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ORIGINAL RESEARCH

To assess the diagnostic role of pleural fluid cholesterol in categorizing type of pleural effusion

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ABSTRACT

Aim: The present study was conducted to assess the diagnostic role of pleural fluid cholesterol in categorizing type of pleural effusion.

Material and methods: The present prospective observational study was conducted on 51 patients hospitalized to the Department of Pulmonary Medicine, TMMC & RC, TMU, Moradabad, for a period of one and a half years. Patients with definite clinical diagnosis and pleural effusion evidenced by radiological imaging and thoracentesis yields a sufficient good quantity of pleural fluid for examination was included in the study. Pleural fluid cholesterol was investigated and compared according to Light's criteria.

Results: Maximum subjects were suffering from moderate amount of pleural effusion. Exudative pleural effusion was found in 94.1%, 86.3%, 72.5% of the subjects while transudative pleural effusion was found in 5.9%, 13.7%, 27.5% of the subjects according to Light's criteria, cholesterol at cut off 45 and 60 respectively. The mean pleural fluid cholesterol level in the exudates and transudates was 85.11±34.13 and 31±7.21 mg/dl with statistically significant difference as p=0.009. Cholesterol at cut of 45 was found to be better predictor of exudative and transudative pleural effusion considering Light's criteria as gold standard.

Conclusion: Cholesterol effusion has the advantage of avoiding plasma protein, sLDH, pleural fluid protein, and LDH. Cholesterol at 45 was the best cut for detecting pleural effusion. As a result, distinguishing exudates from transudates is more efficient, easier, and cost-effective.

Keywords: Pleural Effusion, Light Criteria, Cholesterol

INTRODUCTION

Pleural effusion, a pathological collection of fluid in the pleural space, is a common occurrence. Its causes are many, ranging from relatively innocuous effusions associated with viral pleuritis to prognostically significant effusions associated with congestive heart failure or malignancy. The one-year death rate for patients with a non-malignant pleural effusion ranges from 25% to 57 percent.[1] Although pleural effusion can be caused by a variety of conditions, the most common causes in adults include heart failure, cancer, pneumonia, tuberculosis, and pulmonary embolism, while pneumonia is the most common cause in children.[2,3]

Pleural effusions are classified as either transudates or exudates depending on the biochemical properties of the fluid, which often reflect the physiologic mechanism of generation. Exudative effusions can be distinguished from transudative effusions utilizing Light's criteria in clinical practise. To distinguish between transudative and exudative pleural effusion, Light et al offered biochemical markers such as protein and lactate dehydrogenase (LDH).[4]

However, adopting Light's criteria, the other researchers were only able to reproduce specificity of 70–86%. Also, according to Light's criteria, 25% of patients with transudative pleural effusion are misdiagnosed as having exudative effusion. The transudative PE has significant protein content in patients with heart failure who are on diuretic medication.[5]

Pleural fluid cholesterol, which misclassifies fewer cases than any other Light's parameter, can be used to classify exudates and transudates.[6] Heffner et al. in 2002 identified pleural effusion of the exudative type with at least one of the following conditions based on a meta-analysis.[7]

(i) Pleural fluid protein >2.9 gm/dL.
(ii) Pleural fluid cholesterol >45 mg/dL (1.16 mmol/L).
(iii)Pleural fluid LDH >2/3rd of upper limit of serum.

Pleural cholesterol is hypothesized to come from degenerating cells and increased permeability, which leads to vascular leakage. We need distinct diagnostic measures to discriminate between exudative and transudative effusions because we live in a country where pleural effusion is a prevalent clinical disease. Because pleural fluid cholesterol level may distinguish transudates from exudates as a single factor rather than the multiple characteristics used in Light's criteria, it can be the parameter of choice for physicians or health workers to quickly comprehend the type of fluid and continue. On the other hand, it might be cost-effective and produce results in a timely manner.[8]

There are very few studies on Indian patients along with lack of sufficient data of pleural fluid cholesterol to differentiate exudative and transudative. No studies have been conducted in the state of Uttar Pradesh till date. Hence the present study was conducted to assess the diagnostic role of pleural fluid cholesterol in categorizing type of pleural effusion.

MATERIAL AND METHODS

The present prospective observational study was conducted on 51 patients hospitalized to the Department of Pulmonary Medicine, TMMC & RC, TMU, Moradabad, for a period of one and a half years**.** Time Bound sampling was done. All the patients of pleural effusion coming to pulmonary medicine IPD for a period of 18 months after clearance from ethical committee were included in the study. The inclusion and exclusion for the present study is mentioned below:

INCLUSION CRITERIA

(i) Age ≥18 years of both sexes
(ii) Patients with definite clinical diagnosis and PE evidenced by radiological imaging, where thoracentesis yield a sufficient good quantity of pleural fluid for examination
(iii)Patients giving consent.

