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DIAGNOSTIC UTILITY OF CANCER RATIO IN DIFFERENTIATING MALIGNANT FROM NON-MALIGNANT PLEURAL EFFUSIONS: A RETROSPECTIVE STUDY

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Abstract

Background:

Differentiating malignant pleural effusions (MPEs) from non-malignant effusions is crucial but the definitive diagnostic method is biopsy, which relies on histopathological examination. However, biomarker ratios, such as cancer ratio like serum LDH to pleural ADA (S-LDH:P-ADA), offer minimally invasive alternatives with promising potential.

Aim and Objectives:

This study aimed to evaluate the diagnostic utility of cancer ratio in distinguishing malignant from non-malignant pleural effusions (non-MPEs).

Materials and Methods:

Aretrospective analysis of patient recordsof 69 participants (18 MPE, 51 non-MPE) was conducted at Saveetha Medical College. Biomarker levels and ratios were calculated and analysed using ROC curve analysis and multivariate logistic regression.

Results:

P-LDH:S-CRP demonstrated the highest diagnostic accuracy (AUC = 0.874). Although S-LDH:P-ADA was not statistically significant, its predictive metrics (PPV = 38.7%, NPV = 86.5%, PLR = 1.893, NLR = 0.469) suggest potential with larger cohorts. Notably, combining biomarker ratios, particularly P-LDH:S-LDH and P-LDH:S-CRP, further improved diagnostic performance, yielding an AUC of 0.869, underscoring the added value of integrating multiple biomarkers in MPE differentiation.

Conclusion:

P-LDH:S-CRP and P-LDH:S-LDH ratios demonstrated superior diagnostic accuracy, improving sensitivity and specificity in differentiating malignant from non-malignant pleural effusions. Combining biomarker ratios enhanced diagnostic performance, supporting their role as non-invasive alternatives to traditional methods. Further validation in larger cohorts is warranted.

Keywords: Pleural effusion, malignant effusion, biomarker ratios, LDH, ADA

INTRODUCTION

Pleural effusion, defined as the pathological accumulation of fluid within the pleural space, is commonly encountered in clinical practice and arises from diverse aetiologies, including infectious, inflammatory, and malignant conditions. Among these, malignant pleural effusions (MPEs) pose significant diagnostic and therapeutic

challenges, as they are often indicative of advanced-stage cancer with limited survival outcomes. The differentiation of malignant from non-malignant effusions, such as tuberculous pleural effusion (TPE) and parapneumonic effusion, is considered critical for guiding appropriate clinical management. Traditional diagnostic approaches, including cytological analysis and pleural biopsy, have been utilized; however, their utility is limited by few factors such as invasiveness and high resource demands(1, 2). As a result, the identification of minimally invasive and reliable diagnostic biomarkers for the differentiation of MPEs from benign effusions has been recognized as a priority (3-5).

Biochemical markers, such as lactate dehydrogenase (LDH), adenosine deaminase (ADA), and C-reactive protein (CRP), in pleural fluid and serum have been extensively investigated for their diagnostic utility. Ratios derived from these markers, including the cancer ratio (CR = serum LDH/pleural ADA), have demonstrated promise in recent studies. High sensitivity and specificity for CR at specific cutoffs have been reported by Verma et al. (2015)(6), and its diagnostic performance has been further validated in subsequent research by Aramareerak et al. (2023)(7) and Zhang et al. (2021)(8), particularly when combined with other biomarkers such as carcinoembryonic antigen (CEA) (9, 10). Despite these findings, variability in diagnostic performance across populations and clinical settings has been documented, highlighting the necessity for further exploration (3, 11).

In this study, the diagnostic utility of several biomarker ratios, with a focus on the serum LDH to pleural ADA ratio (S-LDH:P-ADA), has been assessed in the differentiation of malignant and non-malignant pleural effusions. Previous studies have suggested that S-LDH:P-ADA may serve as a robust predictor of malignancy (12, 13), but inconsistent diagnostic performance has also been noted in the literature (14-16). Additional ratios, including pleural LDH to serum CRP (P-LDH:S-CRP) and pleural LDH to serum LDH (P-LDH:S-LDH), have been investigated, as these ratios have shown potential in smaller studies but have yet to be validated in diverse patient cohorts(17, 18).

The analysis of these ratios was conducted in patients with pleural effusion to identify simple and accessible diagnostic tools. Biomarker ratios were hypothesized to provide an integrative approach by capturing systemic inflammation, tumour activity, and pleural pathology. Their diagnostic accuracy was evaluated alongside conventional biomarkers to clarify clinical utility and limitations. By calculating and analysing these ratios, this study aims to enhance diagnostic precision, minimize invasive procedures, and improve patient outcomes.

MATERIALS AND METHODS

Study Design and Participants

This study was a retrospective analysis conducted at in the Department of Respiratory Medicine, Saveetha Medical College, and Hospitals over a period of 6 months. A total of 69 participants were included, comprising 18 individuals with malignant pleural effusions and 51 with non-malignant pleural effusions. Patient data were retrospectively conformed by clinical suspicion subjected to thoracentesis and sample sent for analysis and classified as exudate and transudative as per Light's criteria. Inclusion criteria were adults aged ≥18 years with pleural effusions confirming by imaging studies. Patients with incomplete clinical or biochemical dataor effusions of uncertain aetiology were excluded.

