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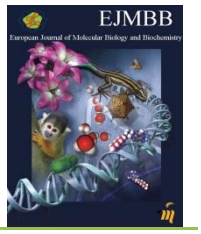


# CORRELATION OF SEAG WITH PLEURAL FLUID PROTEIN THIOLS AS PARAMETER TO DIFFERENTIATE EXUDATES FROM TRANSUDATES

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**ABSTRACT**

Recently SEAG has been reported as good parameter with sensitivity and specificity of 95% and 100%. SEAG is thought to directly reflect the colloidal osmotic pressure. The main advantage of SEAG was reduction in number of patient with transudate receiving concurrent diuretic therapy being misclassified as exudates. Oxidative status of pleural fluid has been analyzed by taking pleural fluid malondialdehyde level (PMDA) as well as different antioxidant enzymes to differentiate transudates from exudates. A total of 56 patients of pleural effusion were taken with diverse etiology, and then venous blood sample and pleural fluid were collected from these patients after diagnosing clinically, radiologically and after thoracocentesis. The greater differential value was found with a combination of SEAG and pleural fluid protein thiols, which correctly classified 92.31% of transudates and 93.34% of exudates with sensitivity and specificity of 92.31% and 83.34% and 93.34% and 92.31% respectively.

## INTRODUCTION

Pleural effusion is a common clinical disorder and is either a manifestation or a complication of one or other respiratory or non-respiratory disease.1 An effusion is termed as transudate when its formation is due to alteration in mechanical factor such as hydrostatic pressure, colloid oncotic pressure, leading to transudative effusion and the causes for this are congestive cardiac failure, pulmonary embolism, nephrotic syndrome, severe anemia, cirrhosis of liver etc. In contrast exudative pleural effusion occurs due to accumulation of fluid or destruction of pleural integrity by inflammatory or infiltration in pleural cavity leads to increase in micro vascular permeability. Causes of pleural effusion are T.B., pneumonia and malignancy [1,2].

So the first step in evaluation of type of pleural effusion is whether it is transudative or exudative [3] and this can be done by light's criteria but many pleural effusion has been misclassified as transdates and exudates [2]. For the past several decades trasudates have been differentiated from exudates, according to light's criteria [4] by measurement of levels of protein and LDH in the serum and the pleural fluid. Since then, several alternative measurements have been proposed, for making this distinction, viz. Serum effusion albumin gradient, protein gradient [5,6] pleural fluid cholesterol [7] pleural fluid/serum cholesterol ratio [7,8] pleural fluid Bilirubin [9] etc. The criteria of Light's et al remain the best method for distinguishing exudates from 2 transudates. The serum-effusion albumin gradient (SEAG) is useful when patients are receiving concurrent diuretic therapy [10].

Light's criteria for exudates are very sensitive but an albumin gradient of 1.2 gm/dl or less tends to be more specific especially in congestive cardiac failure (CCF) on diuretics [10,11]. Light's criteria are the most sensitive for identifying exudates but have lower specificity than other criteria. The main disadvantage of the lights criteria, however, appears to be the occurrence of an exudative

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range of protein levels in many patients with congestive heart failure (CHF) a phenomenon first noted by Pillay [12] in 1965, and later confirmed by Chakko et al [13,14]. This may lead to unnecessary investigations being done in these patients. The problem of high protein transudates is more common in the evaluation of ascites too, which has led to the development of serum - ascites albumin gradient. A gradient of less than 1.1 g/dl has been shown to be the best predictor of exudative ascites and has become an accepted method for differentiating exudate from transudate [15]. It was recommended that if the clinical appearance suggests a transudative effusion but the pleural effusion is an exudate according to Light's criteria, then the difference between serum and pleural fluid albumin levels by a level of more than 1.2 gm/dl would suggest the effusion to be a transudate.

The disadvantage of light's criteria is low specificity and misclassification in about 20-30%.the most widely accepted light's criteria is

a. Pleural protein to serum protein rates greater than 0.5
b. Pleural fluid to serum LDH ratio >0.6
c. Pleural fluid LDH>200 IU/L denoting an exudates.

But the main disadvantage is misclassification of transudates as exudates.

Recently SEAG has been reported as good parameter with sensitivity and specificity of 95% and 100%. SEAG is thought to directly reflect the colloidal osmotic pressure. The main advantage of SEAG was reduction in number of patient with transudate receiving concurrent diuretic therapy being misclassified as exudates. Oxidative status of pleural fluid has been analyzed by taking pleural fluid malondialdehyde level (PMDA) as well as different antioxidant enzymes to differentiate transudates from exudates. The imbalance between oxidants and antioxidants referred as oxidative stress has been associated with various respiratory disorders . Albumin a major plasma protein contains an exposed –SH group over cysteine -34 residues provide the bulk of total thiol pool. These reduced thiol groups that exist both intracellular and extracellular contribute majority of the total antioxidant capacity of the plasma. With the above fact the present study is designed to evaluate SEAG and pleural fluid protein thiol level as parameter to differentiate transudates from exudates.

