ISSN: 2717-8161 RESEARCH ARTICLE

New Trend Med Sci 2022; 3(1): 27-35. https://dergipark.org.tr/tr/pub/ntms

The Importance of Bıochemical and Hematological Parameters in Pleural Effusion Etiology

Iclal Hocanli[1], Atalay Sahin[2]

[1]Departman of Chest Diseases, Şanlıurfa Mehmet Akif Inan Training and Research Hospital, Health Sciences University, Şanlıurfa, Turkey
[2]Department of Thoracic Surgery, Faculty of Medicine, Harran University, Sanliurfa, Turkey

Article History
Received 22 Aug 2021
Accepted 26 Sep 2021
Published Online 15 Jan 2022

****Corresponding Author***
Dr.Iıclal Hocanli
Departman of Chest Diseases,
Şanlıurfa Mehmet Akif Inan Training and Research Hospital,
Health Sciences University,
Şanlıurfa, Turkey
Phone: +90 5078528290
E-mail: iclalhocanli2163@gmail.com

Authors' ORCIDs
Iclal Hocanli
http://orcid.org/0000-0003-3283-9639
Atalay Sahin
http://orcid.org/0000-0003-0498-4935

Abstract: Pleural effusion, the pathological collection of fluid in the pleural space, is very widespread. Light's criteria are still the most commonly used initial laboratory test to determine the etiology of pleural effusion. We purposed to examine the usability of routine laboratory parameters in the differentiation of exudate-transudate. The 150 patients hospitalized in the chest diseases service due to pleural effusion etiology were retrospectively analyzed between January 2018 and December 2019. The patients were divided into two groups according to Light's criteria as exudate and transudate. The pleural fluid data, routine laboratory parameters and radiological image features compared between both groups. Significantly higher serum C-reactive protein (C-RP) values were found in patients with exudative pleural effusion, and significantly higher serum mean platelet volume (MPV) and lower serum platelet values were found in patients with transudative pleural effusion. The serum MPV was negatively correlated with serum platelet. The serum MPV, platelet and C-reactive protein values may be candidate parameters to support the Light's criteria in the differential diagnosis of transudate and exudate pleural fluid.
Keyword: Pleural Effusion; Exudate-Transudate; MPV, Platelet; C-RP.

1. Introduction

Pleural effusion, the pathological collection of fluid in the pleural space, is very widespread. The etiological distribution of pleural effusions is related to the age of the patient, the region, s/he lives in, clinic or hospital where the study was conducted and the advances in diagnostic methods (1). Its the most common causes are cancer, pneumonia and congestive heart failure. In addition, tuberculosis is a significant reason of pleural effusion in our country (2, 3).

Light's criteria are still the most commonly used initial laboratory test to determine the etiology of pleural effusion (4). Whether a pleural effusion is a transudate or an exudate determines its further evaluation and treatment. Laboratory parameters used for light criteria; LDH, total protein, and albumin. Also, when the cholesterol and LDH concentration are evaluated together, a very specific result is obtained in the presence of exudate (5, 6). However, sometimes these

Cite this article as: Hocanli I and Sahin A. The Importance of Bıochemical and Hematological Parameters in Pleural Effusion Etiology. *New Trend Med Sci* **2022**; 3(1): 27-35.

criteria may be insufficient to distinguish between exudate and transudate, and clinicians may have difficulties in approaching patients. therefore, there is a need for new parameters that are easily accessible, inexpensive and reproducible.

Biochemical and hematological blood parameters such as C-reactive protein (C-RP), albumin, platelet, neutrophil and MPV play important roles in reflecting reactions such as inflammation and immune response (7). Recently, the platelet-lymphocyte ratio (PLR), neutrophil-lymphocyte ratio (NLR), C-RP albumin ratio (CAR) obtained from routine laboratory parameters have been shown as new inflammatory biomarkers in many studies (8-10). There are many studies emphasizing that these parameters may be a diagnostic/prognostic factor in patients with pleural effusion (11-15).

In this study, we purposed to examine the usability of routine laboratory parameters and a new inflammatory biomarker obtained from these parameters in the differentiation of exudate-transudate.

2. Material and Methods

Research and Publication Ethics has been complied with at all stages, with the realization and preparation of the study.

