ORIGINAL RESEARCH PAPER
Volume - 12 | Issue - 03 | March - 2023 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

DIAGNOSTIC UTILITY OF CANCER RATIO IN DIFFERENTIATING MALIGNANT PLEURAL EFFUSION FROM NON-MALIGNANT EXUDATIVE PLEURAL EFFUSION.

Respiratory Medicine

Dr T. Ganesh Final Year Postgraduate, Department Of Respiratory Medicine, Trichy SRM Medical College Hospital And Research Centre, Irungalur, Trichy-621105

Dr. P. H. Santhoshkumar M.D, Professor And Hod, Department Of Respiratory Medicine, Trichy SRM Medical College Hospital And Research Centre, Irungalur, Trichy-621105

Dr. R. Velraj M.D, Associate Professor, Department Of Respiratory Medicine, Trichy SRM Medical College Hospital And Research Centre, Irungalur, Trichy-621105

ABSTRACT

Introduction: Malignant pleural effusion (MPE) is caused by malignant tumors originating in the pleura or metastasis of malignant tumors from other locations to the pleura, Pleural fluid cytological or pleural pathological examination is helpful for the diagnosis of MPE, but the positive rate of MPE is approximately 60%, the serum lactate dehydrogenase (sLDH)/ pleural fluid adenosine deaminase (pfADA) ratio had high sensitivity and specificity for diagnosing MPE and it was called cancer ratio. Our study aimed to study the role of cancer ratio (Serum LDH / Pleural fluid ADA) in predicting malignancy in patients with exudative pleural effusion. **Methodology:** This study is done as a Retrospective study in 80 patients admitted with exudative pleural effusion. In a period of one year 6 months from September 2020 to May 2022. Patients with age more than 18 and less than 80 were included. While patients with transudative pleural effusion and other comorbidities were excluded. **Results:** In our study population of 80 patients, 60 were male and 20 were female. Among these 45 patients had Tuberculosis, 15 had parapneumonic effusion and the rest 20 had malignancy. We evaluated the Cancer ratio and other pleural fluid parameters. Pleural LDH and ADA were increased in TB and parapneumonic effusion whereas in malignant patients the ADA levels were less which in turn ended up in significantly higher cancer ratio values. Sensitivity was 92% and specificity was 86%. **Conclusion:** CR has high diagnostic accuracy for MPE.Sensitivity and specificity are two basic metrics of a diagnostic tool. Both were higher in our study. Hence it's advisable to explore further studies to genuinely consider CR as a reliable marker.

KEYWORDS

Cancer ratio, Malignant Pleural effusion, Pleural fluid.

INTRODUCTION

Pleural effusion (PE) is one of the frequently encountered illnesses among patients who visit the department of emergency, respiratory or thoracic diseases (1). Etiologies of PE are many, with the most common reason being tuberculosis pleural effusion (TPE), parapneumonic effusion (PPE), malignant pleural effusion (MPE), heart failure (HF), and others (2). The diagnosis of MPE is typically made with PE cytology or thoracentesis with pleural biopsy. Cytology is a cheap diagnostic tool with high specificity. Pleural biopsy is commonly used for MPE diagnosis.

At present differentiation between two types of pleural effusion - exudate and transudate is the initial investigative methodology used in patients with pleural effusion. Further evaluation of specific diseases associated with the formation of pleural exudate usually requires a more in-depth analysis of pleural fluid, including total and differential cell count, pH and glucose levels, adenosine deaminase (ADA) activity, as well as cytological and microbiological examinations. If inconclusive, the tests are followed by more invasive diagnostic procedures.

In some patients, the clinical, radiological, and laboratory results might be confusing and not particularly helpful in making a reliable diagnosis. This refers not only to patients with rare diseases but also to those with common causes of pleural involvement, such as malignant pleural effusion (MPE). Although MPE can be diagnosed by simple pleural fluid cytology, this method has significant limitations, including a highly variable sensitivity, ranging from as low as 11.6% to as high as 71%.

Biomarkers in PE have been considered to be useful tools for MPE diagnosis (3). Compared with biopsy and cytology, biomarker has some advantages, including inexpensiveness, mini-invasiveness, and objective results.

Recently, Verma et al reported a new biochemical parameter that showed high diagnostic accuracy for pleural malignancies (4). This is a quotient of serum lactate dehydrogenase (LDH) and pleural fluid ADA, termed by the authors as the "cancer ratio" (CR). At the cut-off level of more than 20, the CR showed high sensitivity and specificity for identifying patients with MPE. The high diagnostic performance of this parameter is based on the observations that MPE is usually associated with high serum LDH levels, while TP—is with high pleural fluid ADA levels. Based on this aim of our study is to evaluate the Diagnostic utility of the cancer ratio in differentiating malignant pleural effusion from non-malignant exudative pleural effusion.

