Section: Respiratory Medicine

Original Research Article

DIAGNOSTIC POTENTIAL OF CANCER RATIO (SERUM. LDH: PLEURAL. ADA) IN PREDICTING MALIGNANT PLEURAL EFFUSION

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ABSTRACT

Background: Malignant pleural effusion (MPE) is a common complication of advanced malignancies and often poses diagnostic challenges. The cancer ratio, calculated as the ratio of serum lactate dehydrogenase (LDH) to pleural fluid adenosine deaminase (ADA), has emerged as a potential non-invasive biomarker for differentiating malignant from non-malignant pleural effusions. The aim is to evaluate the diagnostic utility of the cancer ratio (serum LDH/pleural ADA) in predicting malignant pleural effusion among patients with exudative pleural effusions. **Materials and Methods:** This prospective observational study was conducted in the Department of Pulmonology, Mediciti Institute of Medical Sciences, Hyderabad, over 18 months. Sixty adult patients with exudative pleural effusions diagnosed according to Light's criteria were enrolled. Detailed clinical evaluation, imaging studies, serum biochemical analysis, and pleural fluid investigations including LDH, ADA, microbiology, and cytology were performed. The cancer ratio was calculated as serum LDH divided by pleural fluid ADA. Final diagnoses were established through cytology, histopathology, microbiological investigations, and clinical follow-up. Receiver operating characteristic (ROC) curve analysis was used to assess the diagnostic performance of the cancer ratio. **Results:** The mean age of participants was 45.4 ± 15.7 years, with males comprising 63.3% of the study population. Tubercular pleural effusion (60.0%) was the most common diagnosis, followed by malignant pleural effusion (21.7%) and parapneumonic effusion (18.3%). The mean cancer ratio was significantly higher in patients with MPE (32.3 ± 19.5) compared to tubercular pleural effusion (5.4 ± 7.0) and parapneumonic effusion (7.4 ± 6.3) ($p<0.001$). ROC analysis demonstrated excellent discriminatory ability of the cancer ratio for identifying MPE, with an area under the curve (AUC) of 0.96 (95% CI: 0.91–1.00; $p<0.001$). A cancer ratio >20 yielded a sensitivity of 92.3%, specificity of 93.6%, positive predictive value of 80.0%, negative predictive value of 97.8%, and overall diagnostic accuracy of 93.3%. **Conclusion:** The cancer ratio is a simple, inexpensive, and highly accurate non-invasive biomarker for differentiating malignant pleural effusion from other exudative pleural effusions. A cutoff value greater than 20 demonstrated excellent sensitivity and specificity, supporting its use as an adjunctive diagnostic tool in the evaluation of pleural effusions.

INTRODUCTION

Pleural effusion is a common clinical condition characterized by the accumulation of excess fluid in the pleural space, the area between the lungs and the chest wall. It can result from a wide range of etiologies, including infections (such as tuberculosis and pneumonia), congestive heart failure, pulmonary embolism, and malignancies. Pleural effusions are broadly classified into transudative and exudative

types based on Light's criteria, with exudative effusions being associated with inflammation, infection, or malignancy. Diagnostic evaluation typically includes pleural fluid analysis, cytology, and imaging studies to determine the underlying cause.[1,2,3]

In recent years, attention has turned to biochemical markers such as serum lactate dehydrogenase (LDH) and pleural fluid adenosine deaminase (ADA), which reflect tumor metabolism and immune activity, respectively. The cancer ratio, defined as serum LDH divided by pleural ADA, has emerged as a potentially valuable, non-invasive diagnostic marker for MPE.[4]

This study explores the diagnostic utility of the cancer ratio in predicting malignant pleural effusions, addressing the need for reliable alternatives to invasive diagnostic techniques. Serum LDH is a marker of cellular breakdown and is typically elevated in malignancy. Pleural fluid ADA is most commonly associated with tuberculous effusions and is used to distinguish tuberculosis from other causes. Based on the contrasting behavior of these markers in different disease states, the cancer ratio (serum LDH: pleural ADA) has been proposed as a simple, cost-effective method to distinguish malignant from non-malignant exudative effusions. Several preliminary studies have suggested its potential as a supportive diagnostic tool.[4]

With cytological analysis often yielding inconclusive results and invasive procedures being impractical in many cases, there is a pressing need for reliable, non-invasive markers that can aid in the early diagnosis of MPE. The cancer ratio, derived from easily obtainable serum and pleural fluid samples, offers a practical and affordable alternative. By systematically evaluating the cancer ratio in patients with exudative pleural effusions and correlating it with final diagnostic outcomes, this study seeks to validate its diagnostic performance and assess its sensitivity and specificity. The findings may help determine whether the cancer ratio can serve as a supportive tool in identifying MPE and guide further diagnostic decisions.[5]

MATERIALS AND METHODS

This prospective observational study was conducted in the Department of Pulmonology, Mediciti Institute of Medical Sciences, Hyderabad, over a period of 18 months after obtaining approval from the Institutional Ethics Committee. Adult patients presenting to the Pulmonology Outpatient Department or admitted to the hospital with pleural effusion and diagnosed as having exudative pleural effusion according to Light's criteria were consecutively enrolled in the study.

