Serum to Pleural Fluid Albumin Gradient to Differentiate Transudative and Exudative Pleural Effusion

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Summary

A total 105 cases of pleural effusion,65 male and 40 females having different etiology were analysed for pleural fluid albumin gradient. The findings were analysed and compared with Lights criteria to differentiate exudates from transudate. The pleural fluid to serum albumin cut off value 1.2gm/dl to differentiate between exudates and transudate showed sensitivity of 95.50%. Specificity of 87.5%.Positive predictive value 97.70% and efficiency of 94.28%.

Keywords: - Pleural effusion, transudate, exudates, serum to pleural fluid albumin gradient.

Introduction

Established clinical practice recommends the determination of the exudative or transudative nature of pleural effusion as first step in identifying cause. As per Lights[1] criteria the exudative pleural effusion are identified by one or more of the following-

1. Pleural fluid LDH>2/3rd of upper limit of serum value
2. Pleural fluid to serum LDH >0.60 and LDH >200units in pleural fluid,
3. Pleural fluid protein to serum protein>0.50.

Conversely patients with Congestive cardiac failure, Hepatic cirrhosis, Nephritic syndrome, other hypoproteinemic conditions undergoing diuresis assume exudative property.[2] Pleural effusion is a common finding in a number of both pulmonary and extra pulmonary diseases. It is essential to establish etiological diagnosis for therapeutic approach. Now a day's many parameters are used by various authors pleural fluid bilirubin, cholesterol choline esterase alkaline phosphatase, creatinine kinase, uric acid Malon dialdehyde (MDA).[3-9] Pleural fluid Adenosine deaminase (ADA). Pro-brain natriuretic peptide.[10-11] The serum to pleural fluid albumin gradient has been found to be very valuable in distinguishing transudate from exudates. It is a better parameter, adopted by Lights et.al.[1] Peural fluid to serum

albumin gradient is stastistically equivalent to lights criteria.[12] It is an essential marker for the separation of transudates and exudates. There are many inconclusive views regarding the diagnostic efficacy of serum albumin to pleural fluid albumin gradient to differentiate transudative and exudative pleural effusion. So we analysed serum to pleural fluid albumin gradient at Chandulal Chandrakar Memorial Medical College, Durg.

The problem of high-protein transudates is more common in the evaluation of ascites and has led to the development of the serum-ascites albumin gradient (serum albumin level minus the ascites albumin level). 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 of distinguishing exudates from transudates.[13] The albumin gradient has not previously been evaluated in pleural effusions. Therefore, we prospectively measured serum and pleural effusion albumin levels to calculate a serum-effusion albumin gradient (serum albumin level minus the effusion albumin level) in 59 consecutive patients undergoing diagnostic or therapeutic thoracentesis and compared the serum-effusion albumin gradient to the criteria of Light et al.[14] Using preset diagnostic criteria, the etiology of each pleural effusion was determined, and the best discriminating level of the serum-effusion albumin gradient between transudates and exudates was established.

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Materials and Methods

The present study was carried out in the Department of Respiratory Medicine in collaboration with Department of Biochemistry. A total of 105 patients having pleural effusion of diverse etiologies admitted to Respiratory Medicine department from September 2015 to October 2017 were included in our study. Patients having HIV seropositive and Diabetes mellitus were excluded from our study.

All the cases included were of proven etiology. The cases were meticulously analysed with demographic profile, clinical examination, disease severity, duration, hospital stay, therapeutic intervention, previous diagnostic thoracentesis was performed in all the patients. Fluid samples obtained underwent naked eye, biochemical, and cytological, histopathological and microbiological analysis. In some cases pleural biopsy was done. Blood samples were drawn on the same day for biochemical status. Biochemical parameters of blood and pleural fluid were determined with auto analyser (Hitachi 912).LDH was measured with the Boehringer Mannheim Gmbsl kit and expressed in

International units normal value taken at 30degrees Celsius is 160-320. Protein concentration was estimated using the Biuret method and albumin concentration grams per deciliter was measured using Bromocresol green. Both of

which are Spectrophotometric method. Tubercular pleural effusion was diagnosed by pleural biopsy, ADA, CBNAAT, sputum culture.