MATERIALS AND METHODOLOGY

This study was done as a retrospective study in 80 patients; all the patients admitted with exudative pleural effusion above age of 18 years to 80 years in the time period of September 2020 to March 2022 were included in the study. Patients with congestive cardiac failure, chronic renal failure, decompensated liver disease, AIDS patients, trauma patients and pancreatic pleural effusion were excluded from the study.
This study was conducted in the Department of Respiratory Medicine, Trichy SRM medical college Hospital and Research center, a tertiary care center, TrichyThe details of the Patients admitted with pleural effusion were collected, those in whom pleural effusion was transudative were excluded from analysis, we collected data on the biomarkers like serum LDH, pleural fluid protein, sugars, LDH, and ADA levels,

In case of malignancy the conformation of the final diagnosis was based on pleural fluid cytology or pleural biopsy histology, in tuberculosis pleural effusion the diagnosis was based on pleural fluid microbiology results, histopathology results and raised ADA levels. In case of Parapneumonic effusion, the diagnosis was based on low levels of pH, glucose, neutrophilic predominance, and growth of pyogenic organisms on pleural fluid culture. We analyzed the serum LDH: pleural fluid ADA ratio as a predictor of malignant pleural effusion.
Institutional ethical committee approval was obtained for this study with waiver of consent;we used SPSS(v22) software for all statistical analysis.

RESULTS

In our study of 80 patients, 50 patients (62%) were male and the rest 30 (38%) were females. Coming to age group most of the patients were in age group 51- 60 years (n=21). This was followed by 41-50 years (n=17), 61-70 years (n=15), while 10 patients were above 70 years.
Among 80 patients 45 were diagnosed with tuberculosis, para pneumonic effusion was in 15 patients and malignancy was in 20 patients.

We next did the pleural fluid analysis and mean serum protein was higher in malignancy, similar sugar levels were also high in malignancy and tuberculosis, Pleural fluid LDH and ADA, and serum

LDH was higher in parapneumonic effusion.

Table 1: Plural fluid analysis

Mean Valaues	Tb Pleural Effusion	Parapneumonic Effusion	Malignancy
PROTEIN	4.9	5.1	5.5
SUGAR	77	48	80
PL FLUID LDH	447	683	669
PL FLUID ADA	77	85	32
SR LDH	217	308	248

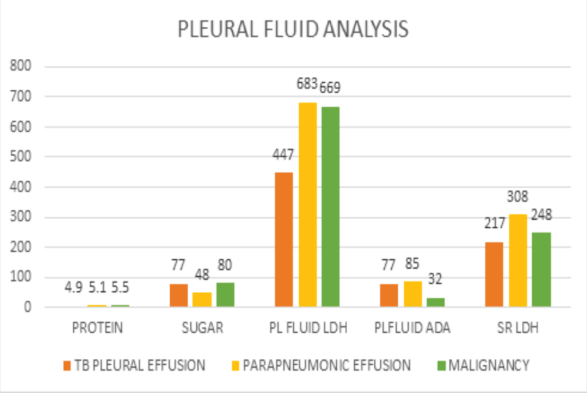

Chart 1: Pleural fluid analysis

Next, we analyzed serum LDH: pleural fluid ADA ratio which is considered as the cancer ratio, both categorically and using mean values, categorically the CR ratio was increased in 95% (n=19) of patients having malignancy which was statistically significant too.

Table 2: Cancer ratio

Diagnosis	Cancer Ratio	
	Increased	Normal
TB PLEURAL EFFUSION	2	43
PARAPNEUMONIC EFFUSION	3	12
MALIGNANCY	19	1
P VALUE - 0.001		
SIGNIFICANT		
CHI-SQUARE TEST		

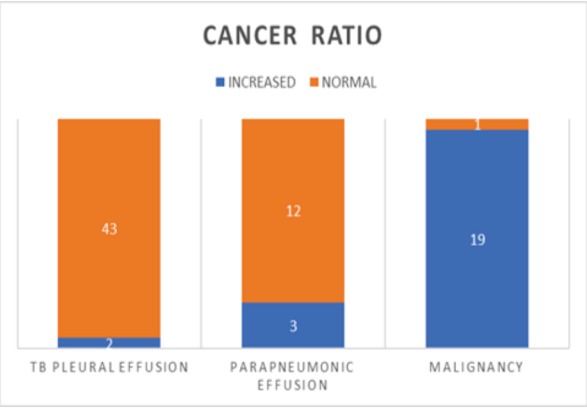

Chart 2: Cancer ratio

Similarly, the mean cancer ratio was calculated and it was very high in patients diagnosed with malignancy as compared to that of tuberculosis and para pneumonic effusion with a p-value 0f 0.013 which was statistically significant.

