

Original Research Article

“A STUDY ON EVALUATION OF THE UTILITY OF PLEURAL FLUID CHOLESTEROL AND LACTATE DEHYDROGENASE (LDH) IN DIFFERENTIATING EXUDATIVE FROM TRANSUDATIVE PLEURAL EFFUSIONS”

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ABSTRACT:

Background: Prevalence of Pleural effusion is approximately 400 /100000 population. Pleural effusion can manifest as a result of several diseases, both pulmonary and extrapulmonary. The pleura is susceptible to infections due to its direct apposition to other structures. For example, the parietal pleura over the diaphragm and chest wall is resistant to infection, whereas the parietal pleura lying over the mediastinum can be easily invaded by organisms.

OBJECTIVES:

1. To determine pleural fluid Cholesterol and LDH from pleural fluid analysis.
2. To determine the cut-off levels for pleural fluid cholesterol and LDH in our set up, given the variability of results from one laboratory to another.

MATERIAL & METHODS: Study Design: Prospective hospital based cross - sectional study. **Study area:** The present study was conducted in the department of TB & Respiratory medicine, Subbaiah Institute of Medical Sciences, Shimoga, Karnataka. **Study Period:** Mar. 2021 – Feb. 2022. **Study population:** Patients with Pleural Effusion evaluated in Department of Respiratory Medicine in Subbaiah Institute of Medical Sciences, Shimoga, Karnataka. **Statistical analysis: Analysis of variance (ANOVA)** has been used to find the significance of study parameters between three or more groups of patients, Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters.

Results: Analysing pleural fluid LDH and Cholesterol in exudative pleural effusions using student t test mean LDH level $772.52 + 144.56$ was moderately significant and mean cholesterol level $81.36 + 5.30$ was strongly significant. Analysing pleural fluid LDH and Cholesterol in transudative pleural effusions using student t test mean LDH level $116.06 + 32.89$ was moderately significant and mean cholesterol level $26.25 + 3.64$ was strongly significant.

CONCLUSION: From our study it can be concluded that, Pleural fluid cholesterol and LDH were found to be excellent pleural fluid parameters for differentiating exudative and transudative effusions from the study. They are both cost effective as well as technically feasible to analyse and hence could serve as better guides in the proper management of pleural effusion.

Keywords: pleural fluid Cholesterol and LDH, Pleural effusion, exudative and transudative effusions

INTRODUCTION:

Pleural Effusion refers to an abnormal or excessive accumulation of fluid in the pleural cavity. Pleural effusion is a commonly encountered medical problem by pulmonologists as well as general physicians caused by diverse pathological conditions. It is very important to establish accurate etiological diagnosis to treat the patient in an appropriate manner as about 15 to 20% of cases remain undiagnosed¹.

Prevalence of Pleural effusion is approximately 400 /100000 population². Pleural effusion can manifest as a result of several diseases, both pulmonary and extrapulmonary. The pleura is susceptible to infections due to its direct apposition to other structures. For example, the parietal pleura over the diaphragm and chest wall is resistant to infection, whereas the parietal pleura lying over the mediastinum can be easily invaded by organisms³.

Based on pathological abnormality and mechanism of formation, effusions may be transudative or exudative. Transudates occur when there are alterations of mechanical factors influencing formation or reabsorption. Exudates results from inflammation or irritation or other disease process involving the pleura, resulting in increased permeability.

Exudative pleural effusions are a common diagnostic problem in clinical practice, as the list of causes is quite exhaustive, although sometimes they can be inferred from the clinical picture⁴. The etiological distribution of pleural effusions depends on the geographical location, patient's age, and treatment of the underlying causes. Exudative effusions need to be separated into infectious, non-infectious and malignant depending on the underlying etiology.

Tuberculosis is the most common cause of exudative effusion in India followed by Malignancy⁵ whereas in the west malignancy and parapneumonic effusions are more common⁶. Pleural tuberculosis is second in frequency after TB lymphadenitis among extra pulmonary tuberculosis⁷. Sometimes etiological diagnosis of pleural effusion is difficult despite cytological, biochemical and microbiological tests⁸. Pleural biopsy is helpful to reach

an etiological diagnosis of exudative pleural effusion, particularly when malignancy is suspected or detailed pleural fluid study are inconclusive⁹.

Though there are many criteria to classify pleural effusions as transudative or exudative, the most commonly and extensively used has been LIGHT'S CRITERIA. The validity and reliability of other criteria for example the one to be used in the present study (COSTA'S CRITERIA) needs to be studied.

There are many studies in Western literature but very few studies in Indian literature, which have assessed the role of pleural fluid cholesterol and lactate dehydrogenase in differentiating between transudative and exudative pleural effusions. Using only cholesterol and lactate dehydrogenase level lowers the cost of the diagnostic procedure which is important in developing countries like India. There is hence a role for defining the best cost effective and diagnostic approach for quicker diagnosis of pleural effusion and hence the need for the present study.