The 150 patients hospitalized in the chest diseases service due to pleural effusion etiology were retrospectively analyzed between January 2018 and December 2019. The study protocol was approved by the Harran University Faculty of Medicine, Ethics Committee (Approval No: HRU/21.10.02 and Approval Date: 24.05.2021). Patients over 18 years of age with radiological pleural fluid, patients with pleural fluid laboratory data obtained by thoracentesis (pleural fluid protein, LDH, albumin, glucose, cell count, pH values), and patients with routine laboratory data were included in the study. Patients under 18 years of age, patients with radiological pleural fluid detected but not applied thoracentesis and/or patients without pleural fluid laboratory data were excluded from the study (thirty-six patients). As a result, a total of one hundred and fourteen patients were included in this study. Demographic and laboratory information of the patients were obtained from the recorded data. Age, gender, clinical diagnosis, pleural fluid characteristics, radiological image features (anatomical region and amount of effusion), biochemical and haematological laboratory data of all patients were recorded. According to the amount of effusion according to the PA chest X-ray; non-massive fluid if one or both costophrenic sinuses are closed; submassive fluid if the area from the diaphragm to the level of the hilum is radiopaque; the fluid above the hilus level was defined as massive fluid. Glucose, total protein, LDH and albumin levels were measured in pleural fluid taken by thoracentesis and in peripheral venous blood taken simultaneously. The patients were divided into two groups according to Light's criteria as exudate and transudate (4). The classic Light's criteria are; fluid is considered exudative if it meets one or more of the following criteria: the absolute pleural fluid lactate dehydrogenase (LDH) level is >200; the pleural: serum LDH ratio is >0.6; and/ or the pleural: serum protein ratio is >0.5. The pleural fluid data, routine laboratory parameters, radiological image features, adenosine deaminase (ADA) levels and values such as the NLR, PLR, LMR and CAR were accepted as new inflammatory biomarkers compared between both groups.

2.1. Statistical analysis

Descriptive statistics are presented as Means±Standard Deviation or medians (25-75 interquartile range). The Kolmogorov-Smirnov test was used to determine whether the data were normally distributed. The student's t-test test was used to compare normally distributed data and the Mann-Whitney U test was used for non-normally distributed data. Spearman's correlation coefficient was used for correlation analysis. To predict exudative fluid according to ADA, C-RP and platelet levels, the cut-off value was determined using receiver operating characteristic (ROC) curve analysis. To predict transudative fluid according to MPV the cut-off value was determined using receiver operating characteristic (ROC) curve analysis. The level of statistical significance was set at $p<0.05$.

3. Results

A total of 114 patients (48 women and 66 men) were included in the study. Table 1 shows the pleural fluid characters, anatomical localizations and volumes, and clinical diagnoses of the patients. There was transudate-qualified pleural fluid in 31 patients and exudate-qualified pleural fluid in 83 patients. The most common diseases in all patients were malignancy, parapneumonic effusion, congestive heart failure and tuberculous pleurisy.

It was statistically significant that the fluids were seen in the right pleural space and the fluid volume was non-massive in the exudate group. When both groups were compared in terms of cell characteristics of the pleural fluid, there was a significant lymphocyte and neutrophil dominance and low pH value in the exudate group (Table 2).

Demographic and laboratory data of the patients in both groups were compared in Table 3. There was a significant difference between the groups in gender ratio and the mean age ($p=0031$, $p<0.001$). When both groups were compared; urea, creatinine and MPV values were found to be significantly higher in patients in the transudate group, while C-RP, ADA, and platelet values were found to be statistically higher in patients in the exudate group.

Correlation between variables was demonstrated using Spearman's test. The serum MPV was negatively correlated with serum platelet (r:-0.563; p<0.001) (Table 4).

According to the roc analysis, the cut-off value of C-RP≥4.3 with a sensitivity of 55% and specificity of 70%, and the cut-off value of platelet ≥279.5 predicted exudate pleural fluid with a sensitivity of 64% and specificity of 63% (Figure 1).

According to the roc analysis, the cut-off value of MPV ≥7.0 predicted transudative pleural fluid with a sensitivity of 66% and specificity of 64% (Figure 2).

Table 1: Clinical and radiological data of patients with pleural fluid.

	Number of patients (n=114)
Fluid type	
Transudate	29
Exudate	85
Anatomical region of fluid	
Right	52
Left	26
Bilateral	36
Amount of Fluid	
Nonmassive	49
Submassive	46
Massive	19
Clinical diagnosis	
CHF	21
PPE	25
TB pleurisy	14
Malignancy	35
Empyema	10
CKF	4
PTE	5

CHF, Congestive heart failure; PPE, parapneumonic effusion; TB, tuberculosis; CKF, chronic kidney failure; PTE, pulmonary thromboembolism.

Table 2: Comparison of pleural fluid features between groups.

