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Characteristics of Genetic Susceptibility in Lung Cancer Patients in North Sumatra Population, Indonesia

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Abstract

Lung cancer remains a major global health problem and the leading cause of cancer-related mortality worldwide. Although smoking and environmental exposure are the dominant risk factors, genetic susceptibility and family history may also contribute to lung cancer development, particularly among individuals with inherited cancer predisposition. This study aimed to describe the characteristics of genetic susceptibility among lung cancer patients in the North Sumatra population, Indonesia, with emphasis on family history of lung cancer and other cancers. A descriptive observational design was employed, conducted from August to November 2024 at Adam Malik Hospital, Universitas Sumatera Utara Hospital, and Santa Elisabeth Hospital. A total of 240 patients with histopathologically confirmed small-cell lung cancer and non-small-cell lung cancer were included through consecutive sampling. Data were collected from medical records, including sociodemographic characteristics, clinical information, and family cancer history, and were analyzed descriptively using IBM SPSS version 26. The results showed that patients had a mean age of 59.12 ± 13.22 years, were predominantly male, and were mostly of Batak ethnicity. Regarding familial susceptibility, 5.4% had a family history of lung cancer, 34.2% had a family history of other cancers, and 60.4% had no family history of cancer. These findings indicate that family history should be considered in lung cancer risk assessment. Integrating familial cancer evaluation into routine clinical practice may support early screening, prevention, and personalized intervention strategies.

INTRODUCTION

Lung cancer is a malignant disease originating from the epithelial cells of the bronchi and alveoli and is the leading cause of cancer-related mortality worldwide (Torre et al., 2015; World Health Organization, 2020). It is classified into non-small-cell lung cancer (NSCLC) and small-cell lung cancer (SCLC), with NSCLC accounting for approximately 85% of cases (American Cancer Society, 2020). In 2020, there were over 2.2 million new cases and 1.8 million deaths globally due to lung cancer (Torre et al., 2015). In Indonesia, lung cancer is the primary cause of cancer deaths (12.6%) and ranks third in incidence (8.7%) (World Health Organization, 2020).

While environmental factors, particularly tobacco smoking, are responsible for more than 80% of lung cancer cases, genetic predisposition accounts for less than 20% (Pikor et al., 2013). A study by Bromen et al. (2020) highlighted a significantly higher incidence among individuals with a family history of lung cancer, especially in younger patients. In general, hereditary

cancer contributes to approximately 10–15% of all cancer cases (Greenberg, 2016), emphasizing the importance of understanding genetic components in lung cancer development.

Recent advancements have focused on identifying germline variants and somatic mutations involved in lung cancer, such as point mutations, gene fusions, and amplifications (Pacheco & Rodriguez, 2019; Song et al., 2021). Although several studies have linked a family history of cancer to increased lung cancer risk (Lee et al., 2019; Zhang et al., 2018), the specific influence of different familial cancer types remains uncertain. Clarifying these associations is crucial for refining risk prediction and enabling early detection strategies (Turner, 2020; Ueno & Yamamoto, 2017).

Given the high burden of lung cancer and the fact that only a minority of smokers develop the disease, genetic susceptibility likely plays a key role in its pathogenesis (Laguna et al., 2024). This study aims to explore the characteristics of genetic susceptibility among lung cancer patients in the North Sumatra population, Indonesia, to support better identification of high-risk individuals and inform targeted prevention efforts.

In Indonesia, lung cancer represents a major cancer burden and is of particular importance among men. National cancer data show that Indonesia recorded more than 408,000 new cancer cases and more than 242,000 cancer-related deaths in 2022, with lung cancer among the leading causes of cancer mortality. The Indonesian context is significant because smoking prevalence, environmental exposure, delayed diagnosis, and unequal access to early detection may worsen lung cancer outcomes. Moreover, regional variations in ethnicity, lifestyle, healthcare access, and familial cancer patterns may influence how lung cancer develops across different populations. Studies focusing on local populations are therefore essential for understanding the characteristics of lung cancer risk beyond general national or global estimates.

