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Characteristics of Tumor Marker on Mediastinal Tumors

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Abstract

Mediastinal tumors are rare thoracic malignancies that pose diagnostic and therapeutic challenges due to their anatomical proximity to vital organs and diverse histopathological features. Early detection and accurate characterization are essential for effective management. This study aimed to describe the characteristics of tumor markers and their diagnostic relevance in patients with mediastinal tumors treated at Adam Malik General Hospital, Medan, Indonesia. A descriptive observational study using a case series design was conducted on 43 patients diagnosed with histopathologically confirmed mediastinal tumors from 2020 to 2024. Data on demographics, tumor histopathology, tumor location, and tumor marker levels (LDH, AFP, β-HCG, and CEA) were collected from medical records. Statistical analysis was performed using SPSS 26.0, with categorical variables expressed as frequencies and percentages, and numerical variables as mean ± standard deviation. The results indicated that the majority of patients were male (76.7%), with a mean age of 40.7 ± 15.5 years. Lymphoma (39.5%) and thymoma (37.2%) were the most common tumor types, predominantly located in the anterior mediastinum (76.7%). LDH was elevated in 76.7% of cases, particularly in germ cell tumors and lymphomas, while AFP and β-HCG elevations were mainly observed in germ cell tumors. CEA had limited diagnostic utility. The study concludes that integrating clinical, histopathological, and tumor marker data enhances diagnostic accuracy, and that LDH, AFP, and β-HCG serve as valuable supportive biomarkers for mediastinal tumor evaluation.

INTRODUCTION

Mediastinal tumors account for approximately 3% of all thoracic cavity tumors. A study at Dr. Hasan Sadikin Hospital, Bandung, Indonesia, identified 82 cases of mediastinal tumors from January 2011 to December 2016, with thymoma being the most common histopathological type (68.4%) (Navas-Blanco, 2021; Giovani et al., 2018). Similarly, Adam Malik Hospital in North Sumatra reported 26 cases from 2019 to January 2023 (Soeroso, 2024).

The mediastinum, located between the right and left lungs, is divided into anterior, middle, and posterior compartments (Moore et al., 2025; Nakanishi, 2026; Rizvi et al., 2023; Suvarna & Lloyd, 2024). Half of mediastinal masses are found in the anterior compartment and are commonly referred to as the "4Ts": thymoma, teratoma, thyroid tissue, and "terrible" lymphoma (Soeroso, 2024; Almeida & Daniel, 2024; Amin, 2013). These masses present a wide range of histopathological characteristics, making diagnosis and classification crucial (Moore et al., 2025; Nakanishi, 2026; Rizvi et al., 2023; Suvarna & Lloyd, 2024).

Mediastinal tumors represent a relatively rare but clinically significant subset of thoracic malignancies, accounting for approximately 3% of all thoracic cavity tumors worldwide. The rarity of these tumors, combined with their proximity to vital organs such as the heart, great

vessels, and major airways, presents substantial challenges for timely diagnosis and effective treatment. Globally, mediastinal tumors have been associated with varied histopathological types, most commonly thymoma, lymphoma, and germ cell tumors, with patient outcomes heavily dependent on early detection and accurate classification (Navas-Blanco, 2021; Almeida & Daniel, 2024).

Epidemiological data indicate that the incidence of mediastinal tumors varies across regions, influenced by population demographics and healthcare access. For instance, a retrospective study at Dr. Hasan Sadikin Hospital in Indonesia identified 82 cases between 2011 and 2016, with thymoma comprising 68.4% of cases, highlighting a predominance in middle-aged adults (Giovani et al., 2018). Similarly, Adam Malik Hospital reported 26 cases between 2019 and 2023, underscoring the regional clinical burden of these tumors and emphasizing the need for local research to optimize diagnostic and therapeutic strategies.

Mediastinal tumors exhibit diverse histopathological characteristics, with anterior mediastinal masses accounting for approximately 50% of cases globally. The so-called "4Ts" — thymoma, teratoma, thyroid tissue, and "terrible" lymphoma — represent the most frequent anterior mediastinal masses. This anatomical concentration, along with the varied tumor biology, necessitates a precise and multimodal diagnostic approach, including imaging, histology, and tumor marker analysis, to guide treatment decisions effectively and improve prognosis (Almeida & Daniel, 2024; Amin, 2013).

