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Comparison Between Serum To Pleural Fluid Albumin Gradient Against Light's Criteria For Distinguishing Transudative From Exudative Pleural Effusion

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Abstract:
Background*:Many diseases -local or systemic present with pleural effusion. Thus its of utmost importance to delineate between transudates and exudates to aid in differential diagnosis. The excess pleural liquid accumulates due to excessive production or decreased lymphatic drainage. The criteria proposed by Light et al(1) in 1972 have been the standard method of differentiating exudates from transudates. Light's criteria is more accurate in identifying exudates. However, it may confound about 25% of transudative effusion cases as exudatives. Dhar et al.(2), established that when the serum - effusion albumin gradient and Light's criteria were compared, Light's criteria correctly identified all the exudates but misdiagnosed 2 of 5 transudates (cases of heart failure).In cases of cardiac failure treated with diuretic therapy the transudates have high protein content.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 is the best predictor of exudative ascites and is an accepted method for differentiating exudate from transudate(3). In the present study was undertaken to calculate SPAG and Light's criteria and to compare SPAG with Light's criteria in analysing pleural effusions. We have used the criteria of Roth et al,(4) that serum-fluid albumin gradient of 1.2 g/dl or less suggests exudate and a gradient above 1.2 g/dl suggests transudate.*
Materials and Methods*: The study was an observational study done in 60 patients who were admitted with Pleural effusion, in Medical wards, Department of General medicine, Government Medical college, Kottayam. The study was carried for a period of 9 months.Pleural fluid aspirate study was done for these patients. Information was collected through a proforma and the data collected was analysed using SPSS*
Results*: For classifying transudates SPAG was 100% sensitive and 93.33% specific and for exudates the sensitivity was 93.33%, specificity is 100%. Sensitivity, Specificity of Lights criteria for classifying transudates were 60% and 97.78% respectively, and for classifying exudates the sensitivity and specificity were 97.78% and 60%.*
The overall accuracy of SPAG was 95% and was 88.33% for Lights criteria for differentiating transudative pleural effusion from exudative pleural effusion.
Conclusion: *For classifying transudates, serum to pleural fluid albumin gradient was 100% sensitive and 93.33% specific and for classifying exudates the sensitivity was 93.33%, specificity was 100%.*
The overall accuracy of serum to pleural fluid albumin gradient was higher, with an accuracy of 95% when compared to 88.33% for Lights criteria, to differentiate transudative and exudative pleural effusion.
Key Word*:Pleural effusion, lights criteraia , pleural fluid analysis SPAG(serum to pleural fluid albumin gradient) , serum albumin*

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I. Introduction

The excessive or abnormal accumulation of fluid within the pleural space is called pleural effusion. A common medical issue, pleural effusion is brought on by a number of underlying clinical disorders. Depending on the underlying pathophysiology, pleural effusion may be classified as either "transudative" or "exudative." When the mechanical parameters affecting the generation or reabsorption of pleural fluid are changed, such as by

a drop in plasma proteins or an increase in systemic or pulmonary hydrostatic pressure, transudates result. Exudates cause increased permeability as a result of pleural inflammation, irritation, or other illness processes.

In our country, pleural effusion is a significant source of morbidity and can occasionally result in mortality. Therefore, it is crucial to identify the origin of the effusion and begin treatment as soon as feasible.

Our study aims to achieve this by using Serum to pleural fluid albumin gradient, as a marker to differentiate exudative vs transudative effusion

II. Material And Methods

This prospective comparative study was carried out on patients of the Department of General Medicine, at Government medical college hospital Kottayam,Kerala, India. A total 60 adults subjects (both male and females) of aged ≥ 18 years were for in this study.

Study Design: Prospective observational study

Study Location: This was a tertiary care teaching hospital based study done in Department of General Medicine, at Government medical college hospital Kottayam,Kerala, India

Study Duration: period of 9 months

Sample size: 60 patients.

Sample size calculation: A study by Roth et al.(4) 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.
N= Z 2 (specificity (1-specificity)).
(Deviation)2 ×P
D = 20% of specificity.
Prevalence = 320/1000000=0.032
Z = 1.96
N = (1.96)2[0.92(1-0.92)]
(0.18)2 × 0.32
= (3.84 ×0.153) /(0.032×0.32)
= 0.587 /0.01
= 58.7
Hence the minimum sample size required would be - 60

Subjects & selection method: Patients admitted in department of medicine diagnosed with pleural effusion

Inclusion criteria:
The patients admitted in the department of general medicine with history and clinical examination suggestive of pleural effusion.