North Sumatra provides an important setting for studying lung cancer susceptibility, as the region comprises diverse ethnic groups, distinct sociocultural patterns, and referral hospitals that manage patients from different districts and backgrounds. In the present study, lung cancer patients were recruited from three central hospitals in North Sumatra — namely Adam Malik Hospital, Universitas Sumatera Utara Hospital, and Santa Elisabeth Hospital — from August to November 2024. The study involved 240 histopathologically confirmed lung cancer patients, including both small-cell lung cancer and non-small-cell lung cancer. The observed patient profile showed that most patients were older adults, predominantly male, and largely from the Batak ethnic group, suggesting that demographic and regional characteristics must be considered when evaluating lung cancer risk in this population.

Previous research has consistently demonstrated that family history is associated with increased lung cancer risk. A systematic review and meta-analysis by Matakidou et al. reported that individuals with affected relatives had a significantly increased risk of lung cancer, particularly when the affected relative was diagnosed at a younger age or when multiple family members were affected. Similarly, Kanwal et al. found that having a first-degree relative with lung cancer increased lung cancer risk by approximately 50% compared with individuals without such a family history. These findings suggest that familial clustering may reflect shared genetic factors, shared environmental exposure, or a combination of both. Family history therefore remains a practical and clinically relevant marker for identifying individuals who may require closer risk assessment.

More recent studies have strengthened the relevance of genetic susceptibility in lung cancer. Ang et al. emphasized that familial lung cancer risk is influenced by both genetic and environmental factors, particularly in Asian populations where exposure to second-hand smoke, air pollution, and household environmental hazards may interact with inherited predisposition. Research on germline variants has also shown that inherited mutations may contribute to lung cancer susceptibility and may interact with somatic mutations in cancer development. In small-cell lung cancer, recent systematic review evidence suggests that a meaningful proportion of patients may carry pathogenic or likely pathogenic germline variants, highlighting the potential role of genetic screening in selected high-risk groups. These findings support the need to incorporate familial and genetic information into lung cancer risk assessment.

Despite growing evidence, several gaps remain in the understanding of genetic susceptibility among lung cancer patients in Indonesia, particularly in regional populations such as North Sumatra. First, most studies continue to focus primarily on smoking and environmental exposure, while family history is often recorded only as a secondary clinical variable. Second, there is limited local evidence describing whether lung cancer patients have a direct family history of lung cancer or histories of other cancers among relatives. Third, the relationship between ethnicity, familial cancer background, and lung cancer susceptibility remains underexplored in Indonesian populations. These gaps limit the ability of clinicians and public health practitioners to design population-specific risk screening models and targeted prevention programs.

The urgency of this research lies in the need to improve early identification of individuals at high risk for lung cancer. Lung cancer is often diagnosed at an advanced stage, when treatment options are more limited and survival outcomes are poorer. If family history and genetic susceptibility indicators can be systematically assessed, clinicians may be better positioned to identify high-risk individuals earlier, recommend appropriate screening, encourage smoking cessation, and provide more personalized counseling. In regions with a high lung cancer burden and limited screening access, straightforward tools such as structured family history assessment may offer a feasible entry point for improving prevention and early detection strategies.

The novelty of this study lies in its focus on the characteristics of genetic susceptibility among lung cancer patients in the North Sumatra population, using family history of cancer as a key indicator. Unlike studies that describe only general clinical profiles or smoking-related risk factors, this research highlights familial cancer patterns — including direct family history of lung cancer, history of other cancers in relatives, and the number of affected family members. By examining these characteristics in a local Indonesian population, the study provides region-specific evidence that may enrich understanding of lung cancer susceptibility in Southeast Asian settings. This approach also reinforces the argument that lung cancer prevention should not rely solely on environmental risk reduction, but should also take into account hereditary and familial risk indicators.

This study aims to explore the characteristics of genetic susceptibility among lung cancer patients in North Sumatra, Indonesia, particularly by assessing family history of lung cancer and other cancers among relatives. The objective is to describe sociodemographic characteristics, clinical profiles, and familial cancer patterns among patients with

histopathologically confirmed lung cancer. The expected contribution of this study is both scientific and practical. Scientifically, it adds local evidence to the literature on familial and genetic susceptibility in lung cancer. Practically, it may support clinicians in identifying high-risk individuals, guide early screening recommendations, strengthen patient education, and encourage the development of personalized prevention strategies for lung cancer in Indonesia.

