Original Research Article

Study of pleural fluid cholesterol and lactate dehydrogenase to differentiate exudate from transudate and compared with Light's criteria

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Abstract

Background: Pleural effusion is the one of the most common Respiratory diseases admitted in the medical ward, most often diagnosed by clinical, radiological and pleural fluid analysis.
Materials and methods: This was a cross-sectional study conducted in Government Royapettah hospital in the Department of Medicine during the period January 2016 to August 2016. Patients admitted as in-patients in medical wards and newly diagnosed to have pleural effusion clinically and radiologically were included in the study.
Results: 10 cases out of fifty cases in the study were below the age of thirty years comprising 20% of total cases. 17 cases between 31-40 years comprised 34% of total cases. Lymphocytic pleural effusion was 21 cases out of 50 cases comprising 42%.
Conclusion: Pleural fluid cholesterol and LDH test is useful to differentiate pleural fluid exudate and transudate with the advantage of requiring only two laboratory parameters and no simultaneous blood sample especially in countries like India, with financial and technical constraints.

Key words

Pleural fluid, Cholesterol, Lactate dehydrogenase, Transudate, Exudate, Light's criteria.

Introduction

Pleural effusion is the one of the most common Respiratory diseases admitted in the medical ward, most often diagnosed by clinical, radiological and pleural fluid analysis. Lights Criteria is used to differentiate exudative from transudative pleural effusion. Serum protein, serum Lactate dehydrogenase, pleural fluid protein and pleural fluid lactate dehydrogenase are required for the same. A major drawback of this is that it is expensive to measure all the parameters. Several studies conducted in India have investigated into finding cost effective alternatives to Lights criteria. Our objective was to find the diagnostic value of pleural fluid Cholesterol and Lactate dehydrogenase in differentiating exudative and transudative effusion compared to Light's criteria and to find the place of pleural fluid cholesterol and Lactate dehydrogenase in diagnostic algorithm of pleural effusion. Cholesterol level in pleural effusion has been studied by many authors to differentiate exudate and transudate [1, 2]. Cholesterol is synthesized by cells lining the pleura, depending on metabolic activity and needs [3-5]. Cholesterol in pleural fluid is increased by degenerated leucocytes and erythrocytes [6]. Increased vascular permeability of pleural capillaries adds to the increased pleural fluid cholesterol level [7]. Cholesterol cut off value of more than 45 mg/dl is taken in studies to differentiate exudative and transudative effusion [2, 8]. Pleural fluid cholesterol of more than 200mg/dl suggests chyliform effusion [7]. Pleural fluid cholesterol and LDH have been studied to separate exudates and transudate. A pleural fluid cholesterol of >45mg/dl or LDH of >200 IU/L was found to be diagnostic of exudate [8]. This test was found to be comparable to light's criteria. Another study done in India found that pleural fluid analysis of cholesterol and LDH with cut off value of >45mg/dl and >200 IU/L respectively has a higher sensitivity and specificity than any other combinations in differentiating exudate and transudate [9]. Hence the requirement of a simple cost effective biochemical test to differentiate between transudate and exudate in pleural effusions is the need of the day [11].

Materials and methods

This was a cross-sectional study conducted in Government Royapettah hospital in the Department of Medicine during the period January 2016 to August 2016. Patients admitted as in-patients in medical wards and newly diagnosed to have pleural effusion clinically and radiologically were included in the study. Traumatic pleural effusion and Patients already started on treatment for pleural effusion were excluded from the study. A sample size of 50 was calculated and included in the study. After taking detailed history from the patient, they were subjected to complete clinical examination. All the patients with suspected pleural effusion clinically were further subjected to radiological investigations chest x ray and ultra-sonogram chest if needed, to confirm the presence of pleural effusion. Thoracocentesis was explained to the patient, after getting consent from the patient and under strict aseptic precaution, thoracocentesis was performed and pleural fluid sent for analysis. Pleural fluid analysis comprising of glucose, protein, LDH, cholesterol, cytology, AFB, gram stain was done. Complete blood count, blood urea, serum creatinine, liver function tests, serum protein and serum LDH, serum cholesterol was also done. Sputum gram stain and AFB was also obtained. Light's criteria were used to classify the patients into exudate and transudate. Transudate group were subjected to further investigations viz. ultrasound abdomen, echocardiogram, etc., to find the etiology of transudate. Pleural fluid cholesterol of more than 45mg/dl and LDH of more than 200IU/L was taken as cut off value and presence of any one or both parameter is diagnostic of exudate, as per previous study references.

