



**DIAGNOSTIC ACCURACY OF PLEURAL FLUID CHOLESTEROL IN DIAGNOSIS
OF EXUDATIVE PLEURAL EFFUSION****SARWER MI⁴, TARIQ N², FAROOQ U³, ZAFAR S⁴, AHMAD S⁴ AND MALIK A^{1*}****1:** Institute of Molecular Biology and Biotechnology (IMBB), The University of Lahore,**2:** M.Islam Medical and Dental College, Gujranwala-Pakistan**3:** Department of pathology, Gujranwala Medical College, Gujranwala-Pakistan**4:** Quaid-e-Azam Medical College, Bahawalpur

Corresponding Author: Arif Malik (PhD): E Mail: arifuaf@yahoo.com*Received 8th March 2019; Revised 11th April 2019; Accepted 10th May 2019; Available online 1st Nov. 2019****<https://doi.org/10.31032/IJBPAS/2019/8.11.4861>****ABSTRACT**

Pleural effusion (PE) is defined as the abnormality that is characterized as the accumulation of fluid in the pleural space that results from collective factors i.e., excess fluid production or decreased absorption. The Light's criteria serve as a good starting point in the separation of transudates from exudates. Pleural fluid cholesterol (PFC) is a useful parameter in ruling out the differences in between pleural exudates and transudates and exudates. 100 patients aging from 30-80 years were recruited in current study. Using 5cc BD syringe venous blood was drawn by staff nurse for the examination of protein, LDH and cholesterol. Data was analyzed using SPSS version 17. Reports for PFC and for Light's criteria were assessed and EPF was labeled "positive" or "negative". A 2x2 table was generated for the calculation of sensitivity, specificity, PPV, NPV and also to find out the diagnostic accuracy of the PFC which was taking as light's criteria. Patients mean age was 55.78±13.53 years including 65% males and 35% females. Current study concludes that the determination of pleural effusion with the help of light's criteria is less expensive and more accurate method. It also signifies the importance of cholesterol as a parameter for the determination of disorder with higher specificity and sensitivity.

**Keywords: Light's criteria, Pleural Cholesterol, Exudative, Pleural Effusion,
Estimation, Accuracy**

INTRODUCTION

Pleural fluid (PF) accumulates between the two pleural layers and it would become difficult for the expansion of lungs during respiration. This excess fluid is medically examined by chest x-ray, Pleural effusion microscopy and PF also diagnosed by Gene Xpert and ZN Staining [1]. Fibrinogen plays a vital role as concentration of plasma protein and lipoprotein influenced pleural viscosity [2]. Pleural effusion is present mostly in those patients who are suffering from respiratory disease. Diagnostic attempt simplifies the plural fluid is a transudates and exudates in detecting pleural effusion. Large number of tests are available which differentiate between these two classes [3]. Valdes et al. in his study explained that 57 (22%) patients showed pleural effusion of transudate and 202 (75%) are EPF patients and light criteria serve as gold standard for the separation of transudate and exudates [4]. If a patient showing a disease which is transudative plural effusion but the light's criteria showing a marginal exudative symptom then confirmed by serum fluid protein gradient examination [5].

Pleural fluid cholesterol is a useful parameter for the differentiation b/w transudate and exudates but pathophysiologic mechanism for exudates is not clear. The sensitivity, specificity and accuracy was also reported that pleural

fluid cholesterol (>710mg/dl) were 88%, 100% and 92%. Which is also used in diagnostic of exudates as light's criteria is a gold standard and it's cleared that Plural fluid cholesterol is an effective and less expansive method for the diagnostic of EPF. Present study was designed to explain the diagnostic accuracy of plural fluid cholesterol for diagnostic of EPF in Pakistan population. Light's criteria assured to be gold standard for the diagnostic of EPF but more work is required for the evolution of light's criteria although Plural fluid Cholesterol is the only one parameter [6]. Aim of current study was to determine the diagnostic accuracy of pleural fluid cholesterol (PFC) estimation as the parameter for the determination of exudative pleural effusion (EPE) as light's criteria.

MATERIAL AND METHODS

Sample Collection

The cross sectional study was done at Department of Pathology, Quaid-e-Azam Medical College Bahawalpur from 10/8/2018 to 10/2/2019. 100 cases were selected with 95% confidence level and 7.5% margin of error and expected %age was 78% and sensitivity was 83% and 100% respectively and light's criteria is taken as gold standard for diagnosis of exudative PE.

Inclusion Criteria

30-80 years of Patient age was including with either gender have EPF (excessive accumulation of pleural fluid) in between the two layers and the accumulation was affirmed with the help of Chest X-ray.

Exclusion Criteria

In this criteria Smoking >10 pack per year or any other symptomatic chronic or acute diseases of respiratory system such as, history of chronic obstructive pulmonary disease (COPD) or history of thoracentesis (within previous 4 weeks), bleeding time (PT>20sec, aPTT>15sec), or the patients on any of the diuretics were excluded out of the current study.