METHOD

Study design and ethical approval

This study employed a descriptive observational was conducted between August and November 2024 across three tertiary referral hospitals in North Sumatra, Indonesia: Adam Malik General Hospital, Universitas Sumatera Utara Hospital, and Santa Elisabeth Hospital. Ethical approval was obtained from the Ethics Committee of the Faculty of Medicine, Universitas Sumatera Utara (Approval No. 1134/KEPK/USU/2024).

Study population and sampling

The study population included patients diagnosed with lung cancer, comprising both small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). Diagnosis was confirmed through histopathological examination and supported by clinical assessment, including history taking and physical examination. Participants were enrolled consecutively from outpatient pulmonary oncology clinics and inpatient wards using a non-probability consecutive sampling method. A minimum sample size of 240 participants was calculated to achieve sufficient statistical power.

Inclusion and exclusion criteria

Inclusion criteria were: (1) patients aged 18 years or older, (2) histopathologically confirmed diagnosis of lung cancer, and (3) complete clinical and family history data available in the medical records. Exclusion criteria included: (1) incomplete or missing medical record data, and (2) patients who declined participation or withdrew consent.

Data Collection

Data were collected using a structured data collection form and included sociodemographic variables (age, gender, and ethnicity) and family cancer history (presence of cancer among first- or second-degree relatives and total number of affected family members). Data were obtained from both electronic and paper-based medical records and verified by trained research staff for accuracy and completeness.

Statistical analysis and software

Descriptive statistics were applied to summarize patient characteristics. Categorical variables were reported as frequencies and percentages, while continuous variables were expressed as means with standard deviations (SD). All data were analyzed using IBM SPSS Statistics for Windows, Version 26.0.

RESULT AND DISCUSSION

A total of 240 lung cancer patients were included in this study, with a mean age of 59.12 ± 13.22 years. The majority were male (75%) and of Batak ethnicity (64.2%), followed by Javanese (26.7%) and Malay (4.2%). Regarding family susceptibility, 13 patients (5.4%) had a family history of lung cancer, 80 patients (34.2%) had a history of other cancers, and 147 patients (60.4%) had no family history of cancer. In terms of the number of affected family

members, 82 patients (34.2%) reported one family member with cancer, 11 patients (4.6%) had two, and 147 patients (60.4%) had none.

Table 1. Characteristics and family susceptibility of lung cancer patients

Characteristics	n (%) / Mean ± SD
Age (years)	59.12 ± 13.22
Gender	
Male	180 (75.0%)
Female	60 (25.0%)
Ethnicity	
Aceh	1 (0.4%)
Banten	0 (0.0%)
Batak	154 (64.2%)
Mixed	0 (0.0%)
Indian	0 (0.0%)
Javanese	64 (26.7%)
Malay	10 (4.2%)
Minangkabau	4 (1.7%)
Nias	1 (0.4%)
Chinese	6 (2.5%)
Family History of Cancer	
Yes, Lung Cancer	13 (5.4%)
Yes, Other Cancers	80 (34.2%)
None	147 (60.4%)
Number of Family Members with Cancer	
One	82 (34.2%)
Two	11 (4.6%)
None	147 (60.4%)

The demographic shift toward an aging population contributes to an increased incidence of age-related diseases, including lung cancer, which predominantly affects older individuals. Notably, fewer than 0.5% of lung cancer-related deaths occur in individuals under the age of 40, with the highest incidence observed among the elderly (Ferlay et al., 2020). In this study, the mean age of lung cancer patients was 59.12 ± 13.22 years, aligning with previous research by Logawathi and Mariedina (2021), who reported a predominance of elderly patients, particularly in the 65–69-year age group, at Haji Adam Malik Hospital, Medan. Similarly, a study study by Ernawati et al. (2019) at Dr. M. Djamil Padang General Hospital in 2021 found that most lung cancer patients were over the age of 40. This pattern may be attributed to prolonged exposure to carcinogens from environmental and domestic sources, with effects manifesting over time and the highest risk evident in those over 40 years (Siegel et al., 2023).

