Serum to pleural effusion albumin gradient and serum to pleural fluid protein gradient a better criterion than light's criteria to distinguish between pleural transudates and exudates

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Abstract This prospective study was carried out to compare Serum to pleural fluid albumin gradient and Serum to pleural fluid protein gradient with traditional Light's Criteria. The aim was to determine the predictive accuracy to currently identify Exudative effusion by these methods. We collected pleural fluid samples from 64 patients with pleuraleffusion who are admitted in Bharat Hospital, Sangli during the period December 2013to December 2014. SE-AG and SE-PG were compared with single parameter of Lights' Criteria. In SE-AG, Serum Albumin- Pleural fluid Albumin level of 1.2gm/dl or less indicates Exudates and greater than 1.2gm/dl indicates Transudates In SE-PG, Serum Protein-Pleuralfluid protein levels of 3.1gm/dl or less indicates Exudates and greater than 3.1gm/dl indicates Transudate. Lights' Criteria of Pleural fluid protein to Serum Total protein ratio of more than 0.5 indicates Exudates and less than 0.5 indicates transudate for clinical diagnosis of the patient. Biochemical tests on Serum and Pleural effusion fluid were done. SE-AG andSE-PG were compared with Lights' Criteria. We found that Lights' Criteria correctly identified all exudates but misclassified 4 cases of transudate as exudates. SE-AG and SE-PG could correctly classify those 4cases as transudates. These cases were of CCF on diuretic therapy. So these gradients could assist in reclassifying Pleural Effusion as transudates, which were misclassified as exudates by Lights' Criteria.

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INTRODUCTION

Distinguishing an exudates from a transudate is the cornerstone of the evaluation of Pleural effusion[1,2]. Because of the high sensitivity in identifying exudates, the criteria proposed by Light *et al*. In 1972, has been the standard method for making this distinction3. But the main disadvantage of this classification was that it misclassified patients of CCF having transudate effusionsas exudates[3]. This observation of exudative range protein levels in patients with CCF was first noted by Pillay4 in 1965 and later confirmed by Chakko *et al*[5], who showed that diuresis will increase the effusion protein. This may lead to unnecessary investigations being done in these patients. Recently it has been reported that SE-AG and SE- PG are good parameters to reduce the incidence of misclassified cases of transudative effusion, as exudative. It has been found to have 97% sensitivity and 100% specificity[6]. Therefore, a stepwise approach consisting the use of Lights' Criteria with albumin and protein gradient to correctly identify exudative effusion seems logical. This may improve the diagnostic accuracy andmaintain simplicity without increasing the number of tests performed and maintaining the costs.

MATERIALS AND METHODS

This prospective study was conducted in Dept. of Medicine in Bharati Hospital, Sangli during the period of December 2014. We studied 64 patients of pleural effusion of diverse etiology who were admitted in our hospital. Out of those 63% were males and 37% were females, ages ranging from 17-80yrs. Mean for each patient, detailed clinical history, physical examination and laboratory test were done to arrive at firm clinical diagnosis. The following test were performed on pleural effusion samples-total protein, albumin, Glucose, cytology with differential count, gram stain, AFB stain bacterial culture, ADA level were done, pleural biopsy and CT Scan only in few cases to arrive at firm diagnosis.

ESTIMATION

Serum total protein and pleural fluid protein were estimated by routine Biuret method. Serum albumin and pleural fluid albumin level were done by BCG (Bromo Cresol Green) method.

RESULT

Out of 64 effusion studies 68.75% were exudates and 31.25% transudate by etiology.

Table 1: Shows Distribution Of Cases According To Etiology

	Causes	No. of Patients	Percentage
Transudate	Ccf	16	25
	Hypoprotinemia	2	3.12
	Nephrotic Syndrome	2	3.12
	Tuberculosis	24	37.5
	Malignancy	7	11
	Pneumonia	6	9.3
Exudate	Liver abscess	1	1.56
	Pulmonary Embolism	4	4.68
	Ccf with pneumonia	1	1.56
	Ccf with malignancy	1	1.56

Table 2: Distribution of cases according to Etiology and mean SE-AG and SE-PG

	Etiology	Seag	Sepg
Exudate	Tuberculosis	0.7	2.8
	Malignancy	1.0	3.0
	Pneumonia	0.8	2.5
	Pulmonary Embolism		
	Liver abscess	0.55	2.4
Transudate	Ccf	1.6	3.4
	Hypoproteinemia	1.7	3.6
	Nephrotic syndrome	1.4	3.2

Table 3: Cases Separated by SE-AG of 1.2 g/dl

Types of Pleural fluid	No. Of cases differentiated by Lights'criteria	No. Of cases differentiated By SE-AG	No. Of Cases Truly classified	No. Of case Falsely Classified	P value
Exudate	48	44	44	4	Z=0.681 P=0.496
Transudate	16	20	20	4	Z=0.590 P=0.555

Table 4: Cases separated by se-pg of 3.1 g/dl

Types of Pleural fluid	No. Of cases differentiated by light's criteria	No. Of cases differentiated By SPAG	No. of Cases Truly classified	No. Of case Falsely Classified	P value
Exudate	48	44	44	4	Z=0.681 P=0.496
Transudate	16	20	20	4	Z=0.590 P=0.555

Table 5: distribution of cases according to etiology and mean serum protein, fluid protein and fluid serum protein ratio (light's criteria)

Types	Etiology	Serum Protein	Fluid Protein	Fluid serum Protein Ratio
Exudate	Tuberculosis	6.4	4.3	0.67
	Malignancy	5.7	4.45	0.78

