

# Serum pleural effusion albumin gradient in differentiating exudative from transudative pleural effusion

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## ABSTRACT

**INTRODUCTION:** In pleural effusion, the first step is to determine whether the effusion is exudative or transudative. This study is carried out to know the diagnostic value of Serum Pleural Effusion Albumin Gradient (SPEAG) criteria in comparison to Light's criteria to differentiate exudative from transudative pleural effusion.

**METHODS:** Patients having pleural effusion admitted in Bir Hospital and Shree Birendra Army Hospital from April 2012 to April 2013 were enrolled in the study. Study population was grouped as exudatives and transudatives etiologically taking clinical diagnosis as the gold standard and was compared with Light's and SPEAG criteria. Sensitivity and specificity of each parameter of Light's criteria were also compared with that of serum pleural effusion albumin gradient.

**RESULTS:** In total 64 patients enrolled in the study, Pleural fluid LDH index of Light's criteria was found to have sensitivity of 100%, specificity of 100%, positive predictive value (PPV) of 100%, negative predictive value (NPV) of 100% and p-value 0.001. Pleural fluid to serum LDH ratio had sensitivity of 100%, specificity of 50%, PPV of 93.75%, NPV of 100%, and p-value 0.01. Similarly, pleural fluid protein/serum protein ratio of 0.5 parameter had sensitivity of 100%, specificity of 75%, PPV of 98.36%, NPV of 100%, and p-value <0.01. SPEAG of 1.2gm/dl was found to have sensitivity of 100%, specificity 100%, PPV of 100% and NPV of 100%. And p-value of 0.001.

**CONCLUSION:** SPEAG was found to differentiate more correctly exudative from transudative pleural effusion than Light's criteria.

**KEY WORDS:** Exudative, Light's criteria, Pleural effusion, Serum pleural effusion albumin gradient.

## INTRODUCTION

When a patient is found to have pleural effusion, an effort should be made to find out the cause. The first and vital step for this is to determine whether the effusion is exudative or transudative. In most setting Light's Criteria is followed to distinguish a case of pleural effusion as exudative or transudative.<sup>1</sup> But, several reports have shown that light's criteria misclassified a large number of pleural effusion, especially transudative<sup>2</sup>.

Pleural effusion has classically been divided into exudative and transudative. An effusion that occurs due to pleural disease resembles like plasma protein rich fluid (resulting from increased capillary permeability) is called exudative effusion<sup>1</sup>. Exudative pleural effusion is more commonly seen

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in inflammatory condition that results in a compromised pulmonary or pleural microvasculature which in turn leads to increased fluid leaking, a higher protein concentration and a decrease in plasma- pleural effusion albumin gradient<sup>2</sup>. Both albumin and globulin fraction in pleural fluid are believed to originate from serum by diffusion. However some proteins like lactic dehydrogenase (LDH) come from within pleural space i.e. from pleural fluid leukocytes<sup>3</sup>. The major advantage of serum pleural effusion albumin gradient is that it is decreased in patients with transudates receiving concurrent diuretic therapy thereby being misclassified as exudates<sup>4</sup>. Therefore, serum pleural effusion albumin gradient is studied for possible reliable tool to differentiate exudates from transudates.

Light's criteria classifies pleural effusion as exudative if it meets one or more of the following criteria<sup>5</sup> : (a) A pleural fluid serum protein ratio 0.5; (b) A pleural fluid LDH concentration >200 IU/ml; (c) A pleural fluid /serum LDH ratio >0.6. Light's criteria have become the standard method for separation as

it has got maximum sensitivity in identifying exudates. But many pleural effusion cases were misclassified by Light's criteria<sup>6</sup>. Therefore, other biochemical parameters like pleural cholesterol<sup>7</sup>, pleural fluid to serum bilirubin ratio<sup>8</sup>, pleural fluid to serum cholinesterase ratio<sup>9</sup>, alkaline phosphatase<sup>10</sup>, creatinine kinase, <sup>11</sup> uric acid<sup>12</sup>, malondialdehyde<sup>13</sup> have been analyzed but none has been found to be 100% sensitive or specific. Recently, plasma-pleural effusion albumin gradient has been reported as a good parameter with 97% sensitivity and 100% specificity<sup>14</sup>. So, this study was carried out to know usefulness of this parameter in our set up.