In terms of gender, the current study found a male predominance (75%), consistent with prior findings by Kandayah (2023) and Ramadhaniah et al. (2015), where male patients represented the majority of lung cancer cases. This trend is likely influenced by external factors, particularly smoking habits, which are more common among men and have been strongly associated with lung cancer incidence (Thun et al., 2013). Additionally, occupational

exposures and lifestyle differences may contribute to this gender disparity (Youlden et al., 2008).

Ethnic distribution showed the majority of patients were Batak (64.2%), followed by Javanese (26.7%) and Malay (4.2%). This is consistent with the findings of Butar (2010), who reported similar ethnic distributions at Dr. Pringadi Hospital, Medan. However, no significant correlation between ethnicity and lung cancer incidence was established in that study. Nonetheless, other studies have indicated that certain ethnic groups may have higher lung cancer rates due to genetic predispositions and environmental exposures. For instance, a study in England found that British Bangladeshi men have the highest rates of lung cancer, highlighting the importance of considering ethnic background and social circumstances in cancer risk assessments (Ellison-Loschmann et al., 2012).

Family history is a crucial factor in cancer risk. Prior studies have shown that individuals with a first-degree relative (FDR) affected by lung cancer, particularly at an early age or involving multiple family members, face a significantly elevated risk (Li et al., 2012). Research indicates that individuals with a family history of lung cancer among FDRs have approximately a 50% higher risk than those without such a history. Familial clustering may result from shared genetic factors, environmental exposures, or a combination of both. Therefore, family history can serve as a useful marker for identifying high-risk individuals and tailoring prevention strategies (Amos et al., 2008).

The current study revealed that 60.4% of participants had no family history of cancer, which aligns with findings from Ernawati et al. (2019) and Wiriansya et al. (2021), where 91.3% and 81.8% of patients, respectively, reported no familial cancer history. Although environmental factors such as smoking contribute to over 80% of lung cancer cases, genetic predisposition remains relevant, accounting for approximately 20% of cases (Pikor et al., 2013). Some studies have demonstrated a familial risk increase of 1.77% when a parent is affected, and a higher risk of 2.15% among siblings, suggesting a potential hereditary component (Sellers et al., 1990). Cytogenetic analyses have shown that mutations in oncogenes and tumor suppressor genes drive carcinogenesis, influence cell growth regulation, and promote cancer progression, making molecular testing a critical component of personalized treatment strategies (Pacheco & Rodriguez, 2019).

Moreover, the growing number of cancer survivors has led to an increased incidence of second primary cancers, including second primary lung cancer (LCa-2). Individuals with family members diagnosed with LCa-2 may still face elevated risk, although this relationship differs from that of primary lung cancer due to differences in exposure and treatment history. A study by Ji et al. (2022) found that the familial relative risk (RR) of lung cancer was 1.96 for LCa-1 family history and 1.89 for LCa-2, indicating a similar degree of risk. These findings underscore the importance of considering both primary and secondary cancer histories in familial risk assessments.

CONCLUSION

This study concludes that lung cancer patients in the North Sumatra population are predominantly older adults, male, and mostly from the Batak ethnic group, with a mean age of 59.12 years. Although environmental factors, particularly smoking and long-term carcinogenic exposure, remain dominant contributors to lung cancer occurrence, the findings also indicate

that familial and genetic susceptibility may play an important role in a subset of patients. Among 240 lung cancer patients, 5.4% had a direct family history of lung cancer, while 34.2% had a family history of other cancers, suggesting that family cancer background should not be overlooked in clinical risk assessment. These results reinforce the importance of integrating family history evaluation into routine lung cancer assessment, especially for identifying individuals who may require earlier screening, preventive counseling, and more personalized health interventions.

Future research is recommended to apply an analytical or cohort design to examine the strength of association between family history, genetic susceptibility, and lung cancer risk in the Indonesian population. Further studies should include molecular or germline genetic testing to identify specific inherited variants that may contribute to lung cancer development, particularly among patients with first-degree relatives affected by lung cancer or multiple family members with cancer. In addition, future research should involve larger and more diverse populations across different regions of Indonesia to compare ethnic, environmental, and lifestyle-related risk patterns. Combining clinical data, smoking history, occupational exposure, family history, and genetic testing may provide a more comprehensive risk prediction model and support the development of targeted lung cancer screening and prevention strategies in Indonesia.

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