Exclusion criteria:
Patients with age less than 18yrs, pregnant females, patients with empyema, hemothorax , post pleurodesis and chylothorax, postoperative effusion, and multiple disease*
Etiology of effusion was determined by the following criteria(5),
1.Patients with pedal edema, radiological evidence of cardiomegaly, congested lungs, and responded to treatment for congestive heart failure were categorized as having congestive heart failure.
2.Patients with pedal edema, decreased urine output, raised blood urea, and serum creatinine levels were diagnosed with renal failure.
3.Patients with proteinuria, edema, and hypoalbuminemia were diagnosed as nephrotic syndrome.
4.Patients with ascites and based on histopathological evidence, USG, biochemical reports, cirrhosis of liver was diagnosed.
5.Malignant pleural effusion was diagnosed with evidence of malignant cells either in cytological examination or in biopsy specimen.
6.Acute fever with purulent expectoration, pulmonary infiltrate on X-ray, and a good response to antibiotic treatment, or identification of the organism in the pleural effusion is diagnostic of parapneumonic effusion
Patients without clinical diagnosis were excluded from the study.

The clinical presumption of the nature of the effusion (transudate or exudate) was based on all the available information obtained just before performing thoracocentesis (like clinical features, microscopy, cytology, biopsy, pleural fluid study, radiography and response to treatment) and was compared with that obtained from biochemical criteria.

This preset diagnostic criteria was used as gold standard for final diagnosis of the etiology.

Pleural effusion due to congestive cardiac failure, cirrhosis of liver, nephrotic syndrome, svc obstruction were considered as transudative, whereas TB, pneumonia, carcinoma, collagen vascular disease, uremia were considered causes for exudative effusions. Effusions due to pulmonary embolism will be classified as exudative according to Burgess et al(6)

*multiple diseases – patients with two of more diseases that could cause pleural effusion

Procedure methodology

After getting clearance from the institutional review board and written informed consent from the patient or immediate relatives, the selected patients diagnosed to have pleural effusion were taken for study. A history was taken, previous records were analysed in detail. A detailed clinical examination was done. Pleural fluid of patients who met the inclusion and exclusion criteria were collected, and pleural fluid was 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. End points of study were discharge from the hospital or death of the patient.

Statistical analysis

Data was entered in Microsoft excel and analyzed using IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp. IBM Corp. Categorical variables were expressed as frequency (percentage) and continuous variables were expressed in mean and standard deviation. Comparison of mean Pleural fluid protein, Serum protein, Serum albumin, Pleural fluid albumin, Pleural fluid LDH and Serum LDH between the type of effusion was performed by independent t-test. The mean ratios SEAG, Pleural to serum protein and Pleural to serum LDH were also compared between the effusion type using independent t- test. Association of age group with type of effusion was evaluated using Pearson Chi-square test, and Association of gender with type of effusion was evaluated using Fisher's Exact test. Sensitivity, specificity, positive predictive value, negative predictive values were used to compare the efficacy of SEAG criteria and Lights criteria. For all these statistical interpretations, $p<0.05$ was considered the threshold for statistical significance.

III. Result

The present study was conducted among 60 patients with Pleural effusion from the Department of General Medicine.

Among them, 1.7% were of age group <30 years and 6.7% of 31-40 years, 5% of 41-50 years age, 33.3% of 51 – 60 years and 11.7% of age more than 70 years.

From the final diagnosis at discharge, there were 15 (25%) transudative effusion and 45 (75%) exudative pleural effusions.

Table 7.1: Age Distribution of Study Population

Age	Frequency	Percentage
< 30 years	1	1.7
31 - 40 years	4	6.7
41 - 50 years	3	5.0
51 - 60 years	20	33.3
61 - 70 years	25	41.7
> 70 years	7	11.7