Sample Size: A total of 60 patients with exudative pleural effusion were included in the study.

Inclusion Criteria

- Patients aged ≥18 years.
- Patients diagnosed with exudative pleural effusion based on Light's criteria.
- Patients willing to provide written informed consent.

Exclusion Criteria

- Patients with transudative pleural effusions.
- Patients with congestive cardiac failure, chronic kidney disease, liver failure, or other systemic disorders likely to cause transudative pleural effusions.
- Patients unwilling to participate in the study.
- Patients with incomplete clinical or laboratory data.

Data Collection: After obtaining written informed consent, detailed demographic and clinical information was recorded, including age, sex, presenting symptoms, comorbidities, smoking status, personal and family history, and relevant medication history. A thorough general and respiratory system examination was performed in all participants.

Laboratory Investigations: Venous blood samples were collected for routine biochemical investigations, including serum protein and serum lactate dehydrogenase (LDH) levels. Diagnostic thoracentesis was performed under aseptic precautions, and pleural fluid samples were analyzed for:

- Protein concentration
- Lactate dehydrogenase (LDH)
- Adenosine deaminase (ADA)
- Cytological examination
- Microbiological analysis, including Gram staining, Ziehl–Neelsen staining, and culture where indicated

Pleural effusions were classified as exudative or transudative according to Light's criteria. An effusion was considered exudative if one or more of the following were present:

- Pleural fluid protein/serum protein ratio >0.5
- Pleural fluid LDH/serum LDH ratio >0.6
- Pleural fluid LDH > two-thirds of the upper limit of normal serum LDH

Imaging Evaluation: All patients underwent chest radiography. Contrast-enhanced computed tomography (CT) of the thorax and transthoracic ultrasonography were performed whenever clinically indicated to assess the extent and characteristics of pleural effusion and associated pulmonary or pleural abnormalities.

Diagnostic Confirmation: The final diagnosis of malignant pleural effusion was established by positive pleural fluid cytology and/or histopathological confirmation obtained through ultrasound-guided closed pleural biopsy or medical thoracoscopy-guided pleural biopsy. Non-malignant pleural effusions were diagnosed based on microbiological, cytological, histopathological findings and clinical follow-up.

Cancer Ratio Calculation: The Cancer Ratio (CR) was calculated for each participant using the following formula:

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Cancer Ratio=Serum LDH/Pleural Fluid ADA

The diagnostic performance of the Cancer Ratio in predicting malignant pleural effusion was evaluated by comparing values between malignant and non-malignant exudative pleural effusions.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using Statistical Package for Social Sciences (SPSS) version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD) or median (interquartile range) as appropriate, while categorical variables were expressed as frequencies and percentages. Comparisons between groups were performed using the independent Student's t-test or Mann–Whitney U test for continuous variables and Chi-square test or Fisher's exact test for categorical variables. Receiver Operating Characteristic (ROC) curve analysis was performed to determine the optimal cutoff value of the Cancer Ratio for predicting malignant pleural effusion and to calculate sensitivity, specificity, positive predictive value, negative predictive value, and area under the curve (AUC). A p-value <0.05 was considered statistically significant.

RESULTS

Table 1: Age and Gender distribution of study participants

Age groups (years)	Number	Percentage
0-30	12	20.0
31-50	23	38.3
51-60	15	25.0
>60	10	16.7
Total	60	100.0

The mean (SD) age was 45.4 (15.7) years with the minimum of 13 and maximum 0f 77 years. Out of 60 participants included in the study, the highest proportion (38.3%) belonged to the 31–50 years age group, indicating that middle-aged individuals formed the largest segment of the study population. This was followed by 25.0% in the 51–60 years age group and 20.0% in the 0–30 years age group. Participants aged above 60 years constituted the smallest proportion at 16.7%. Out of all the participants included, 63.3% were male (n=38) and 36.7% were female (n=22), indicating a predominance of male participants.

