International Journal of Advances in Medicine
Sujatha G et al. Int J Adv Med. 2017 Apr;4(2):457-462
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933
DOI: http://dx.doi.org/10.18203/2349-3933.ijam20171041

Original Research Article

Significance of serum-pleural effusion albumin gradient in differentiating transudative and exudative pleural effusions in comparison to light's criteria

Sujatha G.[1], Vindhya P.[2]*, Kalyan Kumar K.[3]

[1]Assistant Professor, [3]Senior Resident, Department of Pulmonary Medicine, Kamineni Academy of Medical Sciences and Research Centre, LB Nagar, Hyderabad, Telangana, India
[2]Assistant Professor, Department of Pulmonary Medicine, Malla Reddy Institute of Medical Sciences, Suraram, Hyderabad, Telangana, India

Received: 13 January 2017
Accepted: 17 February 2017

***Correspondence:**
Dr. Vindhya P.,
E-mail: vindhyareddy.ponna@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Approximately one million patients develop pleural effusion every year. It is a common clinical disorder and is either a manifestation or a complication of one or other respiratory or non-respiratory disorders. It leads to serious prognosis, if not diagnosed and treated properly. To calculate SEAG and Light's criteria and to compare SEAG with Light's criteria in analyzing pleural effusions.
Methods: A total of hundred patients were selected for the study. Pleural fluid of patients who met the inclusion and exclusion criteria were collected, when pleural fluid is being tapped for diagnostic thoracocentesis. Venous blood sample was collected along with diagnostic thoracocentesis or within 24 hours of thoracocentesis. Written informed consent was obtained from them for thoracocentesis.
Results: In our study we compared the clinical outcome with outcome as per Pleural fluid/Serum protein ratio (p value of <0.0001), pleural fluid/serum LDH (p value of <0.0001) and pleural fluid LDH (p value of <0.0001) separately and the p values were statistically significant. The sensitivity, specificity, PPV and NPV of Light's criteria were 77.2%, 100%, 100%, 93.9% respectively. We compared Light's criteria outcome with clinical outcome and the difference was statistically significant (p value of <0.0001). SEAG showed 100% sensitivity, 97.43% specificity, 91.6% PPV and is 91.66% and NPV is 100%. We compared the clinical outcome with SEAG and there was statistically significant difference (p value of <0.0001). We compared SEAG with Light's criteria and the difference was statistically significant (p <0.0001). We compared Light's plus pleural fluid protein gradient with SEAG and the difference is statistically significant (p value of <0.0001).
Conclusions: SEAG is more sensitive for classifying transudates and more specific for exudates than Light's criteria.

Keywords: Exudate, Effusion, Pleural effusion, Transudate

INTRODUCTION

It is estimated that every year one million people have pleural effusion.[1] Pleural effusion is very common. It results as a complication of respiratory disorder or non respiratory disorder. It can also result as a manifestation of respiratory disorder or non respiratory disorder.[2] If pleural effusion is not diagnosed and treated at an early stage, it can lead serious complication and prognosis may be hampered.

Whenever a physician sees a patient with pleural effusion, he should try to find out the cause in terms of whether it is transudate or exudates. The altered systemic factors can lead to transudate pleural effusion that influence the pleural fluid formation and absorption. Left ventricular failure and cirrhosis of liver are considered as important causes of transudate pleural effusion. The altered local factors can lead to exudates pleural effusion that influence the pleural fluid absorption and formation. Bacterial pneumonia, viral infection etc. are considered as important causes of exudates pleural effusion.[3]

Hence classification of pleural effusion as transudate or exudates is important from treatment point of view. Light's criteria is used to classify the pleural effusion. As on whole, the exudates type of pleural effusion should fulfil at least one criteria and the transudate type of pleural effusion should not fulfil any criteria for proper classification.[4]