Sample Collection and Laboratory Analysis

Pleural fluid and serum samples were collected from all participants at the time of diagnosis. Standard protocols were followed for sample collection, storage, and analysis. Serum lactate dehydrogenase (LDH), pleural LDH, pleural adenosine deaminase (ADA), serum C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR) were analysed using standard biochemical assay methods, including spectrophotometry for LDH and ADA, immunoturbidimetry for CRP, and Westergren method for ESR, in accordance with the laboratory guidelines at Saveetha Medical College.

Data Collection and Categorization

Demographic and clinical data, including age, gender, and underlying aetiology of pleural effusion, were recorded. Based on definitive diagnoses, pleural effusions were categorized into malignant or non-malignant groups. Non-malignant effusions were further classified into tuberculosis (TB), parapneumonic effusions, or other infections, while malignant effusions were subcategorized by cancer type. Diagnostic confirmation was achieved through cytological analysis, pleural biopsy, or clinical-radiological correlation.

Biomarker Ratio Calculation

Biomarker ratios, including serum LDH to pleural ADA (S-LDH:P-ADA), pleural LDH to serum CRP (P-LDH:S-CRP), and pleural LDH to serum LDH (P-LDH:S-LDH), were calculated. These ratios were selected based

on their proposed diagnostic value in distinguishing malignant from non-malignant pleural effusions as reported in prior literature.

Statistical Analysis

Data were analysed using GraphPad PRISM version 9 and IBM SPSS version 25. Continuous variables were expressed as mean ± standard deviation and compared using the Student's t-test for normally distributed data or the Mann-Whitney U test for non-normally distributed data. Categorical variables were presented as frequencies and percentages and analysed using the chi-square test or Fisher's exact test. Receiver operating characteristic (ROC) curves were generated to assess the diagnostic accuracy of biomarker ratios, and the area under the curve (AUC) was calculated. Optimal cutoff values for ratios were determined using the Youden Index. Multivariate logistic regression was performed to identify independent predictors of malignant pleural effusion, adjusting for age and gender. A p-value <0.05 was considered statistically significant.

Ethical Considerations

The study was conducted in accordance with the Declaration of Helsinki.The study obtained the ethical approved by the Institutional Ethics Committee at Saveetha Medical College.Data confidentiality and participant anonymity were maintained throughout the analysis.

RESULTS

The baseline characteristics of the study participants are summarized in Table 1. The study included 69 participants, of whom 66.67% (n=46) were male and 33.33% (n=23) were female, as illustrated in Figure 1. The mean age of participants with malignant pleural effusions was significantly higher (60.11 ± 13.35 years) compared to those with non-malignant effusions (46.2 ± 15.44 years, p=0.0011). Serum LDH levels were also significantly elevated in malignant cases (362.3 ± 179.5 U/L) compared to non-malignant cases (279.5 ± 125.9 U/L, p=0.0454), while pleural LDH levels were markedly higher in malignant effusions (2951 ± 863.2 U/L) compared to non-malignant effusions (814.9 ± 259.2 U/L, p=0.0022). In contrast, pleural ADA levels, ESR, and serum CRP levels did not show significant differences between the two groups.

The pleural effusion types in the cohort were predominantly exudative, accounting for 86.96% (n=60), while transudative effusions were less frequent, representing 13.04% (n=9), as shown in Figure 2. Among the exudative effusions, 30% (n=18) were malignant, while 70% (n=42) were non-malignant, as illustrated in Figure 3. Further analysis of the non-malignant group revealed that tuberculosis (TB) was the most common diagnosis, contributing 56.86% (n=29) of cases, followed by parapneumonic effusions at 23.53% (n=12). Other causes included Enterobacteria infections (9.80%, n=5), MRSA infections (5.88%, n=3), and fungal infections (3.92%, n=2), as depicted in Figure 4.

The distribution of cancer diagnoses among the malignant effusions (n=18) is shown in Figure 5. Adenocarcinoma was the most prevalent diagnosis, observed in 33.33% (n=6) of patients. Small cell lung carcinoma accounted for 22.22% (n=4), while metastatic adenocarcinoma, squamous cell carcinoma, ductal carcinoma with metastasis, and benign tumours each contributed 11.11% (n=2) of cases.

Biomarker ratios were analysed between malignant and non-malignant pleural effusions and are presented in Figure 6. The P-LDH:S-CRP ratio was significantly higher in malignant effusions ($p<0.01$), as was the P-LDH:S-LDH ratio ($p<0.05$). However, no significant differences were observed for the L/N ratio or the S-LDH:P-ADA ratio. Spearman's correlation analysis, shown in Table 2, demonstrated strong positive correlations between pleural LDH and pleural ADA ($r=0.812$, $p<0.01$) and between pleural LDH and ESR ($r=0.985$, $p<0.01$) in malignant samples. Additionally, the P-LDH:S-CRP ratio was highly correlated with pleural LDH ($r=0.918$, $p<0.01$). In contrast, non-malignant samples exhibited weaker or non-significant correlations.