EXCLUSION CRITERIA

(i) Patients with history of PE due to trauma (penetrating or nonpenetrating).
(ii) Patients previously diagnosed and already on treatment;

METHODOLOGY (FIGURE 1)

1. 51 PE patients after admission from the emergency or outpatient department were recruited in the study.
2. Detailed history taking and clinical examination was performed.
3. Patients were assessed for the history of fever, productive or dry cough, night sweats, hemoptysis, chest pain, lower extremity edema, orthopnea, paroxysmal nocturnal dyspnea, decreased urine output, and other relevant symptoms.
4. Clinical assessment including general survey and systemic examination was done.

INVESTIGATIONS

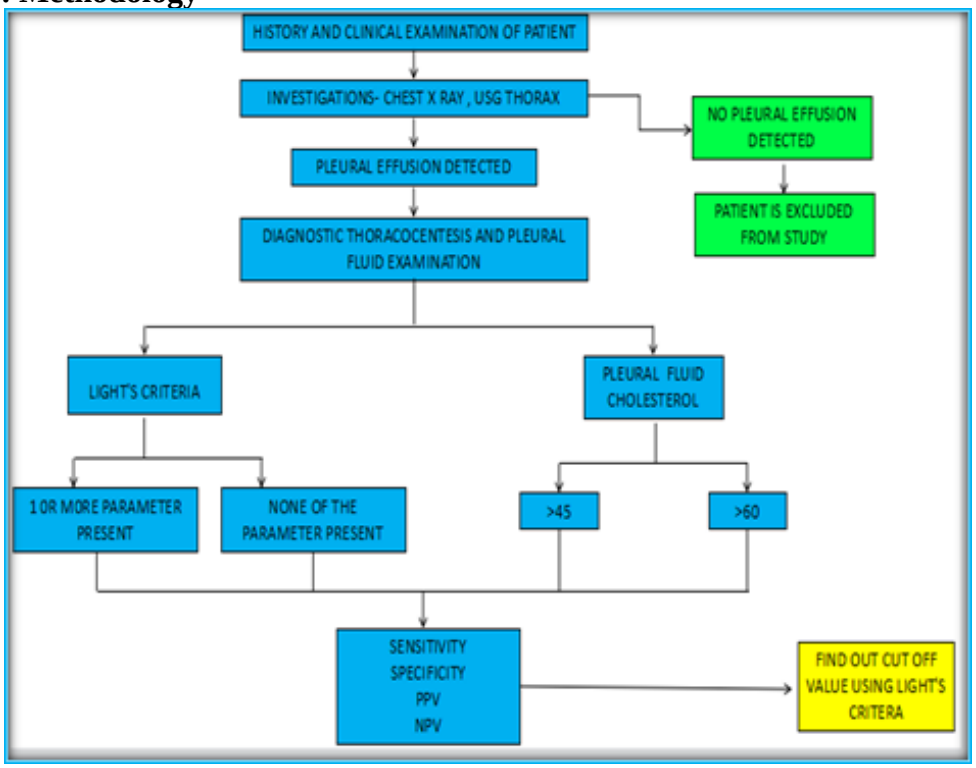
1. Routine Investigations- Hb, TLC, Platelet count, s.Bilirubin, Urea, Creatinine, SGOT,SGPT
2. S.protein
3. S.LDH
4. Chest x-ray
5. Biochemical examination of pleural fluid-

- Protein
- Sugar
- AFB
- LDH
- DLC
- Cholesterol
- ADA

1. Ultrasonography of thorax (selected patients)

Cholesterol was measured on cobas c 501 analyzer by using colorimetric principle.
Lactate dehydrogenase was measured on cobas c 501 analyzer using UV assay colorimetric principle.
Protein was measured on cobas c 501 analyzer by colorimetric assay.

Figure 1: Methodology



STATISTICAL ANALYSIS

The study included descriptive and inferential statistical analysis using SPSS software version 24. Continuous measurement results are reported as Mean + SD (Min-Max), while categorical measurement results are displayed as Number (percent). Diagnostic efficacy was assessed using sensitivity, specificity, true predictive and negative predictive value.

RESULTS

Out of 51 subjects, 25 (49.02%) subjects were from age group of 41-60 years. Minimum subjects were from age group of <20 years (5.88%). Mean age among the study subjects was 45.57±17.48 years. Males (70.6%) were comparatively more as compared to females (29.4%) in our study (table 1).