	Transuda (n=29)	Exuda (n=85)	P
Amount of Fluid (%)			
Nonmassive	13 (44.8)	36 (42.4)	0.069
Submassive	15 (51.7)	31 (36.5)	
Massive	1 (3.4)	18 (21.2)	
Anatomical region of fluid (%)			
Right	5 (17.2)	47 (55.3)	**<0.001**
Left	2 (6.9)	24 (28.2)	
Bilateral	22 (75.9)	14 (16.5)	
Pleural fluid lymphocyte, $\times 10^3$/mL	0.01 (0.0-0.23)	0.07 (0.03-0.22)	**0.007**
Pleural fluid neutrophil, $\times 10^3$/mL	0.0 (0.0-0.05)	0.02 (0.01-0.13)	**0.032**
Pleural fluid monocyte, $\times 10^3$/mL	0.0 (0.0-0.04)	0.0 (0.0-0.05)	0.188
Pleural fluid pH	7.43 ± 0.06	7.35 ± 0.17	**0.004**
ADA levels, U/L	12.2 (7.3-35.7)	38.6 (24.6-58.0)	**0.004**
Clinicals diagnosis			
CHF	21	0	
PPE	0	25	
TB pleurisy	0	14	**<0.001**
Malignancy	0	35	
Empyema	0	10	
CKF	4	0	
PTE	4	1	

ADA, adenosine deaminase; CHF, Congestive heart failure; PPE, parapneumonic effusion; TB, tuberculosis; CKF, chronic kidney failure; PTE, pulmonary thromboembolism.

Table 3: Comparison of demografic and laboratory data between groups.

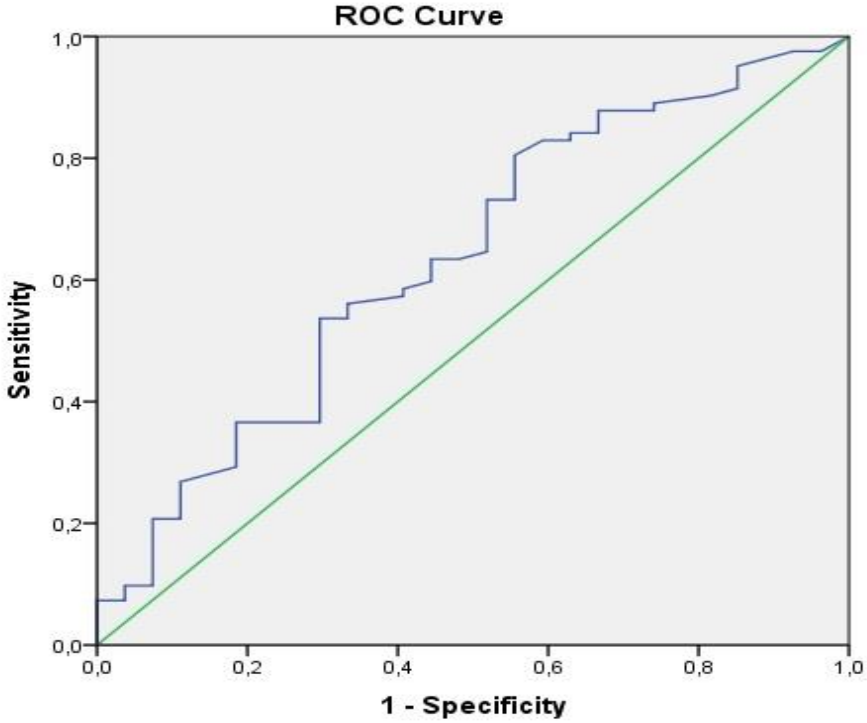
	Transuda (n=29)	Exuda (n=85)	P
Age, years	70.0 (57.5-79.5)	51.0 (32.0-69.0)	**<0.001**
Gender, f/m	8/21	40/45	0.067
Glucose, mg/dl	121.0 (95.0-169.5)	109.0 (91.0-138.5)	0.172
Urea, mg/dl	59.0 (42.8-107.0)	28.5 (20.0-40.2)	**<0.001**
Creatinine, mg/dl	1.2 (0.7-1.8)	0.7 (0.6-0.8)	**<0.001**
AST, U/L	20.0 (12.0-35.0)	20.0 (13.2-27.7)	0.493
ALT, U/L	19.0 (14.0-41.0)	21.0 (12.0-30.7)	0.677
T.Bilirubin, mg/dl	0.7 (0.4-0.9)	0.5 (0.3-0.7)	0.094
Albümin, g/dl	2.7 ± 0.8	3.2 ± 0.5	0.059
Sodium, meq/l	137.8 ± 3.8	136.7 ± 3.7	0.756
Potassium, meq/l	4.4 ± 0.8	4.2 ± 0.5	0.089
CRP, mg/dL	3.0 (0.6-8.6)	5.2 (1.6-12.3)	**0.036**
WBC count, $\times 10^3$/mL	8.0 (7.1-12.5)	10.3 (7.8-13.2)	0.166
Lymphocytes, $\times 10^3$/mL	1.5 (0.8-2.3)	1.6 (0.9-2.4)	0.851
Neutrophils, $\times 10^3$/mL	6.1 (4.6-10.0)	7.2 (5.1-10.3)	0.325
Monocytes, $\times 10^3$/mL	0.7 (0.4-0.8)	0.7 (0.5-1.1)	0.141
Eosinophils, $\times 10^3$/mL	0.0 (0.0-0.2)	0.1 (0.0-0.3)	0.060
Hemoglobin, g/dL	10.9 ± 2.6	11.9 ± 2.3	0.206
Hemotocrit, %	35.1 ± 7.9	38.4 ± 7.2	0.189
MPV, fL	7.6 (6.6-8.2)	6.6 (5.8-7.4)	**0.005**
MCV, fL	86.8 ± 8.6	84.2 ± 7.9	0.977
Platelet count, $\times 10^3$/mL	227.0 (177.5 -346.0)	334.0 (235.7-444.7)	**0.009**
RDW, %	14.0 ± 2.1	13.6 ± 2.6	0.210
ERS, h	29.5 (4.5-72.0)	50.0 (20.5-64.5)	0.220
NLR	4.9 (2.9-8.5)	4.5 (2.5-9.6)	0.981
LMR	2.0 (1.2-3.5)	2.1 (1.1-3.5)	0.975
PLR	160.0 (114.3-269.2)	211.6 (133.9-314.7)	0.085
CAR	1.3 (0.2-3.3)	1.6 (0.5-4.0)	0.228

