

The diagnostic separation of transudates and exudates in pleural effusion

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Abstract

The present study was undertaken to compare plasma-pleural effusion albumin gradient with Light's traditional criteria for differentiating exudates from transudate in pleural effusion who were undergoing diagnostic and therapeutic thoracentesis in whom the etiology of effusion could be determined were studied. Blood and pleural fluid chemistries were measured to determine plasma-pleural effusion albumin gradient and Light's criteria parameters like pleural fluid proteins, fluid to plasma protein ratio, fluid LDH and fluid to serum LDH ratio and we observed some misclassifications in exudates and transudates. Using an albumin gradient of 1.2 gm/dl or less to indicate exudate and >1.2 gm/dl to indicate transudate, none of the transudates were found to be misclassical, but 1 case of exudate (malignant pleural effusion) was misclassical. We conclude that although Light's criteria for exudates are very sensitive, albumin gradient of 1.2 gm/dl or less tends to be more specific to exudates.

Key Words: Plasma-pleural effusion, albumin gradient, exudate, transudate, light's criteria.

Introduction

Approximately one million patients develop pleural effusion every year¹. It is a common clinical disorder and is either a manifestation or a complication of one or other respiratory or non-respiratory disorders². It leads to serious prognosis, if not diagnosed and treated properly.

To treat pleural effusion in a proper way, it should be classified either as an exudate or a transudate. The classification of pleural effusion fluid was based on Light's criteria i.e 1). Pleural fluid protein to plasma protein ratio >0.5, 2). Pleural fluid LDH to serum LDH ratio >0.6. 3). Absolute pleural fluid LDH >200 IU/L denoting as an exudate³. This has become the standard

method for separation as they have maximum sensitivity in identifying exudates. But many pleural effusions were misclassified using these criteria. Therefore, other biochemical parameters like pleural fluid cholesterol⁴, pleural fluid to serum bilirubin ratio⁵, pleural fluid cholinesterase⁶, alkaline phosphatase⁷, creatin kinase, uric acid⁸ and pleural fluid MDA⁹ have been analyzed. But, none has been found to be 100% sensitive or specific.

Recently, plasma-pleural effusion albumin gradient (PPEAG) has been reported as a good parameter with 97% sensitivity and 100% specificity¹. The present study was conducted to evaluate PPEAG for differentiating exudates from transudates.

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Materials and methods

The present study was conducted in Department of Biochemistry in collaboration with department of TB & Chest Medicine of Prathima Institute of Medical Sciences, Nagunur, Karimnagar, Andhra Pradesh. Informed consent was obtained from all the participants of the study and followed the ICMR ethical guide lines-2006. A total of 52 patients having pleural effusion of diverse-etiology were taken and divided into 2 groups:

Group-I(Transudates) – comprising of 13 patients (6 cases of nephrotic syndrome; 5 cases of congestive cardiac failure; 2 cases of hypoproteinemia).

Group-II(Exudates) – comprising of 39 patients (20 cases of Pulmonary TB; 7 cases of Malignancy; 12 cases of pneumonia).

The cases in which neither no cause was definitely diagnosed or more than one cause was present were excluded from the study. After obtaining detailed history and thorough clinical examination of the patient, blood samples were collected.

After the admission of the patients in the hospital, pleural fluid samples were collected in a sterile clean container through thoracocentesis and the following biochemical parameters were analyzed: Blood for Plasma total proteins, plasma albumin and serum LDH, pleural Fluid for fluid protein, fluid albumin and fluid LDH.

Other investigations like x-ray chest, ultra sonography, pleural biopsy, pleural fluid cell counts, differential counts and ADA levels were performed as per requirement.

Estimation

- Total proteins were estimated by routine Biuret Method¹⁰.

- Albumin was measured by BCG method¹¹.
- LDH was estimated by modified IFCC method in which rate of oxidation of NADH to NAD was measured as a decrease in absorbance that was proportional to LDH activity of the sample¹².

All these biochemical parameters were analyzed through Erbachem-7 semi auto analyzer, Statistical analysis of the data was performed using unpaired 't' test.

Results

Of 52 cases of pleural effusion, 38 were males and 14 were females with mean age of 46.98 ± 16.78 years. 39 patients had exudative pleural effusion (Pulmonary TB=20, malignancy=7, pneumonia=12) and 13 patients had transudative pleural effusion (nephrotic syndrome=6, CCF=5, hypoproteinemia=2). The results of estimation of fluid and blood parameter were based on Light's criteria and compared with PPEAG levels. The reference values of Light's criteria taken for various parameters were¹³:

- i) Pleural fluid protein >3.0 gm/dl as an exudate, <3.0 gm/dl as transudate.ii)
- ii) Pleural fluid to plasma protein ratio >0.5 as an exudate and <0.5 as transudate.
- iii) Pleural fluid LDH >200 IU/L as an exudate; <200 IU/L as transudate.
- iv) Pleural fluid to serum LDH ratio >0.6 as an exudate, <0.6 as transudate.

Table-I shows the mean and SD of all parameters studied which were significantly higher for exudates than transudates with $P<0.001$, but PPEAG was

significantly lower in exudates than from transudates (P<0.0001). Table-II shows sensitivity, specificity, Positive Predictive value (PPV) and Negative Predictive value (NPV) of all parameters studied. Comparing PPEAG with other parameters of Light's

criteria, PPEAG showed sensitivity of 97%, 100% specificity, 100% PPV and NPV of 92.3%. When PPEAG was compared to Light's criteria none of the transudates were misclassified, but 2.8% of exudates were misclassified (Table-III).

