Research Article

A study of the utility of lactate dehydrogenase, total proteins, and adenosine deaminase in the diagnosis of pleural exudates: A new statistical approach

Mihir Mehta, Simbita Marwah, Hitesh Shah, Amit Trivedi

Department of Biochemistry, Pramukhswami Medical College and Shree Krishna Hospital, Karamsad, Anand, Gujarat, India.
Correspondence to: Mihir Mehta, E-mail: mihirdmehta@rediffmail.com

Received October 21, 2014. Accepted December 1, 2014

Abstract

Background: Pleural fluid (PF) may be transudative or exudative. Total protein estimation from PF is used to detect exudative pleural effusion.

Objectives: To determine the role of new suggested criteria consisting of lactate dehydrogenase (LDH), total proteins (TP), and adenosine deaminase (ADA) in diagnosis of pleural effusion and differentiate it into transudative and exudative and also to compare it with Light's criteria.

Materials and Methods: This was a cross-sectional study comprising 101 patients with pleural effusion, classified by previously established criteria as transudates or exudates. The study was carried out in a 550-bedded tertiary-care, rural-based, teaching hospital for 1 year. Diagnostic parameters mentioned in Light's criteria were performed from PF and serum, whereas parameters of the new criteria used in our study (LDH, TP, and ADA) were performed from PF. Receiver-operating characteristic curve was used to determine the cutoffs, multiple parallel tests were applied to combine individual test markers to optimize diagnostic accuracy and sensitivity, and specificity and diagnostic accuracy for each test were calculated.

Results: After using multiple parallel tests, the sensitivity, specificity, and accuracy of Light's criteria for diagnosing exudates were 98.9%, 75%, and 95% and those for transudates were 95.29%, 80%, and 93%, respectively. Whereas for the proposed new criteria, sensitivity, specificity, and accuracy for diagnosing exudates were 98.81%, 93.75%, and 98% and those for transudates were 95.23%, 87.5%, and 94%, respectively. The accuracy of new criteria was comparable to that of Light's criteria (p = 0.0018).

Conclusion: From our study, it can be concluded that PF analysis of LDH, TP, and ADA has high sensitivity and specificity for diagnosing pleural effusions and can be used as useful markers to suggest exudative effusions.

KEY WORDS: Pleural exudates, lactate dehydrogenase, total proteins, adenosine deaminase

Introduction

Pleural effusion can be classified as transudative and exudative.[1] Estimation of total proteins (TP) from pleural fluid (PF) is routinely used to differentiate transudates from exudates with a cutoff of 3 g/dL, frequently being used but many times this has led to the misinterpretation of effusions.[2,3]

Access this article online	
Website: http://www.ijmsph.com	Quick Response Code:
DOI: 10.5455/ijmsph.2015.2110201453	

To find parameters that can differentiate transudates from exudates, Light et al. proposed the criteria in 1972, according to which pleural effusion is likely to be exudative if at least one of the following exists: (1) the ratio of PF protein to serum protein greater than 0.5; (2) the ratio of PF lactate dehydrogenase (LDH) and serum LDH greater than 0.6; and (3) PF LDH greater than 2/3 times the normal upper limit of serum LDH.[1] Different laboratories have different values for the upper limit of serum LDH, that is, 200 and 300 U/L,[4] the sensitivity of which is good but specificity is not satisfactory.[5] Hence, several other studies were carried out to propose classifications that included estimation of PF cholesterol,[6,7] ratio of PF/serum cholesterol, PF/serum bilirubin,[7,8] and albumin gradient.[9,10] Later many studies were carried out on adenosine deaminase (ADA),[11,12] which proved that it is a useful biochemical marker to differentiate transudates from exudates.

The aim of this study was to assess the clinical utility of PF LDH, TP, and ADA in the diagnosis and differentiation of transudative and exudative pleural effusion. The rationale of this study was also to compare the usefulness of the new criteria with classical Light's criteria.