AST, aspartate transaminase; ALT, alanine transaminase; CRP, C-reactiveprotein; WBC, white blood cell; MPV, mean platelet volume; MCV, mean corpuscular volume; RDW, red cell distribution width; ESR, erythrocyte sedimentation rate; NLR, neutrophil-lymphocyte ratio; LMR, lymphocyte-monocyte ratio; PLR, platelet-lymphocyte ratio; CAR, C-reactive protein to albumin ratio.

Table 4: Spearsman Correlation of Variables.

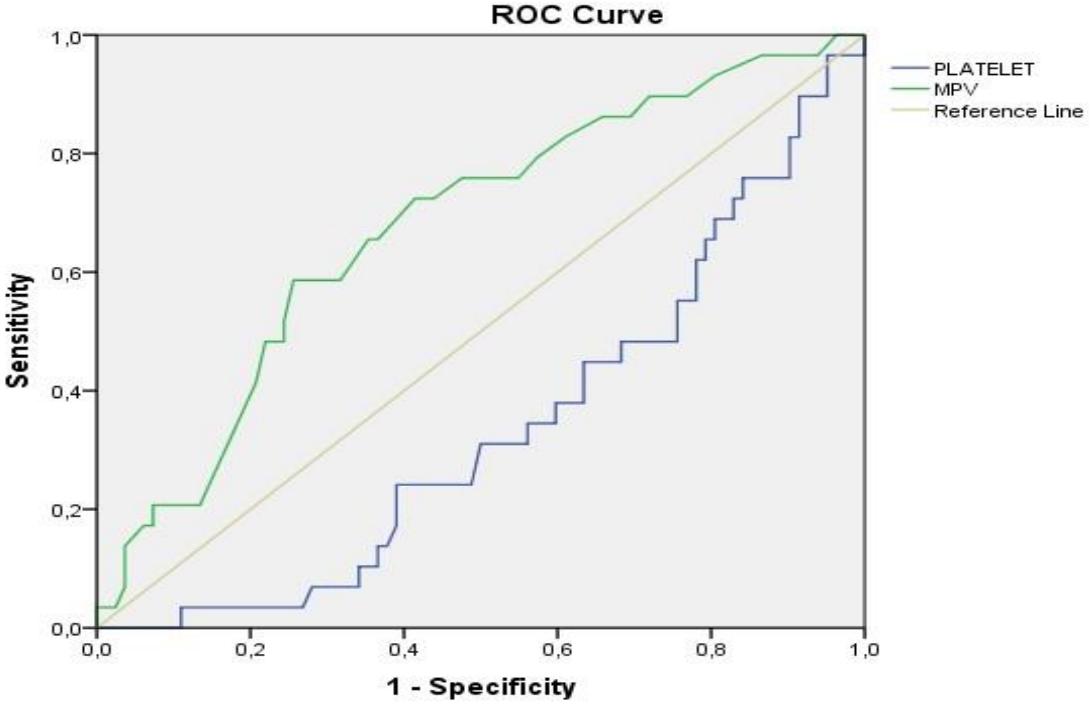
Variables	**Mean**	**SD**	**1**	**2**	**3**
1. MPV, fL	7.0	1.4	—	- 0.563**	- 0. 043*
2. Platelet,$\times 10^3$/mL	324.2	150.4		—	0.069*
3. C-RP, mg/dL	7.3	8.0			—

