ORIGINAL RESEARCH

Diagnostic value of pleural fluid/serum bilirubin ratio Vs pleural fluid protein/serum protein ratio to differentiate transudative from exudative pleural effusion

Dr. Priya Babool[1], Dr. Sat Pal Aloona[2], Dr. Sapna[3], Dr. Harmohinder Kumar Attri[4], Dr. Niharika Khunger[5], Dr. Bibekapal Singh Aloona[6]

[1]Junior Resident 3[rd]year, [2]Professor, [3]Assistant Professor, Department of Medicine, Govt. Medical College & Hospital, Amritsar, Punjab, India
[4]Assistant Professor, Department of Biochemistry, Govt. Medical College & Hospital, Amritsar, Punjab, India
[5]Intern, [6]MBBS, Govt. Medical College & Hospital, Amritsar, Punjab, India

Corresponding Author
Dr. Sat Pal Aloona
Professor, Department of Medicine, Govt. Medical College & Hospital, Amritsar, Punjab, India

ABSTRACT
Background: Transudative effusions are the ultrafiltrates of plasma that have been forced out of the pleura by an imbalance between the oncotic and hydrostatic forces in the chest which creates an imbalance. Also, exudative effusions occurs resulting from various inflammatory conditions.
Methods: A total of 100 patients were enrolled to conduct a study comparing the diagnostic usefulness of pleural fluid bilirubin/serum bilirubin ratio to pleural fluid protein/serum protein ratio to distinguish between exudative and transudative pleural effusion.
Results: Based on pleural fluid bilirubin to serum bilirubin ratio, 45% of the effusions were exudates and 55% were transudates. There were a total of 47% transudates and 53% exudates based on the criterion of pleural fluid protein to serum protein ratio. Significant correlation was seen between effusion type based on pleural fluid protein to serum protein and pleural fluid bilirubin and serum bilirubin.
Conclusion: As a diagnostic tool, the pleural fluid bilirubin/serum bilirubin ratio exhibits potential in distinguishing between transudativeandexudativepleuraleffusions.

INTRODUCTION

The pleural membrane that envelopes the lung parenchyma, diaphragm, chest wall, and mediastinum is an essential structure. The visceral pleura is directly attached to the lung surface, the pleural space, located between the visceral and parietal pleurae, contains approximately 10 milliliters of fluid.[1]An imbalance between hydrostatic and oncotic pressures leads to transudates. These are the ultrafiltrates of plasma that have been forced out of the pleura by an imbalance between the oncotic and hydrostatic forces in the chest. Exudative effusions result from various inflammatory conditions and typically require a more comprehensive evaluation and treatment strategy than transudates.Reduced lymphatic outflow at the pleural borders or pleural inflammation are the two main causes of exudative effusions. Various tests are performed to confirm the pleural effusion such as X-Rays, CT scans, and other general tests like pleural fluid analysis etc..[2]The purpose of this study was to determine whether the pleural fluid bilirubin to serum bilirubin ratio is a useful tool for distinguishing between exudative and transudative pleural effusions.

MATERIALS AND METHODS

A total of 100 patients were enrolled in the Department of Medicine, Government Medical College, Amritsar to conduct a study comparing the diagnostic usefulness of pleural fluid bilirubin/serum bilirubin ratio to pleural fluid protein/serum protein

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ratio to distinguish between exudative and transudative pleural effusion.

INCLUSION CRITERIA
- Patients who, regardless of sex or aetiology, had a clear clinical diagnosis and radiographic evidence of pleural effusion and who were at least 15 years of age.

EXCLUSION CRITERIA:
- Less than 14 years old.
- Individuals suffering from traumatic effusion, pulmonary embolism, hypoproteinemia, dyslipidemia, or jaundice.
- Patients with prior diagnosis who were currently receiving therapy.
- Every patient had a thorough case history obtained, and a thorough clinical examination was performed in accordance with the proforma and Regular blood tests must be carried out. Laboratory investigations were carried out: Serum and pleural fluid proteins, Serum and pleural fluid LDH levels and Bilirubin levels in serum and pleural fluid.In our study, to diagnose exudates the following parameters were used:
- A ratio of serum to pleural fluid proteins greater than 0.5 mg/dl.
- A ratio of greater than 0.6 mg/dl between bilirubin in the pleural fluid and serum bilirubin.

To estimate the protein the Biuret technique and for LDH Pyruvate kinetic method was employed.

STATISTICAL ANALYSIS
At the end of study, the data was collectedand analysedusing appropriate statistical methods. The statistical software SPSS was used for statistical analysis. The mean ± standard deviation was calculated .The values of P <0.05 were considered as significant. The qualitative variables were compared using the chi-square test. Univariate correlation analysis was used to confirm the significance of the variables.