Results

Using the SPSS 20.0 software the Sensitivity, Specificity, Positive predictive value and Negative predictive value of Pleural fluid

cholesterol and LDH test was analysed and Chi-Square test was used to test the association. Measure of agreement between two test and kappa value was calculated. A P value of <0.05 was taken as significant. 10 cases out of fifty cases in the study were below the age of thirty years comprising 20% of total cases. 17 cases between 31-40 years comprised 34% of total cases. 6 cases were between 41-50 years comprising 12% of total cases. 10 cases were between 50-60 years comprising 20% of total cases. 7 cases were above 60 yrs comprising 14% of total cases Out of 50 cases chest x ray showed right sided pleural effusion in 28 cases comprising 56%, 17 cases of left sided pleural effusion with 34%, 5 cases of bilateral effusion which comprises 10%.

Lymphocytic pleural effusion was 21 cases out of 50 cases comprising 42%. All the lymphocytic cases were of tuberculous etiology. 13 pleural effusions wereneutrophilic in nature which comprised 26%. 11neutrophilic effusions were parapneumonic and there were 2 cases of empyema. 6 cases were malignant pleural effusion. 10 pleural effusions were acellular (20%). All the acellular pleural effusions were transudative in nature.

Out of 50 cases, Light's criteria diagnosed 40 cases as exudates which is 80% of total cases and 10 cases as transudates which is 20% of total cases (**Table – 1**).

Table - 1: Classification into transudate and exudate according to Lights criteria.

TYPE	FREQUENCY	PERCENT
Exudate	40	80.0
Transudate	10	20.0

Mean serum protein level in tuberculosis effusion patients was 6.5gm/dl. In Para pneumonic effusion cases mean serum protein level was 6.6gm/dl. Mean serum protein level in transudate effusion cases was 5gm/dl. In patients with malignant effusion, the mean serum protein level was 5.9 gm. /dl. In empyema patients, mean serum protein level was 6.6gm/dl (**Table - 2**).

Table - 2: Mean serum protein levels.

ETIOLOGY	N	MEAN (gm./dl)	SD
TB	21	6.557	0.263
Para Pneumonic	11	6.636	0.366
Transudate	10	5.840	0.636
Malignancy	6	5.967	0.196
Empyema	2	6.600	0.282

In patients with tuberculosis pleural effusion the mean serum LDH level was 351IU/L. In patients with parapneumonic effusion, the mean serum LDH value was 358 IU/L. In transudative effusion patients the mean serum LDH value was 331IU/L. In malignant effusion cases, the mean serum LDH was 384 IU/L. In empyema cases, the mean serum LDH level was 385 IU/L (**Table - 3**).

Table - 3: Mean LDH levels.

ETIOLOGY	N	MEAN (IU/L)	SD
TB	2	351.33	30.622
Para Pneumonic	11	358.18	28.375
Transudate	10	331.80	16.612
Malignancy	6	384.00	11.524
Empyema	2	385.00	15.556

In tuberculous pleural effusion patients, the mean value of serum cholesterol was 174mg/dl. In parapneumonic effusion patients, the mean level was 181mg/dl. In transudative effusion cases, the mean serum cholesterol was found to be 208mg/dl. In malignant cases, the mean serum cholesterol level was 190mg/dl. In cases of empyema, the mean level was found to be 173 mg /dl. Mean pleural fluid protein level in tuberculous effusion patients was 4.3gm/dl. In parapneumonic effusion patients, the mean pleural fluid protein level was 4.7 gm/dl. Trasudative pleural effusion patients showed pleural fluid mean protein level of 2.4gm/dl. Malignant cases showed pleural fluid protein

value of 6.1gm/dl. In empyema patients, the mean value was 6.1gm/dl (**Table - 4**).

Table - 4: Mean pleural fluid protein levels.