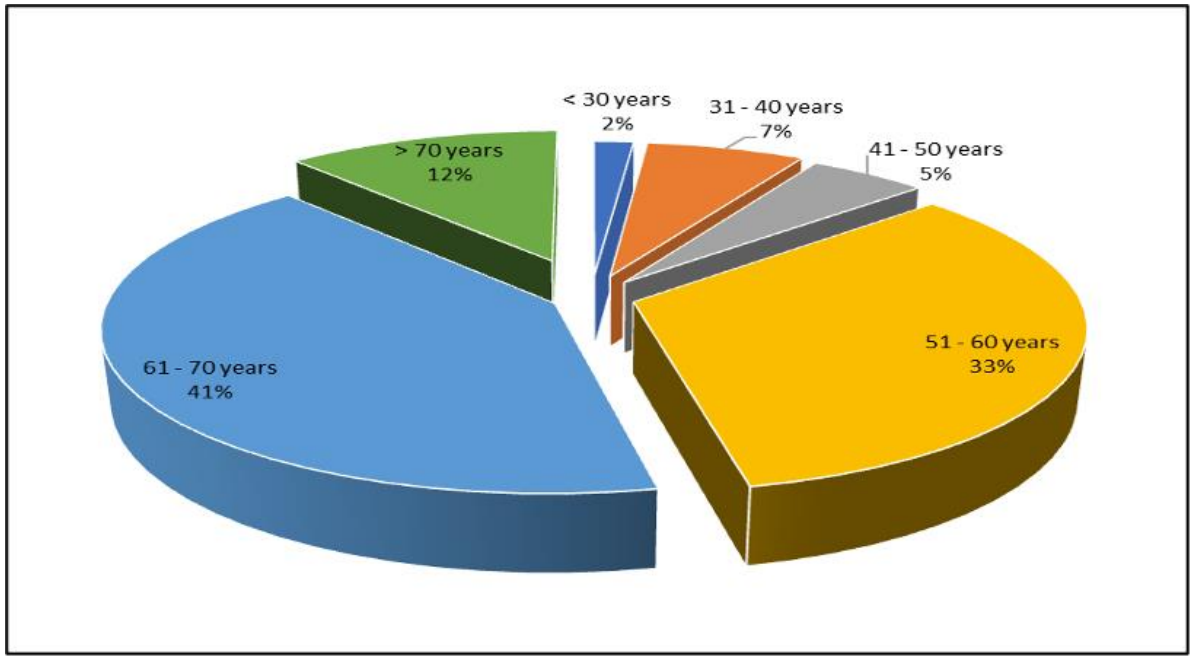

Figure 7.1: Age Distribution of Study Population

Table 7.2: Gender Distribution of the Study Population

Variables	Levels	Frequency	Percentage
Gender	Female	18	30.0
	Male	42	70.0

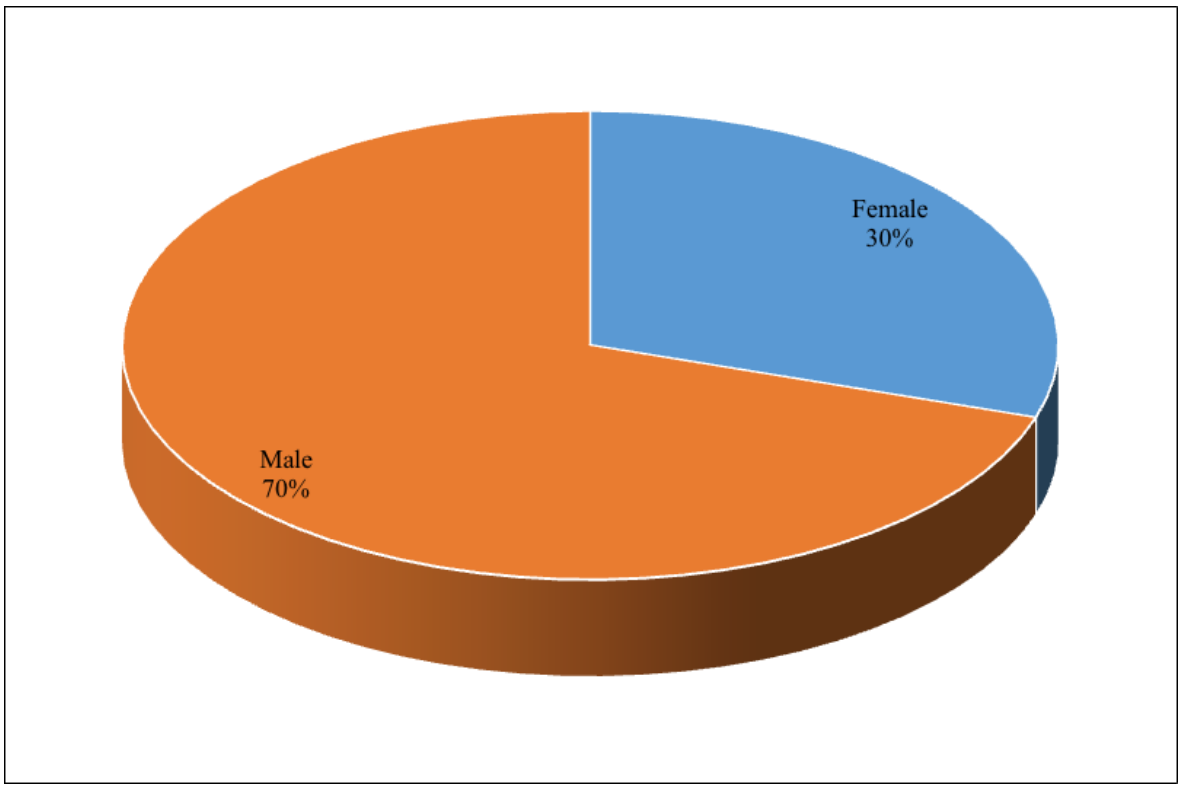

Figure 7.2: Sex Distribution of Study Population

The study population had 18 (30%) females and 42(70%) males.