*p>0.05, **p<0,001.



Variables	AUC	95%Cl	P
C-rp	0.635	0.512-0.757	0.036

Figure 1: Receiver operating characteristics (ROC) curve of C-rp for predicting the exudate fluid.



Variables	AUC	95%Cl	P
MPV	0.676	0.564-0.788	0.005
Platelet	0.337	0.229-0.445	0.009

Figure 2: Receiver operating characteristics (ROC) curve of MPV and platelet for predicting the transudative fluid.

4. Discussion

In this study, we found significantly higher serum C-RP values in patients with exudative pleural effusions, while we found significantly higher serum MPV and lower serum platelet values in patients with transudative pleural effusions.

Pleural effusion is a common pathological condition that may occur due to many different underlying diseases. The first step in determining the cause of an effusion is to differentiate the fluid from transudate to exudate. In many clinical studies performed, it has been observed that pleural effusions with exudate characteristics are caused by malignancy, parapneumonic effusion and tuberculosis, respectively, while pleural effusions with transudate characteristics are mostly caused by CHF (16-19). Our study was consistent with the literature data. The most transudate fluid was found in CHF, and the exudate fluid was most intense in malignancy, PPE, and tuberculosis. Pleural fluid cell analysis and pH value can also help detect fluid character. Neutrophil (parapneumonic effusion and empyema) and lymphocyte cell dominance (tuberculosis and malignancy) are more common in exudate-characterized pleural fluids (5, 20). In transudative effusions, the pH is usually alkalosis (21). pH<7.2 is one of the typical findings for complicated parapneumonic effusion with exudate character (22). In our study, there was significant neutrophil and lymphocyte cell dominance in exudate-qualified pleural effusions and transudate-qualified fluid pH was significantly prone to alkalosis.

Adenosine deaminase (ADA) is a hydrolytic enzyme that plays an important role in purine metabolism. Many studies are showing that pleural fluid ADA (p-ADA) is especially associated with tuberculous (TB) pleurisy. (23, 24). The pleural ADA cut-off value >40 is widely accepted for the diagnosis of TB pleurisy (25). However, in different studies, it has been stated that p-ADA can be a biomarker that can be used to differentiate pleural transudates from exudates (26, 27). In our study, p-ADA levels were found to be significantly higher in the exudate pleural fluid group. this is because inflammatory diseases with lymphocyte dominance are included in this group (TB, empyema cancer, etc).

Separation of exudate and transudate in pleural effusion is very important in patient management. Sometimes the Light criteria may not be sufficient for this distinction. Therefore, there is a need to evaluate other biochemical and haematological parameters. It has been shown that in inflammatory status, IL-6, IL-1, and TNF-α can stimulate precursor cells of blood platelets (28). Therefore, blood platelets are the first cells to accumulate at the site of injury in inflammatory conditions. Mean platelet volume (MPV), which is easily calculated by haematological analyzers, is one of the routine blood parameters. During inflammation, there is an inverse relationship between platelets and MPV values. While platelets undergo activation and ageing at the site of inflammation, mean platelet volume (MPV) decreases in patients with ongoing inflammation (29). This means that increased platelet production is accompanied by a decrease in the mean platelet volume. When we searched the literature, there were very few studies investigating the relationship between MPV and platelet in patients with pleural effusion. In a study conducted with transudative-qualified pleural effusion patients, it was emphasized that high MPV and low platelet might be poor prognostic criteria (30). Hyperreactivity of blood platelets has been shown to markedly increase patients' susceptibility to acute cardiovascular events (31, 32). Ohuchi et al. stated that increased platelet count and decreased MPV values are prognostic factors in exudate-qualified malignant pleural effusion patients (15). As we know, MPV and platelet values were compared for the first time in our study between transudate and exudate qualified pleural effusion patients. Patients with transudative effusion had significantly higher MPV and low platelet values and there was a negative correlation between MPV and platelet the according to Spearman's test. This may be explained by the presence of cardiovascular and low-grade inflammatory diseases in this group. Therefore high MPV and low platelet count can be laboratory parameters that can be used in the separation of transudate and exudate.