## METHODOLOGY

A total of 56 patients of pleural effusion were taken with diverse etiology, then venous blood sample and pleural fluid were collected from these patients after diagnosing clinically, radiologically and after thora cocentesis.

**Inclusion Criteria:**

Cases clinically diagnosed as having pleural effusion with diverse etiology

**Exclusion Criteria:**

Cases with either no cause were definitely diagnosed or more than one cause present will be excluded from the study.

Data was collected on standard Proforma, detailing the medical history, physical examination and investigation.

**Parameters Studied:**

1. Serum Albumin
2. Serum Total Proteins
3. Serum Lactate dehydrogenase
4. Serum protein thiols
5. Pleural Fluid Albumin
6. Pleural Fluid Total Protein
7. Pleural Fluid Lactate dehydrogenase
8. Pleural Fluid Protein thiols

**Other Investigations:**

1. Chest X-Ray – PA view
2. C-T Scan of Chest

The biochemical parameters were estimated and calculated.

1. Criteria of light et al (namely: pleural fluid/serum protein ratio, pleural fluid/serum LDH ratio, pleural fluid LDH concentration)
2. Albumin gradient (serum albumin concentration minus pleural effusion albumin concentration)
3. Protein gradient (serum total protein concentration minus pleural effusion total protein concentration) when separating transduates from exudates cut off points recommended in literature were used.

The clinical presumption of nature of effusion (transudate or exudates) was based on all available information obtained just before performing thoracocentesis and was compared with that obtained from biochemical criteria.

Biochemical parameters were determined using semi auto analyzer chem.-7 and spectrophotometer.

## RESULTS

In the present study, in a series of 56 patients, used the serum- effusion albumin gradient for the classification of pleural effusions with a cut-off value of 1.2 g/dl, of 24 of 26 transudates, and 28 of the 30 exudates were classified correctly. The mean albumin gradients were significantly raised in transudates (3.82 ± 0.45g/dl) as compared to exudates (3.08 ± 0.44g/dl) with p value of <0.001 .This method resulted in a sensitivity of 92.31%, and a specificity 92.31% respectively. The present study has shown that even though taking into account the light's criteria and SEAG in differentiating exudates and transudates. The greater differential value was found with a combination of SEAG and pleural fluid protein thiols, which correctly classified 92.31% of transudates and 93.34% of exudates with sensitivity and specificity of 92.31% and 83.34% and 93.34% and 92.31% respectively.

**Table 1. Sex Distribution**

| Total No | 56 | Transudates | Exudates |
|---|---|---|---|
| Males | 34 | 12 | 22 |
| Females | 22 | 14 | 8 |

**Table 2. Final Diagnosis**

| Transudates | Exudates |
|---|---|
| CCF:14 | TB :21 |
| Anemia:05 | Malignancy :07 |
| Cirrhosis;07 | Empyema :02 |
| **Total :26(46.42%)** | **Total :30(53.58%)** |

**Table 3. Exudative effusions**

| Final diagnosis | | SEAG | | Light's Criteria | |
|---|---|---|---|---|---|
| TB | 21 | TB | 20 | TB | 18 |
| Malignancy | 07 | Malignancy | 06 | Malignancy | 04 |
| Empyema | 02 | Empyema | 02 | Empyema | 01 |
| **Total** | **30** | **Total** | **28** | **Total** | **23** |

**Table 4. Transudative effusions**

| Final Diagnosis | | SEAG | | Light's Criteria | |
|---|---|---|---|---|---|
| **CCF** | **14** | **CCF** | **13** | **CCF** | **11** |
| **Cirrhosis** | **07** | **Cirrhosis** | **06** | **Cirrhosis** | **05** |
| **Anemia** | **05** | **Anemia** | **05** | **Anemia** | **04** |
| **Total** | **26** | **Total** | **24** | **Total** | **20** |

**Table 5 a. Sensitivity, Specificity and PPV of SEAG**

| SEAG | Exudate | |
|---|---|---|
| | **Present** | **Absent** |
| **Positive** | **28(tp)** | **02(fp)** |
| **Negative** | **02(fn)** | **24(tn)** |

