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A cross sectional study of efficacy of the ratio of pleural fluid alkaline phosphatase to serum alkaline phosphatase level in classifying pleural effusion as exudative and transudativeat IRD, SMS Medical College, Jaipur

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Abstract

Background: To study of efficacy of the ratio of pleural fluid Alkaline Phosphatase to serum Alkaline Phosphatase level in classifying pleural effusion as exudative and transudative**.**

Methods: This study was conducted among 60 patients with pleural effusion, attending the Institute of Respiratory Diseases, Jaipur (Rajasthan). Patients with clinical and radiological evidence of pleural effusion, irrespective of etiology, both sexes with age > 12 years were included. Patients with clinical and radiological evidence of pleural effusion are to be included in the study. Then they are classified in to exudates and transudates on the basis of the clinical, radiological and biochemical evaluation. Pleural fluid alkaline phosphatase & Serum alkaline phosphatase ratio is compared with results of the classification of exudates and transudates done on the basis of Light’s criteria.

Results: In our study by applying the Lights criteria, about 22.22 % of exudative pleural effusion was misclassified as transudative, and by applying Pleural fluid alkaline phosphatase the misclassification was 8.88%. Whereas by Pleural fluid / Serum alkaline phosphatase ratio, the misclassification was only 6.67%.

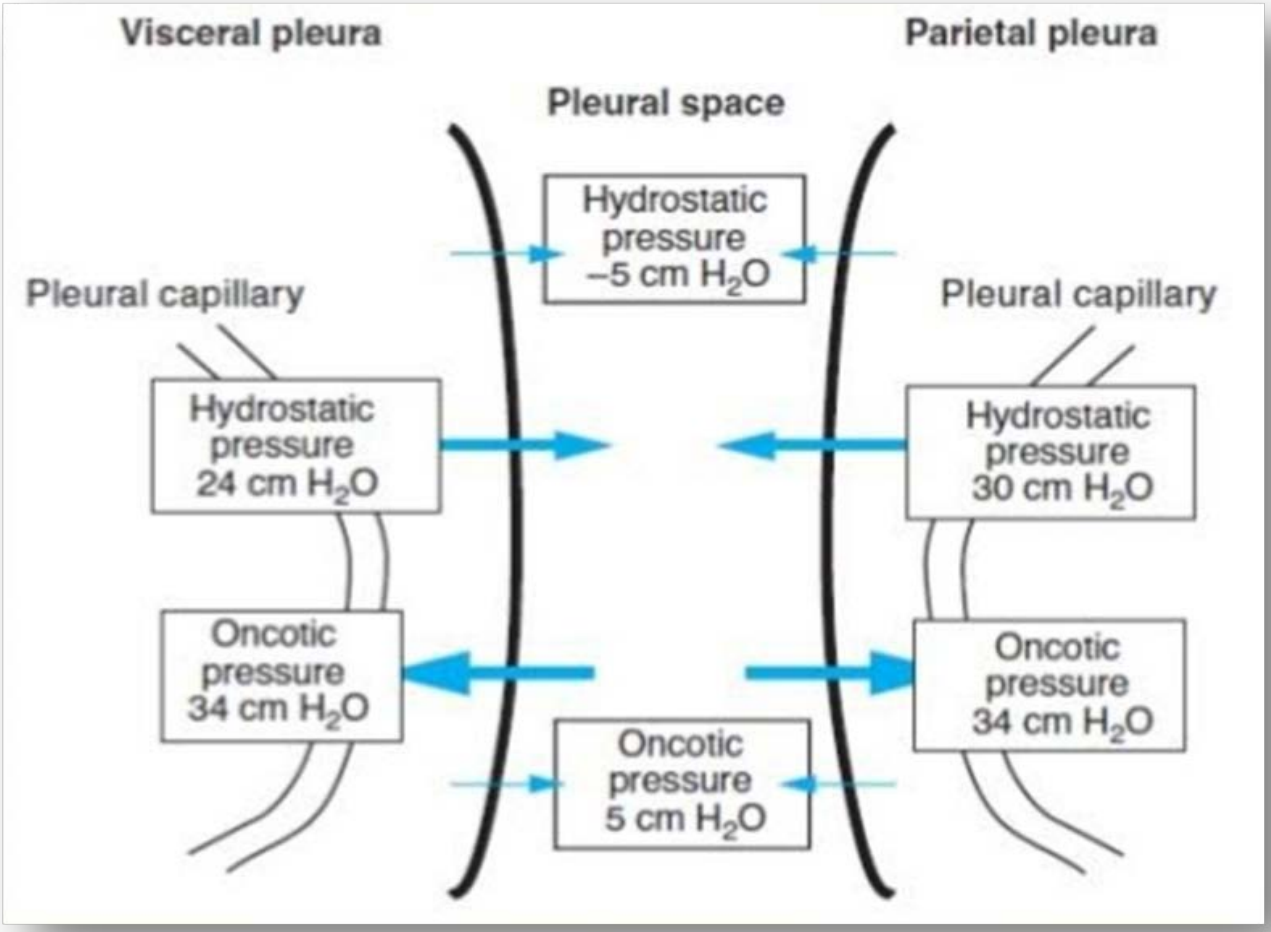
Conclusion: The pleural effusions from tuberculosis, lung cancer and pneumonia, heart failure chronic kidney and liver diseases are more common as compared to other etiologies in emergency department. Pleural fluid alkaline phosphatase and its ratio to serum levels ratio can be useful for differentiating the nature of pleural effusion and is comparable to light's criteria in resource limited settings of rural district hospitals.