ETIOLOGY	N	MEAN (gm./dl)	SD
TB	21	4.386	0.377
Para Pneumonic	11	4.791	0.270
Transudate	10	2.400	0.722
Malignancy	6	6.167	0.367
Empyema	2	6.100	0.424

288 IU/L was the mean pleural fluid LDH value in tuberculous effusion cases. In parapneumonic effusion patients, the mean pleural fluid LDH value was 342 IU/L. In transudates the mean pleural fluid LDH was 137 IU/L. In empyema, the mean pleural fluid LDH was 424 IU/L. In malignant effusion, the mean pleural fluid LDH was found to be 621 IU/L (**Table - 5**).

Table - 5: Mean pleural fluid LDH levels.

ETIOLOGY	N	MEAN (IU/L)	SD
TB	21	288.48	11.677
Para Pneumonic	11	342.18	35.535
Transudate	10	137.40	26.298
Malignancy	6	621.67	44.279
Empyema	2	424.00	.000

In pleural effusion due to tuberculosis, the mean pleural fluid cholesterol was 63mg/dl. In parapneumonic effusion patients, the mean value of pleural fluid cholesterol was 67mg/dl. In transudates, the mean pleural fluid cholesterol was found to be 36mg /dl. In malignant pleural effusion cases, the mean pleural fluid cholesterol value was 85mg/dl. In empyema cases, the mean value was 73mg/dl (**Table - 6**).

Out of 50 total cases, as per aetiology, 40 cases were exudates and light's criteria diagnosed all the 40 cases correctly as exudates. The newer test pleural fluid cholesterol and LDH, diagnosed 38 cases correctly as exudates and two cases were misclassified as transudates. Out of 10 transudate cases by aetiology, Light's diagnosed all the 10 cases as transudates correctly. Pleural fluid cholesterol and LDH test diagnosed 8 cases correctly as transudates and misclassified two transudates as exudates (**Table - 7**).

Table - 6: Mean pleural fluid cholesterol levels.

ETIOLOGY	N	MEAN	SD
TB	21	63.71	4.529
Para Pneumonic	11	67.09	4.323
Transudate	10	36.40	3.502
Malignancy	6	85.33	6.154
Empyema	2	73.00	4.243

As already seen, the routinely used light's criteria diagnosed 40 cases as exudates. The pleural fluid cholesterol and LDH test diagnosed 38 cases as exudates out of 40 cases diagnosed by Light's criteria as exudates. Two exudates were only misclassified as transudates. Similarly pleural fluid cholesterol and LDH test misclassified only two transudates as exudates, which were diagnosed as transudates by Light's criteria (**Table – 8**).

Pleural fluid cholesterol and LDH was compared with the standard LIGHTS criteria and the results showed sensitivity to be 95%, specificity to be 80%, positive predictive value 95%, negative predictive value 80%, p value of $<0.001^{**}$ was significant in measure of agreement, kappa value was 0.75 which showed good correlation. Out of 50 cases tuberculosis comprises 21 cases with 42%, parapneumonic effusion cases are 11 with 22%,transudates are 10 cases with 20%, malignancy are 6 cases with 12%, empyema comprises 2 cases with 4% (**Table – 9**).

Measure of agreement between these two tests was calculated using kappa value which also showed significant agreement between these two tests with kappa factor of 0.75 and P value of 0.01** which was highly significant.

Table - 7: Correlation of Lights criteria with Actual etiology.

		ACTUAL ETIOLOGY		Total	P VALUE
		EXUDATE	TRANSUDATE		
LIGHTS CRITERIA	EXUDATE	40	0	40	0.001**
	TRANSUDATE	0	10	10	
Total		40	10	50	

Table - 8: Correlation of Light's Criteria with Pleural fluid cholesterol and LDH values.

		PLEURAL FLUID CHOLESTEROL+LDH		Total	P VALUE
		EXUDATE	TRANSUDATE		
LIGHTS CRITERIA	EXUDATE	38	2	40	0.001**
	TRANSUDATE	2	8	10	
Total		40	10	50	

Table - 9: Etiology of Pleural effusion.