CRP is a biomarker of inflammation and infection. It is synthesized in hepatocytes after stimulation by different cytokines and released into the blood in response to the inflammation (33). Many studies are showing that CRP can be used as prognostic and diagnostic in patients with malignant and parapneumonic pleural effusion (34-36). In two different studies, it has been suggested that pleural fluid HsCRP values and CRP values are parameters that can be used in the separation of transudate and exudate (37, 38). In our study, there was a significant difference between the two groups in terms of serum CRP value. Therefore, serum CRP value can be a non-invasive, inexpensive and easily accessible parameter that can be used to differentiate between transuda and exudate.

In recent studies, new inflammatory biomarkers such as NLR, LMR, PLR, and CAR have been found that can be easily calculated from routine parameters. These biomarkers have been observed to have diagnostic and prognostic values in many pathologic states (39-41). In a study, it was shown that the pleural fluid neutrophil-lymphocyte ratio is an inexpensive and easily calculated haematological parameter that can be used in the differential diagnosis of pleural effusion (42). Studies are showing that NLR and PLR can predict survival in malignant effusions (43, 44). In our study,

NLR, PLR, LMR and CAR biomarkers were compared for the first time in the differentiation of transudate exudate, but no significant results were obtained. This may be due to the small number of our patients.

5. Conclusions

As a result, we found high serum MPV and low serum platelet levels significant for transudate pleural fluids, and high serum C-reative protein levels for exudate pleural fluids. In the differential diagnosis of transudate and exudate pleural fluid serum MPV, platelet and C-reactive protein values may be candidate parameters to support the Light's criteria. We think that our study may lead to studies being conducted in larger populations.

Limitations of the Study

There are some limitations of our study. It can be listed as being a single-centre-retrospective study and inclusion of fewer patients in the study due to insufficient registered laboratory data.

Acknowledgement

None.

Conflict of Interests

The all authors have no conflicts of interest to declare.

Financial Support

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author Contributions

Concept- Hocanli I.; Design- Hocanli I.; Supervision- Hocanli I., Sahin A.; Data Collection and/or Processing- Hocanli I.; Analysis and/or Interpretation - Hocanli I.; Literature Search- Hocanli I., Sahin A.; Writing Manuscript- Hocanli I.; Critical Review- Hocanli I., Sahin A.

Ethical Approval

The study protocol was approved by the Harran University Faculty of Medicine, Ethics Committee (Approval No: HRU/21.10.02 and Approval Date: 24.05.2021).

Data sharing statement

Data and mareials are available upon request. Hyperlink: 'mail to: iclalhocanli@2163mail.com

Consent to participate

Consent for the study was obtained from all participants for the study.

Informed Consent

Informed consent form was obtained from all participants for the study.