**Table 5 b. Sensitivity, Specificity and PPV of SEAG**

| SEAG | Exudate | |
|---|---|---|
| | **Present** | **Absent** |
| **Positive** | **24(tp)** | **5(fp)** |
| **Negative** | **02(FN)** | **25(TN)** |

**Figure 1. Correlation of pleural fluid protein thiols with SEAG in exudates**

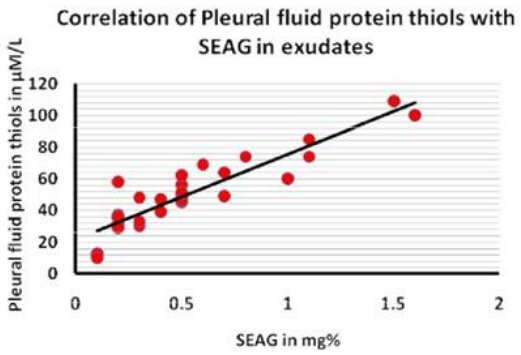
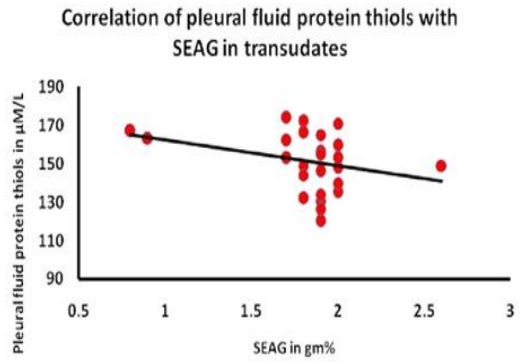



**Figure 2. Correlation of pleural fluid protein thiols with SEAG in transudates**




## DISCUSSION

Both albumin and globulin fraction in pleural fluid are believed to originate from serum via diffusion. However some protein like LDH comes from within pleural space i.e from pleural leucocytes. As pleural fluid albumin is originating from serum, measurement of serum effusion albumin gradient (SEAG) was considered as effective measure in discriminating exudates from transudates[5]. A study conducted by Roth et al [6] used serum-effusion albumin gradient for the classification of

pleural effusions. With a cut-off value of 1.2 g/dI, all transudates and exudates were classified correctly with sensitivity and specificity of 87%, and 92%, respectively. A similar study conducted by Arijit Kumar Das [17] et al and K.B. Gupta [18] et al also showed that though the criteria of light's helps in differentiation of exudates from transudates. But criteria used by light's et al misclassified 33% in transudates and 14% in exudates. But after taking into account the SEAG with a cut off value of 1.2g/dl none of the transudates and only 2% of exudates were misclassified with sensitivity specificity and PPV of 97.9%, 100% and 100% respectively. This has led for consideration of SEAG as parameter to differentiate exudates from transudates. In our present study which comprised of 56 patients after taking into account SEAG with a cut off value of 1.2g/dl, 24 of 26 transudates and 28 of 30 exudates were classified correctly. The mean albumin gradients were significantly raised in transudates (3.82 ± 0.45g/dl) as compared to exudates (3.08 ± 0.44 g/dl) with p value of <0.001.This method resulted in a sensitivity of 92.31% and a specificity 92.31% respectively.

The results presented in this study demonstrate that the concentration of protein thiol in serum was markedly reduced in patients with exudates compared to transudates.

The decreased plasma thiol levels may be due to enhanced free radical generation in patients with exudates, which is mainly due to several inflammatory condition associated with exudative pathology. On contrary transudative effusion is not related majorly to inflammatory pathology but results from an imbalance between hydrostatic and oncotic pressure. Therefore there is no much generation of free radicals in transudates. Serum albumin correlated positively with serum protein thiols (r=0.570, p<0.001) in exudates, but no correlation seen in transudates. Pleural fluid protein thiols correlated positively with SEAG (r=0.276, p<0.001) in exudates and correlated negatively in transudates (r =- 0.357, p<0.001). Thus in the group of well characterized pleural effusion the measurement of serum and pleural fluid protein thiols could be a better marker for differentiation of exudates and transudates and measurement of protein thiols could provide better sensitivity and specificity for the characterization of effusion as an exudate when compared to light's criteria. However, to overcome the limitation of misclassification by using criteria of light et al, SEAG along with estimation of serum and pleural fluid protein thiols in addition to light's criteria could be a better alternative in differentiation of exudates and transudates in clinical practice.

## CONCLUSION

However to overcome the limitation of misclassification by using light's criteria, we advocate measurement of serum and pleural fluid protein thiols along with SEAG could be better alternative in differentiation of exudates and transudates in clinical practice.

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