Malignancy by cytology and biopsy. Infective etiology by blood and pleural fluid culture and microscopy. Other exudates like pancreatitis, connective tissue disorder, collagen vascular disease etc. The diagnosis of congestive heart failure as a cause of pleural effusion with enlarged heart elevated CVP or engorged neck veins, pitting edema, ventricular cardiac gallop, absence of pulmonary infiltrates, purulent sputum and clearing of the effusion in response to therapeutic cardiac regimen. Other transudates such as Nephrotic syndrome when patients have proteinuria, oedema and hypoalbuminemia when serum albumin was <3gm/dl. Proven liver cirrhosis the pleural fluid to serum LDH, protein, albumin and serum to pleural fluid albumin gradient were analysed. In addition the utility of all Biochemical parameter for identifying exudates from transudates was analysed.

Observations and Results

Out of 105 patients 65 were male and 40 were females. Maximum number of cases is in the age group between 41 to 60 years, minimum cases are in the age group of less than 20 years.

Table I showing age wise distribution

Age group	Male	Female	Total
Less than20	03	04	07
21-40	12	15	27
41-60	35	12	47
More than 61	15	09	24
Total	65	40	105

Tubercular effusion in 67, malignancy 14, congestive cardiac failure in 7, Pneumonia in 6, chronic liver disease in 4, hypoproteinemia in 3, Rheumatoid Arthritis in 2, Nephrotic syndrome in 2 cases were diagnosed.

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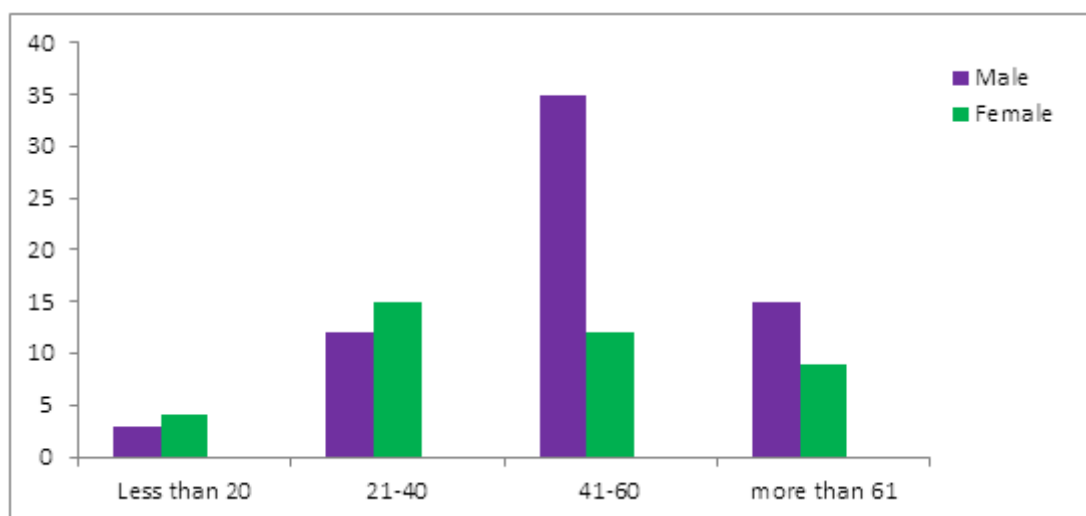*Available online at - www.ijirms.in*

Table II gives the average value obtained in respect of 16 transudates and 89 exudates. Average values obtained in transudative and exudative pleural effusion

Sr.no.	Parameters	Transudates n=16	Exudates n=89
1	Pleural fluid protein (gm%)	2.63	4.71
2	Pleural fluid/serum protein ratio	0.47	0.75
3	Pleural fluid LDH	172.80	837.30
4	Pleural fluid serum LDH ratio	0.49	1.40
5	Serum to pleural fluid albumin gradient	1.62	0.95

Pleural fluid LDH had maximum number of misclassified cases in transudates (31.25%) as over exudates (9.78%) while serum to pleural fluid gradient had least number of misclassified cases in transudates (12.5%) and exudates (4.49%).

Table IV Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and efficiency of parameters studied.

Parameters	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Efficacy (%)
Pleural fluid protein	91.01	75	95.29	60	88.57
Pleural fluid/serum protein	93.25	81.25	96.50	68.42	91.42
Pleural fluid LDH	89.88	68.75	94.17	55	86.66
Pleural fluid serum LDH	93.25	68.75	94.31	64.70	89.52
Pleural fluid/serum albumin gradient	95.50	87.50	97.70	77.77	94.28

As per Lights criteria out of 16 transudates 6 cases were misclassified as exudates and 2 exudates were misclassified as transudates. As per serum pleural fluid albumin gradient only 2 transudates were misclassified as exudates and 4 exudates were misclassified as transudates. Serum pleural fluid albumin gradient had greater no. of misclassified exudates and lesser no. of misclassified transudates as compared to Lights criteria.