References

1. Valdés L, Alvarez D, Valle JM, Pose A, San José E. The etiology of pleural effusions in an area with high incidence of tuberculosis. *Chest* **1996**; 109: 158-162.
2. Unlu M, Sahin U, Akkaya A, Dogan A. Investigation of the etiology of pleural effusions. *Respir Dis* **2001**; 12: 212-215.
3. Ozkara S, Fırat S, Dinc M, et al. The incidence and etiology of massive pleural effusions. *Breathing* **1996**; 12: 423-428.
4. Light RW, Macgregor MI, Luchsinger PC, Ball WC Jr. Pleural effusions: the diagnostic separation of transudates and exudates. *Ann Intern Med* **1972**; 77: 507-513.
5. Jany B, Welte T. Pleural Effusion in Adults-Etiology, Diagnosis, and Treatment. *Dtsch Arztebl Int* **2019**; 116: 377-386.
6. Yilmaz A, Tunaboyu IK, Akkaya E, Bayramgürler B. A comparative analysis of the biochemical parameters used to distinguish between pleural exudates and transudates. *Respir* **2000**; 5: 363-367.
7. Henriot I, Launay E, Boubaya M, et al. New parameters on the hematology analyzer XN-10 (SysmexTM) allow to distinguish childhood bacterial and viral infections. *Int J Lab Hematol* **2017**; 39: 14-20.
8. Seringec Akkececi N, Yildirim Cetin G, Gogebakan H, Acipayam C. The C-Reactive Protein/Albumin Ratio and Complete Blood Count Parameters as Indicators of Disease Activity in Patients with Takayasu Arteritis. *Med Sci Monit* **2019**; 25: 1401-1409.
9. Kalyan S, Goshtesabi A, Sarray S, Joannou A, Almawi WY. Assessing C reactive protein/albumin ratio as a new biomarker for polycystic ovary syndrome: a case-control study of women from Bahraini medical clinics. *BMJ Open* **2018**; 8: e021860.
10. Ventura JC, Hauschild DB, Moreira EAM, et al. C-reactive protein/albumin ratio is associated with lung function among children/adolescents with cystic fibrosis: a three-year longitudinal study. *Sao Paulo Med J* **2018**;136:29-36.
11. Castaño Vidriales JL, Amores Antequera C. Use of pleural fluid C-reactive protein in laboratory diagnosis of pleural effusions. *Eur J Med* **1992**; 1: 201-207.
12. Zou MX, Zhou RR, Wu WJ, Zhang NJ, Liu WE, Fan XG. The use of pleural fluid procalcitonin and C-reactive protein in the diagnosis of parapneumonic pleural effusions: a systemic review and meta-analysis. *Am J Emerg Med* **2012**; 30: 1907-1914.
13. Garcia-Pachon E, Soler-Sempere MJ, Zamora-Molina L, Baeza-Martinez C, Grau-Delgado J, Padilla-Navas I. Platelet-to-Lymphocyte Ratio and Survival in Malignant Pleural Effusion. *Clin Lab* **2020**; 1: 66(8).
14. Li D, Shen Y, Qin J, et al. Diagnostic performance of C-reactive protein for parapneumonic pleural effusion: a meta-analysis. *Ann Transl Med* **2019**; 7: 1.
15. Ohuchi M, Inoue S, Ozaki Y, Ueda K. Platelet count and mean platelet volume are associated with not only bone, soft tissue, and lymph node metastases but also with malignant pleural effusion

in lung cancer patients. *Neoplasma* **2017**; 64: 140-147.

16. Hamm H, Brohan U, Bohmer R, Missmahl HP. Cholesterol in pleural effusions. A diagnostic aid. *Chest* **1987**; 92: 296-302.

17. Marel M, Stastny B, Melínová L, Svandová E, Light RW. Diagnosis of pleural effusions. Experience with clinical studies, 1986 to 1990. *Chest* **1995**; 107: 1598-1603.

18. Romero-Candeira S, Hernández L, Romero-Brufao S, Orts D, Fernández C, Martín C. Is it meaningful to use biochemical parameters to discriminate between transudative and exudative pleural effusions? *Chest* **2002**; 122: 1524-1529.

19. Bayrak MG, Erkan L, Uzun O, Hazelnut S, Atici AG, Ozkaya S. Evaluation of 153 patients with pleural effusion. *Respir Dis* **2006**: 17; 66-72.

20. Hooper C, Lee YCG, Maskell N: Investigation of a unilateral pleural effusion in adults: British Thoracic Society pleural disease guideline 2010. *Thorax* **2010**; 65 (Suppl 2): ii4–17.

21. Light RW, MacGregor MI, Ball WC Jr, Luchsinger PC. Diagnostic significance of pleural fluid pH and PCO2. *Chest* **1973**; 64: 591-596.

22. Heffner JE, Brown LK, Barbieri C, DeLeo JM. Pleural fluid chemical analysis in parapneumonic effusions. A meta-analysis. *Am J Respir Crit Care Med* **1995**; 151: 1700-1708.

23. Liang QL, Shi HZ, Wang K, Qin SM, Qin XJ. Diagnostic accuracy of adenosine deaminase in tuberculous pleurisy: a meta-analysis. *Respir Med* **2008**; 102: 744-754.

24. Reechaipichitkul W, Kawamatawong T, Teerajetgul Y, Patjanasoontorn B. Diagnostic role of pleural fluid adenosine deaminase in tuberculous pleural effusion. *South Asian J Trop Med Public Health* **2001**; 32: 383-389.

25. Porcel JM. Tuberculous pleural effusion. *Lung* **2009**; 187: 263-270.

26. Maranhão BHF, da Silva Junior CT, Barillo JL, et al. Diagnostic Accuracy with Total Adenosine Deaminase as a Biomarker for Discriminating Pleural Transudates and Exudates in a Population-Based Cohort Study. *Dis Markers* **2021**; 2021: 6648535.