Despite advances in imaging and surgical techniques, challenges remain in the early and accurate diagnosis, particularly in differentiating germ cell tumors, lymphomas, and thymomas. Tumor markers, such as lactate dehydrogenase (LDH), alpha-fetoprotein (AFP), and beta-human chorionic gonadotropin (β-HCG), have emerged as valuable adjuncts in clinical assessment. LDH, for example, is consistently elevated across multiple tumor types and is indicative of tumor activity, while AFP and β-HCG are more specific to germ cell tumors, facilitating both diagnosis and treatment planning.

Prior studies have highlighted regional variations in mediastinal tumor presentation. Al-Khalifa et al. (2020) documented a mean patient age of 46.6 years with a predominance of fourth-decade cases, whereas Shahana et al. (2023) reported peak incidence in the 21–30-year age group. These discrepancies underscore the necessity of context-specific research to inform diagnostic criteria and therapeutic pathways appropriate to local populations. Moreover, male predominance in mediastinal tumors is a consistent global observation, although certain subtypes, such as thymoma, exhibit a more balanced gender distribution.

A significant research gap exists in systematically characterizing tumor markers in mediastinal tumors within the Indonesian context, particularly in correlating LDH, AFP, and β-HCG levels with specific histopathological types. While international studies have outlined marker utility, limited local data constrain evidence-based clinical decision-making, making it difficult to implement standardized diagnostic protocols. Addressing this gap is crucial to improving early detection rates and optimizing patient outcomes in Indonesia.

The urgency of this research is accentuated by the potential severity of mediastinal tumors, which can present asymptomatically or lead to life-threatening complications due to their proximity to critical thoracic structures. Rapid, accurate diagnosis not only guides therapeutic interventions but also reduces morbidity and mortality. Furthermore, understanding

tumor marker profiles allows for improved prognostication and monitoring of treatment response, supporting personalized medicine approaches in thoracic oncology.

This study introduces novelty by integrating comprehensive tumor marker profiling with histopathological and demographic data in a local Indonesian cohort. By evaluating the prevalence and elevation patterns of LDH, AFP, β-HCG, and CEA across lymphoma, thymoma, germ cell, and neurogenic tumors, the research provides actionable insights that have not been systematically documented in prior regional studies. Such integration enhances diagnostic precision and supports evidence-based clinical pathways.

The purpose of this research is to describe the characteristics of tumor markers in mediastinal tumors, assessing their diagnostic relevance and potential utility in prognostication. By establishing correlations between marker elevation and specific tumor types, the study aims to enhance early detection strategies, support treatment planning, and provide data-driven guidance for clinicians managing mediastinal tumors in Indonesia.

Consequently, the contributions of this study extend to both clinical practice and academic research. For clinicians, the findings offer a refined framework for interpreting tumor markers in mediastinal tumors, improving diagnostic accuracy and patient management. For researchers, the study provides a foundation for further investigations into biomarker-based diagnostics, enabling subsequent studies to explore prognostic modeling, treatment response monitoring, and, potentially, the development of novel therapeutic targets. Ultimately, the research objectives and benefits align with enhancing patient outcomes, optimizing healthcare resources, and advancing knowledge in thoracic oncology within the regional and global context.

METHOD

This study employed a descriptive observational design using a case series approach to investigate the characteristics of tumor markers in mediastinal tumors. The research was conducted at Adam Malik General Hospital, Medan, Indonesia, covering the period from 2020 to 2024. The population consisted of all patients diagnosed with histopathologically confirmed mediastinal tumors during this period. Inclusion criteria required definitive histopathological confirmation, while patients with other primary tumors or known malignancies outside the mediastinum were excluded. A non-probability consecutive sampling method was applied to select participants who met the eligibility criteria, ensuring that all accessible cases were included for comprehensive analysis.

Data collection involved extracting demographic variables (age and sex), histopathological and cytological classifications, tumor location, and tumor marker levels (CEA, LDH, AFP, and β-HCG) from medical records. The research instrument was a structured data extraction form designed to standardize the collection of relevant clinical and laboratory parameters. To ensure reliability and consistency, data entry and coding procedures were cross-verified by two independent researchers, and descriptive statistics were used to assess the distribution and completeness of variables. Validity was supported by utilizing laboratory values confirmed through standardized hospital protocols, while reliability was ensured by cross-checking medical records against laboratory reports to minimize errors.

