VOLUME - 10, ISSUE - 05, MAY- 2021 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Pulmonary Medicine

A CROSS SECTIONAL STUDY OF EFFICACY OF THE RATIO OF PLEURAL FLUID BILIRUBIN TO SERUM BILIRUBIN 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 Bilirubin to serum Bilirubin 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 bilirubin & Serum bilirubin ratio is compared with results of the classification of exudates and transudates done on the basis of Light's criteria.

Results: Pleural bilirubin to serum ratio shows non significance to differentiate between exudates and transudates pleural effusion etiology.

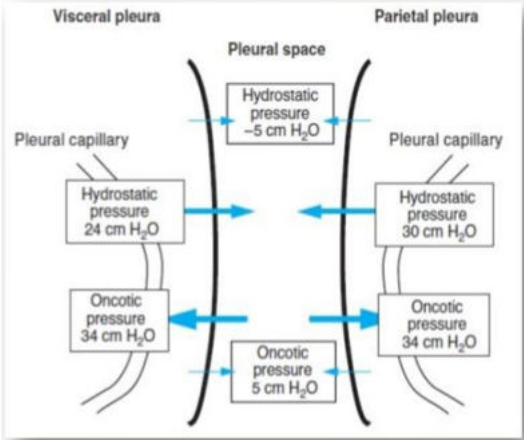
Conclusion: The pleural effusions from tuberculosis, lung cancer and pneumonia, heart failure chronic kidney and liver diseases are more common as compared to other etiologies in emergency department. Pleural fluid bilirubin and its ratio to serum levels ratio can be useful for differentiating the nature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

KEYWORDS : Bilirubin ratio; exudates; Light's criteria; pleural effusion; transudates.

INTRODUCTION:

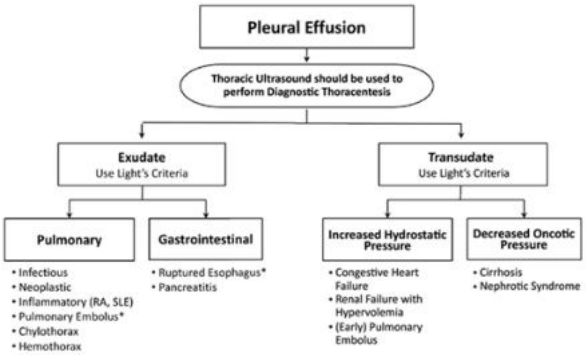
Pleural effusion (PE) is a common condition in clinical practice. A correct diagnosis of the underlying disease is essential for the management of pleural effusion. A definitive diagnosis is not established in approximately 20% of cases. An undiagnosed PE is defined as one that remains of unknown origin 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

Bilirubin has a high molecular weight (584). With respect to its concentration between serum and protein it behaves in a

manner identical to that of the high molecular weight proteins. Any serous membrane inflammation often leads to increased capillary permeability and this enables the diffusion of high molecular weight bilirubin.

A pleural fluid bilirubin of more than 0.48 mg / dl and a pleural fluid bilirubin to serum bilirubin ratio of more than 0.62 is considered as exudates.

MATRERIAL & 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
- Prgnancy
- 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 Bilirubin & Serum Bilirubin,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 Bilirubin & Serum Bilirubin 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 Bilirubin82.22% and Plural fluid Bilirubin/ serum Bilirubin reveals that 84.44% cases can be correctly classified as exudates.

Table-1Descriptive 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 Bilirubin 60.0% and Plural fluid Bilirubin/ serum Bilirubinreveals that 66.67% 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 Bilirubinthe misclassification was 17.77%. Whereas by Pleural fluid / Serum Bilirubinratio, the misclassification was only 15.55%.

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 by applying the Lights criteria, about 46.66 % of transudative pleural effusion was misclassified as exudative, and by applying Pleural fluidBilirubin the misclassification was 40.0%. Whereas by Pleural fluid / Serum Bilirubinratio, the misclassification was only 33.33%.

Among the parameters used most specific and sensetive test to classify an exudative pleural effusion from a transudative pleural effusion is pleural fluid total protein which is 83.33 % ,72.20% respectively.

In other hand p-value of pleural to serum bilirubin ratio was insignificant.

In our study the positive predictive value, negative predictive value of pleural fluid/ serum Bilirubin ratio classify an exudative pleural effusion from a transudative pleural effusion is higher which is 93.30% , 86.60 % respectively, but this study data shows that bilirubin level not signify etiology of pleural effusion as compare with Light's criteria.

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 transudative pleural 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]

Since protein ratio was being used widely, researchers had been interested in assessing the efficiency of pleural fluid serum Bilirubin ratio. The efficacy was comparable to that of pleural fluid protein and pleural fluid serum protein ratio. The mean Bilirubin ratio for exudates exceeded that for transudates. The observed difference was statistically non-significant, P value from t test being >0.05. Considering the cutoff point of 0.6.Meisel et al revealed the sensitivity of 96% and specificity of 83%.[11] Pleural fluid alkaline phosphatase, Bilirubin and its ratio to serum levels fulfilled the criteria and misplaced as exudates. In the rural setting the facility for LDH level is not easily available, the facility for bilirubin level is not found that can be utilized in work up for pleural effusion, but in our study alkaline phosphatase level found that can be utilize in work up for pleural effusion.

Pleural fluid to serum bilirubin ratio can't replace Light's criteria in differentiation between exudates and transudate pleural effusion. Pleural fluid to serum bilirubin ratio is not a reliable test because of insignificant p-value(>0.05)

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 bilirubin 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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