OBJECTIVES:

1. To determine pleural fluid Cholesterol and LDH from pleural fluid analysis.
2. To determine the cut-off levels for pleural fluid cholesterol and LDH in our set up, given the variability of results from one laboratory to another.

MATERIAL & METHODS:

Study Design: Prospective hospital based cross - sectional study.

Study area: The present study was conducted in the department of TB & Respiratory medicine, Subbaiah Institute of Medical Sciences, Shimoga, Karnataka.

Study Period: Mar. 2021 – Feb. 2022.

Study population: Patients with Pleural Effusion evaluated in Department of Respiratory Medicine in Subbaiah Institute of Medical Sciences, Shimoga, Karnataka.

Sample size: Sample size was calculated using the N-master software based on the study by Judith and Jorge¹⁰. A minimum sample of 76 patients was required to achieve statistically significant results with 95% confidence and 10% relative precision.

Sampling method: Simple random Sampling Technique.

Inclusion criteria:

1. Patients aged > 18 years with pleural effusion.
2. Patients diagnosed with Pleural Effusion based on history, clinical examination and appropriate imaging modality (Chest radiography, USG Chest, CT Scan Chest).

Exclusion criteria:

1. Patients who are hemodynamically unstable.
2. Previous Thoracentesis
3. Traumatic pleural tap
4. Procedure related pleural effusion
5. Suspected Pulmonary Thromboembolism
6. Chylothorax, Haemothorax
7. Patients who are unwilling to participate in the study.

Ethical consideration: Institutional Ethical committee permission was taken prior to the commencement of the study.

Study tools and Data collection procedure:

- Structured proforma.
- Demographic data, detailed clinical history, and clinical examination findings were recorded.
- Laboratory tests –Relevant laboratory tests including Serum Cholesterol and LDH were performed in all patients.
- Pleural Fluid Analysis will include levels of protein,sugar,Adenosine De Aminase(ADA),cholesterol,LDH and albumin.Other parameters like cell count, malignant cytology,AFB stain and aerobic bacterial culture were done.
- Reports of Chest x-ray, USG Chest, CT Scan Chest were recorded.

The cost of the additional pleural fluid investigations was borne by the researcher.

Statistical analysis:

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean \pm SD (Min-Max) and results on categorical measurements are presented in Number (%). **Analysis of variance (ANOVA)** has been used to find the significance of study parameters between three or more groups of patients, Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. **Chi-square/ Fisher Exact test** has been used to find the significance of study parameters on categorical scale between two or more groups. Results with a p value of <0.05 was considered statistically significant.

OBSERVATIONS & RESULTS:

Table 1: Age distribution of patients

Age in years	No. of patients	%
<20	5	6.6
20-30	9	11.8
31-40	10	13.2
41-50	14	18.4
51-60	16	21.1
61-70	14	18.4
71-80	7	9.2
>80	1	1.3
Total	76	100.0

In the present study out of 76 patients, majority of patients 57.9% (n=44) belonged to the age group of 40-70 yrs with mean age of 48.97±17.03 yrs. Out of 76 patients, 69.7%(n=53) were males and 30.3% (n=23) were females.

TABLE 2: TYPE OF PLEURAL EFFUSION

	No. of patients (n=76)	%
Exudate	62	81.6
Transudate	14	18.4

In our present study of 76 pleural effusions, 81.6%(n=62) were exudates and 18.4%(n=14) were transudates. Among exudative pleural effusion the most common type was tubercular seen in 50%(n=38) patients followed by parapneumonic(15.8%) , empyema(6.6%) , malignant(3.9%) and paramalignant effusion(6.6%).Among paramalignant effusions; 2 were k/c/o Ca oesophagus, 1 was a case of brain metastasis with unknown primary, 1 was diagnosed with Ca ovary and 1 with Ca Endometrium. Among transudative pleural effusion CKD was the most common cause seen in 13.15%(n=10) of patients followed by CLD and CCF seen in 2.6%(n=2) of patients.

TABLE 3: Comparison of Hemoglobin, TLC and ESR in relation to Type of Effusion of patients studied

Variables	Type of Effusion					P value
	Tubercular	Parapneumonic	Empyema	Malignant	Paramalignant	
Hemoglobin (g/dl)	12.58±1.16	12.55±0.90	11.90±1.02	12.60±1.22	12.06±1.22	0.866

TLC	8840.91±2161.47	13557.5±5966	12150±4907.52	9370±147.99	8732.00±1293.24	0.001**
ESR	56.21±13.45	37.83±13.42	59.20±16.84	27.00±6.08	28.80±5.26	<0.001**

Among blood parameters studied; total leucocyte count was high among parapneumonic and empyema patients with ESR being high among tubercular and empyema patients and were statistically significant.

