Research Article / Araştırma Makalesi

Pleural Fluid Gas Analysis in Diagnosing and Differentiating Pulmonary Diseases

Plevral Sıvı Gaz Analizinin Pulmoner Hastalıkların Tanısında ve Ayırımında Kullanımı

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Abstract

Background: This study aimed to evaluate pleural fluid gas parameters in patients with different underlying pulmonary diseases to assess their diagnostic implications.
Materials and Methods: This study conducted at Akdeniz University Pulmonology Department and Harran University Pulmonology Department. The retrospective study included 118 patients with pleural effusion confirmed via imaging between January 2018 and December 2024. Pleural fluid samples collected by thoracentesis underwent gas analysis (pO_2, pCO_2, pH, HCO_3) and standard biochemical and cytological evaluations. Comparative analysis of gas characteristics was performed across diagnostic categories with a significance threshold of $p < 0.05$.
Results: In this study, 87 of 118 patients underwent arterial blood gas analysis, with a mean age of 66.4±14.2 years and 72.4% being male. Acidic, normal, and alkaline pleural fluid pH values were observed in 25.3%, 26.4%, and 48.3% of patients, respectively. Most effusions were exudative (83.9%), and unilateral (81.6%), with malignancy (29.9%), pneumonia (35.6%), and heart failure (16.1%) being the leading causes. Among pneumonia cases, 45.1% had complicated effusions or empyema. Transudative effusions were associated with older age, higher pH, and lower LDH, pCO_2, and protein levels ($p<0.05$). Compared to other causes, pneumonia-related effusions were more likely to be exudative, occur in males, and have higher protein levels. Malignant effusions showed significantly higher HCO_3 and protein levels ($p<0.05$).
Conclusions: Pleural fluid gas analysis may offer valuable diagnostic insights, particularly in differentiating infectious from non-infectious effusions.

Keywords: Pleural Fluid Analysis, Pneumonia, Pulmonary Diseases

Öz

Amaç: Bu çalışma, farklı altta yatan pulmoner hastalıkları olan hastalarda plevral sıvı gaz parametrelerini değerlendirerek tanısal etkilerini incelemeyi amaçlamaktadır.
Materyal ve Metod: Akdeniz Üniversitesi ve Harran Üniversitesi Göğüs Hastalıkları Bölümü'nde gerçekleştirilen bu retrospektif çalışma, Ocak 2018 ile Aralık 2022 arasında görüntüleme ile doğrulanmış plevral efüzyonu olan 118 hastayı içermektedir. Torasentez ile toplanan plevral sıvı örneklerine gaz analizi (pO_2, pCO_2, pH, HCO_3) ve standart biyokimyasal ve sitolojik değerlendirmeler yapıldı. Gaz özellikleri, tanı kategorileri arasında karşılaştırmalı olarak analiz edildi ve anlamlılık eşiği $p < 0,05$ olarak belirlendi.
Bulgular: Bu çalışmada, 118 hastanın 87'sine arteriyel kan gazı analizi uygulandı; hastaların ortalama yaşı 66,4±14,2 yıl olup, %72,4'ü erkekti. Plevral sıvı pH değeri hastaların %25,3'ünde asidik, %26,4'ünde normal ve %48,3'ünde alkalen olarak saptandı. Plevral sıvıların büyük çoğunluğu (%83,9) eksüdatif ve %81,6'sı unilateraldi. En sık nedenler malignite (%29,9), pnömoni (%35,6) ve kalp yetmezliği (%16,1) olarak belirlendi. Pnömoni tanısı alan olguların %45,1'inde komplike efüzyon veya ampiyem vardı. Transüdatif efüzyonlar daha ileri yaş, daha yüksek pH ve daha düşük LDH, pCO_2 ve protein düzeyleri ile ilişkiliydi ($p<0,05$). Pnömoniye bağlı efüzyonlar, diğer nedenlere kıyasla daha çok erkeklerde görülmekte, daha yüksek protein düzeylerine sahip olmakta ve daha sık eksüdatif özellik göstermekteydi. Malignite grubunda ise HCO_3 ve total protein düzeyleri anlamlı olarak daha yüksekti ($p<0,05$).
Sonuç: Plevral sıvı gaz analizi, özellikle enfeksiyöz ve enfeksiyöz olmayan efüzyonları ayırt etmede yararlı tanısal bilgiler sunabilir.