Table 7.3: Distribution of Type of Effusion (Final Diagnosis)

Variables	Levels	Frequency	Percentage
type of effusion	exudative	15	25.0
	transudative	45	75.0

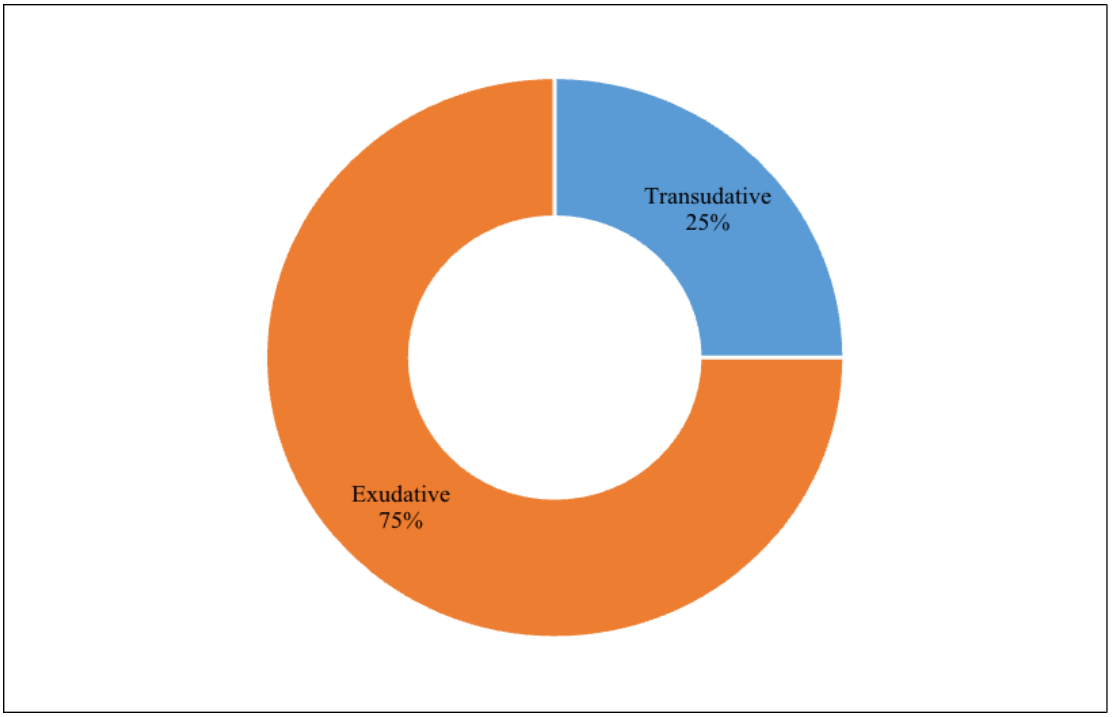

Figure 7.3: Frequency of Type of Effusion

From the final diagnosis made at the time of discharge, out of the 60 cases,15 cases were of transudative pleural effusion and 45 cases were of exudative pleural effusion, with a percentage of 25% and 75% respectively.

Table 7.4: Distribution of Etiology in Transudative Effusion

Type of effusion	Etiology	Frequency	Percentage
Transudative	CCF	7	46.7
	CKD	2	13.3
	Cirrhosis of liver	4	26.7
	Nephrotic syndrome	2	13.3