Materials and Methods

This was an observational, cross-sectional study comprising 101 samples of PF and venous blood from different patients of pleural effusion from the medical wards and intensive care units of a tertiary-care hospital between February 1, 2013 and December 31, 2013. Tuberculous effusion was diagnosed by culture examination of PF and pleural tissue, or on the basis of pleural biopsy. Malignant effusions were diagnosed on the basis of cytopathological investigations. We excluded those cases of effusion in whom cause was not identified despite exhaustive investigations. We excluded samples of patients with hemothorax, on diuretic therapy, on anticoagulant or thrombolytic agents, and tested positive for HIV. Other causes of effusions were already diagnosed on the basis of all clinical data and investigations. We also excluded hemolyzed, lipemic, icteric, and fibrin-containing fluid samples. Samples of PF and venous blood were obtained in plain vacutainer and immediately centrifuged for 15 min at 3000 rpm. The supernatant fluid and serum were separated and measurements of LDH, TP, and ADA were taken. TP was estimated using colorimetric endpoint biuret method whereas LDH was estimated using colorimetric assay DGKC (pyruvate to lactate), both were performed on Cobas Integra 400 plus autoanalyzer (Roche). ADA was analyzed using colorimetric endpoint method on RA-50 semi-autoanalyzer.

Statistical Analysis

Statistical analysis was performed using MedCalc software, version 12.5. Values of $p < 0.05$ were considered significant. The receiver-operating characteristic (ROC) curve was used to determine the cutoff or reference value of each parameter. Multiple parallel tests were applied to combine individual test markers to optimize diagnostic accuracy. Combined ROC curves were also obtained after applying multiple parallel tests to compare the significance. We calculated sensitivity, specificity, and diagnostic accuracy for each test with a 95% confidence interval (95% CI) to evaluate diagnostic or validity parameters of a given test. We used positive and negative likelihood ratios as overall indicators of concordance.

Results

Table 1 shows the distribution of the causes of exudates (in 85 patients) and transudates (in 16 patients) in the cases under study. Among patients with exudates (60 males and 25 females), the mean age was 45.2 years (range 15–50 years). However, in case of transudates (9 men and 7 women), the mean age was 61.5 years (range 40–89 years). Among patients with exudates, 76% had tuberculosis whereas 14% had lung carcinoma and 2% had systemic lupus erythematosus (SLE). In case of transudates, 50% patients had congestive cardiac failure (CCF), 25% chronic renal failure, and 13% cirrhosis. While hypoproteinemia and cirrhosis were constituting 6% each as the cause of transudates.

Table 2 shows analysis of the diagnostic parameters included in Light's criteria, which include ratio of LDH in PF and serum (LDH-PF/S), ratio of TP in PF and serum (TP-PF/S), and LDH in PF (LDH-PF). These parameters were run as isolated tests for the diagnosis of transudates and exudates. From the analysis it is evident that in case of exudates, the sensitivity and specificity of LDH-PF/S ratio are 84.52% (95% CI: 74.62–91.18) and 68.75% (95% CI: 41.48–87.87), respectively, which shows low specificity. However, sensitivity and specificity of TP-PF/S ratio in case of exudates are 95.18% (95% CI: 87.45–98.44) and 70.59% (95% CI: 44.05–88.62), respectively, and those of LDH-PF ratio are 91.76% (95% CI: 83.24–96.34) and 60% (95% CI: 32.89–82.54), respectively, which show very low specificity as compared to other diagnostic parameters. The cutoff point of LDH-PF was 200 U/L as recommended in Light's criteria. Thus, it is evident that in case of exudates if we run these parameters as isolated tests then the specificity is very low. On the contrary, it is evident that in case of transudates the specificity is on higher side as compared to exudates. For example, the specificity of

Table 1: Proportions of patients diagnosed with various diseases who presented with pleural exudates and transudates

Classification	Diagnoses	Patients, *n* (%)	Males	Females
Exudate, *N* = 85	Tuberculosis	65 (76)	46	19
	Small-cell lung carcinoma	1 (1)	01	00
	Non-small-cell lung carcinoma	10 (13)	07	03
	Systemic lupus erythematosus	2 (2)	01	01
	Pleural empyema	7 (8)	05	02
Transudate, *N* = 16	Congestive cardiac failure	8 (50)	05	03
	Chronic renal failure	4 (25)	02	02
	Hypoproteinemia	1 (6)	00	01
	Cirrhosis	2 (13)	01	01
	Atelectasis	1 (6)	01	00