27. Atalay F, Ernam D, Hasanoglu HC, Karalezli A, Kaplan O. Pleural adenosine deaminase in the separation of transudative and exudative pleural effusions. *Clin Biochem* **2005**; 38: 1066-1070.

28. Linke B, Schreiber Y, Picard-Willems B, et al. Activated Platelets Induce an Anti-Inflammatory Response of Monocytes/Macrophages through Cross-Regulation of PGE_2 and Cytokines. *Mediators Inflamm* **2017**; 2017: 1463216.

29. Afsar N, AfrozeI A, Tahniath H, Abid Z. Role of mean platelet volume as an adjunct in evaluation of acute inflammation. *Annals Pathol Lab Med* **2017**; 4: 466-469.

30. Garcia-Pachon E, Soler-Sempere MJ, Cerda-Guilabert P, et al. Prognostic Value of Hematological Inflammatory Markers in Patients with Pleural Effusion Due to Heart Failure. *Clin Lab* **2020**; 1: 66(3).

31. Endler G, Klimesch A, Sunder-Plassmann H, et al. Mean platelet volume is an independent risk factor for myocardial infarction but not for coronary artery disease. *Br J Haematol* **2002**; 117: 399-404.

32. Araz O, Albez FS, Ucar EY, Kerget B, Yılmaz N, Akgun M. Predictive Value of Mean Platelet Volume for Pulmonary Embolism Recurrence. *Lung* **2017**; 195: 497-502.

33. Späth C, Srinivasa S, Walsh M, Singh P, Rodgers M, Koea J. Role of post-operative serum C-reactive protein levels as a predictor of complications in upper gastrointestinal surgery. *ANZ J Surg* **2019**; 89: 74–78.

34. Park DS, Kim D, Hwang KE, et al. Diagnostic value and prognostic significance of pleural C-reactive protein in lung cancer patients with malignant pleural effusions. *Yonsei Med J* **2013**; 54: 396-402.

35. Li D, Shen Y, Qin J, et al. Diagnostic performance of C-reactive protein for parapneumonic pleural effusion: a meta-analysis. *Ann Transl Med* **2019**; 7: 1.

36. Kogan Y, Sabo E, Odeh M. Diagnostic Value of C-Reactive Protein in Discrimination between Uncomplicated and Complicated Parapneumonic Effusion. *Diagnostics (Basel)* **2020**; 10: 829.

37. Rezaeetalab F, Parizadeh SM, Esmaeely H, Akbari H, Akbari F, Saberi S. Tumor necrosis factor alpha and high sensitivity C-reactive protein in diagnosis of exudative pleural effusion. *J Res Med Sci* **2011**; 16: 1405-1409.

38. Izhakian S, Wasser WG, Fox BD, Vainshelboim B, Kramer MR. The Diagnostic Value of the Pleural Fluid C-Reactive Protein in Parapneumonic Effusions. Dis Markers 2016;2016:7539780.

39. Balcioglu YH, Kirlioglu SS. C-Reactive Protein/Albumin and Neutrophil/Albumin Ratios as Novel Inflammatory Markers in Patients with Schizophrenia. *Psychiatry Investig* **2020**; 17: 902-910.

40. Kalyoncuoglu M, Durmus G. Relationship between C-reactive protein-to-albumin ratio and the extent of coronary artery disease in patients with non-ST-elevated myocardial infarction. *Coron Artery Dis* **2020**; 31: 130-136.

41. Shen Y, Wang H, Li W, Chen J. Prognostic significance of the CRP/Alb and neutrophil to lymphocyte ratios in hepatocellular carcinoma patients undergoing TACE and RFA. *J Clin Lab Anal* **2019**; 33: e22999.

42. Akturk UA, Ernam D, Akbay MO, Koçak ND, Ogur E, Irmak I. Role of theNeutrophil-LymphocyteRatio in the Differential Diagnosis of

Exudative Pleural Effusion. *Clinics (Sao Paulo)* **2016**; 71: 611-616.

43. Popowicz N, Cheah HM, Gregory C, et al. Neutrophil-to-lymphocyteratio in malignantpleuralfluid: Prognosticsignificance. *PLoSOne* **2021**; 16: e0250628.

44. Garcia-Pachon E, Soler-Sempere MJ, Zamora-Molina L, Baeza-Martinez C, Grau-Delgado J, Padilla-Navas I. Platelet-to-LymphocyteRatioandSurvival in Malignant Pleural Effusion. *Clin Lab* **2020**; 66(8).

https://dergipark.org.tr/tr/pub/ntms