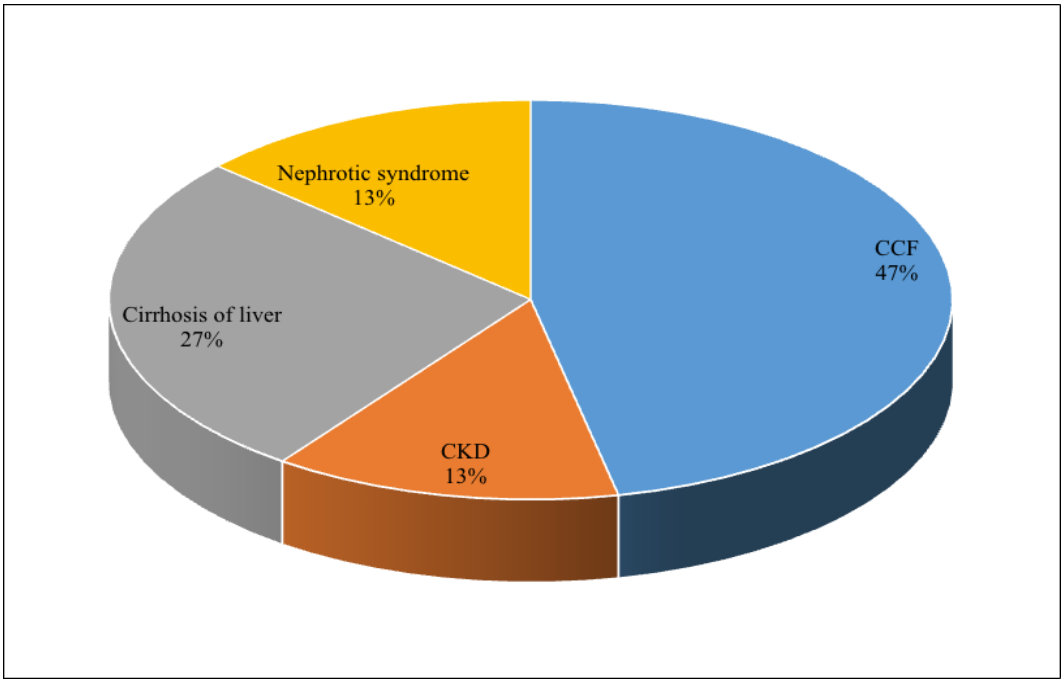

Figure 7.4: Distribution of Etiology of Transudative Effusion

Of the 15 cases of transudative pleural effusions diagnosed, 46.7% constituted pleural effusion due to congestive heart failure and 13.3% due to chronic kidney disease and 26.7% due to cirrhosis of liver and 13.3% due to nephrotic syndrome.

Table 7.5: Distribution of Etiology in Exudative Effusion

Type of effusion	Etiology	Frequency	Percent
Exudative	parapneumonic	10	22.2
	Tubercular	28	62.0
	Malignant	7	15.6

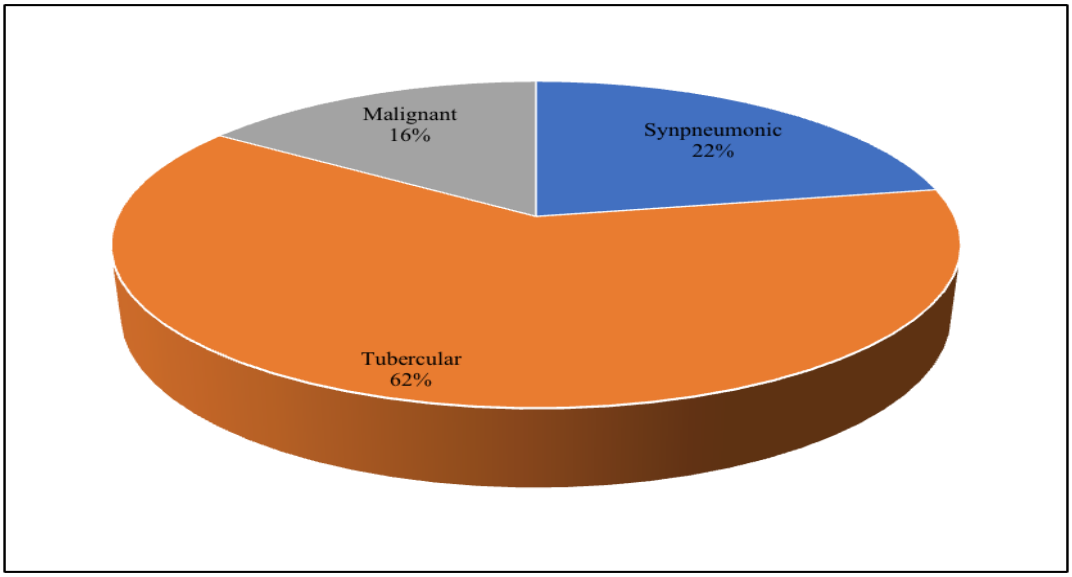

Figure 7.5: Distribution of Etiology of Exudative Effusion

Among the 45 cases of exudative effusions diagnosed, 62% were due to tubercular etiology and 22% were due to parapneumonic effusion and 15.6% effusions were due to malignancy.

Table 7.6: Association of Age and Gender with Type of Effusion

		Final diagnosis of type of pleural effusion		χ2	p value
		Transudative n (%)	Exudative n (%)		
Age group#	< 30 years	0(0.0)	1 (100.0)	5.51	0.36
	31 - 40 years	1 (25)	3 (75)		
	41 - 50 years	1 (33.33)	2 (66.7)		
	51 - 60 years	8 (40.0)	12 (60.0)		
	61 - 70 years	5 (20.0)	20 (80.0)		
	> 70 years	0 (0.0)	7 (100.0)		
Gender °	Female	5 (27.8)	13 (72.2)	0.11	0.75
	Male	10 (23.8)	32 (76.2)		

P value <0.05 is considered statistically significant.
Pearson Chi-square test
° Fischer's exact test