Sometimes transudates can be classified as exudates as the origin is uncertain.[5] Pleural capillaries are considered as the source of pleural effusion.[6] The fluid gets transferred from across the pleural space.[7] This is due to the semi permeable nature of endothelium in the pleural area. [7, 2] The diffusion is due to components like globulin and albumin in the serum.[8-10] and the sub pleural lymphatic vessels clear them.[7] The causes of exudates pleural effusion are swelling and reduced diameter of microvasculature. The in case of transudate pleural effusion there is no swelling and reduced diameter of microvasculature. Thus increased fluid leakage is seen in exudates type of pleural effusion. But in transudate pleural effusion, there is loss of balance of hydrostatic forces and loss of balance of osmotic forces.[2,7]

Roth et al stated that this principle can be applied to distinguish between transudate and exudates type of pleural effusion.[11]

Hence present study was undertaken to calculate SEAG and Light's criteria and to compare SEAG with Light's criteria in analysing pleural effusions

METHODS

The sources of data are the patients with pleural effusion based on clinical and radiological basis from the departments of General medicine, Pulmonology, Gastroenterology and Nephrology, Kamineni Hospitals, LB Nagar, Hyderabad, from October 2012 to October 2014.

A total of hundred patients were selected for the study. Pleural fluid of patients who met the inclusion and exclusion criteria was collected, when pleural fluid is being tapped for diagnostic thoracocentesis. Venous blood sample was collected along with diagnostic thoracocentesis or within 24 hours of thoracocentesis. Written informed consent was obtained from them for thoracocentesis.

The patients were followed up to their discharge and classified as exudates or transudates based on the clinical features, microscopy, cytology, biopsy, pleural fluid culture, radiography & response to treatment and were included in the study.

Inclusion criteria

Patients with clinical and radiological evidence of pleural effusion

Exclusion criteria

- Age less than 14 years
- Pregnant females
- Old diagnosed cases of Pleural effusion

Informed consent was obtained from all the subjects included in the study. Blood Samples were collected by venipuncture under aseptic conditions in red capped vacutainers. Pleural fluid is collected in sterile containers from the patient when they are undergoing diagnostic thoracocentesis observing standard safety & aseptic precautions. The blood was allowed to clot.

Blood and pleural fluid were centrifuged for the estimation of total protein & LDH on a fully automated system within 3-4 hours of sample collection. Total proteins were estimated by Biuret method and serum albumin was measured by BCG method. LDH was estimated by modified IFCC method in which rate of oxidation of NADH to NAD was measured as a decrease in absorbance that was proportional to the LDH activity in the sample.

Chest X rays were taken for all the subjects, Ultrasound chest and CT chest were asked in selected patients. By sputum examination [sputum for AFB], Bronchoscopy and BAL, ADA level in the pleural fluid more than 40 U/L, more than 70 U/L (highly suggestive of TB) we diagnosed a case as Tuberculosis.

Malignancy was diagnosed based on the malignant cells in the pleural fluid, Paramalignant effusions based on the underlying malignancy, CECT chest and CT guided biopsy. Para pneumonic effusions were diagnosed based on the sputum examination [gram stain] and cultures for organisms, USG or CT chest, and resolution with antibiotics.

Pancreatitis was diagnosed based on Serum amylase and lipase levels, CT abdomen and Pleural fluid/Serum amylase ratio of 1.0. PPF is diagnosed based on the pleural fluid amylase levels and MRCP. Congestive cardiac failure is diagnosed based on the clinical presentation, 2D ECHO, past history and resolution of effusions with diuretics. Cirrhosis of liver with ascites is

diagnosed based on the history, clinical details and Ultrasound abdomen. Nephrotic syndrome was diagnosed based on 24 hour urine protein and serum albumin levels. Patients without clinical diagnosis were excluded from the study.

Ethics committee of our institution has reviewed the protocol and approved the study. Informed consent was taken from all the patients in the study group.

RESULTS

The present study was conducted on 100 patients with Pleural effusion from the Departments of General medicine, Pulmonology, Nephrology and Gastroenterology, Kamineni hospital, L. B. Nagar, Hyderabad between October 2012 and October 2014.

