3%

The majority of patients in the study population were over 60 years of age, with a higher proportion observed in males and in smokers. Adenocarcinoma was the most common histopathological subtype identified in our study. Prevalence of EGFR Mutation Types has been given below in the Table 2.

Table 2. EGFR Mutation Status and Distribution of Mutation Types

Mutation		N	%
EGFR mutation status	Mutated	21	37.5%
	Wild-type	35	62,5%
Type of EGFR mutation	Exon 18	2	9,5%
	Exon 19	10	47,6%
	Exon 20	1	4,8%
	Exon 21	8	38,1%

The prevalence of EGFR mutations in this study was 37.5%, with 21 mutation-positive cases identified. The most frequently observed mutations were exon 21 mutations, followed by exon 19 mutations. The association between EGFR mutation status and selected clinical characteristics is given below in Table 3.

Table 3. Association Between EGFR Mutation Status and Selected Clinical Characteristics

Characteristics		EGFR mutation status				p
		Mutated		Wild-type		
		N	%	N	%	
Age	**≤60**	5	8.9%	8	14.3%	p>0.05
	>60	16	28,6%	27	48.2%	
Sex	**Male**	7	12,5	27	48,2%	p<0.05
	Female	14	25%	8	14.3%	
Smoking status	**Smoker**	8	14.3%	23	41.1%	p<0.001
	Non-smoker	13	23.2%	12	21.4%	

EGFR mutation status was significantly associated with sex and smoking history. The likelihood of harboring an EGFR mutation was higher in female patients than in male patients. Never-smokers demonstrated a higher prevalence of EGFR mutations compared with smokers. No statistically significant association was observed between EGFR mutation status and patient age.

Table 4. Association Between EGFR Mutation Status and Disease Stage and Histopathology

Characteristics		EGFR mutation status				P
		Mutated		Wild-type		
		N	%	N	%	
Stage	**III**	0	0%	3	5.4%	p>0.05
	IV	21	37.5%	32	57.1%	
Histopathology	**Adenocarcinoma**	20	35.7%	30	53,6%	p<0.001
	Squamous cell carcinoma	1	1.8%	5	8.9%	

EGFR mutations were observed at a substantially higher rate in patients with adenocarcinoma compared with those with squamous cell carcinoma, and this difference was statistically significant.

Discussion

According to global studies, the prevalence of EGFR mutations among patients with non–small cell lung cancer (NSCLC) is higher in Asia compared with other regions, with an average rate of approximately 39.6%. Among Asian countries, Japan has reported the highest prevalence, reaching up to 64.8% [4]. Therefore, patients with lung cancer in Asia in general, and in Vietnam in particular, have a higher likelihood of benefiting from treatment with tyrosine kinase inhibitors (TKIs), making EGFR mutation testing particularly important in clinical practice. In our study of 56 patients with stage III–IV non–small cell lung cancer (NSCLC), the prevalence of EGFR mutations (37.5%) was comparable to that reported in other Vietnamese studies, such as those by Pham Cam Phuong (41.2%) [3] and Mai Trong Khoa (40.7%) [5], and was consistent with the regional average [4]. The slight variations observed among studies may be attributed to differences in inclusion criteria, testing methodologies, or the epidemiological characteristics of the study populations across regions. Specifically, our study included patients with stage III–IV NSCLC in accordance with the recommendations of the Ministry of Health, whereas the study by Mai Trong Khoa enrolled patients from stage I to IV. Additionally, some studies have focused exclusively on patients with adenocarcinoma, a histological subtype known to have a higher prevalence of EGFR mutations compared with other NSCLC subtypes.

Regarding the distribution of mutation types, our findings showed that exon 19 and exon 21 were the two most frequently mutated sites, consistent with the majority of domestic and international reports. In our study, all exon 19 mutations were classified as Del19, whereas exon 21 mutations were predominantly the L858R point mutation. These are considered the two “classical” mutations due to their high prevalence and favorable response to TKI therapy, although treatment outcomes are generally superior in patients harboring Del19 compared with L858R [6]. Exon 18 mutations are regarded as uncommon alterations with a relatively low prevalence; in our study, they accounted for 9.5%. Patients with exon 18 mutations are sensitive to TKIs; however, their response is typically less favorable than that observed in exon 19 and exon 21 mutations. Notably, second-generation TKIs have been shown to provide better therapeutic efficacy than first-generation agents in this subgroup [7]. In contrast, most exon 20 mutations are associated with drug resistance, with T790M being the most common variant. This mutation is rarely detected prior to treatment, with a reported prevalence of approximately 0-5.9%, and often coexists with a sensitizing mutation such as Del19 or L858R. The majority of T790M cases represent acquired resistance mutations that develop after TKI therapy in patients with initially sensitizing EGFR mutations [8].

The results of our study also demonstrated that the likelihood of harboring an EGFR mutation was significantly higher in female patients than in male patients. Similarly, never-smokers exhibited a higher risk of EGFR mutations compared with smokers. The association between sex, smoking history, and EGFR mutation status has been consistently reported as statistically significant in numerous studies. A study conducted by Xiao-Jun Yu et al. involving 100 patients with non–small cell lung cancer (NSCLC) showed that EGFR was the predominant driver gene in never-smokers, whereas titin mutations were more commonly observed in patients who were current or former smokers [9]. The difference in EGFR mutation prevalence between sexes may partly be explained by the higher smoking rates among men, particularly in Asian countries. Some authors have also suggested a potential influence of sex hormones on the occurrence of EGFR mutations; however, current evidence remains inconclusive, and further research is needed to clarify this relationship.

In contrast, when examining the association between EGFR mutation status and age or disease stage, we did not observe any statistically significant differences. Several studies have similarly reported that age does not significantly influence the likelihood of harboring an EGFR mutation; however, age may be associated with specific mutation subtypes. Patients younger than 50 years have been reported to exhibit a higher prevalence of Del19 compared with L858R [10]. Regarding disease stage, most studies conducted in Vietnam and internationally have consistently demonstrated no significant differences in EGFR mutation prevalence across different stages of the disease.

Our findings further support the growing body of evidence highlighting the clinical significance of EGFR mutation testing in guiding targeted therapy for advanced NSCLC. Large international studies have demonstrated that patients with EGFR-mutant tumors experience significantly improved response rates and longer progression-free survival when treated with EGFR-TKIs compared with conventional chemotherapy [11]. For example, the IPASS trial showed that gefitinib provided superior outcomes in patients with EGFR mutations, establishing molecular testing as a critical component of treatment selection. Similarly, subsequent studies evaluating newer-generation TKIs such as osimertinib have reported improved survival outcomes and better central nervous system penetration, further reinforcing the importance of early molecular profiling in advanced lung cancer [12]. These findings emphasize that accurate identification of EGFR mutations not only contributes to epidemiological understanding but also directly impacts therapeutic decision-making and long-term patient prognosis [13-15].

Conclusion

Based on the analysis of 56 patients with stage III–IV non–small cell lung cancer (NSCLC) treated at the Department of Oncology, Gia Lai General Hospital, the following conclusions were drawn: The prevalence of EGFR mutations was 37.5%, comparable to that reported in other domestic studies. Sensitizing mutations were the most frequently observed alterations, particularly exon 19 deletions (Del19) and exon 21 L858R mutations. Primary resistance mutations in exon 20 (T790M) were rarely detected. Female sex and never-smoking status were associated with a higher likelihood of harboring EGFR mutations compared with male patients and smokers.

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