For data analysis, numerical variables, such as age and tumor marker concentrations, were expressed as mean ± standard deviation (SD), while categorical variables, including

tumor type and marker elevation status, were presented as frequencies and percentages. Statistical analysis was performed using SPSS software version 26.0. The analysis focused on identifying patterns of tumor marker elevation across different tumor types and demographic groups, allowing for the evaluation of diagnostic utility and potential correlations between histopathology and biomarker profiles. The procedural framework included ethical approval from the Health Research Ethics Committee of Universitas Sumatera Utara (Approval No. 1132/KEPK/USU/2024), adherence to patient confidentiality, and systematic documentation of all collected data.

RESULTS AND DISCUSSION

This study is a descriptive observational study with a case series design conducted at Adam Malik General Hospital, Medan, Indonesia. The target population included patients diagnosed with mediastinal tumors at Adam Malik Hospital from 2020 to 2024. The inclusion criterion was patients with histopathologically confirmed mediastinal tumors. Patients with other primary tumors or known malignancies outside the mediastinum were excluded. A non-probability sampling technique using a consecutive sampling method was applied.

Data on sample characteristics were obtained from medical records, including demographic variables (age and sex), tumor classification based on histopathological or cytological findings, and tumor marker values (CEA, LDH, AFP, and β-HCG). Statistical analysis was performed using SPSS version 26.0. Categorical variables were presented as frequencies and percentages, while numerical variables were expressed as mean ± standard deviation (SD).

This study was approved by the Health Research Ethics Committee of Universitas Sumatera Utara, with approval number 1132/KEPK/USU/2024.

A total of 43 patients with mediastinal tumors were included in this study, with a mean age of 40.7 ± 15.5 years. Most patients were male (76.7%). Based on histopathological features, the most frequent tumor types were mediastinal lymphoma (39.5%), thymoma (37.2%), germ cell tumors (18.6%), and neurogenic neoplasms (4.7%).

Histopathological classification showed that among lymphoma cases, 14 patients (32.5%) had non-Hodgkin lymphoma and 3 (7%) had Hodgkin lymphoma. For thymoma, type C (thymic carcinoma) was the most common (18.6%), followed by type AB (11.6%), type A (4.7%), and type B2 (2.3%). Among germ cell tumors, non-seminomatous types were most prevalent (9.3%), while seminoma, mature teratoma, high-grade immature teratoma, and germ cell tumor not otherwise specified each accounted for 2.3% of cases. Two cases (4.7%) were neuroendocrine tumors.

Most tumors were located in the anterior mediastinum (76.7%), while 16.3% had an undetermined location. Only 2 cases (4.7%) were located posteriorly, and 1 case (2.3%) was located in the middle mediastinum.

In terms of tumor markers, LDH was the most frequently elevated marker, observed in 76.7% of patients (33 cases). Elevated β-HCG was found in 8 patients (18.6%), AFP in 6 patients (13.9%), and CEA in 4 patients (9.3%). The majority of patients had normal levels of CEA (53.4%), AFP (58.1%), and β-HCG (53.0%). LDH was the only marker with a significant proportion of elevated values, indicating its potential relevance in mediastinal tumor diagnostics.

Table 1. Histophatological and diagnostic characteristics of mediastinal tumors

Variables	Total
Cell Features	
Mediastinal Lymphoma	17 (39,5%)
Thymoma	16 (37,2%)
Germ Cell	8 (18,6%)
Neurogenic neoplasm	2 (4,7%)
Histopathologic Features	
Lymphoma	
Non-Hodgkin lymphoma	14 (32,5%)
Hodgkin lymphoma	3 (7%)
Thymoma	
Thymoma type A	2 (4,7%)
Thymoma type B2	1 (2,3%)
Thymoma type AB	5 (11,6%)
Thymoma type C (Thymic carcinoma)	8 (18,6%)
Tumor Sel Germinal	
Seminoma	1 (2,3%)
Non-seminoma	4 (9,3%)
Mature Teratoma	1 (2,3%)
High Grade Immature Teratoma	1 (2,3%)
Germ Cell Tumor	1 (2,3%)
Neuroendocrine tumor	2 (4,7%)
Diagnostic	
Tumor Location	
Anterior	33 (76,7%)
Posterior	2 (4,7%)
Medial	1 (2,3%)
Difficult to determine	7 (16,3%)
Tumor Marker	
CEA	
Normal	23(53,4%)
High	4 (9,3%)
AFP	
Normal	25 (58,1%)
High	6 (13,9%)
ß–HCG	
Normal	23 (53%)
High	8 (18,6%)
LDH	
Normal	1 (2,3%)
High	33 (76,7%)