The mean age of patients in our study group was 51.85±18.53 years. 57(57%) were males and 43(43%) were female subjects.

Out of 78 subjects, 25 [32%] were Para-pneumonic effusions, 21 [27%] were due to Tuberculosis, 19 [25%] were Para-malignant effusions, 7 [9%] were Malignant effusions, 4 [5%] were due to Pancreatitis, 1 [1%] was due to pancreatico-pleural fistula and the other one [1%] was due to esophageal rupture (Figure 1).

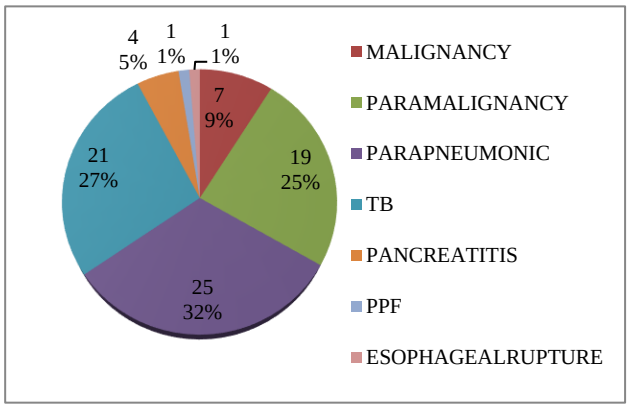

Figure 1: Distribution of exudates.

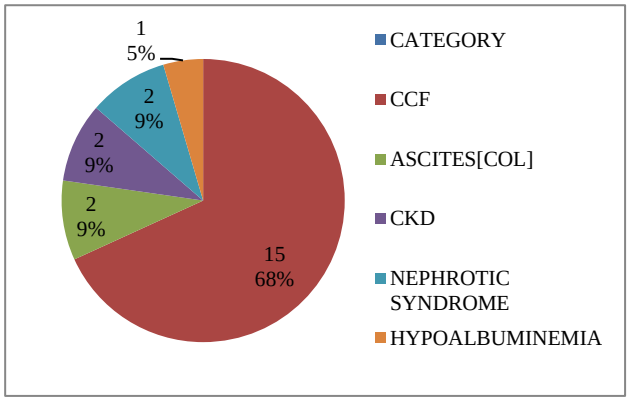

Figure 2: Distribution of transudates.

Out of 22 subjects with transudative effusions 15 [68%] were due to congestive cardiac failure, 2 [9%] each with cirrhosis of liver with ascites, chronic kidney disease, nephrotic syndrome and 1 [5%] with hypoalbuminemia rupture (Figure 2).

The mean of serum protein, serum albumin and serum LDH in our study group are 5.74±1.149 g/dl, 2.96± g/dl, 283.29 U/L respectively (Table 1).

Table 1: Distribution of serum variables.

Statistics	Serum total protein g/dl	Serum albumin g/dl	Serum LDH U/L
N	100	100	100
Mean	5.74	2.96	283.29
Median	5.50	2.50	261.50
Std. deviation	1.149	0.706	126.408
Minimum	4	2	75
Maximum	9	6	900

The men values of Pleural fluid protein, albumin and LDH are 3.78±1.662 g/dl, 2.13±0.988 g/dl, 361.42±246.330 U/L (Table 2).

Table 2: Distribution of pleural fluid variables.

Statistics	Pleural fluid protein g/dl	Pleural fluid LDH U/L	Pleural fluid albumin g/dl
No. of observations	100	100	100
Mean	3.78	361.42	2.13
Median	3.50	340.00	2.00
Std. deviation	1.662	246.330	0.988
Minimum	2	58	0
Maximum	9	1600	7

The mean values for pleural fluid protein/serum protein, pleural fluid LDH/Serum LDH are 0.49±0.249 and 0.91±0.970 respectively (Table 3).

Table 3: Distribution of light's criteria ratios.