Anahtar Kelimeler: Plevral efüzyon, Pnömoni, Pulmoner hastalıklar

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Introduction

Pleural effusion is a common manifestation in various pulmonary diseases, including pneumonia, empyema, tuberculosis, malignancy, and heart failure (1–7) . The evaluation of pleural fluid characteristics is crucial for diagnosing the underlying cause of the effusion. Traditionally, pleural fluid analysis includes the assessment of its physical, chemical, and cytological properties (4,5,7–9). However, the analysis of pleural fluid gas characteristics, such as oxygen (pO2) and carbon dioxide (pCO2) levels, has not been extensively explored. A few studies have thoroughly investigated pH as a characteristic of pleural fluid gas (10–12). Pleural fluid pH is a crucial diagnostic marker, particularly in distinguishing complicated parapneumonic effusion, where pH is typically below 7.0 (10,13). It also serves to differentiate between malignant and tuberculous effusions; a pH below 7.30 strongly suggests tuberculosis, while a value above 7.30 favors malignancy. The biochemical profile of pleural fluid—including pH, pCO_2, pO_2, HCO_3^-, and glucose—varies depending on the total white blood cell (WBC) count and the integrity of the pleura (10). Because blood gas analyzers are widely available in clinical settings, pH and gas measurements can offer rapid, cost-effective diagnostic support compared to culture-based methods (14). An animal study reported that peritoneal fluid pH, PCO2, and PO2 levels could distinguish bacterial infections from other etiologies (15).

The potential diagnostic value of pleural fluid gas analysis lies in its ability to provide insights into the metabolic and respiratory status of the pleural space. Alterations in pleural fluid gas tensions could reflect local pathophysiological processes, such as increased metabolic activity of pleural cells, impaired gas diffusion, or abnormal vascular permeability (8,16–18). This study aims to investigate the pleural fluid gas characteristics in patients with different pulmonary diseases and to evaluate their diagnostic implications.

Materials and Methods

Study Design and Population

This retrospective study was conducted at Akdeniz Universtiy Pulmonology Department and Harran Universtiy Pulmonology Department between Jan 1, 2018 and December 31, 2024. The study included patients presenting with pleural effusion, confirmed by chest X-ray or ultrasound, who underwent thoracentesis for diagnostic purposes. Patients with a history of recent thoracic surgery, chest trauma, or known pleural disease were excluded.

Sample Collection

Pleural fluid samples were obtained via thoracentesis under sterile conditions. Each patient provided informed consent prior to the procedure. Approximately 50-100 mL of pleural fluid was collected in heparinized syringes to prevent clotting. Samples were immediately transported to the laboratory for analysis. There was no need for ice as they are measured immediately.

Pleural Fluid Gas Analysis

Pleural fluid gas analysis was performed using a blood gas analyzer. The following parameters were measured: Partial pressure of oxygen (pO2), Partial pressure of carbon dioxide (pCO2), pH, Bicarbonate (HCO3-).

In addition to gas analysis, pleural fluid was subjected to standard biochemical and cytological analysis, including: Total protein, Lactate dehydrogenase (LDH), Glucose, Cell count and differential, Gram stain and culture, cytological examination.

The cause of pleural effusion was primarily determined based on pathological examination, culture growth, and/or clinical-radiological-biochemical assessments, if available.

Pneumonia was defined as the presence of cough, sputum production, fever (>38°C), elevated acute-phase reactants (e.g., C-reactive protein or procalcitonin), and radiographic evidence of pulmonary infiltration on chest imaging (X-ray or computed tomography).

Complicated Pleural Effusion and Empyema Classification

Pleural fluid samples were further evaluated for the presence of complicated parapneumonic effusion or empyema. Empyema was defined as pleural fluid with purulent appearance or positive Gram stain/culture. Complicated parapneumonic effusion was identified based on low pleural fluid pH (<7.20), low glucose (<40 mg/dL), or loculated effusion on imaging. These definitions were used to categorize the pneumonia-related effusions.