RESULTS
In the present study, majority of patients were in the age group of more than 60 years (30%). 64% of the study population were males and 36 % were females.The patients suffering from cancer, CCF, CKD, CLD, other CTDs, pneumonia, TB, and RA were 3%, 19%, 17%, 11%, 2%, 18%, 27%, and 3% respectively. Different causes of pleural effusion were TB and pneumonia, CLD related effusion, RA related effusion and CKD were seen. The distribution of study participants according to effusion type (based on the bilirubin ratio). There were total 55% transudate and 45% exudates effusion type. The distribution of study participants according to effusion type (based on pleural fluid protein/serum protein). There were total 47% transudate and 53% exudates effusion type.The association of age group and gender with effusion type (based on pleural fluid protein/serum protein) showed non-significant association in the present study. In males, there were 43.80% transudate effusion type and 56.20% were exudates. In females, there were 52.80% transudate effusion type and 47.20 % were exudates. The association of gender with effusion type (based on pleural fluid bilirubin/serum bilirubin) showed that 54.40% males had transudate effusion type and 45.50% were exudates. In females, there were 56.20% transudate effusion type and 43.70% were exudates. Non-significant association was seen.

Table No. 1: Association Of Diagnosis With Effusion Type Based On Pleural Fluid Protein /Serum Protein

DIAGNOSIS	EFFUSION TYPE				TOTAL	
	TRANSUDATE		EXUDATE			
	NO.	%AGE	NO.	%AGE	NO.	%AGE
CANCER	0	0%	3	100%	3	100%
CCF	18	94.7%	1	5.2%	19	100%
CKD	15	88.2%	2	11.7%	17	100%
CLD	9	81.8%	2	18.1%	11	100%
OTHER CTDs	0	0%	2	100%	2	100%
PNEUMONIA	1	5.5%	17	94.4%	18	100%
TB	4	14.8%	23	85.1%	27	100%
RA	0	0%	3	100%	3	100%
TOTAL	47	47%	53	53%	100	100%

Pearson Chi-square Statistic = 65.07; P<0.001 from above table

Table no 1 showed significant association (p<0.001) of diagnosis with effusion type (based on pleural fluid protein / serum protein).

Table No. 2: Association Of Diagnosis With Effusion Type (Based On Pleural Fluid Bilirubin/ Serum Bilirubin)

DIAGNOSIS	EFFUSION TYPE				TOTAL	
	TRANSUDATE		EXUDATE			
	NO.	%AGE	NO.	%AGE	NO.	%AGE
CANCER	1	33.3%	2	66.7%	3	100%
CCF	18	94.7%	1	5.3%	19	100%
CKD	17	100%	0	0%	17	100%
CLD	9	81.8%	2	18.2%	11	100%
OTHER CTDs	0	0%	2	100%	2	100%
PNEUMONIA	4	22.2%	14	77.8%	18	100%
TB	5	18.5%	22	81.5%	27	100%
RA	1	33.3%	2	66.7%	3	100%
TOTAL	55	55%	45	45%	100	100%

Pearson Chi-square Statistic = 55.142 p<0.001 from above table

Table no 2shows association of diagnosis with effusion type (based on pleural fluid bilirubin/serum bilirubin ratio) (p value< 0.001).

TABLE NO. 3: LABORATORY PARAMETERS

LABORATORY PARAMETER	EFFUSION TYPE		P VALUE
	TRANSUDATE (MEAN ± SD)	EXUDATE (MEAN ± SD)	
PLEURAL FLUID PROTEIN (g/dl)	2.91 ± 0.79	4.68 ± 1.00	<0.001
SERUM PROTEIN (g/dl)	6.76 ± 0.73	6.87 ± 0.75	0.484
PLEURAL FLUID PROTEIN/SERUM PROTEIN	0.42 ± 0.12	0.67 ± 0.11	<0.001
PLEURAL FLUID LDH	73.72 ± 37.43	122.81 ± 66.39	<0.001
SERUM LDH	170.77 ±71.05	197.26 ± 90.50	0.110
PLEURAL FLUID LDH/SERUM LDH	0.41 ± 0.08	0.60 ± 0.12	<0.001
PLEURAL FLUID BILIRUBIN	0.34 ± 0.10	0.47 ± 0.10	<0.001
SERUM BILIRUBIN	0.73 ± 0.16	0.70 ± 0.16	0.470
PLEURAL FLUID BILIRUBIN/SERUM BILIRUBIN	0.47 ± 0.18	0.69 ± 0.17	<0.001

According to above table 3, significant association was observed for the mean pleural proteinin transudate and exudates [p value<0.001]; the mean pleural fluid /serum protein [p value<0.001]; Mean pleural LDH [p value <0.001]; The mean pleural fluid to serum LDH [p value<0.001]; Mean pleural fluid bilirubin [p value <0.001] and the pleural fluid bilirubin/serum bilirubinbetween exudates and transudates was found to be statistically significant [p value<0.001].

DISCUSSION
Pleural effusion is a prevalent medical condition that doctors face globally. When a pleural effusion is diagnosed, the most important thing to do is find out if it is exudative or transudative, as this has a big impact on treatment and prognosis.