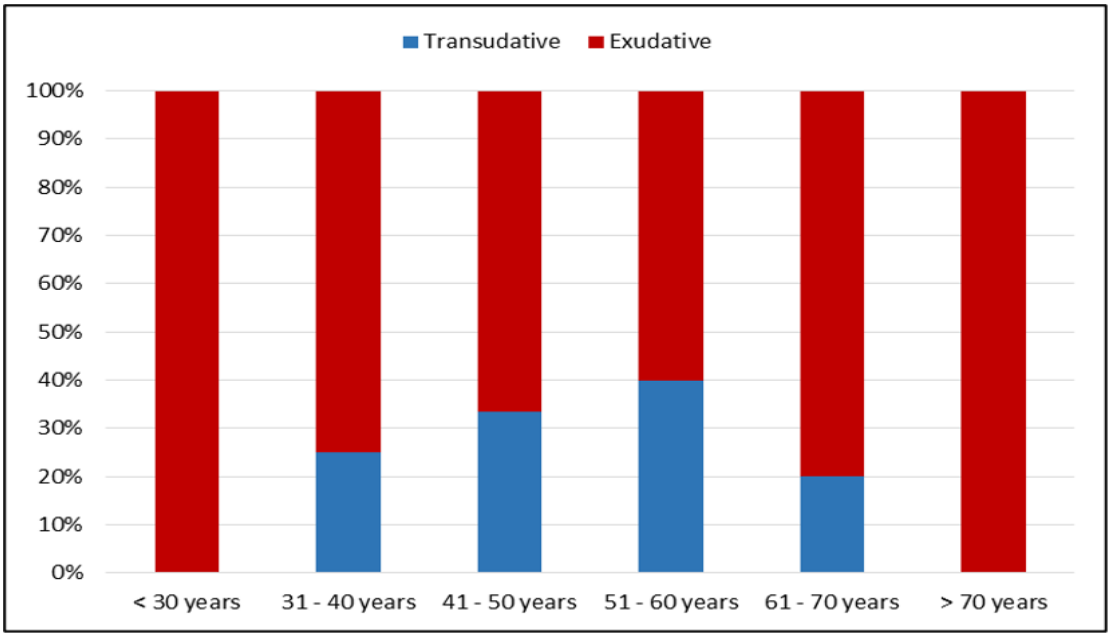

Figure 7.6: Distribution of Type of Effusion in Different Age Groups

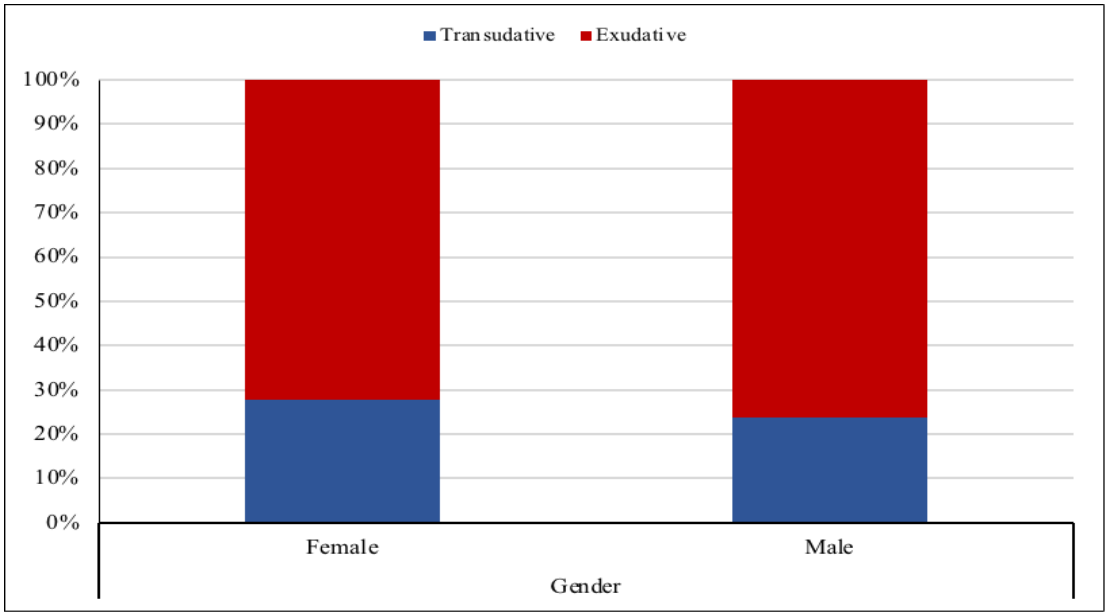

Figure 7.7: Distribution of Type of Effusion According To Gender

Our study included patients of age above 18 years. The majority of the study population were of age group of 61-70 years. Exudative effusion was the major cause of pleural effusion in all the studied age groups.
On comparing the gender and type of pleural effusion, exudative effusion was the main type of effusion in both males (76.2%) and females (72.2%).
Inference
There is no statistically significant association for Age group and gender with type of effusion.