Table 4: Analysis of pleural fluid parameters in Exudative Pleural Effusions

Variables	Type of Effusion					P value
	Tubercular	Parapneumonic	Empyema	Malignant	Paramalignant	
PF Glucose	79.36±19.5	92.58±50.44	2.00±0.71	68.33±14.16	112.2±16.81	<0.001**
PF protein	4.92±0.82	4.31±0.80	5.16±1.09	4.47±1.54	4.46±0.53	<0.001**
PF LDH	623.61±90.67	375.21±22.95	2642.2±101.62	2298±306.87	267.6±53.10	<0.001**
PF Cholesterol	75.42±27.24	100.49±79.85	70.60±16.83	91.67±35.56	79.40±17.54	0.002**
PF ADA	62.61±24.50	21.20±11.27	88.88±48.44	14.77±5.87	16.98±11.08	<0.001**
PF TLC	427.70±94.98	1826.09±272.50	1913.80±257.54	135.33±97.08	72.40±12.81	<0.001**
PF lymphocytes	83.24±12.20	54.55±34.09	46.60±30.95	80.00±10.00	83.00±10.95	<0.001**
PF Neutrophils	14.33±9.84	41.82±34.80	51.00±33.62	20.00±10.00	17.00±10.95	<0.001**

- Pleural fluid Glucose: lowest among empyema cases and p value was statistically significant among groups.
- Pleural fluid Protein: highest among empyema cases and statistically significant among groups.
- Pleural fluid Cholesterol: higher among parapneumonic and malignant effusions. Cut off of 45 mg% was statistically significant.
- Pleural fluid LDH: highest among empyema and malignant effusions. Cut off of 200 mg% was statistically significant.
- Pleural fluid ADA: higher among tubercular and empyema cases. P value was statistically significant.
- Pleural fluid cytology: fluid was found to be more cellular in parapneumonic effusions and Empyema.
- Predominant cells: tubercular, parapneumonic, malignant, paramalignant effusions were found to be lymphocyte predominant effusions and empyema was neutrophil predominant.

Table 5: Analysis of Pleural Fluid parameters in Transudative Pleural Effusions

Variables	TRANSUDATE
PF Glucose	116.57±69.57
PF protein	1.84±0.66
PF LDH	116.06±32.89
PF Cholesterol	26.25±3.64
PF ADA	6.42±4.54
PF TLC	88.43±76.01
PF Lymphocytes	73.93±11.12
PF Neutrophils	21.36±10.10

The mean pleural fluid protein is 1.84 + 0.66, mean LDH 116.06 + 32.89, mean cholesterol 26.25 + 3.64 with lymphocyte predominant effusions.

Analysing pleural fluid LDH and Cholesterol in exudative pleural effusions using student t test mean LDH level 772.52 + 144.56 was moderately significant and mean cholesterol level 81.36 + 5.30 was strongly significant.

Analysing pleural fluid LDH and Cholesterol in transudative pleural effusions using student t test mean LDH level 116.06 + 32.89 was moderately significant and mean cholesterol level 26.25 + 3.64 was strongly significant.

Table 6: Diagnostic value of Pleural Fluid Cholesterol and LDH

VARIABLES	Observation					Correlation					
	TP	FP	FN	TN	Total	Se	Sp	PPV	NPV	Accuracy	P value
Pleural Fluid Cholesterol	59	2	3	12	76	93.7	85.7	96.7	80.0	93	<0.001**
Pleural Fluid LDH	58	3	4	11	76	93.5	78.6	95.1	73.33	91	<0.001**

The sensitivity, specificity, PPV, NPV of pleural fluid Cholesterol was 94%, 86%, 97%, 80% with accuracy of 93% whereas sensitivity, specificity, PPV, NPV of pleural fluid LDH 93.5%, 78.6%, 95%, 73% with accuracy of 91% for classifying exudates and transudates.

Table 7: Analysis of Serum PROTEIN, LDH and Cholesterol in Exudative Effusions

Variables	Exudate		Total	P value
	Yes	No		
SR Protein	6.44±0.59	5.68±0.46	6.30±0.64	<0.001**

SR LDH	221.35±78.05	187.07±29.14	215.03±72.67	0.111
SR Cholesterol	158.64±29.91	172.43±33.66	161.18±30.87	0.132

On simultaneous serum analysis it was found that mean protein level among patients with exudative effusion was $6.44 + 0.59$ which was statistically strongly significant. Mean LDH was $221.35 + 78.05$ and mean Cholesterol $158.64 + 29.91$.