	Pneumonia	6.8	4.8	0.7
	Liver abscess	6.5	4.9	0.75
	Ccf	6.2	2.55	0.41
Traqnsudate	Hypoproteinemia	5.1	2.3	0.45
	Nephprotic syndrome	4.8	2.0	0.41

Table 6: Cases differentiated by pleural, fluid to serum protein ratio of 0.5 (lights' criteria)

Types of pl. fluid	No. Of cases Differentiated By light's criteria	No. Of cases Differentiated By Ethology	No. Of cases truly classified	No. Of cases truly classified	P value
Exudate	48	42	44	4	Z=0.681 P=0.496
Transudate	16	20	20	4	Z=0.590 P=0.555

The commonest cause of exudates was tuberculosis (37.5%) next common cause was CCF (25%), malignancy (11%), Pneumonia (9.3%), Pulmonary embolism and nephritic syndrome and anemia (4.68%) Syndrome and anemia (4.68%) result of estimation of fluid and blood parameters were based on light n criteria and compared with SEAG and SEPG.

DISCUSSION

Differentiation between exudates from transudate is essential in determining the cause of pleural effusion and the decision as to whether further more investigation should be advised for the patient17. Misclassification can lead to unnecessary investigation that can be invasive and expensive. Presently Light's Criteria[3] is used. (Pleural fluid protein / Serum protein ratio >0.5, Pleural effusion LDH / Serum LDH ratio >0.6 and pleural effusion LDH >200U denoted an exudates.) But many Pleural effusions, misclassified have been reported using these criteria. Recently many new parameters like pleural effusion cholesterol[7,8], Pleural effusion to Serum Bilirubin ratio[9], Uric Acid[12] and Pleural effusion malondialdehyde (MDA)[13] have been reported. But none of these could show better sensitivity and specificity than Light's criteria. The sensitivity of Lights' Criteria for exudative effusion is 99%, but the specificity ranges from 65% to 85%[7]. Particularly transudative effusion resulting from CCF with diuretic therapy is misclassified as exudative. To overcome this problems another proposed method to reduce the misclassification of transudative effusion as exudative is the use of SE-AG and SE-PG. In one study SE-AG and SE-PG > 1.2g/dl and3.2g/dl respectively[25], correctly identified 86% and 91% of the transudates. In another study SE-AG and SE-PG correctly identified 85% and 55% of misclassified transudates due to CCF respectively[14,15]. Both question and answers have documented SEAG is better discriminator than Lights' criteria in diagnostic separation of transudate and exudates[16]. On the other hand, Burgess et al1[7] using an albumin gradient of 12g/L found the sensitivity and

specificity to be 87% and 92% respectively and concluded that the criteria by light et al remained the best method for distinguishing exudates and transudate. In our study, we found that 6 patients of CCF were classified as exudates by applying Light's criteria. (Pleural fluid /serum protein>0.5 is exudative). After applying serum fluid albumin and serum protein gradient criteria to this patients, 4patients were classified as transudates, However, 2 patients who showed exudates by these methods were further evaluated found to have pneumonitis in one and malignancy in another patients of CCF, who were classified as exudates by Lights' criteria were on diuretic therapy. By applying P value to the result obtained by Lights' criteria and serum fluid albumin and serum fluid protein gradient. The value was found to be 0.555. This value was not significant. This be due to small number patient's, in our study. The study by Biesla and colleageus[15] included misclassified CHF transudate. Our study was also not specifically designed to evaluate the patient with CHF who received diuretics. Romero, Candeira and colleagues[14] showed that in patients who received diuretic therapy, the serum fluid albumin and serum fluid protein gradients had higher rate of correctly identifying misclassified transudates but similar accuracy who compared with Light's critrria.[18] The pleural microvasculature endothelium is semi permeable, resulting in protein content of pleural fluid being lower than the serum. The pleural albumin and globulin components are believed to originate from the serum via diffusion and then cleared by subpleural lymphatics[20, 21]. Exudative effusion usually involve some type of the case of exudates, there is increased leakage of fluid, which has a higher concentration of proteins resulting in a low gradient between serum and fluid protein (and albumin)[17]. The occurrence of pleural effusion in CHF could probably be attributed to increased leakage of fluid into the pulmonary interstitium and in the pleural space. Chakko et al and showed that diuretic therapy in cases of CHF with pleural effusion leads to concentration of pleural effusion proteins, which can fall in the exudative

range[5,16]. Moreover some animal and human studies have shown that increase in hydrostatic pressure can increase the protein content in effusions[18]. This can be partly explained by opening of large pores in endothelium with elevated hydrostatic pressure[22,23]. Thus in patient of CHF having pleural effusion, amount of proteins in pleural fluid can significantly increase to exudative levels if degree of pulmonary artery pressure causing the formation of effusion was very high. Such a linear correlation between the hydrostatic pressure and the protein content of ascites in patients with portal hypertension has been documented[24]. Therefore this phenomenon may help explain the pathogenesis of exudative effusion documented in CHF when total protein in pleural effusion was used as diagnostic criteria[5,16,18]. Our results conclude, that the SEAG and SPEG increased the predictive accuracy to correctly identify exudative effusion when compared with effusion serum protein ratio of light's criteria. Consequently effusion to serum protein gradient of 0.5 may be used in consideration with SEAG of [1,2] and SPEG of 3.1 when encountering pleural effusion suspected of being transudative that have been misclassified as exudative by light n criteria. This may improve the diagnostic accuracy and maintain simplicity without increasing the number of tests performed and maintaining costs. Light n criteria should still be used as the initial step when encountering pleural effusion, as it is universally known and simple to apply.

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