## METHODS

This study is carried out to know the diagnostic value of proposed Serum Pleural Effusion Albumin Gradient criteria in comparison to Light's criteria to differentiate exudative from transudative pleural effusion and also to compare efficiency of this value with those of light's criteria. This is descriptive observational study. Patients of age 15-75, having pleural effusion and admitted in NAMS, Bir Hospital and Shree Birendra Army Hospital from april 2012 to april 2013 were enrolled in the study. Study population were grouped as exudatives and transudatives etiologically taking clinical diagnosis as the gold standard. Serum pleural effusion albumin gradient of 1.2 gm/dl or less was taken as exudative and the gradient above 1.2 gm/dl was taken as transudative. The result of this tool was compared with those of etiological diagnosis. Similarly, patients were also classified by using light's criteria. Then the results of each parameters of light' criteria like (i) Pleural fluid to serum protein ratio >0.5, (ii) pleural fluid to serum LDH ratio >0.6 (iii) pleural fluid LDH > 2/3<sup>rd</sup> of of the upper limit of normal were compared with those of etiological diagnosis. Then sensitivity and specifity of each parameters of light's criteria were compared with that of serum pleural effusion albumin gradient. Patients having combined or more than one causes of pleural effusion like collagen vascular disease, pancreatic disease, pulmonary embolism etc. and patients with no definite cause diagnosed were excluded from the study. With strict aseptic precaution, pleural fluid aspiration was done and every care was given to prevent complications like infection, bleeding, pneumothorax etc. The following investigations were done routinely in all patients: a) Pleural Fluid: Albumin, total protein, glucose, LDH, total cell count, differential count; b) Blood: Albumin, total protein, glucose and LDH. Patients with Serum pleural effusion albumin gradient of 1.2 was taken as exudative and those with gradient  $\leq 1.2$  was taken as transudative.

## Statistical Methods:

Data were entered and analyzed using Microsoft Office Excel, SPSS ( statistical package for social studies ) software version

17. Independent t-test was was used to compare the results of various parameters among the study patients. All values were expressed as mean  $\pm$  SD. 95% confidence interval was taken and p-value <0.05 was considered as statistically significant. Sensitivity, specifity, positive predictive value and negative predictive value of each parameter of Light's criteria were also compared with that of serum pleural effusion albumin gradient

## RESULTS

In total cases of 64 patients, 60 were male and 4 were female. Cases with pneumonia were 10, and allof them were male. Total patients with tuberculosis were 41, out of which male were 38 and female were 3. Total patients with carcinoma of lungs were 9, out of which male were 8 and female were 1. Only 1 patient had congestive heart failure and it was male. Total patients with cirrhosis of liver with hepatic dysfunction were 3 and all of them were male (100%). Patients with obvious exudative causes of pleural effusion like pneumonia, tuberculosis, carcinoma of lungs were placed in exudative group and those with transudative causes of pleural effusion like congestive heart failure, cirrhosis of liver, hepatic hydrothorax were placed in transudative group. Total patients in exudative group were 60 (93.8%) and with those in transudative group were 4 (6.3%). When adopting serum effusion albumin gradient parameter, 60 (93.75%) cases were separated as exudative and 4 (6.25%) were separated as transudative (Figure 1). This was consistent with number of cases separated on the basis of etiological diagnosis.

When applying pleural fluid LDH 200 U/L criteria in the above cases, 60 (93.75%) cases were separated as exudative and 4 (6.25 %) as transudative . This was consistent with the number of cases separated on the basis of etiological diagnosis; p-value (<0.001). So, exudates classified correctly were 99.95% and transudates classified correctly were 99.21%. When applying pleural fluid to serum LDH ratio of 0.6 index of Light's criteria, 64 (100% ) cases were separated as exudative and 0 (0%) as transudative (Figure 1); p- value was significant (<0.01). Here all exudates were classified correctly but there all transudates were misclassified.

Similarly, when applied serum pleural fluid protein to serum protein ratio of 0.5 index of Light's Criteria, 61(95.1%) were separated as exudative and 3 (4.69%) as transudative. P-value was significant (<0.01). Exudates classified correctly was 99.95% and transudates classified correctly was 99.21%. While applying SPEAG Criteria, exudates classified correctly was 93.75% and transudates classified correctly was 99.21%. (Figure 1)

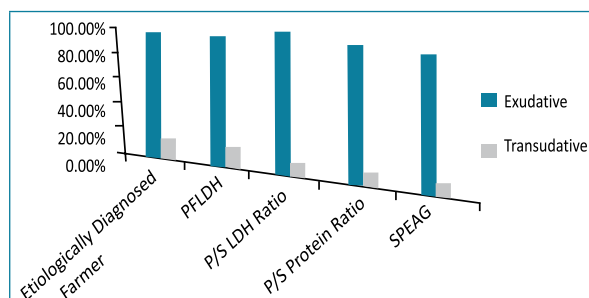


Figure 1. Comparative analysis of parameters of Light's criteria and serum pleural effusion albumin gradient (SPEAG) criteria with the etiological diagnosis of transudate and exudates on discharge (LDH = Lactate dehydrogenase; PF = Pleural fluid; P/S = Pleural fluid / Serum ratio)