Table 2: Analysis of diagnostic parameters as isolated tests

Diagnosis	Parameters	LDH-PF/S	TP-PF/S	LDH-PF	ADA-PF
Exudates	Prevalence	84.15% (75.01–90.3)	83.14% (73.89–89.5)	85.2% (76.15–91.08)	85.19% (76.15–91.08)
	Sensitivity	84.52% (74.62–91.18)	95.18% (87.45–98.44)	91.76 (83.24–96.34)	96.47% (89.32–99.08)
	Specificity	68.75% (41.48–87.87)	70.59 (44.05–88.62)	60% (32.89–82.54)	86.67% (58.39–97.66)
	PPV	93.42% (84.66–97.55)	94.05 (86.04–97.79)	92.86 (84.53–97.06)	97.62% (90.86–99.59)
	NPV	45.83% (26.17–66.76)	75% (47.41–91.67)	56.25 (30.55–79.24)	81.25% (53.69–95.03)
	Significance (p)	<0.0001	<0.0001	<0.0001	<0.0001
	Accuracy	82% (79.3–84.8)	91% (87.3–95.8)	87% (82.3–91.7)	95% (91.8–98.3)
	PLR (C)	2.7 (1.3–5.62)	3.24 (1.55–6.77)	2.29 (1.23–4.28)	7.24 (1.99–26.31)
	NLR (C)	0.23 (0.13–0.39)	0.07 (0.03–0.19)	0.14 (0.06–0.30)	0.04 (0.01–0.13)
	PLR (W)	14.2 (6.07–33.2)	15.8 (6.74–37.03)	13 (6–28.17)	41 (10.42–161.3)
	NLR (W)	1.18 (0.74–1.88)	0.33 (0.14–0.81)	0.78 (0.41–1.49)	0.23 (0.08–0.66)
Transudates	Prevalence	81.14% (71.67–87.89)	83.16% (78.62–86.9)	82.15% (76.6–88.4)	84.16% (75–90.3)
	Sensitivity	86.42% (76.58–92.7)	69.9% (59.37–78.74)	68.18% (57.28–77.48)	95.24% (87.59–98.46)
	Specificity	94.74% (71.89–99.72)	85.71% (42–99.25)	91.67% (59.75–99.56)	75% (47.4–91.67)
	PPV	98.8% (91.35–99.92)	98.48% (90.73–99.92)	98.36% (90.02–99.91)	95.24% (87.59–98.46)
	NPV	0.62 (0.42–0.79)	17.65% (7.39–35.17)	28.21% (15.55–45.1)	75% (47.4–91.67)
	Significance (p)	<0.0001	<0.0001	<0.0001	<0.0001
	Accuracy	88% (84.5–91.5)	93% (89.2–96.8)	71% (68.2–73.8)	92% (88.8–95.2)
	PLR (C)	16.42 (2.43–110.8)	4.89 (0.79–30.18)	8.18 (1.25–53.72)	3.81 (1.63–8.91)
	NLR (C)	0.14 (0.08–0.25)	0.35 (0.25–0.5)	0.35 (0.25–0.48)	0.06 (0.02–0.17)
	PLR(W)	70 (10–490)	65 (9.29–454.7)	60 (8.59–419.24)	20 (7.68–52.1)
	NLR(W)	0.61 (0.37–1.01)	4.67 (3.05–7.14)	2.55 (1.84–3.52)	0.33 (0.14–0.81)

LDH-PF/S, ratio of lactate dehydrogenase in pleural fluid and serum; TP-PF/S, ratio of total proteins in pleural fluid and serum; LDH-PF, LDH in pleural fluid; ADA-PF, adenosine deaminase in pleural fluid; PPV, positive predictive value; NPV, negative predictive value; PLR, positive likelihood ratio; C, conventional; NLR, negative likelihood ratio; W, weighted by prevalence.