Table 7.7: Comparison between SPAG Vs Final Diagnosis and Lights Criteria Vs Final Diagnosis

Comparison	Predictor	TP	TN	FP	FN	Sensitivity	Specificity	PPV	NPV	Accuracy
SPAG vs **Final Diagnosis**	Exudative	42	15	0	3	93.33	100.00	1.00	0.83	95.00
	Transudative	15	42	3	0	100.00	93.33	0.83	1.00	
Lights Criteria vs **Final Diagnosis**	Exudative	44	9	6	1	97.78	60.0	0.88	0.90	88.33
	Transudative	9	44	1	6	60.0	97.78	0.90	0.88	

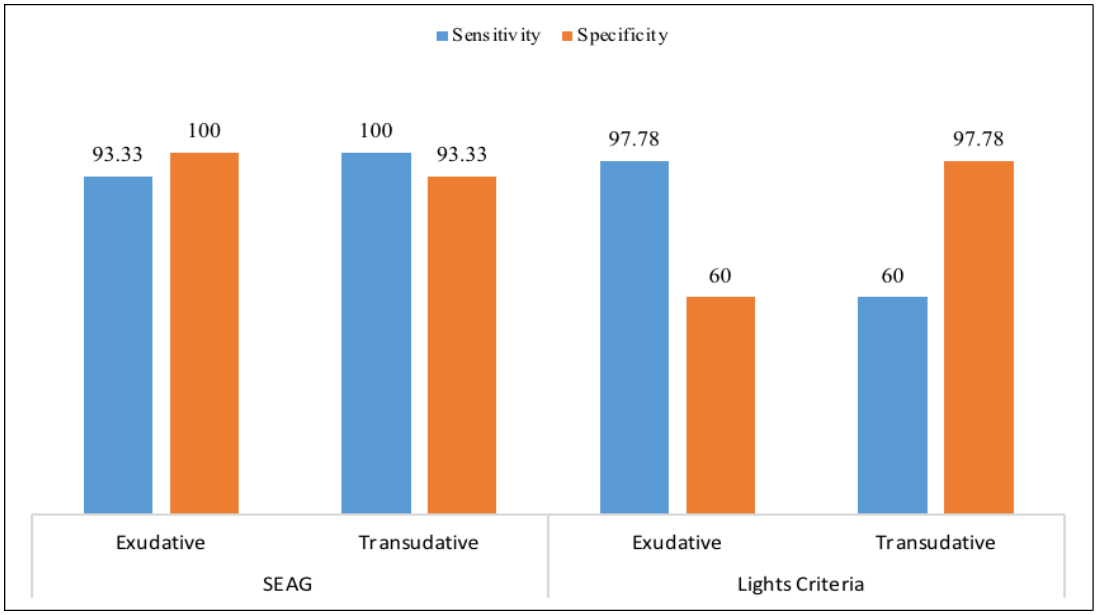

Figure 7.8: Sensitivity and Specificity of SPAG and Lights Criteria

In this study, using serum to pleural fluid albumin gradient above 1.2g/dl as cut off (>1.2g/dl transudative), 18 cases were classified as transudative effusion and 42 cases as exudative effusion.

On comparing above classified with final diagnosis of these pleural effusions, all transudative effusions were correctly identified by serum to pleural fluid albumin gradient. But it was found that, out of those classified as transudative effusion (18 cases), 3 were misclassified as transudative.

Thus, for classifying transudates SPAG was 100% sensitive and 93.33% specific. Positive predictive value was 83%, Negative predictive value was 100% and for exudates the sensitivity was 93.33%, specificity is 100%, positive predictive value was 100%, and negative predictive value was 83%.

Lights criteria identified 50 cases as exudative effusion and 10 cases as transudative pleural effusion.

On comparing this with the final diagnosis of these cases, 6 out of 50 exudates (12.22%) were misclassified by lights criteria.

Among the 10 cases identified by lights criteria as transudates, 1 exudative effusion due to malignancy was misclassified as transudate.

Sensitivity, Specificity of Lights criteria for classifying transudates were 60% and 97.78% respectively, with a Positive Predictive value of 90% and negative predictive value of 88%.

In classifying exudates the sensitivity and specificity were 97.78% and 60%, Positive and Negative predictive values were 88% and 90% respectively.

The accuracy of lights criteria when compared with final diagnosis to differentiate a case of pleural effusion into transudative and exudative was 88.33%.

IV. Discussion

SOCIODEMOGRAPHIC DETAILS

In our study a total of 60 patients with pleural effusion were studied. The study population had 18 (30%) females and 42 (70%) males. Patients with age above 18 years were included in the study. Among them, 1.7% were of age group <30 years and 6.7% of 31-40 years , 5% of 41-50 years age, 33.3% of 51 – 60 years and 11.7% of age more than 70 years. Maximum number of cases were in the age group of 61-70 years, minimum cases are in the age group less than 30 years. Exudative effusion was the major type of pleural effusion in all the studied age groups.

On considering the gender and type of pleural effusion, exudative effusion was the main cause of effusion in males (76.2%) and females (72.2%).

In a study done by Sahi and Dwivedi(7) in which they found that transudative pleural effusion appears in advanced age group but exudative pleural effusion is seen in early age groups.

It was found that there was no statistical significance in the type if effusion and the age and gender of these patients.