Statistics	Pleural fluid protein/ Serum protein	Pleural fluid LDH/ Serum LDH
No of observations	100	100
Mean	0.49	0.91
Median	0.50	0.50
Std. deviation	0.249	0.970
Minimum	0	0
Maximum	2	5

Table 4: Distribution of pleural fluid/serum protein ratio.

	No of patients	% of patients
Transudate	24	24
Exudate	76	76

In our study we found out that taking pleural fluid protein/serum protein cut off as 0.5 (>0.5 as exudate and <0.5 as transudate) there are 76% exudates and 24% transudates (Table 4).

We compared the clinical outcome with Pleural fluid protein/Serum protein ratio outcome and the P value of <0.0001 was significant (Table 5).

Table 5: Pleural fluid/serum protein versus clinical outcome.

Category exudates or transudate	No. of cases as per clinical outcome	No. of cases differentiated by pleural fluid/Serum protein	No. of cases truly classified	No. of cases misclassified classified	P value
Exudate	78	76	73	3 (3.9%)	<0.0001
Transudate	22	24	22	2 (8.3%)	Significant

In present study we found out that taking pleural fluid protein/serum protein cut off as 0.6 (>0.6 as exudate and <0.6 as transudate) there are 83% exudates and 17% transudates (Table 6). Comparing Pleural fluid protein/serum protein ratio, P value of <0.0001 is significant (Table 7).

Pleural fluid LDH of more than 220 U/L is taken as an exudative effusion and below that as transudative effusion. Thus the patients with transudate were 28% and patients with exudate were 72% (Table 8).

Table 6: Distribution of pleural fluid/serum LDH outcome.

	No of patients	% of patients
Transudate	17	17
Exudate	83	83

Table 7: Pleural fluid/serum LDH Vs clinical outcome.

Category- exudate or transudate	No. of cases as per clinical outcome	No. of cases differentiated by pleural fluid/ serum LDH	No. of cases truly classified	No. of cases misclassified classified	P value
Exudate	78	83	83	0	<0.0001
Transudate	22	17	12	5(29.4%)	Significant

Table 8: Distribution of pleural fluid LDH outcome.

	No of patients	% of patients
Transudate	28	28
Exudate	72	72

Pleural fluid LDH of more than 220 U/L is taken as an exudative effusion and below that as transudative effusion (Table 9). Light's criteria classified 83 patients under exudative effusions and 17 patients under transudative effusions (Table 10).

Table 9: Pleural fluid versus clinical outcome.

Category- exudates or transudate	No. of cases as per clinical outcome	No. of cases differentiated by Pleural fluid LDH>220U/L	No. of cases truly classified	No. of cases misclassified classified	P value
Exudate	78	72	65	7(9.7%)	<0.0001
Transudate	22	28	27	1(3.5%)	Significant

P value of <0.0001 is significant.

The sensitivity and specificity of Light's criteria for the separation of transudates is 77.2% and 100% respectively. Positive predictive value and Negative predictive value are 100% and 93.97% respectively. And for exudates the sensitivity, specificity, positive and negative predictive value are 100%, 77.2%, 93.97% and 100%. P value of <0.0001 is significant. We compared Light's criteria outcome with Clinical outcome and the p value was statistically significant (Table 11).

Table 10: Distribution of light's criteria outcome.

	No. of patients	% of patients
Transudate	17	17.0
Exudate	83	83.0

Table 11: Light's criteria versus clinical outcome.

	Clinical -outcome		
Light's criteria outcome	**Transudate**	**Exudate**	**Total**
Transudate	17 (TP)	0 (FP)	17
Exudate	5 (FN)	78 (TN)	83
Total	22	78	100

SEAG classified 24 [24%] subjects as transudates, 76 [76%] as exudates (Table 12).

Table 12: Distribution of SEAG outcome.

	No of patients	% of patients
Transudate	24	24.0
Exudate	76	76.0

Table 13: SEAG versus clinical outcome.