Discussion

The occurrence of pleural effusion may be of various causes mainly due to more fluid formation and less absorption or both. The exudative pleural effusion usually due to inflammation leading to increase leakage of proteinaceous fluid where as transudative effusion usually with intact microvascular endothelium. Therefore the gradient between pleural fluid and serum is low. Akkurt etal (15) with 74 exudates and 27 transudates had found sensitivity and specificity atleast as 100% and 81% when Lights criteria was used compared with 91.9% and 100% respectively when albumin gradient is used.Lesley J.Burges etal in 270 exudates 123 transudates reported sensitivity,specificity and accuracy of 98%,83%,and 93% respectively according to Lights criteria and 87%,92% and 89% respectively when used serum effusion albumin gradient.J. E.Heffner etal(16)out of 1448(1071 exudate and 377 transudates)shows sensitivity and specificity 97.9% and 74.3% by using Lights criteria(17).The sensitivity and specificity of 97.75% and 62.5% as per albumin gradient. In our study sensitivity and specificity and accuracy with respect to Lights criteriaare 97.75%,62.5% and 93.3%.As per serum pleural effusion albumin gradient the sensitivity and specificity and accuracy are 95.5%,87.5%, and 94.28%

respectively. So we concluded that the criteria for Lights having high sensitivity, remains the best method for distinguishing exudates from transudates and serum effusion albumin gradient having high specificity is useful when patients with transudative effusion are on diuretic therapy.

Congestive heart failure probably results in pleural effusions because of increased leakage of fluid into the pulmonary interstitium, which collects in the pleural space, and increased systemic venous pressure, which decreases lymphatic flow and therefore decreases pleural fluid absorption. Diuretics could lead to fluid resolution through multiple mechanisms. By decreasing left atrial pressure, less fluid would leak from the pulmonary microvasculature, leading to decreased fluid formation and eventual resolution by lymphatic drainage. Also, by decreasing systemic venous pressure, the lymphatic drainage would be increased. Finally decreasing systemic arterial pressure could lead to a pressure gradient that favored fluid reabsorption via the pleural micro vessels. Exudative causes for effusions usually involve some type of inflammation and compromise of the pulmonary or pleural microvasculature, which leads to increased leakage of 8uid that has a higher concentration of protein (18).

Roth et al. (19) in a series of 59 patients used the serum-effusion albumin gradient for the classification of pleural effusions. With a cut-off value of 1.2 g/dl, all the transudates and 39 of the 41 exudates were classified correctly and showed that the serum-effusion albumin gradient had a sensitivity and specificity of 87%, and 92%, respectively. However, another study obtained a sensitivity of only 63% and a specificity of 81%.

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In the study of Burgess et al, (20) the gradient had a sensitivity and specificity of 87%, and 92%, respectively. In the present study, this method resulted in a sensitivity of 91.5%, and a specificity of 92.86%.

Chakko et al (21) showed that treatment of patients with congestive heart failure and pleural effusions with diuretics leads to a concentration of pleural fluid protein which can be in the exudative range. Five patients in our series, four of whom had had previous diuretic therapy, were misclassified as "pseudoexudates" by Light's criteria. By applying the criterion of an albumin gradient greater than 1.2 g/dl to indicate a transudate, all five patients were correctly classified. In our series the albumin gradient criterion for exudates was 100 percent specific, while Light's criteria were 72 percent specific.

Regarding the good results obtained, we suggest the use of albumin gradient as an effective means of discriminating exudative from transudative pleural effusions. Since this method only relies on measurements of effusion and serum albumin concentrations, it can be very helpful when other measurements are not available.

Nevertheless, the results should be treated cautiously when the patient is suspected of having degrees of hypoalbuminemia. On account of the very high discrepancy among the results obtained by several researchers, further study is necessary to make a final decision on the efficacy of this method.

Conclusion

On the basis of observation and result we concluded that serum to pleural fluid albumin gradient has a better specificity as compared to LIGHT criteria, suggesting that serum effusion albumin gradients is a simple, extremely cost effective and useful parameter with better discriminatory capability. LIGHT criteria in distinguishing pleural transudates especially due to chronic congestive cardiac failure even in patients on diuretic therapy but has a little less sensitivity in detecting exudative pleural effusion as compared to LIGHTs criteria.

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