The diagnostic utility of biomarker ratios was evaluated using ROC curve analysis (Figure 7, Table 4). The P-LDH:S-CRP ratio exhibited the highest area under the curve (AUC) at 0.874 (95% CI: 0.773–0.975, $p<0.005$), followed by the P-LDH:S-LDH ratio with an AUC of 0.789 (95% CI: 0.649–0.928, $p<0.005$). Combining ratios, such as P-LDH:S-LDH and P-LDH:S-CRP, further improved diagnostic performance, yielding an AUC of 0.869 (95% CI: 0.765–0.972). Sensitivity and specificity values at optimal cutoff levels for the biomarker ratios are summarized in Table 5. The combination of P-LDH:S-LDH and P-LDH:S-CRP achieved the highest positive likelihood ratio (PLR=3.000) and the lowest negative likelihood ratio (NLR=0.384). Although S-LDH:P-ADA was not statistically significant, its predictive metrics (PPV = 38.7%, NPV = 86.5%, PLR = 1.893, NLR = 0.469) highlights its potential as a diagnostic tool for differentiating malignant from non-malignant pleural effusions.

Multivariate logistic regression analysis with malignancy as the outcome variable (Table 3) identified P-LDH:S-CRP as a significant predictor of malignancy in adjusted models (OR=0.981, 95% CI: 0.962–1.000, $p<0.05$). Other biomarkers, including serum LDH, pleural LDH, and pleural ADA, did not achieve statistical significance in predicting malignancy after adjusting for age and sex.

DISCUSSION

The study evaluated the diagnostic potential of biomarkers and their ratios, particularly serum LDH to pleural ADA (S-LDH:P-ADA), for differentiating malignant from non-malignant pleural effusions. Significant differences were found in pleural and serum LDH levels, with notable results for P-LDH:S-CRP and P-LDH:S-LDH ratios. Although S-LDH:P-ADA did not show significant differences, its diagnostic metrics (PPV, NPV, PLR, NLR) suggest potential for further study with larger cohorts. These findings support the growing evidence for biochemical markers in diagnosing malignant pleural effusions.

The observed results align and contrast with several prior studies. Verma et al. (2015) reported a sensitivity of 98% and specificity of 94% for the S-LDH:P-ADA ratio at a cut-off >20, a diagnostic performance much stronger than observed in the current study, where the S-LDH:P-ADA ratio demonstrated modest sensitivity and specificity values(19). Similarly, Aramareerak et al. (2023) showed the potential of S-LDH:P-ADA in a Thai cohort with an AUC of 0.83 at a lower cut-off, emphasizing its contextual variability(7).

Further contextualizing our findings, the distribution of non-malignant pleural effusions in our study (Figure 4) identified tuberculosis (TB) as the most common cause (95.24%)followed by parapneumonic effusions (4.76%). This aligns with Gu et al. (2016), who also reported TB as a significant contributor, emphasizing pleural CEA's role in distinguishing TPE from MPE with a specificity of 94% and AUC of 0.86.For malignant pleural effusions (Figure 5), adenocarcinoma was the predominant diagnosis (66.67%), followed by Metastatic carcinomatous deposits (22.22%) and small cell lung carcinoma (11.11%)(1). Zhang et al. (2020) similarly reported pleural fluid CEA as a reliable marker for lung cancer-associated MPE, achieving high accuracy (AUC 0.978)(10). These findings highlight tumour-specific biomarkers, such as CEA, for distinguishing malignancies like adenocarcinoma.Compared to meta-analyses by Nguyen et al. (2015) and Fan et al. (2022), which noted high specificity but low sensitivity for MPE diagnosis, our results support integrating pleural and serum markers, especially in cytology-negative cases(20, 21). Multi-marker panels, as suggested by Peng et al. (2022), warrant further exploration to improve diagnostic accuracy(22).

Zhang et al. (2021) extended these findings, indicating that combining S-LDH:P-ADA with pleural CEA significantly enhanced diagnostic accuracy, an approach that could be explored in future iterations of the current study(8). Notably, Cavaco et al. (2022) and ElSharawy et al. (2020) highlighted the strength of integrating cancer ratios with clinical features, achieving AUCs of up to 0.94, thereby underscoring the importance of multidimensional approaches(11, 14). In contrast, Huang et al. (2023) noted age-related variability in the diagnostic performance of the S-LDH:P-ADA ratio, suggesting that the sample composition may partly explain the modest results observed here(3).