STUDY OF ETIOLOGICAL PROFILE

In this study out of 60 pleural effusions analyzed, the maximum (75%) were exudative effusions, out of which the most commonly seen were due to Tuberculosis (60%) followed by parapneumonic effusions (22.2%), followed by malignant (17.8%) effusions. These results were comparable to the study of Gongati P et al, Roth et al, Dhar et al,(4) (8)reported in their study that the commonest cause of exudative effusion was tuberculosis (42%).

Among transudative effusion, 7(46.7%) were due to CCF, 2(13.3%) CKD, 4 (26.7%) cirrhosis of liver and 2 (13.3%) nephrotic syndrome. The results were comparable to the study of Roth et al.(4)

In our study, using serum to pleural fluid albumin gradient above 1.2g/dl as cut off (>1.2g/dl transudative), 18 cases were classified as transudative effusion and 42 cases as exudative effusion.

On comparing above classified, with final diagnosis of these pleural effusion, all transudative effusions were correctly identified by serum to pleural fluid albumin gradient. But it was found that, out of those classified as transudative effusion (18 cases), 3 were misclassified as transudative. These included pleural effusions associated with 2 parapneumonic effusions and one malignancy.

Thus, for classifying transudates serum to pleural fluid albumin gradient was 100% sensitive and 93.33% specific. Positive predictive value was 83%, Negative predictive value is 100% and for exudates the sensitivity was 93.33%, specificity was 100%, positive predictive value was 100%, and negative predictive value was 83%.

The overall accuracy was 95% when comparing serum to albumin gradient with final diagnosis for differentiating transudative and exudative pleural effusion.

In the study by Roth et al(4),59 patients with pleural effusion were studied and lights criteria was 100% sensitive at identifying exudates, but specificity was 72% while the serum to pleural fluid albumin gradient was 100% specific and yet very sensitive ,ie, 95%.

In the study done by Mohanty et al(9), using lights criteria 6 cases out of 46 transudates were misclassified as exudative effusion and 2 exudates were misclassified as transudative effusion. And serum to pleural fluid albumin gradient, had greater number of misclassified exudates (4 exudates) and lesser number of misclassified transudates (only 2 transudates) when compared to lights criteria. The sensitivity and specificity and accuracy with respect to lights criteria were 97.75% , 62.5% and 93.3%. and 95.5%, 87.5% and 94.28% were the sensitivity, specificity and accuracy by serum pleural effusion albumin gradient.

In the study by Akkurt et al(12), sensitivity and specificity were 100% and 81% for lights criteria as compared with 91.9% and 100% respectively when serum – effusion albumin gradient were used to study the 74 exudates and 27 transudates of his study population.

Another study by Lesley J burges et al(6), were 270 exudates and 123 transudative effusion were studied, sensitivity, specificity and accuracy with lights criteria were 98%, 83%, 93% respectively and serum to pleural fluid albumin gradient had 87%, 92%, and 89%.

In our study, using Lights criteria 50 cases were identified as exudative effusion and 10 cases as transudative pleural effusion.

On comparing this with the final diagnosis of the cases, 6 out of 50 exudates (12.22%) was misclassified by lights criteria. This included one case of liver cirrhosis and 5 cases of congestive cardiac failure.

Among the 10 cases identified by lights criteria as transudates, 1 exudative effusion of malignancy was misclassified as transudate.

Sensitivity, Specificity of Lights criteria for classifying transudates were 60% and 97.78% respectively, with a Positive Predictive value of 90% and negative predictive value of 88%.

In classifying exudates, the sensitivity and specificity were 97.78% and 60%, Positive and Negative predictive values were 88% and 90% respectively.

The accuracy of lights criteria when compared with final diagnosis to differentiate a case of pleural effusion into transudative and exudative was 88.33%.

Gupta KB et al(10) in his study, found that 4 out of 12 transudates (33.3%) and 7 out of 48 exudates (14.5%) were misclassified using Lights criteria. In the study by Das AK et al(11) , using lights criteria, it was observed that 5 of the exudates & 3 transudates were falsely classified.

So when we compare the final accuracy of SPAG with final diagnosis of type of effusion and lights criteria with final diagnosis of effusion, we can find an accuracy of 95% of SPAG against a 88.33% of Lights criteria.

Therefore, serum to pleural fluid albumin gradient is as an effective means of discriminating exudative from transudative pleural effusions. Since this method uses only the values of effusion and serum albumin concentrations, it can be of great use when other measurements are not available.

V. Conclusion

From this study, it was found that:

1.For classifying transudates, serum to pleural fluid albumin gradient was 100% sensitive and 93.33% specific and for classifying exudates the sensitivity was 93.33%, specificity was 100%.

2.The overall accuracy of serum to pleural fluid albumin gradient when compared to lights criteria was higher, with an accuracy of 95% for serum to pleural fluid albumin gradient against a 88.33% for Lights criteria.

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