The analysis of tumor marker levels across different mediastinal tumor types revealed distinct patterns. In germ cell tumors, LDH was elevated in 87.5% of cases, followed by AFP (50%) and β-HCG (37.5%), supporting their role in diagnosing and monitoring this tumor type. CEA was not elevated in any germ cell tumor case.

In mediastinal lymphoma, elevated LDH was observed in 76.5% of patients, reflecting high cellular turnover, while elevations in CEA and β-HCG were less frequent (17.6% and 11.8%, respectively). AFP remained within normal limits in all lymphoma cases.

Among thymoma patients, LDH elevation was also common (75%), whereas CEA, AFP, and β-HCG were elevated in only a small proportion of cases, indicating limited diagnostic value for these markers in thymoma. In neurogenic tumors, which were limited in number, one case showed elevated CEA and LDH, while the remaining markers were within normal limits.

Overall, LDH emerged as the most consistently elevated marker across all tumor types, particularly in germ cell tumors and lymphoma, suggesting its utility as a general indicator of tumor activity. AFP and β-HCG demonstrated greater specificity for germ cell tumors, while CEA had limited diagnostic relevance in this cohort.

Table 2. Tumor marker profiles by mediastinal tumor type

Variable	Germinal Cell Tumor (n = 8)	Mediastinal Lymphoma (n = 17)	Neurogenic Tumor (n = 2)	Thymoma (n = 16)
CEA				
Normal	4 (50%)	9 (52.94%)	0 (0%)	10 (62.5%)
High	0 (0%)	3 (17.64%)	1 (50%)	1 (6.25%)
AFP				
Normal	3 (37.5%)	12 (70.58%)	1 (50%)	9 (56.25%)
High	4 (50%)	0 (0%)	0 (0%)	2 (12.5%)
ß–HCG				
Normal	4 (50%)	10 (58.82%)	1 (50%)	8 (50%)
High	3 (37.5%)	2 (11.76%)	0 (0%)	3 (18.75%)
LDH				
Normal	1 (12.5)%	0 (0%)	0 (0%)	0 (0%)
High	7 (87.5%)	13 (76.47%)	1 (50%)	12 (75%)

This study aimed to evaluate the demographic, histopathological, and tumor marker characteristics of mediastinal tumors in patients treated at Adam Malik Hospital, Medan. The findings revealed that the mean age of patients was 40.7 ± 15.5 years, with a male predominance (76.7%). These results align with previous literature, which reports that mediastinal tumors are commonly diagnosed in individuals aged 30–50 years, indicating that middle age may be a risk factor for these tumors (Giovani et al., 2018; Jilani et al., 2023). Al-Khalifa et al. (2020) also found the mean age to be approximately 46.6 years, with most cases occurring in the fourth decade of life. In contrast, a study by Shahana et al. (2023) reported a younger age distribution, with a peak incidence in the 21–30-year age group. This variation may reflect differences in population demographics, tumor types, and referral patterns.

The predominance of male patients is consistent with the findings of previous studies by Giovani et al. (2018), Shahana et al. (2023), and Al-Khalifa et al. (2020), all of whom reported a higher incidence of mediastinal tumors in males. Several other studies have indicated that the risk of mediastinal tumors is nearly twice as high in men as in women, suggesting a potential gender-related susceptibility. However, for specific tumor subtypes such as thymoma, the incidence appears to be balanced between males and females.