Table 2: Type of pleural effusion diagnosed

Final diagnosis	Number	Percentage
Tubercular Pleural effusion	36	60.0
Para pneumonic effusion	11	18.3
Malignant pleural effusion	13	21.7

The majority were diagnosed with Tubercular Pleural Effusion, accounting for 36 (60.0%) of the cases. 11 (18.3%) participants were diagnosed with Para Pneumonic Effusion, and 13 (21.7%) had Malignant Pleural Effusion.

Table 3: Cancer ratio (Serum LDH/ Serum ADA)

Cancer ratio	Number	Percentage
Up to 20	45	75.0
>20	15	25.0
Total	60	100.0

Among the 60 participants, the majority, 45 (75.0%), had a Cancer ratio of up to 20, while 15 (25.0%) had a Cancer ratio greater than 20.

Table 4: Comparison of few parameters across the Different kinds of pleural effusion

	TPE		PPE		MPE		P value	Bonferroni P value		
Parameter	Mean	SD	Mean	SD	Mean	SD		P1	P2	P3
Age	39.1	13.4	54.1	14.0	59.7	12.3		0.003	<0.001	1.0
ESR	64.2	13.7	26.2	7.0	67.8	15.6		<0.001	1.0	<0.001
HbA1C	5.8	1.1	6.0	1.0	5.8	1.0	0.82			
Serum LDH	242.1	104.1	157.7	69.1	413.6	189.6		0.08	<0.001	<0.001
Serum Protein	6.4	0.9	6.0	0.3	6.2	0.6	0.22			
Pleural Effusion (l)	1.6	0.9	1.2	0.5	2.5	1.2		0.58	0.03	0.005
Pleural fluid Glucose	71.6	8.2	89.3	15.0	102.6	13.7	<0.001	<0.001	<0.001	0.01
Pleural fluid protein	5.3	0.5	5.0	0.7	4.7	1.5	0.08			
Pleural fluid LDH	655.7	390.4	309.2	48.3	604.7	644.2	0.06			
Pleural fluid ADA	72.7	36.4	23.8	10.1	16.6	12.6	<0.001	<0.001	<0.001	1.0
Pleural effusion cell count	1847.4	935.3	1388.5	393.2	1366.6	200	0.08			
Cancer ratio	5.4	7.0	7.4	6.3	32.3	19.5	<0.001	1.0	<0.001	<0.001

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Difference between TPE and PPE, P2-between TPE and MPE, P3-PPE and MPEAge: The mean age of the TPE group (39.1 years) is significantly lower than both the PPE (54.1 years) and MPE (59.7 years) groups. The P-values show a significant difference between TPE and PPE (P1 = 0.003), as well as between TPE and MPE (<0.001), suggesting that the age of participants with TPE is significantly younger than those with PPE and MPE. There is no significant difference between PPE and MPE (P3 = 1.0). Erythrocyte Sedimentation Rate (ESR): The TPE group has a significantly higher ESR (64.2) compared to both PPE (26.2) and MPE (67.8). The P-values confirm significant differences, with P1 (<0.001) and P2 (<0.001) indicating that ESR is significantly higher in the TPE and MPE groups compared to the PPE group.Serum LDH: Serum LDH is significantly higher in the MPE group (413.6) compared to both the TPE (242.1) and PPE (157.7) groups, as indicated by the P-values for P2 (<0.001) and P3 (<0.001).Pleural Effusion (l): The pleural effusion volume in the MPE group (2.5 liters) is significantly higher than in the TPE (1.6 liters) and PPE (1.2 liters) groups, with significant P-values for P2 (0.03) and P3 (0.005).Pleural Fluid Glucose Pleural fluid glucose is significantly lower in the TPE group (71.6) compared to PPE (89.4) and MPE (102.6), with significant P-values for P1 and P2 (<0.001) and P3 (0.02).

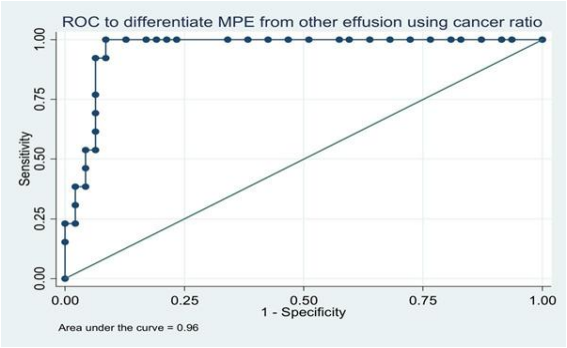

Figure 1: ROC to differentiate the MPE from other effusions using cancer ratio

Table 5: ROC to differentiate the MPE from other effusions using cancer ratio

Parameter	Area under the curve	P value
Cancer Ratio	0.96 (0.91-1.00)	<0.001

The ROC area under the curve was 0.96 showing that the cancer ratio could be used as a marker in differentiating malignant effusion from other kinds of effusion.