TYPE	FREQUENCY	PERCENT
Tuberculosis	21	42.0
Para Pneumonic	11	22.0
Transudate	10	20.0
Malignancy	6	12.0
Empyema	2	4.0

Discussion

Out of 50 cases taken into the study, 40 cases were exudates and 10 cases were transudates etiologically. 26 patients are male and 24 patients are female out of fifty patients. Most of the patients are between 30 to 60 years. Only 7 cases were above 60 years and 10 cases below 30 years. In this study, it was found that tuberculosis was found to be the most common cause of pleural effusion and parapneumonic effusion came next. Transudative effusion comprises only 20%. X-ray chest showed right sided pleural effusion in 56% of cases and left sided effusion in 34% of cases. Bilateral effusion was seen in 10% of cases, all of which were due to transudative etiology. In this study, it was found that lymphocytic effusion predominates and all were due to tuberculosis etiology. The next one is neutrophilic effusion which was due to parapneumonic etiology and empyema. All the transudative effusions were acellular. Sputum AFB was negative in all the patients in the study. Sputum gram stain was positive in ten cases, in which three were gram negative bacilli and seven were gram positive cocci. All were seen with parapneumonic effusion. Mean serum protein level was found to be high in effusion due to parapneumonic cause and empyema with 6.6gm/dl. Mean serum LDH was higher in malignant pleural effusion and empyema with 384 IU/L and 385 IU/L respectively. Mean serum cholesterol was higher in exudative effusion patients with value of 208 mg/dl. Mean pleural fluid protein was 2.4 gm/dl in transudative effusion. In exudative effusion, mean pleural fluid protein was found to be highest in malignancy and empyema with value of 6.1gm/dl. In tuberculosis it was 4.3gm/dl and in parapneumonic 4.7 gm/dl. Mean Pleural fluid LDH in transudate was 137 IU/L. In malignancy, it was highest with 621 IU/L and in empyema, it was 424 IU/L. In tuberculosis, it is 288 IU/L and in parapneumonic effusion, it was 342 IU/L. Mean pleural fluid cholesterol was highest in malignant pleural effusion with 85 mg/dl and next comes empyema with 73 mg/dl. In transudates, it was 36 mg/dl. In tuberculosis cases, it was 63mg/dl and in parapneumonic effusion, it was 67 mg/dl. Light's criteria diagnosed 40 cases as exudates which correctly

matched with etiological diagnosis. In the same way, it diagnosed ten cases as transudates which also correctly matched with etiological diagnosis. So light's criteria showed 100% sensitivity and 100% specificity according to this study. .The pleural fluid cholesterol and LDH test diagnosed 38 cases as exudates when compared with lights criteria and two exudates were only misclassified as transudates. In the same way, this test diagnosed 8 cases as transudates correctly when compared with Light's criteria and 2 transudates were misclassified as exudates. When pleural fluid cholesterol and LDH test was compared with routinely used Light's criteria the pleural fluid cholesterol and LDH test showed sensitivity of 95% and specificity of 80%, positive predictive value of 95% and negative predictive value of 80%. Previous studies showed 99% sensitivity and 98% specificity for pleural fluid cholesterol and LDH combination in differentiating exudate and transudate [3]. An Indian study also showed similar results - sensitivity of 99% and specificity of 98%. Our present study showed 95% sensitivity and 80% specificity [4]. In conclusion, though Light's criteria is the most accepted criteria for differentiating between exudates and transudate in pleural effusion [12], Pleural fluid cholesterol and LDH test in pleural fluid with cholesterol >45 mg/dl and LDH >200 IU/L showed 95% sensitivity and 80% specificity in diagnosing exudates is a very good cost effective alternative. It is comparable with Light's criteria, with a significant measure of agreement between the two, with a significant P value of $<0.01^{**}$. Pleural fluid cholesterol and LDH test is useful to differentiate pleural fluid exudate and transudate with the advantage of requiring only two laboratory parameters and no simultaneous blood sample especially in countries like India, with financial and technical constraints. The limitations of the study would be that it involved a limited number of patients, pleural fluid analysis was done in newly diagnosed patients who were not started on any diuretics and hence the sensitivity and specificity of light's criteria was very high in this study, lastly, the sensitivity and specificity of the new test should further be evaluated by involving a larger number of subjects. There are no conflicts of interests between the authors.

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