LDH-PF/S ratio in case of transudates is 94.74% (95% CI: 71.89–99.72) against 68.75% in case of exudates, that of TP-PF/S ratio is 85.71% (95% CI: 42–99.25) against 70.59% in case of exudates, and that of LDH-PF for transudates is 91.67% (95% CI: 59.75–99.56) against 60% in case of exudates. Hence, in case of the parameters included in Light's criteria, both sensitivity and specificity are not higher for exudates or transudates. If sensitivity was higher then specificity was lower and vice versa. To get high sensitivity and specificity, we performed analysis of ADA from PF and it was found that in case of exudates, sensitivity of ADA-PF was 96.47%, specificity was 86.67%, and diagnostic accuracy was 95%, which was higher than that of parameters of Light's criteria. In case of transudates, the sensitivity, specificity, and diagnostic accuracy were 95.23%, 75%, and 92%, respectively. Hence, the sensitivity and accuracy were better although specificity was lower. Table 2 also comprises other related statistical data of the diagnostic parameters run as isolated tests.

Table 3 summarizes the analysis of diagnostic parameters of Light's criteria for the diagnosis of transudates and exudates, which were run as multiple parallel tests using LDH and TP. Using multiple parallel tests, we found the sensitivity, specificity, and diagnostic accuracy to be 98.9%, 75%, and 95% respectively for diagnosis of pleural exudates, whereas the corresponding values for the diagnosis of pleural transudates were 95.29%, 80%, and 93%, respectively. It is evident that specificity is still lower in both transudates and exudates despite using multiple parallel tests.

To distinguish exudates from transudates, we determined the best cutoff points or reference values for LDH-PF, TP-PF, and ADA-PF with the help of the ROC curve. That is, to determine LDH-PF, the cutoff point to distinguish exudates from transudates was 325 U/L, which means >325 U/L indicates exudate and ≤ 325 U/L indicates transudate. The area under ROC curve (AUC) was 0.956 ($p < 0.0001$). Regarding TP-PF, the cutoff point to distinguish exudates from transudates was 3.4 mg/dL, which means >3.4 mg/dL indicates exudate and ≤ 3.4 mg/dL indicates transudate. The AUC was 0.892 ($p < 0.0001$). Regarding ADA-PF, the cutoff point to distinguish exudates from transudates was 35 U/L, which means >35 U/L indicates exudate and ≤ 35 U/L indicates transudate. The AUC was 0.922 ($p < 0.0001$).

Table 4 shows the analysis of the diagnostic parameters of new criteria for exudates and transudates after applying multiple parallel tests for LDH-PF, TP-PF, and ADA-PF. For the diagnosis of exudates, the sensitivity, specificity, and accuracy were 98.81%, 93.75%, and 98%, respectively, whereas in case of transudates, the corresponding values were 95.23%, 87.5%, and 94%. It is evident that the diagnostic parameters of the new criteria are comparable to those included in Light's criteria.

Table 3: Analysis of diagnostic parameters of Light's criteria for the diagnosis of pleural exudates and transudates

	Estimated value	95% Confidence interval	
		Lower limit	Upper limit
Exudates			
Sensitivity	98.90%	95%	99.95%
Specificity	75%	52.95%	89.40%
Positive predictive value	95.42%	89.87%	98.12%
Negative predictive value	94.74%	71.89%	99.72%
Accuracy	95%	92.20%	98.10%
Likelihood ratios: (C) = conventional; (W) = weighted by prevalence			
Positive (C)	3.97	1.98	7.94
Negative (C)	0.01	0.001	0.076
Positive (W)	20.83	9.52	45.56
Negative (W)	0.056	0.008	0.376
Transudates			
Sensitivity	95.29%	87.73%	98.48%
Specificity	80%	51.37%	94.68%
Positive predictive value	96.42%	89.19%	99.07%
Negative predictive value	75%	47.40%	91.67%
Accuracy	93%	89.90%	96.10%
Likelihood ratios: (C) = conventional; (W) = weighted by prevalence			
Positive (C)	4.76	1.73	13.12
Negative (C)	0.06	0.02	0.16
Positive (W)	27	8.88	82.09
Negative (W)	0.33	0.14	0.81

Table 4: Analysis of diagnostic parameters of new criteria for the diagnosis of pleural exudates and transudates