Table 8: Analysis of SERUM PROTEIN, LDH and Cholesterol in Transudative Effusions

Variables	Transudate		Total	P value
	Yes	No		
SR Protein	5.68±0.46	6.44±0.59	6.30±0.64	<0.001**
SR LDH	187.07±29.14	221.35±78.05	215.03±72.67	0.111
SR Cholesterol	172.43±33.66	158.64±29.91	161.18±30.87	0.132

On simultaneous serum analysis it was found that mean protein level among patients with transudative effusion was $5.68 + 0.46$, mean LDH $187.07 + 29.14$, mean cholesterol $172.43 + 33.66$.

DISCUSSION:

We have done a cross sectional study on pleural effusion patients in a tertiary care hospital. Pleural effusion is a commonly encountered clinical problem. In many cases cause cannot be found in spite of careful clinical evaluation. It is very important to establish an accurate diagnosis to treat the patients in an appropriate manner. A better knowledge of spectrum of clinical history, radiological imaging, biochemical and cytological evaluation helps in narrowing down diagnostic dilemma and aid in management of patients. Our aim was to evaluate the role of pleural fluid Cholesterol and LDH in differentiating exudative and transudative effusions. There are many studies in Western literature but very few studies in Indian literature, which have assessed the role of pleural fluid Cholesterol and LDH in differentiating between transudative and exudative pleural effusions. Results obtained from the study were compared with the studies in the literature.

In our study 69.7% (n=53) of patients were males and 30.3% (n=23) of patients were females. The study done by Marel et al found 66.6% of study population were males and 33.34% were females.¹¹ A study done by Chakrabarti et al on 75 patients with pleural effusion had 64% male subjects.¹² Another study done Valdes et al on 129 patients found 56.5% to be males.¹³ This is consistent with previous studies which had shown that men are more predisposed to tuberculosis and malignancy.¹⁴

In our study mean age of the population was 48.97 ± 17.03 yrs. Majority of patients 57.9% (n=44) belonged to the age group of 40-70 yrs. Patients with tuberculous pleural effusion had

a mean age of 41.29 ± 17.96 which was lower compared to the mean age in patients with malignant and paramalignant pleural effusion (55.67 ± 11.85 and 58.4 ± 17.79). A study conducted by Chan et al on patients with tuberculous pleural effusion revealed mean age of 44 years.¹⁵ Similar to our study, another study conducted by Valdes et al showed a higher mean age of 65 ± 14 in patients with malignancy.¹⁶ This is due to higher incidence of malignancy with progression of age.¹⁷

ESR was high among tubercular (56.21 ± 13.45) and empyema (59.20 ± 16.84) patients. This is in consistent with another study which showed that ESR was highest in empyema (78 ± 8) and tubercular effusion (50 ± 8).¹⁸

In our study mean cholesterol level in exudative pleural effusion was 81.36 ± 5.30 and in transudative pleural effusion was 26.35 ± 3.64 . In a similar study done by Rungta and Jha¹⁹ assessing the role of cholesterol in pleural effusion in 56 patients found that mean cholesterol level in exudates was 72.4 ± 9.2 and in transudates 36.9 ± 5.2 . In our study pleural fluid cholesterol had a sensitivity of 94% and specificity of 86% for distinguishing exudates and transudates with PPV of 96.7% and NPV of 80%. In a study by Guleria et al¹ role of pleural fluid cholesterol was evaluated in 50 patients (25 exudates and transudates each) in differentiating transudates and exudates found that pleural fluid cholesterol had a sensitivity of 88% and specificity of 100% for exudates with an accuracy of 92%. Rungta and Jha⁸⁶ also studied the diagnostic value of pleural fluid cholesterol in 56 patients in differentiating transudate and exudate and concluded from their study that pleural fluid cholesterol and lactate dehydrogenase had a sensitivity of 99% and specificity of 98% in separating transudate and exudate.

Pleural fluid LDH in empyema in our study was very high (2642.2 ± 101.62 U/L) which is similar to other studies proving that LDH is high in patients with empyema.¹⁸ The mean pleural fluid LDH among transudative pleural effusions was 116.06 ± 32.89 which was similar to study by Rungta and Jha¹⁹ in which mean pleural fluid LDH in transudative effusions was 95 ± 24.5 . In our study sensitivity and specificity of pleural fluid LDH for differentiating exudates and transudates was 93.5% and 78.6% with PPV and NPV of 95.08% and 73.33%. In a study by Guleria et al¹ which included 50 patients' pleural fluid LDH had a sensitivity of 80% and specificity of 96% for exudates. In another study (86) including 56 patients' pleural fluid LDH had sensitivity of 79% and specificity of 75% to differentiate transudative and exudative effusions.

CONCLUSION:

From our study it can be concluded that, Pleural fluid cholesterol and LDH were found to be excellent pleural fluid parameters for differentiating exudative and transudative effusions from the study. They are both cost effective as well as technically feasible to analyse and hence could serve as better guides in the proper management of pleural effusion.

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