Keywords: ALP(Alkaline phosphatase, Pleural effusion (PE), Pleural, Serum.

Introduction

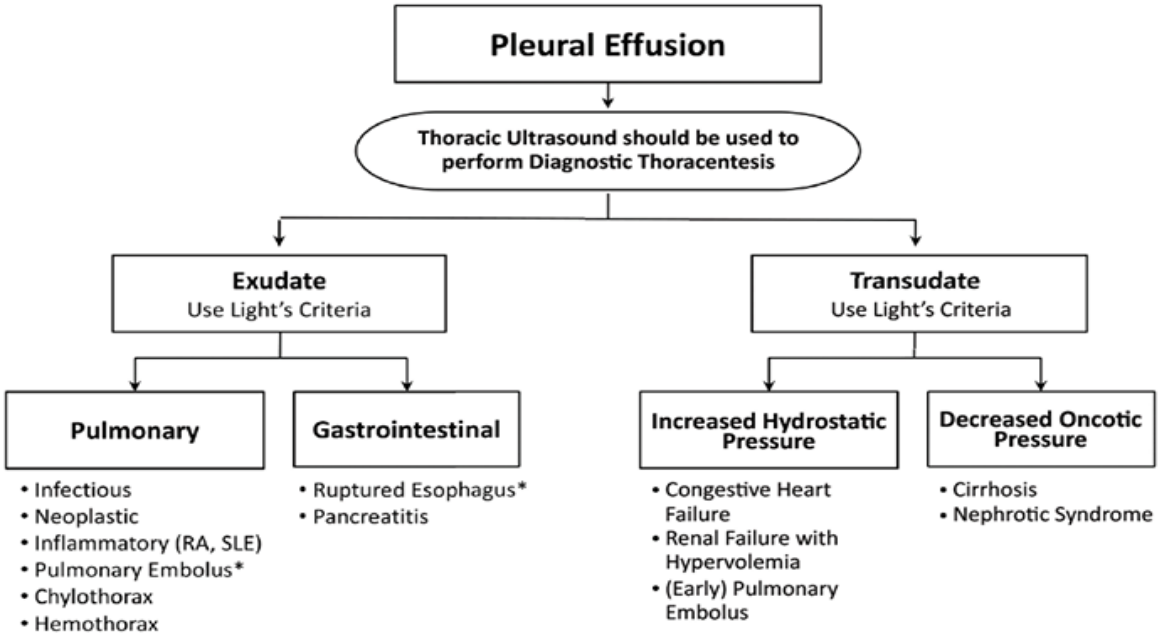
Pleural effusion (PE) is a common condition in clinical practice. A correct diagnosis of the underlying disease is essential for the management of pleural effusion. A definitive diagnosis is not established in approximately 20% of cases. An undiagnosed PE is defined as one that remains of unknown origin after performing complete pleural fluid analysis (nucleated cell counts with differential diagnosis, biochemistry, culture, cytology, and flow cytometry).The aim of this paper is to review the difficulties that may be encountered when attempting to establish the cause of a pleural effusion.

Pleural effusion can be caused by several mechanisms including increased permeability of the pleural membrane, increased pulmonary capillary pressure, decreased negative intra pleural pressure, decreased oncotic pressure, and obstructed lymphatic flow.