	Estimated value	95% Confidence interval	
		Lower limit	Upper limit
Exudates			
Sensitivity	98.81%	92.62%	99.94%
Specificity	93.75%	67.71%	99.67%
Positive predictive value	98.81%	92.62%	99.94%
Negative predictive value	93.75%	67.71%	99.67%
Accuracy	98%	94.40%	99.92%
Likelihood ratios: (C) = conventional; (W) = weighted by prevalence			
Positive (C)	15.81	2.37	105.47
Negative (C)	0.01	0.001	0.089
Positive (W)	83	11.83	582.45
Negative (W)	0.067	0.010	0.448
Transudates			
Sensitivity	95.23%	87.59%	98.46%
Specificity	87.5%	60.41%	97.8%
Positive predictive value	97.56%	90.65%	99.58%
Negative predictive value	77.78%	51.92%	92.63%
Accuracy	94%	90.8%	97.2%
Likelihood ratios: (C) = conventional; (W) = weighted by prevalence			
Positive (C)	7.62	2.08	27.88
Negative (C)	0.05	0.02	0.14
Positive (W)	40	10.17	157.3
Negative (W)	0.29	0.12	0.70

Table 5: Comparison between Light's criteria and new criteria

Diagnosis	Diagnostic yield (accuracy)			Sensitivity		Specificity		Combined ROC curve	
	Light's criteria	New criteria	*p*-Value	Light's criteria	New criteria	Light's criteria	New criteria	Light's criteria	New criteria
Exudate	95%	98%	0.0018	98.9%	98.81%	75%	93.75%	0.884 ($p < 0.0001$)	0.906 ($p < 0.0001$)
Transudate	93%	94%	0.916	95.29%	95.23%	80%	87.5%		

Table 5 summarizes the comparison of diagnostic accuracy of the new criteria of our study with that of Light's criteria. The diagnostic accuracy of new criteria proposed for the diagnosis of exudates was significantly comparable with that of Light's criteria. Furthermore, combined ROC curves for Light's criteria and new criteria were obtained after applying multiple parallel tests.

Figure 1 shows that the AUC for Light's criteria was 0.884 ($p < 0.0001$) whereas that for new criteria was 0.906 ($p < 0.0001$). Hence, it is concluded that new criteria is significantly comparable to Light's criteria.

Discussion

Because pleural effusion is due to an underlying disease, it must be differentiated into transudate or exudate to know its exact etiopathology so that appropriate management can be done. Transudate occurs in conditions such as congestive heart failure, pneumonia, atelectasis, and mediastinal carcinomatosis, whereas an exudate results from diseases such as tuberculosis, carcinoma lung, SLE, and empyema.[2] To distinguish exudates from transudates, LDH, TP, and ADA were used and the cutoffs were determined with the help of ROC curve. The values for AUC were calculated with a trapezoidal method,[13] with values close to 1.0 indicating high diagnostic accuracy.[14,15] We then calculated sensitivity, specificity, and diagnostic accuracy by applying multiple parallel tests.