In our study, age distribution showed that the age group over 60 years old had the highest prevalence of pleural effusion (30%) which means that the chance of an effusion rises with age.The gender breakdown showed male predominance. Similar results were observed in studies byRao et al.[3]and Prabhakaran R et al.[4]

Based on the pleural fluid bilirubin/serum bilirubin ratio, there were 45% exudates and 55% transudates and pleural fluid protein/ serum protein ratio, it revealed 53% of exudates and 47% of transudates.In study done byJaber,Bint Al huda et al among 35 patients,there were 22[62.8%] exudates and 13[37.1%] transudates.[5]Nevertheless, Meisel et al had equal number of exudates & transudates in their study.[6]

In our study the commonest cause of effusion was Tb 27% and others were CCF, pneumonia, CKD, CLD, RA related effusions and CTDs.The majority of effusion cases in a similar study by Agrawal P et al were caused by lung infections. Pneumonia accounted for 35.9%, with tuberculosis coming in second at 23.3%[7].Another study conducted by Jaber, Bint Al Huda also showed maximum number of cases due to pulmonary TB(31.4%) followed by malignancy either due to bronchogenic carcinoma (17.14%)or metastasis (14%)followed by pneumonia(5%).[5]

In studying age distribution of different causes of pleuraleffusion, it was seen that in the younger age groups less than 30 years, lung infections were more common as compared to conditions like CCF,CKD and Cancer.HareeshPathak et al. in GMC Bhopal,280 cases of pleural effusion were taken.Majority of patients (104) belonged to age group of 21–30 years. Out of 202 tubercular effusion patients, 102 belonged

to age group of 21–30 years, followed by 36 patients in age group of 31–40 years. Out of 36 malignant effusions patient majority (20) belonged to age group of more than 60 years. Out of 16 bacteriological effusion patients 6 belonged to age group of 31–40 years followed by 4 patients who were of 41–50-year age group.[8]It was seen that higher rates of cardiovascular disease in older populations led to an increased incidence of heart failure-related pleural effusions with heart failure being a predominant cause in the elderly. Age-Related Trends showedthat greater prevalence of pleural effusions was due to chronic conditions such as heart failure, malignancy, and pulmonary embolism. Younger Populations were more commonly affected by infectious causes such as pneumonia and tuberculosis.[9]

Comparable to pleural fluid protein to serum protein ratio, the effectiveness was similar to the ratio of pleural fluid to serum protein. For exudates, with a P value of <0.001 from the t test, the observed difference was statistically significant. Similarly, the mean pleural fluid to serum bilirubin ratio for exudates was higher than that for transudates in a research by Agrawal P.[7]

Based on the pleural fluid bilirubin/serum bilirubin ratio, the study demonstrated the diagnostic accuracy of effusion type. Sensitivity was 79.25%, specificity was 93.62%, positive predictive value was 93.3%, and negative predictive value was 80% for the pleural fluid bilirubin/ serum bilirubin ratio diagnostic accuracy. This study bears similarities to that conducted by Badve et al. in which the pleural fluid bilirubin/serum bilirubin ratio of >0.6 in pleural fluid demonstrated an 84% specificity and 79% sensitivity in detecting exudates. The sensitivity and specificity of the pleural fluid protein/serum protein ratio were 92% and 88%, respectively, indicating greater diagnostic accuracy.[10]Similar results were obtained by study done by Huang et al.[11] Kim et al. [12]Aloona SP et al.[13]

According to Ismail HJ et al.[14] the bilirubin ratio (pleural fluid bilirubin/serum bilirubin) had 88% and 85% sensitivity and specificity, respectively, while the protein ratio (fluid protein/serum protein) had 88% and 85% sensitivity and specificity.When comparing the accuracy of the parameters, such as the pleural fluid bilirubin/serum bilirubin ratio, to Light's criterion, Adnan Yilmazetal.discovered no discernible differences.[15]Studies comparing pleural fluid protein/serum protein and pleural fluid bilirubin/serum bilirubin ratios have demonstrated that both are useful in distinguishing exudative from transudative effusions. Hence, the results of our study regarding the diagnostic accuracy of pleural fluid bilirubin/serum bilirubin ratio in comparison to pleural fluid protein/serum protein ratio in differentiating exudative from transudative pleural effusions are comparable to the studies done in the past.

CONCLUSION
In conclusion, even though the pleural fluid protein/serum protein ratio is still the gold standard for differentiating between transudates and exudates, the pleural fluid bilirubin / serum bilirubin ratio may improve diagnostic accuracy and evaluation in situations where the clinical diagnosis and the results from this long-used test do not match. As a diagnostic tool, the pleural fluid bilirubin/serum bilirubin ratio exhibits potential in distinguishing between transudative and exudative pleural effusions. It provides diagnostic performance that is comparable to that of the pleural fluid protein/serum protein ratio and could be helpful in situations where more indicators are required to increase diagnostic accuracy or if standard criteria are ambiguous. Pleural fluid bilirubin/serum bilirubin should be done routinely to distinguish transudative from exudative effusions as it is easily available, cost effective and better than other routinely done biochemical tests.

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