Table-I

Comparison of transudations and exudates with respect to different parameters

S. No	Parameters	Transudates		Exudates		'P' value
		Range	Mean ± SD	Range	Mean ± SD	
1.	Pleural Fluid Proteins (gm/dl)	1.6 - 6.2	2.82 ± 1.41	2.1 - 6.5	3.92 ± 1.14	<0.001
2.	Pleural Fluid to plasma protein ratio	0.24 - 1.14	0.49 ± 0.27	0.37 - 1.23	0.70 ± 0.20	<0.001
3.	Pleural fluid LDL IU/L	88 - 298	145.7 ± 61.94	92 - 498	268.85 ± 94.6	<0.001
4.	Pleural fluid to serum LDH ratio	0.30 - 0.85	0.53 ± 20	0.37 - 1.59	0.91 ± 0.34	<0.0001
5.	Plasma pleural effusion albumin gradient (PPEAG)	1.2 - 2.8	1.74 ± 0.52	0.5 - 1.7	0.85 ± 0.24	<0.001

Table – II

Sensitivity, specificity, positive predictive value (PPN), negative predictive value (NPV) of various parameters studied

S.No.	Parameters	Sensitivity	Specificity	PPV	NPV
1.	Pleural fluid proteins	80%	76.9%	99.1%	55.5%
2.	Pleural fluid to plasma protein ratio	82.1%	69.2%	88.8%	56.2%
3.	Pleural fluid LDH	74.4%	76.9%	90.6%	50.0%
4.	Pleural fluid to serum LDH ratio	76.9%	76.9%	90.9%	52.6%
5.	Plasma-pleural effusion albumin gradient	97%	100%	100%	92.3%

Table – III

No. of cases misclassified in transudate and exudate pleural efusions for every parameter studied:

S.No.	Parameter	Transudate No:13	%	Exudates No:39	%
1.	Pleural fluid proteins	3	23.1%	8	20.6%
2.	Pleural fluid to plasma protein ratio	4	30.8%	7	17.9%
3.	Pleural fluid LDH	3	23.1%	10	26.0%
4.	Pleural fluid to serum LDH ratio	3	23.1%	9	23.1%
5.	Plasma-pleural effusion albumin gradient	0	0.0%	1	2.8%

Discussion

Approximately about 4% of patients attending chest clinic may suffer from pleural effusion as a sequelae to diseases of respiratory system, cardio vascular system, renal and other systems. But determining the cause of pleural effusion is not always easy. The initial and most important step in diagnosis is to differentiate them as exudate or transudate. Many criteria have been used like pleural fluid cholesterol; fluid to serum cholesterol ratio, pleural fluid MDA, fluid to serum MDA ratio, fluid to serum bilirubin ratio, fluid to serum cholinesterase ratio, but none of the parameter has yet proved to be satisfactory^{1,13}.

Pleural fluid can be accumulated for a number of reasons, which may be due to increased fluid formation or decreased absorption. Effusion due to pleural disease resembles plasma (exudate) while that occurring with normal pleural membrane due to hemodynamic aberrations or oncotic changes results in formation of ultra filtrate of plasma (transudate). Transudate effusion results from normal microvasculature and maintains the gradient between plasma and pleural fluid protein¹⁴.

Etiology of the production of exudate involves some types of inflammation resulting in a compromised pulmonary or pleural microvasculature, which in turn leads to increased fluid leaking, a higher protein concentration and a decrease in albumin gradient. Albumin in pleural effusion originates from serum via diffusion. However, proteins like LDH come from pleural fluid leucocytes into pleural space¹⁵. Therefore, PPEAG should be taken as an effective means of differentiating exudate from transudate as this method only relies on measurement of plasma and effusion albumin concentration. Taking a cut of value of 1.2 gm/dl of PPEAG, K.B.Gupta et al¹ revealed all the transudates and 95% of all exudates were classified correctly. In the present study also, none of the transudates and 2.8% of exudates were misclassified with sensitivity, specificity, PPV and NPV of 97.9%, 100%, 100% and 92.3% respectively (Table-II). The mean albumin gradient were significantly higher in transudates 1.74 ± 0.52 as compared to exudates 0.85 ± 0.24 with 'P' value of <0.0001 , which correlates well with previous workers.

Based on Light's criteria, there were about 20% to 35% of misclassifications either as transudate or exudate¹. In our study, it was found that pleural fluid to plasma protein misclassified in 30.8% transudates and 17.9% exudates. Pleural fluid LDH misclassified in 23.1% transudates and 20% exudates while fluid to serum LDH misclassified in 23.1% transudates and 19.8% exudates.

In the present study, the exudative pleural effusion based on pleural fluid protein, 8 cases were misclassified (4 cases were of Pulmonary TB, 3 cases of pneumonia, 1 case was of malignancy). In transudative pleural effusion 3 cases were misclassified as exudates. But when PPEAG was evaluated all of the transudates were well classified. Hence PPEAG has been found to better criterion to classify transudate and exudate even in misclassified effusions.

Thus, the present study shows the usefulness of PPEAG in classifying transudate from exudate especially in cases misclassified by Light's criteria. So, PPEAG can be used as a good complementary parameter.

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