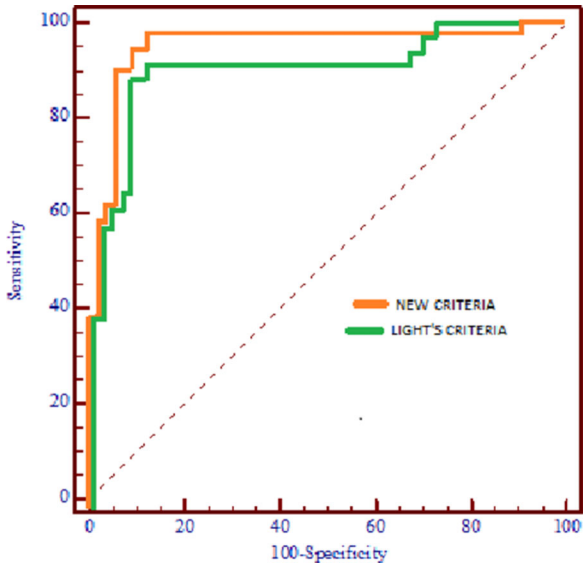

Figure 1: Comparison of combined ROC curve of Light's criteria and new criteria

Maranhão et al.[16] conducted a similar study in which the sensitivity, specificity, and accuracy were 99.4%, 72.6%, and 99.2%, respectively, for the diagnosis of exudates whereas in case of transudates, the corresponding values were 98.5%, 83.4%, and 90%. This clearly states that the specificity in the diagnosis of exudates and transudates is significantly lower as against our study, which can lead to misclassification of exudates and transudates. This was probably because they had used only two parameters, namely LDH and TP using multiple parallel tests whereas we included ADA in addition to LDH and TP and applied multiple parallel tests. Furthermore, the reason behind high sensitivity and low specificity in case of their study could be that they decided a cutoff of LDH as 328 U/L against 325 U/L in our study. In our study, the cutoff values were uniformly selected using a formal technique that maximized sensitivity without markedly decreasing specificity. This technique suggests that the fundamental feature of diagnostic tests is a linkage between sensitivity and specificity, which produces a relatively large decrease in specificity for a small gain in sensitivity when cutoff values are selected to decrease false-negative results to an extreme degree. Bearing this in mind, cutoff points were determined such that specificity would not be compromised by marginally increasing sensitivity.[17]

In our study, we obtained diagnostic parameters that were comparable to those included in Light's criteria.[1] It is evident that the sensitivity of diagnostic parameters of Light's criteria as isolated tests is low in case of transudates, which may lead to misclassification of a transudate as an exudate. Whereas in case of exudates, specificity of those parameters was low that may lead to misclassification of exudates and transudates. Hence, it is advantageous to use multiple parallel tests that will improve the overall sensitivity and specificity. By applying multiple parallel tests in case of diagnostic parameters of Light's criteria, the sensitivity, specificity, and diagnostic accuracy were 98.9%, 75%, and 95%, respectively, whereas in case of transudates, the corresponding values were 95.29%, 80%, and 93%. Light's criteria may have almost 100% sensitivity in diagnosis of exudates but approximately 20% patients with pleural effusion that was caused by CCF may fulfill the criteria of exudative effusion after being treated with diuretics and hence may be misdiagnosed.[18] This clearly states that the lower specificity can lead to misclassification of transudates as exudates. Another advantage of our study is that all tests are to

be performed from PF only, whereas in case of Light's study, both blood and PF samples have to be collected to perform LDH-PF/S and TP-PF/S. Hence, more number of tests will be used and it will increase the cost as well.

Atalay et al.[11] carried out a study on ADA and proved that it was a useful biochemical marker to differentiate transudates from exudates, and it was equally sensitive and specific as albumin gradient. In case of exudates, the sensitivity and specificity were 85.8% and 82.3%, respectively, which were lower as compared to our study. The limitation of this study was that it included only exudates, whereas in our study both exudates and transudates were included.

Heffner et al.[19] conducted a meta-analysis of diagnostic tests that were used to distinguish exudative from transudative pleural effusion wherein they used a number of parameters that included LDH-PF, TP-PF, and cholesterol-PF (C-PF). They derived cutoff points for each parameter and processed them as paired and triplet combinations, that is, LDH-PF/C-PF and TP-PF/LDH-PF/C-PF, respectively. For the diagnosis of exudative effusion, the sensitivity and specificity of LDH-PF/C-PF were 97.5% and 71.9%, respectively, whereas the corresponding values for TP-PF/LDH-PF/C-PF were 98.4% and 70.4%. It is evident that specificity is much lower as compared to our study, which could be because we have replaced cholesterol by ADA.

Conclusion

From this study it can be concluded that PF analysis of LDH, TP, and ADA is easy, simple, cost-effective, and has high sensitivity, specificity, and accuracy for the diagnosis of pleural effusions. By using combined ROC curve it can be concluded that the new criteria is significantly comparable to Light's criteria. The use of new criteria of our study is effective and satisfactory as its diagnostic accuracy is as good as that of Light's criteria. By applying Light's criteria to our study, we obtained diagnostic parameters that were similar to those found in the original study. Because the diagnostic accuracy of the two criteria are comparable, the new criteria can be used as a useful biochemical marker to suggest exudative effusions and can be used in day-to-day laboratory practice.