Most tumors in this study were located in the anterior mediastinum (76.7%). This finding is in agreement with prior studies, which report that the anterior compartment is the most common site for mediastinal tumors due to the presence of thymic tissue, lymph nodes, and fat (Jilani et al., 2023; Marino & Ascani, 2019; Al, 2022). The so-called "4Ts" — thymoma, teratoma, thyroid lesions, and "terrible" lymphoma — are commonly used to

describe the most frequent anterior mediastinal masses (Almeida & Daniel, 2024). In this study, lymphoma (39.5%) and thymoma (37.2%) were the most common tumor types, supporting the predominance of anterior mediastinal masses. Neurogenic tumors, which were the least common in this cohort (4.7%), are more frequently found in the posterior mediastinum (Jilani et al., 2023).

Histopathologically, non-Hodgkin lymphoma (32.5%) was the most frequently observed subtype, followed by thymic carcinoma (18.6%). This aligns with studies by Maru et al. (2024) and Roden et al. (2022), which identified non-Hodgkin lymphoma as the most prevalent subtype among mediastinal lymphomas and noted the aggressive nature of thymic carcinoma as a solitary lesion in the anterior mediastinum (Roden et al., 2020).

Tumor marker evaluation demonstrated elevated LDH levels in 76.7% of all cases. Notably, LDH was elevated in 87.5% of germ cell tumors, 76.47% of lymphomas, 75% of thymomas, and 50% of neurogenic tumors. These findings support the role of LDH as a general biomarker of tumor activity, although it is not specific to any single tumor type (Al, 2022; Bille, 2024). Elevated LDH levels have been associated with increased tumor metabolism, hypoxia, and poor prognosis, as described by Yuan et al. (2016).

AFP and β-HCG were predominantly elevated in germ cell tumors (50% and 37.5%, respectively), consistent with their role as specific markers for non-seminomatous and seminomatous germ cell tumors. In this study, two patients with non-seminomatous germ cell tumors exhibited concurrent elevation of both AFP and β-HCG, which supports their diagnostic value. Elevated levels of these markers can confirm the diagnosis of germ cell tumors without histological verification and may prompt immediate treatment initiation (Verma et al., 2020; Bille, 2024; Marandino & Vogl, 2022).

CEA elevation was observed in 17.6% of lymphoma cases, as well as in one case each of thymoma and neurogenic tumor. Although CEA is a nonspecific marker primarily associated with gastrointestinal malignancies, its elevation may occur in various cancers, including lung, breast, ovarian, and thyroid malignancies (Kankanala et al., 2025). Therefore, while not specific to mediastinal tumors, CEA may still have utility in conjunction with imaging and other markers for diagnosis and monitoring.

This study has several limitations. Being retrospective in nature, it relies on secondary data from medical records, and is therefore constrained by the accuracy and completeness of the documentation. Potential data loss or lack of standardized tumor marker testing across all cases may influence the results.

In summary, the study confirms that mediastinal tumors predominantly affect males in middle age, with the anterior mediastinum being the most common site. Lymphoma and thymoma were the most frequent histopathological types. Tumor markers such as LDH, AFP, and β-HCG provide important diagnostic and prognostic information, particularly in germ cell tumors and lymphomas, although they should be interpreted cautiously given their nonspecific nature.

CONCLUSION

The study concludes that mediastinal tumors in the Indonesian cohort predominantly affect middle-aged males, with the anterior mediastinum being the most frequent site of occurrence. Lymphoma, particularly non-Hodgkin lymphoma, and thymoma were identified

as the most common histopathological types. Tumor marker analysis revealed that LDH is the most consistently elevated biomarker across all tumor types, highlighting its potential utility as a general indicator of tumor activity. AFP and β-HCG elevations were primarily associated with germ cell tumors, confirming their role as specific diagnostic markers, whereas CEA demonstrated limited diagnostic relevance. Integrating clinical, radiological, histopathological, and tumor marker data provides a more comprehensive approach to the accurate diagnosis and management of mediastinal tumors.

For future research, it is recommended to conduct multicenter, prospective studies with larger sample sizes to validate and generalize these findings across diverse populations. Further investigation into additional tumor markers, molecular profiling, and longitudinal follow-up could enhance prognostic accuracy and inform personalized treatment strategies. Incorporating advanced imaging and biomarker-guided therapeutic monitoring may also improve early detection and optimize patient outcomes, ultimately contributing to evidence-based clinical guidelines for mediastinal tumor management.

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