	Light's criteria outcome		
SEAG criteria outcome	**Transudate**	**Exudate**	**Total**
Transudate	17	7	24
Exudate	0	76	76
Total	17	83	100

Table 14: SEAG versus light's criteria.

	Light's criteria outcome		
SEAG criteria outcome	**Transudate**	**Exudate**	**Total**
Transudate	17	7	24
Exudate	0	76	76
Total	17	83	100

For classifying transudates SEAG is 100% sensitive and 97.43% specific. Positive predictive value is 91.66%; Negative predictive value is 100%. For exudates the sensitivity is 97.3%, specificity is 100%, positive predictive value is 100%, and negative predictive value is 91.66%. P value of <0.0001 is significant. SEAG outcome is compared with clinical outcome and the p value of <0.0001 is statistically significant (Table 13).

P value of <0.0001 is significant. In our study we compared SEAG outcome with that of Light's criteria and the p value was statistically significant (Table 14).

DISCUSSION

The mean age of study population was 51.3±18.53 years. Para-pneumonic effusions were seen in all age groups maximum between 20 and 50 years. Tuberculous effusion was equally seen in all age groups. Roth et al found that the average age group was 61 years.[11] Mean ages of the patients was 55.64±17.081 years in the study done by Gongati P et al.[12]

We found that a male to female ratio of 1.32:1. Roth et al [11] found a ratio of 1.68:1.[11] Gongati P et al found a male to female ratio 2.1:1.[12]

Out of 100 pleural effusions analyzed the maximum (78%) are exudative effusions, out of which the most commonly seen are due to Pneumonia, i.e. Para-pneumonic effusions (32%) followed by Tuberculosis (27%) followed by Para-malignant (25%) effusions. These results are comparable to the study of Gongati P et al, Roth et al**,** Dhar et al reported in his study that the commonest cause of exudative effusion was tuberculosis (42%).[11-13]

The commonest cause of transudative effusions was Congestive heart failure (68%). Our results are comparable to the study of Roth et al.[11]

3 out of 76 exudates (3.94%) were misclassified, one para-pneumonic effusion, one para-malignant effusion and one pancreatico-pleural fistula. 2 (CHF) out of 24 transudates (8.33%) were misclassified. Total misclassification rate is 5%. Gupta KB et al [1] found that 4 out of 12 transudates (33.3%) and 7 out of 48 exudates (14.5%) were misclassified.[1] Das AK et al observed that 5 of the exudates & 3 transudates were falsely classified. Total misclassification of 20% occurred.[14]

In our study pleural fluid LDH/serum LDH > 0.6 (i.e. >0.6 as exudates and < 0.6 as transudates) separated 17 as transudates and 83 as exudates. 5 transudates (four with CHF and one cirrhosis of liver) were misclassified as exudates (29.41%). All the exudates were correctly classified. The difference was statistically significant (p<0.0001) when the LDH ratio was compared to the clinical outcome. Our results are comparable to the study done by Gupta KB et al, Mangaraj M et al, Das AK et al, Sunanda V et al.[1,14-16]

Sensitivity, Specificity, Positive Predictive value and Negative predictive value of Lights criteria for classifying transudates are 77.2%, 100%, 100%, 93.9% respectively. In classifying exudates the sensitivity and

specificity are 100% and 77.2%, Positive and Negative predictive values are 93.97% and 100% respectively. There was a statistically significant difference (p<0.0001) between the light's criteria and the clinical outcome. Our results are comparable to the study by Roth et al, and Dhar et al.[11,13]

For classifying transudates SEAG is 100% sensitive and 97.43% specific. Positive predictive value is 91.66%, Negative predictive value is 100%. For exudates the sensitivity is 97.3%, specificity is 100%, positive predictive value is 100%, and negative predictive value is 91.66%.