Table 1: Age and gender distribution among the study subjects

Age Group (in years)	N	%
<20	3	5.88
21-30	11	21.57
31-40	6	11.76
41-50	12	23.53
51-60	13	25.49
>60	6	11.76
Gender		
Male	36	70.6
Female	15	29.4
Total	51	100

Maximum subjects were suffering from moderate amount of pleural effusion. Most common colour of pleural effusion was found to be pale yellow (66.7%). Dark yellow, reddish and turbid colour was reported among11.8%, 9.8% and 9.8% of the subjects respectively (table 2).

Table 2: Amount categorization and colour among the study subjects

Amount	N	%
Loculated	6	11.8
Mild	15	29.4
Moderate	19	37.3
Massive	11	21.6
Colour		
Brown	1	2.0
Dark Yellow	6	11.8
Pale Yellow	34	66.7
Redish	5	9.8
Turbid	5	9.8
Total	51	100

Tubercular effusion was found in 47.1% of the subjects. Malignancy was reported in 17.6% of the subjects. CCF, empyema and parapneumonic effusion was shown in 5 subjects each (table 3).

Table 3: Clinical diagnosis among the study subjects

Diagnosis	N	%
CCF	5	9.8
Empyema	5	9.8

Hepatic hydrothorax	2	3.9
Malignancy	9	17.6
Pancreatic effusion	1	2.0
Parapneumonic effusion	5	9.8
Tubercular	24	47.1
Total	51	100

Table 4 shows the type of pleural effusion according to Light's criteria and cholesterol at cut off 45 and 60. Exudative pleural effusion was found in 94.1%, 86.3%, 72.5% of the subjects while transudative pleural effusion was found in 5.9%, 13.7%, 27.5% of the subjects according to Light's criteria, cholesterol at cut off 45 and 60 respectively.

Table 4: Outcome among the study subjects

Parameters	**Exudative**		**Transudative**	
	N	**%**	**N**	**%**
Light's criteria	48	94.1	3	5.9
Cholesterol: 45	44	86.3	7	13.7
Cholesterol: 60	37	72.5	14	27.5

Protein and protein ratio was found more in exudative pleural effusion as compared to transudative pleural effusion with statistically significant difference as $p<0.05$. The mean pleural fluid cholesterol level in the exudates and transudates was 85.11±34.13 and 31±7.21 mg/dl with statistically significant difference as $p=0.009$ (table 5).

Table 5: Investigative profile according to Light's criteria

Light's criteria		**Sugar**	**Protein**	**LDH**	**ADA**	**Cholesterol**	**TLC**	**Serum Protien**	**Serum LDH**	**Protein ratio**	**LDH ratio**
Exudative	Mean	79.44	4.72	1012.95	61.12	85.11	5771.35	6.67	327.20	.73	3.26
	SD	53.69	1.34	1136.41	35.78	34.31	20899.63	.95	97.423	.22	3.84
Transudative	Mean	131.93	2.67	123.0	40.33	31.0	121.67	7.0	270.0	.36	.46
	SD	41.69	1.15	78.25	21.13	7.21	100.04	0.43	149.86	.12	.14
t test		2.74	6.65	1.81	0.98	7.31	0.22	0.37	0.92	7.93	1.56
p value		0.11	0.013*	0.19	0.33	0.009*	0.65	0.55	0.34	0.007*	0.22

*: statistically significant

Sensitivity, specificity, PPV, NPV and accuracy rate of cholesterol at 45 cut off was 87%, 100%, 100%, 94% and 94.50% respectively while the same at 60 cut off was 100%, 89%, 72%, 100% and 80% respectively. Hence cholesterol at cut of 45 was found to be better predictor of exudative and transudative pleural effusion considering Light's criteria as gold standard [Table 6].

Table 6: Diagnostic efficacy of cholesterol (45) and cholesterol (60) considering Light's criteria as gold standard

Parameters	**Cholesterol (45)**	**Cholesterol (60)**
Sensitivity	87%	100%
Specificity	100%	89%
Positive Predictive Value	100%	72%
Negative Predictive Value	94%	100%
Accuracy Rate	94.50%	80%

DISCUSSION

It is critical to distinguish between exudative and transudative pleural effusions when diagnosing pleural effusion. Light's criteria, according to Vaz MA et al[9], are the most acceptable way for distinguishing between transudative and exudative pleural effusions. Many biochemical markers have been proposed as alternatives to discriminate transudative and exudative pleural effusions to increase diagnostic accuracy. Cholesterol has been demonstrated to be as sensitive as the Light's criterion in most clinical studies, however it is less specific. The optimal cholesterol cutoff point for distinguishing transudative pleural effusions from exudative pleural effusions is yet unknown. The current study was conducted to see how useful pleural fluid cholesterol is in diagnosing different types of pleural effusions.