Table 6: Diagnostic performance of Cancer ratio in differentiating MPE from other effusion

Caner ratio	MPE		Total
	Yes	No	
>20	12	3	15
Up to 20	1	44	45
Total	13	47	60

Parameter	Point estimate	95 % Confidence limit
Sensitivity	92.3	64.0-99.8
Specificity	93.6	82.5-98.7
Positive predictive value	80.0	51.9-95.7
Negative predictive value	97.8	88.2-99.9
Diagnostic accuracy	93.3	83.8-98.2

The sensitivity was 92.3%, indicating that it correctly identified 92.3% of true positive cases, with a 95% confidence interval (CI) ranging from 64.0% to 99.8%. The specificity was also high at 93.6% (95% CI: 82.5%–98.7%). The positive predictive value (PPV) was 80.0% (95% CI: 51.9%–95.7%), and negative predictive value (NPV) was notably high at 97.8% (95% CI: 88.2%–99.9%), indicating that nearly all individuals with a negative test result were truly disease-free. Overall, the diagnostic accuracy of the test was 93.3% (95% CI: 83.8%–98.2%), confirming its reliability as a diagnostic tool.

DISCUSSION

The present study enrolled 60 participants with a mean age of 45.4 years (SD= 15.7), ranging from 13 to 77 years. A majority of patients (38.3%) belonged to the 31–50 age group, followed by 25.0% in the 51–60 range, and 20.0% were ≤30 years. Only 16.7% were older than 60 years, suggesting a predominant middle-aged population affected by pleural effusion. In a study by Verma et al. (2016), a higher mean age was reported (52.3 years), suggesting that malignant pleural effusions tend to occur in older individuals.[1] In terms of gender distribution, males accounted for a higher proportion of participants (63.3%), while females represented 36.7%, indicating a male preponderance among patients presenting with pleural effusion in this cohort. Han et al. (2019) in a large meta-analysis also noted a male predominance in pleural effusion cases, particularly in tubercular and malignant etiologies.[2]

Diagnostically, tubercular pleural effusion (TPE) was the most common cause (60%), followed by malignant pleural effusion (MPE, 21.7%) and parapneumonic effusion (PPE, 18.3%), reflecting the high burden of TB-related effusions in endemic

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areas. Nishanth et al. (2022) also found TPE to be the leading cause (66%) followed by PPE and MPE, reinforcing TB's continued dominance in Indian clinical settings.[3]

Laboratory parameters showed high mean ESR (56.5 mm/hr), pleural ADA (51.6 U/L), and pleural fluid LDH (581.1 U/L). Mean serum LDH was 249.5 U/L, serum protein 6.3 g/dL, pleural fluid protein 5.2 g/dL, glucose 81 mg/dL, and pleural volume drained averaged 1.6 L. The cancer ratio (serum LDH/ADA) had a mean of 11.6, with a wide range (1.1–73.3), suggesting diagnostic variability. Verma et al. (2016) reported comparable ADA levels in TPE (>70 U/L) and lower values in MPE and PPE, affirming ADA's diagnostic utility.[1,6,7]

Comparative analysis across effusion types demonstrated statistically significant age differences: mean age was 39.1 years in TPE, 54.1 in PPE, and 59.7 in MPE ($p < 0.001$). ESR was significantly higher in MPE (67.8) and TPE (64.2) compared to PPE (26.2) ($p < 0.001$). Pleural ADA was markedly higher in TPE (72.7) than PPE (23.8) and MPE (16.6) ($p < 0.001$). Cancer ratio was significantly elevated in MPE (32.3) and PPE (7.4) vs TPE (5.4) ($p < 0.001$). Pleural fluid glucose is significantly lower in the TPE group (71.6) compared to PPE (89.4) and MPE (102.6), with significant P-values for P1 and P2 (<0.001) and P3 (0.02). Pleural volume was largest in MPE (2.5 L), significantly greater than in PPE (1.2 L, $p = 0.03$) and TPE (1.6 L, $p = 0.005$). These intergroup differences are consistent with findings by Verma et al. (2016) and Han et al. (2019), both of whom emphasized ADA and cancer ratio as discriminators between TB and malignant effusions.[1,2]