Sample Collection

Hundred (n=100) patients that were according to the inclusion criteria from the Quaid-e-Azam College Bahawalpur were substituted in the following study after obtaining the informed consent. Demographic details of the population were obtained that includes their name, gender, weight and height. After obtaining such details the blood samples were obtained and were subjected for their serum extraction and samples were then stored at -80°C for their future analysis. Samples were subjected for their protein, cholesterol and LDH concentration. Experienced person following the prescribed procedures

with the help of 10cc BD syringe by thoracentesis obtained pleural samples under aseptic measures. Pathological assessment of the samples and determination of the levels of cholesterol and proteins was carried out in the hospital laboratory.

Data Analysis

SPSS version 17 was used for the analysis of data. Mean \pm was calculated. This data used for the calculation of patient age, frequency and percentage and also used for EPF. A table of 2x2 was used for the calculation of sensitivity, specificity, PPV, and NPV and also used to find out the accuracy of the PFC taking as lights Criteria as a gold standard.

RESULTS

Patients were found to have the mean age of 55.78 ± 13.53 years. Current study included about 35% of patient were females and rest 65% as males. The ratio of female to male patients was 1:1.8. The mean PFC level was 61.67 ± 11 mg/dl. 41% of the patients executed PFC <60 mg/dl and 59% of the patients had PFC >60 mg/dl. The mean SC was 157.50 ± 22.75 mg/dl. The mean PFC to SC ratio was 0.39 ± 0.08 . The mean PFC pleural fluid LDH was 195.49 ± 24.35 . The mean PF to SC ratio was 0.54 ± 0.27 .

Table 1: Descriptive Statistics Of Age (Year)

VARIABLES	(n=100)
Age (years)	55.78±13.5
Sex	
Male	65%
Female	35%

Table 2: LABORATORY INVESTIGATIONS (n=100)

PFC (mg/dl)	61.67±11.00
PFC<60mg/dl	41%
PFC≥60mg/dl	59%
SC (mg/dl)	157.50±22.75
PFC to SC ratio	0.39±0.08
Pleural fluid LDH	195.49±24.35
Pleural fluid to serum cholesterol ratio	0.54±0.27

Table: 3 Accuracy of PFC for diagnosis of EPF against Light's criteria

		EPF Lights criteria		Total
		Positive	Negative	
PFC	Positive	45	8	53
	Negative	3	44	47
Total		48	52	100

Sensitivity = 93.75%, Specificity = 84.62%, PPV = 84.91%, NPV = 93.62%, diagnostic Accuracy = 89%

DISCUSSION

In several pathological conditions the pleural effusion may occur where as many as 20% of the cases fail to execute the proper etiology. The disorder is reported to be useful in featuring the differences in between EPF and transudative [7-10]. Without consisted data there is found another biomarker that is pleural fluid cholesterol and the pleural/serum cholesterol ratio (PC/SC) to lights criteria [11-14]. Present study shows that large percentage of the population suffering from pleural effusion had PFC levels >60 mg/dl. Current study helps in stating the sensitivity of serum cholesterol to be around 93.75% with the specificity at the same time to be around 84.62%. Guleria *et al* data showed that there is a cut off value for all transudates which have

PFC level <60 All transudates had PFC levels <60 mg/dl which showed that 16% of tubular and 8% are non tubular and on the basis of this cut off value is <60mg/dl sensitivity had 88% and specificity 100% for the xudates and that showed 92% accuracy [6]. Romero *et al*, data results of pleural fluid LDH showed higher specificity 95% as compared to lights criteria and they also found that both criteria are equally important for the differentiation between exudates from transudates. Costa *et al*, also describe to same detail [15].

Kalayci *et al* demonstrated in their study that PFC, and he explained about the compared the ratio of PFC P/S and P/S microglobulin (P/S 12 m) and PF characteristic with light criteria and concerted with a threshold value of (0.3)

the sensitivity and specificity of PFC/SC which is 95% and 90% respectively for the diagnosis of exudates [16].

Pleural fluid cholesterol (PFC) levels proved useful in the diagnosis of EPF. Vascular and cellular permeability increases due to degeneration and leakage which cause elevation of PFC level in that area [17]. Its cleared from many studies that PFC increased in pleural exudates which play vital role in differentiating between exudates and transudates as potentially biomarker. It is still not clear from the studies that PFC provides an adequate power. PFC/SC ratios work a potential biomarker for the differentiating exudates to transudates. So for more reliable results we have to be meta-analyzed from literature [18].

Cholesterol is synthesized by the pleural cells by themselves, synthesizes of the cholesterol extrahepatic cells is much more than they were reported earlier. Synthesis is totally dependent upon the metabolic demand of the body. Concentration of cholesterol in the pleural cavity relatively uptakes by the degeneration of leukocytes and erythrocytes as these cells are believed to contain large cholesterol quantities. Light's criteria become gold standard because the sensitivity and specificity of this assay is 100% as light *et al.* used PF and serum level protein and LDH for the

differentiation transudates from exudates [19]. Rufino *et al* described in their study the PC levels demonstrated sensitivity of 97.22%, specificity of 85.71%, PPV of 98.59% and NPV of 75% [11]. Patel *et al.* studied showed that there is a cut off value for PFC level and that is >60mg/dl and for total protein that is 3mg/dl which is used for the differentiation between transudates and exudates [20, 21].