Figure 2 shows pleural fluid LDH index of Light's criteria have sensitivity of 100%, specificity of 100%, positive predictive value (PPV) of 100%, negative predictive value (NPV) of 100% and p-value 0.001. Pleural fluid to serum LDH ratio had sensitivity of 100%, specificity of 50%, PPV of 93.75%, NPV of 100%, and p-value 0.01. Similarly, pleural fluid protein/serum protein ratio of 0.5 parameter had sensitivity of 100%, specificity of 75%, PPV of 98.36%, NPV of 100%, and p-value <0.01. Serum pleural effusion albumin gradient parameter had sensitivity of 100%, specificity of 100%, PPV 100%, NPV of 100% and p-value of 0.001.

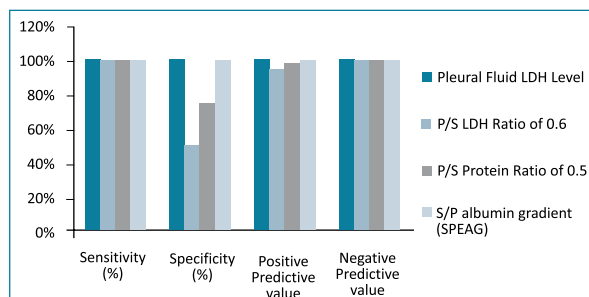


Figure 2. Sensitivity, Specificity, Positive Predictive Value and Negative Predictive Value of Parameters (LDH = Lactate dehydrogenase; P/S = Pleural fluid / Serum ratio; S/P = Serum /Pleural fluid ratio)

## DISCUSSION

Light's Criteria has remained as gold standard in differentiating pleural effusion as exudative and transudative. But, many authors have found transudative pleural effusion been misclassified as exudative, especially those receiving diuretics. Dhar et al.<sup>14</sup> found that Light's Criteria correctly identified all the exudates but misdiagnosed 2 to 5 patients with transudative pleural effusion. But using serum pleural effusion albumin gradient, all patients were correctly diagnosed and the result was compatible with standard aetio-pathological diagnosis made on detailed clinical background. Roth et al found that 57 out of 59 patients were correctly classified by Light's criteria and it was found to have 100% sensitive

and 72% specific, whereas, serum pleural effusion albumin gradient of 1.2 gm/dl or less tends to have 95% sensitive and 100% specific specially in cases of chronic congested heart failure. KB Gupta et al.<sup>7</sup> found that taking a cut off serum pleural effusion albumin gradient of 1.2gm/dl, was able to differentiate between exudates and transudates with sensitivity and specificity of 97.9% and 100% respectively. Chakko et al.<sup>15</sup> performed thoracentesis in patients with effusions due to CHF before and after an average of 6 days of diuresis (SD  $\pm$  2 days). The second thoracentesis showed a significant increase in both protein and LDH level<sup>16</sup> and in 3 of 8 cases, post diuresis chemistry had changed enough to meet the Light criteria for an exudative effusion. Sunanda et al.<sup>17</sup> found in exudative pleural effusion based on pleural fluid protein, 8 cases were misclassified (4 cases Pulmonary TB, 3 Pneumonia and 1 case Malignancy). In transudative effusion 3 cases were misclassified as exudates. But when plasma pleural effusion albumin gradient was evaluated, all of the transudates were well classified. Vazquez F<sup>18</sup> while using the Light's criteria found that a diagnostic accuracy of 82.75% (CI 95%; 73.1- 90%). The albumin gradient did not vary in patients of transudates not receiving diuretics, allowing correct diagnosis of transudates in 93 (82.4 -97.8%) of cases. However in patients who were taking diuretics, classic criteria of protein index defined correctly only in 66% (53.4- 82.1% of cases) (p<0.05 ). But serum pleural effusion albumin gradient allowed the author to establish the correct diagnosis of transudative even in patients taking diuretics. It should be noted that with diuresis, the characteristics of pleural fluid may occasionally change from transudates to those of exudates. However, in such patients, SPEAG, remain above 1.2 g/dl<sup>19</sup>.

## CONCLUSION

Serum pleural effusion albumin gradient (SPEAG) was found to be more useful tool than Light's criteria to differentiate correct & exudative from transudative pleural effusion. It is particularly invaluable at the setting when Light's criteria creates confusion misclassifying transudative pleural effusion as exudative.

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