Beyond the cancer ratio, this study's findings on pleural LDH and its ratios with serum biomarkers resonate with results from other studies. For instance, Hackner et al. (2019) identified strong diagnostic accuracy for pleural CEA ratios in cytology-negative cases, while Pan et al. (2019) and Zhang et al. (2022) achieved high AUCs by combining LDH and pleural markers with decision models(2, 9, 23). These observations highlight the potential of integrating traditional markers with advanced analytic techniques. Despite these promising directions, the current findings show that P-LDH:S-CRP and P-LDH:S-LDH outperformed S-LDH:P-ADA in diagnostic efficacy, warranting further exploration of these ratios in larger

Three key findings were highlighted. First, pleural LDH and its ratios, especially P-LDH:S-CRP, proved to be effective diagnostic tools for differentiating malignant effusions. Second, although the modest performance of S-LDH:P-ADA showcases the potential to differentiate malignant from non-malignant pleural effusions, this cohort highlights the need for a larger sample size and tailored diagnostic thresholds across populations. Third, combining biomarker ratios with clinical data could enhance accuracy, as supported by prior research. Limitations include a small sample size, particularly for malignant cases, which may have impacted the statistical power of S-LDH:P-ADA. Additionally, the absence of external validation limits the findings' generalizability, and the study did not evaluate S-LDH:P-ADA in combination with markers like pleural CEA or VEGF, which have shown promise in another research.

CONCLUSION

This study reinforces the diagnostic utility of pleural LDH and its associated ratios while raising questions about the contextual applicability of the S-LDH:P-ADA ratio. Despite its limited performance here, the ratio's diagnostic metrics - PPV (0.387), NPV (0.865), PLR (1.893), and NLR (0.469) -highlightsto be a potential diagnostic tool for differentiating malignant from non-malignant pleural effusions however larger sample sizes and refined cut-offs is warranted.

Most importantly, combining biomarker ratios, particularly P-LDH:S-LDH and P-LDH:S-CRP, significantly enhanced diagnostic performance, achieving an AUC of 0.869 and improving overall sensitivity and specificity. This underscores the importance of integrating multiple biomarkers rather than relying on a single ratio, as it enhances diagnostic precision and minimizes reliance on invasive procedures.

The findings underscore the broader implications of leveraging biomarker ratios in non-invasive diagnostics, contributing to a growing arsenal of tools for malignant pleural effusion differentiation. Future research should prioritize larger, multicentric studies with diverse populations, integrating biochemical markers with clinical and imaging features to develop robust diagnostic algorithms. A call to action is issued for clinicians and researchers to continue refining and validating these tools, ultimately enhancing the diagnostic precision and care pathways for patients with pleural effusions.

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Authors contribution:

Vijayalakshmi Sivasubramanian conceptualized and designed the study, supervised data collection, performed data interpretation, and acted as the corresponding author. Rishab Rampradeep contributed to data collection, statistical analysis, and manuscript drafting. Gangadharan Vadivelu provided critical revisions to the manuscript, ensuring intellectual content and coherence. All authors have read and approved the final manuscript and agreed to be accountable for all aspects of the work.

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Tables and Figures:

Values are mean ± SD; Values shown in bold showed significant difference. Student t-test to compare between Non-malignant and malignant groups. $p < 0.005$ is considered statistically significant.

Table 1: Base line characteristics of anthropometric parameters, biomarkers of inflammation, LDH and ADA

Variables	Non-Malignant samples (n = 51)	Malignant samples (n = 18)	p value
Age	46.2 ± 15.44	60.11 ± 13.35	0.0011
Male, n(%)	32 (62.75%)	14 (77.78%)	
Serum LDH	279.5 ± 125.9	362.3 ± 179.5	0.0454
Pleural LDH	814.9 ± 259.2	2951 ± 863.2	0.0022
Pleural ADH	37.86 ± 31.23	37.41 ± 18.65	0.9591
ESR	88.42 ± 36.72	88.72 ± 29.92	0.9775
Serum CRP	125.6 ± 89.17	83.52 ± 66.85	0.1010

Table 2: Spearman's correlation of inflammatory biomarkers, LDH, and ADA.

Variables	Combined samples	Non-Malignant samples	Malignant samples
Serum LDH U/L			
Pleural LDH U/L	**0.401****	0.181	**0.992****
Pleural ADA U/L	0.105	-0.079	**0.940****
ESR mm/hr	0.127	-0.003	**0.877****
Serum CRP mg/L	-0.012	-0.176	**0.753***

L/N Ratio	-0.227	-0.243	0.068
S-LDH : P-ADA	**0.361****	**0.455****	-0.469
P-LDH : S-LDH	0.153	-0.152	**0.770***
P-LDH : S-CRP	**0.430****	**0.350***	**0.918****
Pleural LDH U/L			
Pleural ADA U/L	**0.391****	**0.360****	**0.812****
ESR mm/hr	0.094	-0.014	**0.985****
Serum CRP mg/L	0.257	0.237	**0.886****
L/N Ratio	-0.221	-0.235	-0.206
S-LDH : P-ADA	0.74	-0.012	-0.396
P-LDH : S-LDH	**0.924****	**0.907****	**0.901****
P-LDH : S-CRP	**0.651****	**0.554****	**0.806****
Pleural ADA U/L			
ESR mm/hr	0.179	0.093	**0.900****
Serum CRP mg/L	0.017	-0.113	**0.800****
L/N Ratio	0.197	0.225	-0.091
S-LDH : P-ADA	**-0.639****	**-0.648****	**-0.620***
P-LDH : S-LDH	**0.445****	**0.440****	**0.664****
P-LDH : S-CRP	**0.282***	**0.303***	**0.886****
ESR mm/hr			
Serum CRP mg/L	**0.542****	**0.436****	**0.900****
L/N Ratio	-0.254	-0.201	**-0.667***
S-LDH : P-ADA	0.032	0.085	**-0.837****
P-LDH : S-LDH	0.075	-0.046	**0.960****
P-LDH : S-CRP	-0.224	**-0.345***	**0.788****
Serum CRP mg/L			
L/N Ratio	-0.231	-0.180	**-0.821****
S-LDH : P-ADA	0.097	0.194	**-0.714***
P-LDH : S-LDH	**0.306***	**0.354***	**0.911****
P-LDH : S-CRP	**-0.444****	**-0.550****	0.591
L/N Ratio			
S-LDH : P-ADA	-0.127	-0.078	-0.054
P-LDH : S-LDH	-0.228	-0.188	**-0.609***
P-LDH : S-CRP	-0.271	-0.199	-0.556
S-LDH : P-ADA			
P-LDH : S-LDH	-0.230	**-0.416****	-0.156
P-LDH : S-CRP	-0.21	-0.163	**-0.830****
P-LDH : S-LDH			
P-LDH : S-CRP	**0.664****	**0.542****	**0.697***