CONCLUSION

Current study reveals that rather than light's criteria a less expensive pleural fluid cholesterol is a beneficial parameter in differentiating pleural transudates from exudates due to its high sensitivity and specificity.

ACKNOWLEDGEMENTS

The authors are highly thankful to the IMBB, the University of Lahore and the students of IMBB LAB-313 for providing support and help to carry out the investigations.

CONFLICT OF INTEREST

Authors declare no conflict of interest.

REFERENCES

- [1] Wong CL, Holroyd-Leduc J, Straus SE. Does this patient have a pleural effusion? *J Am Med Assoc* 2009; 301(3): 309-17.
- [2] Yetkin F, Kayabas U, Ersoy Y, Bayindir Y, Toplu SA, Tek I. Cerebrospinal fluid viscosity: a novel

- diagnostic measure for acute meningitis. *South Med J* 2010; 103(9): 892-5.
- [3] Janda S, Swiston J. Diagnostic accuracy of pleural fluid NT-pro-BNP for pleural effusions of cardiac origin: a systematic review and meta-analysis. *BMC pulmonary medicine* 2010; 10(1):58.
- [4] Valdés L, San-José E, Estévez JC, González-Barcala FJ, Álvarez-Dobaño JM, Golpe A, *et al.* Cholesterol in pleural exudates depends mainly on increased capillary permeability. *Translational Research* 2010; 155(4): 178-84.
- [5] Light RW. The Light criteria: the beginning and why they are useful 40 years later. *Clinics in chest medicine* 2013; 34(1): 21-6.
- [6] Guleria R, Agarwal S, Sinha S, Pande J, Misra A. Role of pleural fluid cholesterol in differentiating transudative from exudative pleural effusion. *The National medical journal of India* 2003; 16(2): 64-9.
- [7] Storey DD, Dines DE, Coles DT. Pleural effusion: a diagnostic dilemma. *JAMA* 1976; 236(19): 2183-6.
- [8] Hirsch A, Ruffie P, Nebut M, Bignon J, Chretien J. Pleural effusion: laboratory tests in 300 cases. *Thorax* 1979;34(1):106-12.
- [9] Chandrasekhar AJ, Palatao A, Dubin A, Levine H. Pleural Fluid Lactic Acid Dehydrogenase Activity: Value in Diagnosis. *Archives of internal medicine* 1969; 123(1): 48-50.
- [10] Peterman TA, Speicher CE. Evaluating pleural effusions: a two-stage laboratory approach. *JAMA* 1984; 252(8): 1051-3.
- [11] Rufino R, Marques BL, de Lima Azambuja R, Mafort T, Pugliese JG, da Costa CH. Pleural Cholesterol to the Diagnosis of Exudative Effusion. *The open respiratory medicine journal* 2014; 8:14.
- [12] Ortega L, Heredia J, Armengol R, Mir I, Romanillas T, Armengol J. [The differential diagnosis between pleural exudates and transudates: the value of cholesterol]. *Medicina clinica* 1991; 96(10): 367-70.
- [13] Costa M, Quiroga T, Cruz E. Measurement of pleural fluid cholesterol and lactate dehydrogenase: a simple and accurate set of indicators for separating exudates from transudates. *CHEST Journal* 1995; 108(5): 1260-3.
- [14] Hooper C, Lee Y, Maskell N. on behalf of the BTS Pleural Disease Guideline Group. Investigation of a unilateral pleural effusion in adults: British Thoracic Society Pleural

- Disease Guideline 2010. Thorax 2010; 65.
- [15] Romero S, Martinez A, Hernandez L, Fernandez C, Espasa A, Candela A, et al. Light's criteria revisited: consistency and comparison with new proposed alternative criteria for separating pleural transudates from exudates. Respiration 2000; 67(1): 18-23.
- [16] Kalayci AG, Gurses N, Adam B, Albayrak D. Significance of pleural fluid cholesterol and beta-2 microglobulin levels for the differentiation of pleural effusions in childhood. Clinical pediatrics 1996; 35(7): 353-8.
- [17] Hillerdal G. Chyliform (cholesterol) pleural effusion. CHEST Journal 1985; 88(3): 426-8.
- [18] Heffner JE, Brown LK, Barbieri CA. Diagnostic value of tests that discriminate between exudative and transudative pleural effusions. CHEST Journal 1997; 111(4): 970-80.
- [19] Light RW, Macgregor MI, Luchsinger PC, Ball WC. Pleural effusions: the diagnostic separation of transudates and exudates. Annals of Internal Medicine 1972; 77(4): 507-13.
- [20] Patel AK, Choudhury S. Combined pleural fluid cholesterol and total protein in differentiation of exudates and transudates. 2013.
- [21] Hernando HV, Jimenez JM, Juncal LD, García-Buela JP, Â±a MME, Bueso JF. Meaning and diagnostic value of determining the lysozyme level of pleural fluid. CHEST Journal 1987; 91(3): 342-5.