SEAG is more sensitive for classifying transudates and more specific for exudates than Light's criteria. There was a statistically significant difference (p<0.0001) between the SEAG criteria and the clinical outcome. Our results are comparable to the study done by Roth et al, and Dhar et al.[11,13]

SEAG correctly classified all the transudates but misclassified two exudates (para malignant effusions) as transudates. SEAG is more sensitive for transudates and more specific for exudates than Light's criteria.

CONCLUSION

It was found that SEAG is a good parameter to differentiate the groups. SEAG is more sensitive than Light's criteria for classifying transudates and is more specific for exudates. SEAG was found to be a better criterion than Light's for classifying transudates. Also only single parameter of pleural fluid is used in SEAG criteria which is easy to apply when compared to Light's criteria where three parameters are needed. Light's criteria with pleural fluid protein gradient is better than SEAG and very promising for classifying pleural effusions.

ACKNOWLEDGEMENTS

The authors would like to acknowledge statistician Mrs. Sucharita Suresh for her invaluable contribution.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee

REFERENCES

1. Gupta KB, Aggarwal SK, Kumar S, Manchanda M. Evaluation of plasma-pleural effusion albumin gradient for differentiating between pleural transudate and exudate. Indian J Tuberculosis. 2003;50-3.
2. Sahn SA. The pleura. Am Rev Respir Dis. 1988;138:184-234.
3. Light RW. In: Fauci AS, Kasper DL, Hauser SL, Longo DL, Jameson JL, Joseph Loscalzo, et al., editors. Harrison's Principles of Internal Medicine. 18th ed. New York: McGraw Hill; 2012. p. 2178.
4. Light RW, MacGregor I, Luchsinger PC, Ball WC. Pleural effusions: the diagnostic separation of transudates and exudates. Ann Intern Med. 1972;77:507-13.
5. Hamun H, Broham U, Bohmer R, Missmahl HP. Cholesterol in pleural effusion a diagnostic aid. Chest. 1987;92:296-302.
6. Broaddus VC, Light RW. What is the origin of pleural transudates and exudates? Chest. 1992;102:658-9.
7. Pistolesi M, Miniati M, Guintini C. Pleural liquid and solute exchange. Am Rev Respir Dis. 1989;140(3):815-47.
8. Zinneman HH, Johnson JJ, Lyon RH. Proteins and microproteins in pleural effusions. Am Rev Respir Dis. 1957;76:247-55.
9. Shallenberger DW, Daniel TM. Quantitative determination of several pleural fluid proteins. Am Rev Respir Dis. 1972;106:121-2.
10. Broaddus VC, Staub NC. Pleural liquid and protein turnover in health and disease. Semin Respir Med. 1987;9:7-12.
11. Roth BJ, O' Meara TF, Cragun WH. The serum-effusion albumin gradient in the evaluation of pleural effusion. Chest. 1990;98:546-9.
12. Paramjyothi K. Comparison of SEAG and ALP against Light's criteria for distinguishing transudates from exudates. Asian J Medical Research. 2013;2(2):45-50.
13. Dhar MC, Chaudhary S, Basu K, Sau Tj, Pal D, K Mitra K. Significance of Serum effusion albumin gradient in the differential diagnosis of pleural effusion. Ind J Tub. 2000;18:241-5.
14. Das AK. A study on Significance of Serum effusion albumin gradient in the differential diagnosis of pleural effusion. Jk science. 2009;11(3):124-5.
15. Mangaraj M, Kumari S, Nandu R, Pattnaik MR, Mohapatra PC, et al. Pleural fluid MDA & serum – effusion albumin gradient in pleural effusion. IJCB. 2008;23;1.81-4.
16. Sunanda V, Shravanthi K. The diagnostic separation of transudates and exudates in pleural effusion. J Coll Med Sci Nepal. 2011;7(3):24-8.

Cite this article as: Sujatha G, Vindhya P, Kumar KK. Significance of serum-pleural effusion albumin gradient in differentiating transudative and exudative pleural effusions in comparison to light's criteria. Int J Adv Med 2017;4:457-62.