The numbers in the open arrow indicate the net magnitude of pressure gradient between the hydrostatic and oncotic pressure across the visceral and parietal pleura

Etiology



Many criteria have been used to distinguish them, but none of them have been found to be satisfactory. The most frequently used Light's criteria, though still considered as the gold standard; sometimes misclassify a transudate as an exudate. Light's criteria is the most commonly used method for this classification.[1,2]

As noted in various previous studies exudates have a high concentration of alkaline phosphatase in pleural effusion when compared to that of transudates and the same feature has been used in distinguishing transudates and exudates successfully.[3,4,5,6]

Light's Criteria[7]

The pleural fluid is an exudates if one or more of the following criteria are met:

1. Pleural fluid protein / Serum Protein > 0.5
2. Pleural fluid LDH / Serum LDH > 0.6
3. Pleural fluid LDH more than 2/3rd the upper limits of normal Serum LDH

"Alkaline phosphatase is a hydrolase enzyme which catalyze the removal of phosphate groups from nucleotides, proteins, alkaloids etc. It is mostly produced by liver and bone and these are the predominant forms. Other sites of production include kidney, intestine, placenta, pleura etc. Alkaline phosphatase levels are also used to differentiate transudative and exudative pleural effusion. A cut off value of 60 IU for Pleural fluid ALP and Pleural fluid/Serum ALP ratio of 0.35 is applied to classify pleural effusion into transudate or exudates."

Material & Methods

This is a hospital based prospective analytical study done on 60 patients admitted with pleural effusion at Institute of Respiratory Diseases, SMS Medical College, Jaipur during a one year period. Necessary permission was taken from the Ethical Committee and Research Review Board of SMS Medical College, Jaipur.

Inclusion criteria

•In Patients with clinical and radiological evidence of pleural effusion irrespective of etiology, both sex.

- Age > 12 years

Exclusion criteria

- "Age less than 12 years
- Pregnancy
- Jaundice
- Bone lesions

The patients had pleural effusion with clinical background of congestive cardiac failure, chronic liver disease, chronic kidney disease, tuberculosis, parapneumonic effusions and malignancy. The patients are examined clinically with the following parameters and after apply inclusion and exclusion criteria patients were included in the study after taking an informed consent.

Total 60 patients are taken for study In all the patients following investigation are done to classify them as exudates and transudates.

Pleural fluid alkaline phosphatase & Serum alkaline phosphatase,total protein are estimated and the patients are classified Then the patients are classified in to exudates and transudates on the basis of Light's criteria."

"Now the classification of exudates and transudates done on the basis of Pleural fluid alkaline phosphatase & Serum alkaline phosphatase is compared with results of the classification of exudates and transudates done on the basis of Light's criteria."

- "Sensitivity, Specificity, Positive predictive value, Negative predictive value of each tests are calculated" in to exudates and transudates.

Results

In our study data reveals that based on Light's Criteria 77.77% were correctly classified as exudates. However, on the basis of Plural fluid alkaline phosphatase 91.12% and Plural fluid alkaline phosphatase/ serum alkaline phosphatase reveals that 93.33% cases can be correctly classified as exudates.

Table 1: Descriptive statistics of pleural fluid protein, serum protein and their ratio:

Descriptive statistics	Pleural Fluid protein (gm/dl)	Serum protein (gm/dl)	Pleural fluid protein/ serum protein
Mean	3.69	6.49	0.569
SD	1.22	0.67	0.191
Minimum	1.20	3.80	0.273
Maximum	6.70	8.60	1.240

In our study data reveals that based on Light's Criteria 53.33% were correctly classified as transudates. However, on the basis of Plural fluid alkaline phosphatase 80.0% and Plural fluid alkaline phosphatase/ serum alkaline phosphatase reveals that 86.67% cases can be correctly classified as transudates.

Table 2: Descriptive statistics of pleural fluid bilirubin, serum bilirubin and their ratio:

Descriptive statistics	Pleural Fluid bilirubin	Serum bilirubin	Pleural fluid bilirubin / serum bilirubin
Mean	0.922	0.848	1.223
SD	0.420	0.416	0.662
Minimum	0.270	0.330	0.163
Maximum	2.780	2.490	4.00

In our study by applying the Lights criteria, about 22.22 % of exudative pleural effusion was misclassified as transudative, and by applying Pleural fluid alkaline phosphatase the misclassification was 8.88%. Whereas by Pleural fluid / Serum alkaline phosphatase ratio, the misclassification was only 6.67%.

In our study by applying the Lights criteria, about 46.66 % of transudative pleural effusion was misclassified as exudative, and by applying Pleural fluid alkaline phosphatase the misclassification was 20.0%. Whereas by Pleural fluid / Serum alkaline phosphatase ratio, the misclassification was only 13.33%.