Values shown in bold showed significant difference. $p < 0.005$ is considered statistically significant.

Table 3: Multivariate logistic regression analysis with malignancy as the outcome variable				
Variable	**Model**	**OR**	**95% CI**	
			Lower	**Upper**
Serum-LDH U/L	**A**	0.999	0.996	1.001
	B	0.996	0.991	1.000
Pleural-LDH U/L	**A**	1.000	0.99	1.000
	B	**1.000***	**0.99**	**1.000**
Pleural-ADA U/L	**A**	1.000	1.000	1.001
	B	1.000	0.999	1.002
ESMR mm/hr	**A**	1.000	0.980	1.020
	B	0.987	0.961	1.014
Serum CRP mg/L	**A**	1.007	0.997	1.016
	B	1.005	0.993	1.017
L/N Ratio	**A**	1.024	0.974	1.076
	B	1.074	0.966	1.195
S-LDH : P-ADA	**A**	1.005	0.970	1.041
	B	0.996	0.960	1.033
P-LDH : S-LDH	**A**	1.001	0.971	1.033
	B	0.985	0.951	1.020
P-LDH : S-CRP	**A**	0.992	0.978	1.006
	B	**0.981***	**0.962**	**1.000**
S-LDH : P-ADA + P-LDH : S-LDH	**A**	1.007	0.981	1.003
	B	0.990	0.996	1.014
S-LDH : P-ADA + P-LDH : S-CRP	**A**	1.000	0.987	1.013
	B	0.982	0.965	1.000
P-LDH : S-LDH + P-LDH : S-CRP	**A**	0.998	0.987	1.009
	B	0.986	0.971	1.000
S-LDH : P-ADA + P-LDH : S-LDH + P-LDH : S-CRP	**A**	1.000	0.989	1.011
	B	0.985	0970	1.000

S-LDH: Serum lactate dehydrogenase, P-LDH: Pleural lactate dehydrogenase, S-ADA: Serum adenosine deaminase, P-ADA: Pleural adenosine deaminase, S-CRP: Serum C-reactive protein; ESR: Erythrocyte Sedimentation Rate; Models: A-unadjusted, B-adjusted for age and sex; OR: odds ratio; CI: confidence interval.

Table 4: Area under the curve analysis of LDH, ADA and CRP			
Variable	**Area**	**95% C.I**	
		Lower	**Upper**
S-LDH : P-ADA	0.580	0.422	0.738
P-LDH : S-LDH	**0.789***	**0.649**	**0.928**
P-LDH : S-CRP	**0.874******	**0.773**	**0.975**
S-LDH : P-ADA + P-LDH : S-LDH	0.636	0.482	0.789
S-LDH : P-ADA + P-LDH : S-CRP	**0.780***	**0.645**	**0.915**
P-LDH : S-LDH + P-LDH : S-CRP	**0.869******	**0.765**	**0.972**
S-LDH : P-ADA + P-LDH : S-LDH + P-LDH : S-CRP	**0.786***	**0.653**	**0.918**

S-LDH: Serum lactate dehydrogenase; P-LDH: Pleural lactate dehydrogenase; S-ADA: Serum adenosine deaminase; P-ADA: Pleural adenosine deaminase; S-CRP: Serum C-reactive protein. Values shown in bold showed significant difference. $p < 0.005$ is considered statistically significant.