Out of 51 subjects, 25 (49.02%) subjects were from age group of 41-60 years. Minimum subjects were from age group of <20 years (5.88%). Mean age among the study subjects was 45.57±17.48 years in our study. Similar age distribution was revealed by Sat Pal Aloonaet al[10], RogérioRufino et al[11] and R. Guleria et al.[12]

Males (70.6%) were comparatively more as compared to females (29.4%) in our study. RogérioRufinoet al[11], Sat Pal Aloona et al[10] and R. Guleria et al[12] too in their showed more males as compared to females.

In the present study; tubercular effusion was found in 47.1% of the subjects. Malignancy was reported in 17.6% of the subjects. CCF, empyema and parapneumonic effusion was shown in 5 subjects each in this study. CK Liam et al[13] in their study too revealed tuberculosis as the most common cause of pleural effusion. Similarly in a study by AB Hamalet al[14] the most common cause was tuberculosis followed by cancer. RogérioRufinoet al[11] in their study too found tuberculosis as the most common cause of pleural effusion.

Exudative pleural effusion was found in 94.1%, 86.3%, 72.5% of the subjects while transudative pleural effusion was found in 5.9%, 13.7%, 27.5% of the subjects according to Light's criteria, cholesterol at cut off 45 and 60 respectively in the present study. Valdes L et al[6] Sat Pal Aloona et al[10] and Hamm et al[14] also found more exudative as compared to transudative cases.

Protein, cholesterol and protein ratio was found more in exudative pleural effusion as compared to transudative pleural effusion with statistically significant difference as $p<0.05$ in our study. Sat Pal Aloonaet al[10] in their study found that cholesterol level was more in exudative as compare to transudative effusion, which is similar to our study. According to Hamal AB et al[14] it suggests that pCHOL is highly correlated for exudate which is significant at the $p<0.05$. Hamm et al[15] in their study reported similar findings too(42.27 mg% in transudative and 70.56 mg% in exudative).

In the present study; sensitivity, specificity, PPV, NPV and accuracy rate of cholesterol at 45 cut off was 87%, 100%, 100%, 94% and 94.50% respectively while the same at 60 cut off was 100%, 89%, 72%, 100% and 80% respectively. Hence cholesterol at cut of 45 was found to be better predictor of exudative and transudative pleural effusion considering Light's criteria as gold standard. Similar to our study, SrinathDhandapaniet al[16] too reported that best cutoff value of cholesterol to classify exudative and transudative pleural effusion was 45. These findings are similar to our study. According to AB Hamalet al[14] cholesterol cut of at 45.24 (1.16 mmol/L), sensitivity, specificity and PPV was found to be 97.7%, 100% and 100% respectively, which is approximately similar to our study. Sat Pal Aloonaet al[10] in their study reported that cholesterol had sensitivity and specificity of 94.12% and 100% respectively, which is approximately similar to our study. However they didn't mention the cutoff value.

Valdes et al,[7] in their study showed that cholesterol cut of at 55; sensitivity, specificity and PPV was found to be 91% and 100% respectively. PCHOL levels of 60 mg per 100 ml were

found to be superior to conventional measurements of protein level, LDH, and Light's criteria in Hamm et al's[15] prospective study of 70 pleural effusions. In their study, Patel AK and colleagues[17] found that pleural fluid cholesterol and total serum proteins are simple, cost-effective, and relevant indicators for distinguishing between transudative and exudative pleural effusion.

Cholesterol is beneficial in the diagnosis of pleural exudates, according to Shenet al[18] Cholesterol was shown to be more specific and sensitive at the 45 cutoff than at the 60 cutoff in this investigation. According to our research, the optimal cuttoff for distinguishing between transudative and exudative pleural effusion was 45. As a result, it is advised that pleural fluid cholesterol estimate be made a normal part of pleural evaluation.

Cholesterol was shown to be more specific and sensitive at a cutoff of 45 than it was at a cutoff of 60 in the current investigation. The optimal cutoff to distinguish transudative from exudative pleural effusion, according to our research, was 45. As a result, it is recommended that pleural fluid cholesterol be estimated as part of routine pleural evaluation.

CONCLUSION

It is concluded that pCHOL has comparable findings with respect to pleural effusion considering Light's criteria. Cholesterol effusion has the advantage of avoiding plasma protein, sLDH, pleural fluid protein, and LDH. Cholesterol at 45 was the best cut for detecting pleural effusion. As a result, distinguishing exudates from transudates is more efficient, easier, and cost-effective. This study also shows that in situations of pleural effusion, determining pCHOL should be standard practise.

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