Among the parameters used most specific test to classify an exudative pleural effusion from a transudative pleural effusion is pleural fluid total protein which is 81.25 % and most sensitive test is pleural fluid/ serum alkaline phosphatase ratio which is 95.45 %.

Table 3: Data showing correctly classified exudates and wrongly classified transudate by different methods:

Crireria	Correctly classified as exudates	Wrongly classified as transudate	X^2 (with respect to Light's criteria)	p
Light's criteria	35 (77.77%)	10(22.22%)		
Pleural Fluid Bilirubin	37 (82.22%)	8 (17.77%)	1.22	0.368
Pleural Fluid Bilirubin/Serum Bilirubin	38(84.44%)	7 (15.55%)	1.38	0.458

Table 4: Data showing correctly classified transudate and wrongly classified exudates by different methods:

	Correctly classified as transudate	Wrongly classified as exudates	X^2(with respect to Light's Criteria)	p
Light's criteria	8 (53.33%)	7 (46.66%)		
Plural Fluid Bilirubin	9(60.00%)	6(40.00%)	1.29	0.255
Plural Fluid Bilirubin/Serum Bilirubin	10(66.66%)	5 (33.33%)	0.24	0.62

In our study the positive predictive value, negative predictive value of pleural fluid/ serum alkaline phosphatase ratio classify an exudative pleural effusion from a transudative pleural effusion is higher which is 93.30 % , 86.60 % respectively .

In this study sensitivity, specificity, positive predictive value, negative predictive value and diagnostic

accuracy of Light's criteria are 83.3% , 72.2% , 77.7% , 53.33% , respectively .

Discussion

"One of the most common disease entity encountered by physicians worldwide is pleural effusion. In a situation where undiagnosed pleural effusion has come upon, the first and foremost thing to be resolved is whether the fluid is a transudate or exudate. The most frequently used Light's criteria, though still considered as a gold standard, often misclassify a transudate as an exudate. The present study was undertaken to evaluate the efficacy of pleural fluid alkaline phosphatase and its ratio to serum levels respectively, and pleural fluid total protein in distinguishing pleural fluid transudates and exudates and its correlation with Light's criteria.

For many decades Light's criteria had been used widely to differentiate exudative from transudativepleural effusion. But it also misclassified 25 % of transudates as exudates, so there was a need to identify new parameters which would prove to be superior or supportive to the array of tests at present.

This study was conducted at Institute of Respiratory Diseases, Sawai Man Singh Medical College, Jaipur. 60 patients diagnosed with pleural effusion who were admitted in our institute during 2019-2020, were included in the study. Patients having complaints like fever, cough, chest pain, shortness of breath.

In this study The patients with TB were younger than the patients with malignancy. Their mean age was 36 years, consistent with Luis Valdes et al (34 years)[8] and S.K. Sharma et al (33 years). [9]

In our study we demonstrated that massive effusion was most commonly seen in malignant effusion group (3%) but other study by Maher et al shows as high as 55%massive effusion seen in malignant effusion group. [10]

Although, previous studies[6,11]have made an attempt to use ALP for differentiating tuberculous from other types of pleural effusion, but none of them have clearly differentiated tuberculous from non-tuberculous pleural effusion. Francisco Carrion and Miguel Perpina94 found in their study that P ALP was significantly raised in malignant pleural effusion as compared to tuberculous, non-tuberculous and effusions due to miscellaneous causes. Further, while differentiating exudates from transudates, Muzaffer Metintas[12]found that P ALP and P/S ALP ratio were significantly raised in tuberculous pleural effusion as compared to neoplastic effusion, other exudates and transudates. However, Mushtaq A Lone[13] again while differentiating exudates from transudates reported that ALP did not differentiate tuberculous from other causes of effusion, including malignancy, parapneumonic effusion and nonspecific. In view of above controversy, we aimed to assess the value of ALP in differentiating exudate from transudate pleural effusion and found that ALP is a useful biochemical marker for such differentiation.

To conclude, ALP is helpful in separating exudate from transudate pleural effusion. However, further studies, involving larger number of patients, to evaluate the parameter covered in our study are needed in order to draw any conclusion or to achieve higher sensitivity.

Conclusion

The pleural effusions from tuberculosis, lung cancer and pneumonia, heart failure chronic kidney and liver diseases are more common as compared to other etiologies in emergency department. Pleural fluid alkaline phosphatase and its ratio to serum levels ratio can be useful for differentiating the nature of pleural effusion and is comparable to light's criteria in resource limited settings of rural district hospitals.

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