Table 5: Sensitivity and specificity at optimal cutoff levels							
	Optimal cut-off level	**Sensitivity**	**Specificity**	**PPV**	**NPV**	**PLR**	**NLR**
S-LDH : P-ADA	≥ 9.574	0.706	0.627	0.387	0.865	1.893	0.469
P-LDH : S-LDH	≥ 2.226	0.588	0.784	0.476	0.851	2.722	0.526
P-LDH : S-CRP	≥ 7.739	0.588	0.745	0.435	0.844	2.306	0.553
S-LDH : P-ADA + P-LDH : S-LDH	≥ 12.955	0.706	0.627	0.387	0.865	1.893	0.469
S-LDH : P-ADA + P-LDH : S-CRP	≥ 21.55	0.588	0.686	0.385	0.833	1.873	0.601
P-LDH : S-LDH + P-LDH : S-CRP	≥ 10.68	0.706	0.765	0.500	0.886	3.000	0.384
S-LDH : P-ADA + P-LDH : S-LDH + P-LDH : S-CRP	≥ 23.195	0.706	0.667	0.414	0.872	2.120	0.441

S-LDH: Serum lactate dehydrogenase; P-LDH: Pleural lactate dehydrogenase; S-ADA: Serum adenosine deaminase; P-ADA: Pleural adenosine deaminase; S-CRP: Serum C-reactive protein; PPV: positive predictive value; NPV: negative predictive value; PLR: positive likelihood ratio; NLR: negative likelihood ratio.