References

1. Light RW, MacGregor ML, Luchsinger PC, Ball WC. Pleural effusions: the diagnostic separation of transudates and exudates. Ann Intern Med 1972;**77**(4):507–13. .
2. Kumar V, Abbas A, Fausto N. Acute and chronic inflammation. In: *Pathologic Basis of Disease*, 7th edn, Robbins SL and Cotran RS (Eds.). Philadelphia: Saunders, Elsevier, 2004. pp. 49–53.
3. Carr DT, Power MH. Clinical value of measurements of concentration of protein in pleural fluid. N Engl J Med 1958;259(19):926–7.
4. Joseph J, Badrinath P, Basran GS, Sahn SA. Is the pleural fluid transudate or exudate? A revisit of the diagnostic criteria. Thorax 2001;56(11):867–70.
5. Valdes L, Pose A, Surez J, Gonzales-Juanatey JR, Sarandeses A, Jose ES, et al. Cholesterol: a useful parameter for distinguishing between pleural exudates and transudates. Chest 1991;99(5): 1097–102.
6. Hamm H, Brohan U, Bohmer R, Missmahl HP. Cholesterol in pleural effusions: a diagnostic aid. Chest 1987;92(2):296–302.
7. Metintas M, Alatas O, Alatas F, Colak O, Ozdemir N, Erginel S. Comparative analysis of biochemical parameters for differentiation of pleural exudates from transudates Light's criteria, cholesterol, bilirubin, albumin gradient, alkaline phosphatase, creatine kinase, and uric acid. Clin Chim Acta 1997;264(2):149–62.
8. Meisel S, Shamis A, Thaler M, Nussinovicht N, Rosenthal T. Pleural fluid to serum bilirubin concentration ratio for the separation of transudates from exudates. Chest 1990;98(1):141–4.
9. Roth BJ, O'Meara TF, Cragun YM. The serum effusion albumin gradient in the evaluation of pleural effusions. Chest 1990;98(3): 546–9.
10. Romero-Candeira S, Hernández L. The separation of transudates and exudates with particular reference to the protein gradient. Curr Opin Pulm Med 2004;10(4):294–8.
11. Atalay F, Ernam D, Hasanoglu HC, Karalezli A, Kaplan O. Pleural adenosine deaminase in the separation of transudative and exudative pleural effusions. Clin Biochem 2005;38(12):1066–70.
12. Ocaña I, Martinez-Vazquez JM, Segura RM, Fernandez-De-Sevilla T, Capdevila JA. Adenosine deaminase in pleural fluids. Test for diagnosis of tuberculous pleural effusion. Chest 1983;84(1):51–3.
13. DeLeo JM, Campbell G. The fuzzy receiver operating characteristic function and medical decisions with uncertainty. In: Proceedings of the First International Symposium on Uncertainty Modeling and Analysis, Ayyub BM (Ed.). New York: IEEE Computer Society Press, 1990. pp. 694–9.
14. Hanley JA, McNeil BJ. The meaning and use of the area under a receiver operating characteristic (ROC) curve. Radiology 1982; 143(1):29–36.
15. McNeil BJ, Hanley JA. Statistical approaches to the analysis of receiver operating characteristic (ROC) curves. Med Decis Making 1984;4(2):137–50.
16. Maranhão BH, Silva Junior CT, Chibante AM, Cardoso GP. [Determination of total proteins and lactate dehydrogenase for the diagnosis of pleural transudates and exudates: redefining the classical criterion with a new statistical approach]. J Bras Pneumol 2010;36(4):468–74.
17. Riegelman RK, Hirsch RP. Questions to ask in studying a study and testing a test. In: How to Read the Medical Literature, 2nd edn, Laplante M (Ed.). Boston: Little Brown, 1989. pp. 75–7.
18. Porcel JM, Vives M, Vicente de Vera MC, Cao G, Rubio M, Rivas MC. Useful tests on pleural fluid that distinguish transudates from exudates. Ann Clin Biochem 2001;38(Pt 6):671–5.
19. Heffner J, Brown L, Barbieri C. Diagnostic value of tests that discriminate between exudative and transudative pleural effusions. Primary Study Investigators. Chest 1997;111(4):970–80.

How to cite this article: Mehta M, Marwah S, Shah H, Trivedi A. A study of the utility of lactate dehydrogenase, total proteins, and adenosine deaminase in the diagnosis of pleural exudates: A new statistical approach. Int J Med Sci Public Health 2015;4: 286-291

Source of Support: Nil, **Conflict of Interest:** None declared.