Table 3: Mean cancer ratio

Cancer Ratio	Tb Pleural Effusion	Para Pneumonic Effusion	Malignancy
MEAN	5.8	8.03	20.9
SD	0.89	1.32	1.89
ANOVA			
P VALUE -0.013			
SIGNIFICANT			

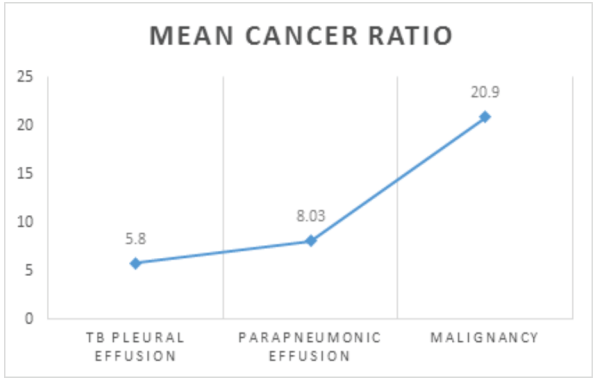

Chart 3: mean caner ratio

The sensitivity and specificity were 95 % and 91.67 %, respectively. The Positive predictive value (PPV) was 79.17% and the negative predictive value was 98.21 %. CR>20 has a p-value of 0.001

DISCUSSION

The cancer ratio is the ratio of serum LDH and pleural fluid ADA. ADA level is known to be low in malignant effusion. However, it is not appropriate to use these low levels to diagnose malignant effusion due to a lack of linear biochemical relationship between them. Serum LDH, however, is high in malignancies and is a well-known finding. Thus theoretically, the serum LDH: Pleural fluid ADA ratio should be significantly higher in patients presenting with malignant pleural effusion and hence help to discriminate between malignant and non-malignant effusion.

Serum LDH is a ubiquitous cellular enzyme, which rises in reaction to tissue injury. Raised serum LDH is found in many clinical situations, very high and isolated serum LDH might be a marker of specific illnesses. Serum LDH is elevated in cancer as the cancer cells don't depend on oxidative phosphorylation for energy utilization, instead preferential use of glycolysis for energy by tumor cells, a switch in the ATP generation pathway which is intermediated by LDH.

ADA is a known biomarker of tuberculous pleural effusion. ADA plays an important role in purine nucleoside metabolism and is secreted by mononuclear cells, lymphocytes, neutrophils, and RBCs. High levels show a relationship with infective conditions such as TB (ADA-2) and empyema (ADA1).MPE patients characteristically show low levels of ADA, but whether this can help MPE diagnosis is unclear.

For undiagnosed exudative pleural effusion, the clinical usefulness of CR for the diagnosis of MPE is that it can help guide treatment plans: patients with high CR values (>20) must be treated with caution, and further diagnostic examinations such as repeated cytological test, invasive procedures such as medical thoracoscopy and pleural biopsy should be considered.

In our study dominant etiology of exudative pleural effusion was tuberculosis which is in similarity to a few studies from India where tuberculosis was the most common etiology. Our study findings were not in concordance with the study by Akash Verma (5) et al where the incidence of malignant pleural effusions was 61.3%.

Cough and dyspnea were observed to be the most common presenting symptoms in our study. The most common symptom encountered by patients with pleural effusions related to nonmalignant variants is a dry cough, followed by breathlessness, fever, and chest pain.In a study by Arun Gopi et al the most common symptom was chest pain followed by dry cough.(6)

In the present study, we have observed that the serum LDH is significantly higher among the parapneumonic effusion and malignant pleural effusion when compared to other etiologies. This is in concordance with the study conducted by Akash Verma et al.(5)

Cancer ratio with a cut-off level of ≥20 is highly predictive of malignancy in patients with exudative pleural effusion with high sensitivity (98%) and specificity (94%) in the study done by Akash verma et al.(5) Our study had a sensitivity and specificity of 95 % and 91.67% respectively. We had almost similar sensitivity and specificity in comparison to the above study. Thus as per our study, the diagnostic

cut-off of 20 gives a better diagnostic prediction and would help in differentiating between malignant and nonmalignant etiologies and also guide us to look for malignancy elsewhere if the cancer ratio is more than 20.

CONCLUSION

CR has high diagnostic accuracy for MPE. Sensitivity and specificity are two basic metrics of a diagnostic tool. Both were higher in our study. Hence it's advisable to explore further studies to genuinely consider CR as a reliable marker.

REFERENCES

1. Porcel JM, Azzopardi M, Koegelenberg CF, et al. The diagnosis of pleural effusions. Expert Rev Respir Med. 2015; 9:801–15.
2. Light RW. Clinical practice. Pleural effusion. N Engl J Med. 2002; 346:1971–7.
3. Huo ZY, Peng L. Is Xpert MTB/RIF appropriate for diagnosing tuberculous pleurisy with pleural fluid samples? A systematic review. BMC Infect Dis. 2018; 18:284.
4. Verma A, Abisheganaden J, Light RW. Identifying malignant pleural effusion by a cancer ratio (Serum LDH: Pleural Fluid ADA Ratio). Lung. 2016; 194:147–53.
5. Verma A, Dagaonkar RS, Marshall D, et al. differentiating malignant from tubercular pleural effusion by cancer ratio plus (cancer ratio: pleural lymphocyte count). Can Respir J. 2016; 2016:7348239.
6. Arun Gopi,Sethu M.Madhavan,Surendra K.Sharma,Steven A.Sahn.Diagnosis and treatment of Tuberculous pleural effusion.chest journal :2007;March 131(3):880-889.