The ROC analysis for the cancer ratio showed excellent discriminatory power for MPE with an area under the curve (AUC) of 0.91–1.000 ($p < 0.001$), indicating near-perfect diagnostic performance. Verma et al Demonstrated a high AUC (~1.0) for cancer ratio in diagnosing MPE and reported sensitivity, specificity, PPV, NPV, and accuracy values comparable to your findings.[1] Diagnostic performance parameters showed that a cancer ratio >20 had a sensitivity of 92.3% and specificity of 93.6% for identifying MPE, with a positive predictive value (PPV) of 80% and negative predictive value (NPV) of 97.8%.[8,9,10]

The overall diagnostic accuracy was 93.3% (95% CI: 83.8–98.2), emphasizing the robustness of cancer ratio as a non-invasive biomarker for malignancy-related pleural effusions. Han et al found pooled AUC >0.95, with sensitivity ~90% and specificity ~96–100%, reinforcing the diagnostic power of cancer ratio >20.[2,11,12]

CONCLUSION

This study highlights that tubercular pleural effusion remains the predominant cause of pleural effusions in a middle-aged Indian population, with malignant and parapneumonic effusions more common in older patients. A clear male predominance was observed. Clinical features such as cough, fever, and dyspnea were common across all groups. Diagnostic parameters, particularly pleural ADA and the cancer ratio (serum LDH/ADA), proved highly effective in differentiating tubercular from malignant effusions. The cancer ratio >20 demonstrated excellent sensitivity and specificity, validating its role as a reliable non-invasive biomarker for malignant pleural effusion diagnosis. These findings underscore the importance of integrating clinical, biochemical, and demographic data to optimize diagnosis and management of pleural effusions in endemic settings.

REFERENCES

1. Verma A, Abisheganaden J, Light RW. Identifying Malignant Pleural Effusion by A Cancer Ratio (Serum LDH: Pleural Fluid ADA Ratio). Lung. 2016 Feb;194(1):147–53.
2. Han YQ, Zhang L, Yan L, Ouyang PH, Li P, Hu ZD. Diagnostic accuracy of cancer ratio for malignant pleural effusion: a systematic review and meta-analysis. Ann Transl Med. 2019 Oct;7(20):554.
3. Nishanth PS, Devassy TV, Jose T. Diagnostic utility of cancer ratio in differentiating malignant from non-malignant pleural effusions in a tertiary care centre in central Kerala. Int J Adv Med. 2022 Jan 25;9(2):102.
4. Verma A, Dagaonkar RS, Marshall D, Abisheganaden J, Light RW. Differentiating Malignant from Tubercular Pleural Effusion by Cancer Ratio Plus (Cancer Ratio: Pleural Lymphocyte Count). Can Respir J. 2016;2016:1–6.
5. Huang JH, Chen H, Zhang ZC, Gu J, Yan L, Jiang MP, et al. Age affects the diagnostic accuracy of the cancer ratio for malignant pleural effusion. BMC Pulm Med. 2023 Jun 7;23(1):198.
6. Porcel JM, Azzopardi M, Koegelenberg C, Maldonado F, Rahman N, Lee Y. The diagnosis of pleural effusions. Expert Rev Respir Med. 2015 Nov 2;9(6):801–15.
7. Light RW. Pleural Effusion. N Engl J Med. 2002 Jun 20;346(25):1971–7.
8. Heffner JE. Diagnosis and management of malignant pleural effusions. Respirology. 2008 Jan;13(1):5–20.
9. Jacobs B, Sheikh G, Youness HA, Keddissi JI, Abdo T. Diagnosis and Management of Malignant Pleural Effusion: A Decade in Review. Diagnostics. 2022 Apr 18;12(4):1016.
10. Maskell N, Gleeson F, Davies R. Standard pleural biopsy versus CT-guided cutting-needle biopsy for diagnosis of malignant disease in pleural effusions: a randomised controlled trial. The Lancet. 2003 Apr;361(9366):1326–30.
11. Feller-Kopman DJ, Reddy CB, DeCamp MM, Diekemper RL, Gould MK, Henry T, et al. Management of Malignant Pleural Effusions. An Official ATS/STS/STR Clinical Practice Guideline. Am J Respir Crit Care Med. 2018 Oct 1;198(7):839–49.
12. Rolston D, Diaz-Guzman E, Budev MM. Accuracy of the physical examination in evaluating pleural effusion. Cleve Clin J Med. 2008 Apr 1;75(4):297–303.

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