Figure 1

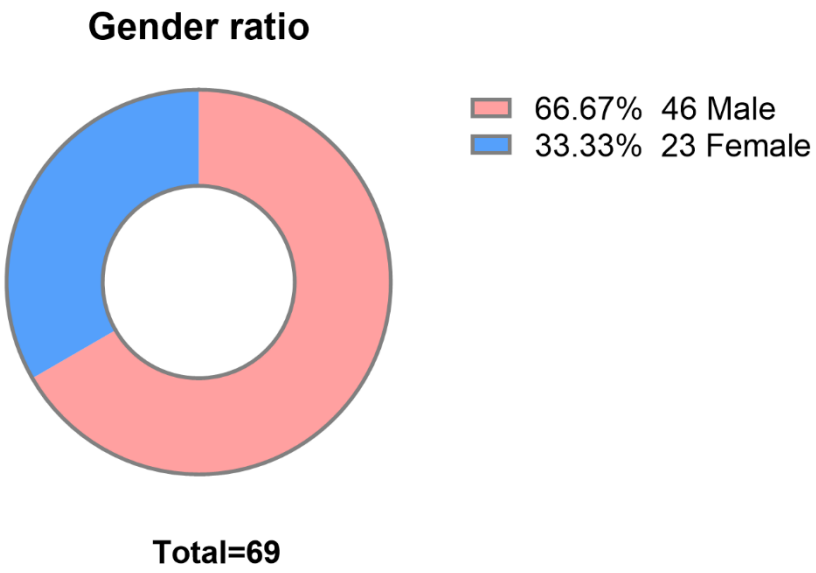

Figure 1: Gender Distribution of Study Participants

Figure 2

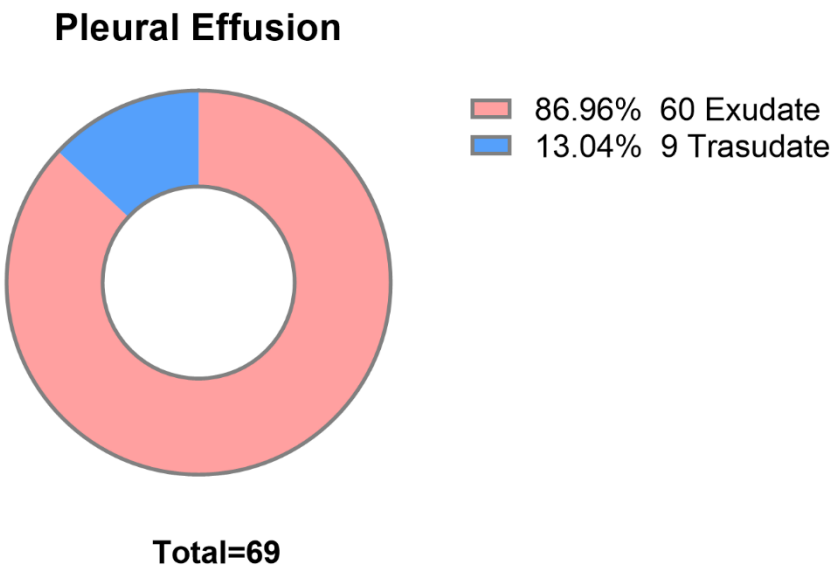

Figure 2: Distribution of Pleural Effusion Types

Figure 3

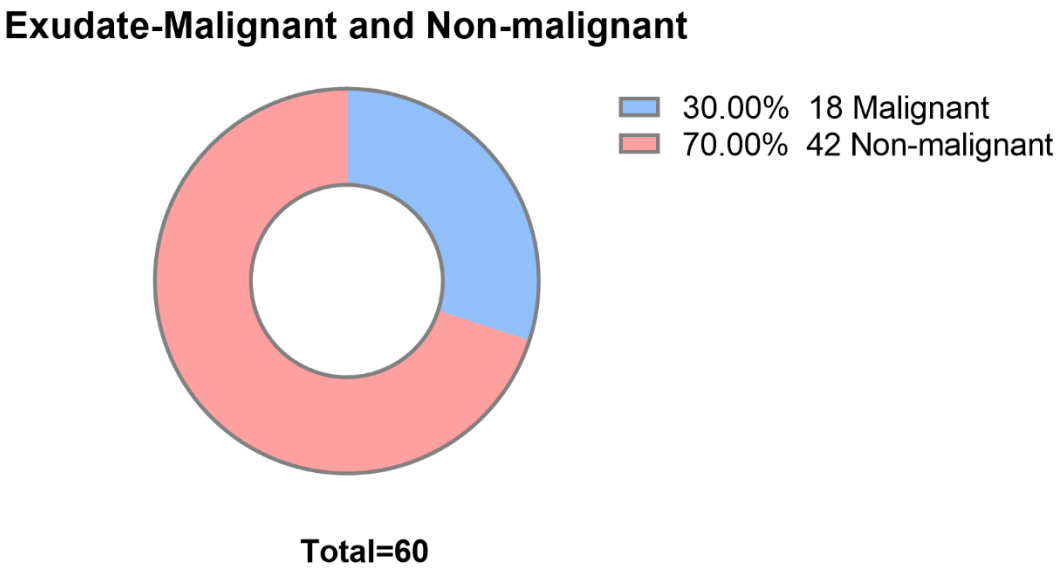

Figure 3: Proportion of Malignant and Non-Malignant Exudative Pleural Effusions

Figure 4

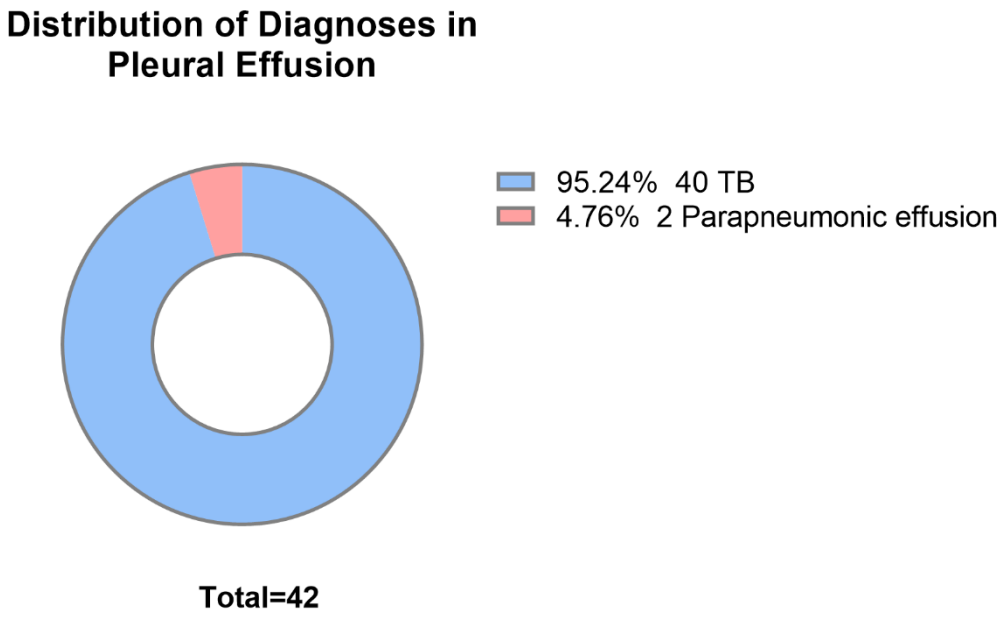

Figure 4: Distribution of Diagnoses in Non-Malignant Pleural Effusions

Figure 5

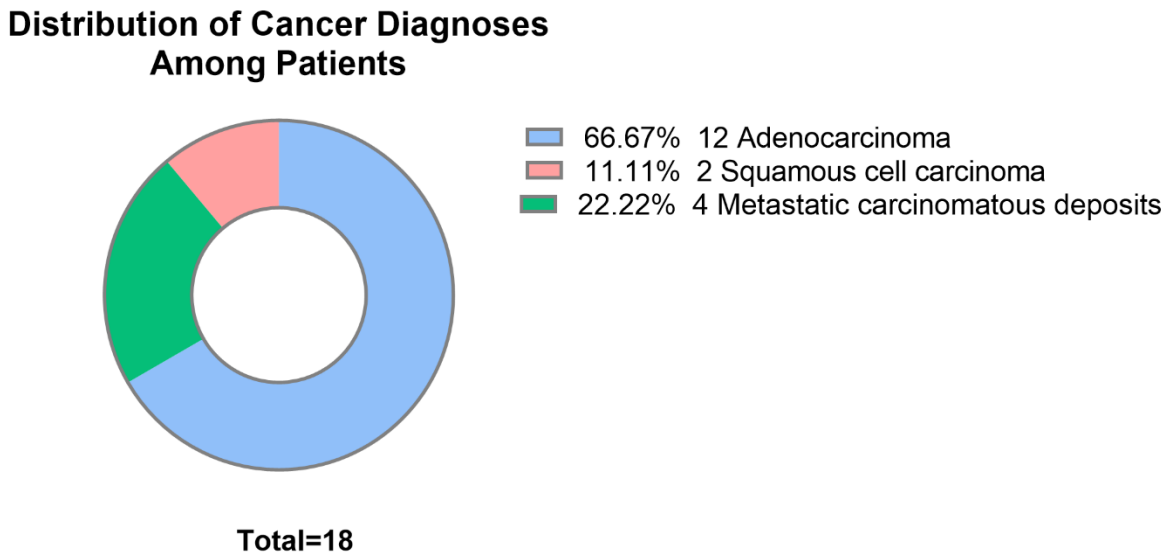

Figure 5: Distribution of Cancer Diagnoses Among Patients with Malignant Pleural Effusions

Figure 6

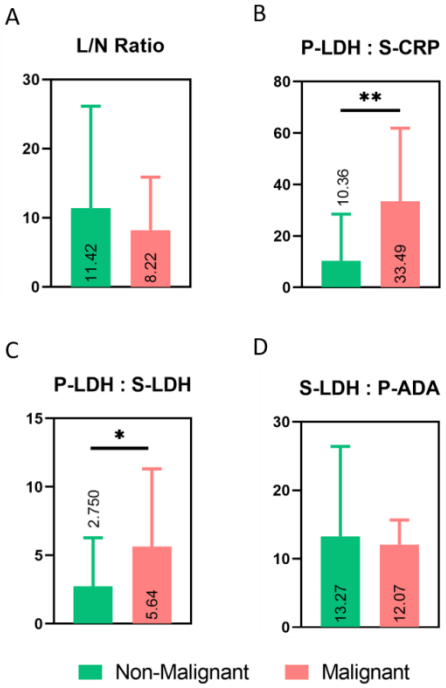

Figure 6: Comparison of Biomarker Ratios Between Malignant and Non-Malignant Pleural Effusions. Bar plots represent the mean ± standard deviation of various biomarker ratios, (A): L/N Ratio, (B): P-LDH:S-CRP, (C): P-LDH:S-LDH, and (D): S-LDH:P-ADA, between malignant and non-malignant pleural effusion groups. Statistical analysis was performed using Student's t-test, with significance levels indicated as *p < 0.05 and **p < 0.01.

Figure 7

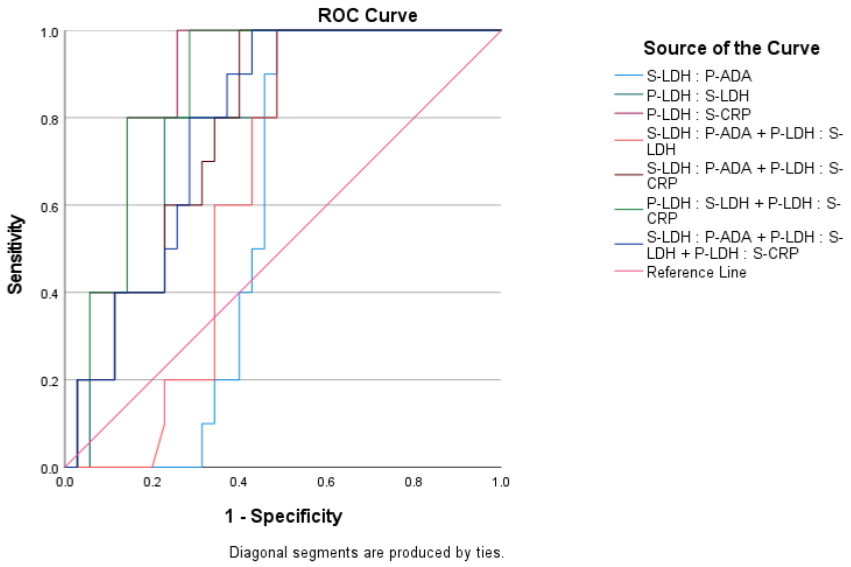

Figure 7: ROC Curve Analysis for Diagnostic Utility of Biomarker Ratios in Predicting Malignancy. Receiver Operating Characteristic (ROC) curves depicting the diagnostic performance of various biomarker ratios, including S-LDH:P-ADA, P-LDH:S-LDH, P-LDH:S-CRP, and combined ratios, in differentiating malignant from non-malignant pleural effusions. The Area Under the Curve (AUC) values for each ratio highlight their discriminatory power. The reference line represents random chance (AUC = 0.5).

List of abbreviations
ADA: Adenosine Deaminase
AUC: Area Under the Curve
CEA: Carcinoembryonic Antigen
CI: Confidence Interval
CR: Cancer Ratio
CRP: C-Reactive Protein
ESR: Erythrocyte Sedimentation Rate
LDH: Lactate Dehydrogenase
MPE: Malignant Pleural Effusion
NLR: Negative Likelihood Ratio
NPV: Negative Predictive Value
OR: Odds Ratio
PLR: Positive Likelihood Ratio
PPV: Positive Predictive Value
ROC: Receiver Operating Characteristic
S-ADA: Serum Adenosine Deaminase
S-CRP: Serum C-Reactive Protein
S-LDH: Serum Lactate Dehydrogenase
P-ADA: Pleural Adenosine Deaminase
P-CRP: Pleural C-Reactive Protein
P-LDH: Pleural Lactate Dehydrogenase
TB: Tuberculosis
TPE: Tuberculous Pleural Effusion