Data Analysis

Descriptive statistics were used to summarize the demographic and clinical characteristics of the study population. The pleural fluid gas parameters were compared across different diagnostic categories using appropriate statistical tests (e.g., indepent t-test, chi-square test). In the chi-square analysis, due to the insufficient number of cases for each cause of pleural effusion, the other groups were combined and compared with the pneumonia group. Similarly, the malignancy group was compared with the combined of other groups. Statistical significance was set at $p < 0.05$

Results

In this study, a total of 118 patients were evaluated. Of these patients, 87 underwent arterial blood gas analysis. The average age of the patients was 66.4 years, with a standard deviation of 14.2 years. Among these 87 patients, 24 were female (27.6%) and 63 were male (72.4%). Pleural fluid analysis showed that 22 patients (25.3%) had acidic pleural fluid, 42 patients (48.3%) had alkaline pleural fluid, and 23 patients (26.4%) had pleural fluid within the normal range. In the medical histories, 27 patients (31%) had a history of malignancy, 35 patients (40.2%) had hypertension, 17 patients (19.5%) had heart failure, and 18 patients (20.7%) had diabetes mellitus.

Pathological examination of the pleural fluid revealed malignancy in 5 (5.7%) patients, and pleural fluid cultures showed bacterial growth in 7 (8.0%) patients. Regarding the nature of

the pleural fluid, 14 (16.1%) patients had transudative pleural fluid, while 73 (83.9%) had exudative pleural fluid. Chest X-rays indicated unilateral pleural effusion in 71 (81.6%) patients and bilateral pleural effusion in 16 (18.4%) patients. Additionally, 54 (62.1%) patients had a history of smoking.
Based on further investigations, the pleural effusion was attributed to malignancy in 26 patients (29.9%), heart failure in 14 patients (16.1%), pneumonia in 31 patients (35.6%), and the cause remained undetermined in 16 patients (18.4%). Among the 31 patients diagnosed with pneumonia, 8 patients (25.8%) were classified as having empyema, and 6 patients (19.3%) had complicated parapneumonic effusions without frank empyema. Thus, a total of 14 patients (45.1%) with pneumonia had either complicated effusions or empyema. The remaining 17 patients (54.9%) had uncomplicated parapneumonic effusions. The basic characteristics of the patients are provided in Table 1.

Table 1. The basic characteristics of the patients

	Features	n	%
Sex	Male	63	72.4
pH	Asidic	22	25.3
	Alkalic	42	48.3
	Normal	23	26.4
Light	Transudative	14	16.1
	Exudative	73	83.9
Smoking	Current/exsmoker	54	62.1
	Nonsmoker	23	26.4
	Unknown	10	11.5
X-ray	Unilateral	71	81.6
	Bilateral	16	18.4
Culture growths	Positivity	7	8.0
Pathologic examintaion	Diagnostic	5	5.7
Pleural fluid etiology	Malignancy	26	29.9
	Heart failure	14	16.1
	Pneumonia	31	35.6
	Unknown	16	18.4
		Mean	sd
Age	years	66.4	14.2
Pleural fluid	pH	7.39	0.19
	pCO2 (mmHg)	42.5	16.3
	pO2 (mmHg)	119.7	31.4
	hCO3 (mmol/L)	25.1	5.8
	Total protein (g/L)	30.9	16.4
	LDH (U/L)	562.8	1005.3
	Albumin (g/L)	35.4	9.3
	White blood cell (thousand/mm3)	2.1	1.4

When comparing transudative and exudative fluids, it was found that patients with transudative effusion were older (73.8 vs 67.2, p=0.035) and had higher pH (7.48 vs 7.38, p=0.001), and lower LDH levels (142 vs 640, p=0.001), pCO2 levels (36.5 vs 43.7, p=0.009) and total protein levels (28.0 vs 31.5, p=0.039) (Table 2).

Table 2. Comparison of transudative and exudative fluids

	Transudative (n=14)	Exudative (n=73)	p
Age, yr (mean±sd)	73.8±7.9	67.2±11.7	0.035
pH (mean±sd)	7.48±0.1	7.38±0.2	0.001
pCO2, mmHg (mean±sd)	36.5±6.3	43.7±17.4	0.009
pO2, mmHg (mean±sd)	123.0±31.9	119.1±31.5	0.670
hCO3, (mmol/L) (mean±sd)	27.4±6.5	26.1±5.9	0.137
LDH ,(U/L) (mean±sd)	142.3±68.7	640.9±1077.4	0.001
Total protein (g/L) (mean±sd)	28.0±11.3	31.5±17.4	0.045
Albumin, (g/L) (mean±sd)	18.7±5.6	22.7±6.6	0.039
White blood cell (mean±sd)	1.6±1.1	1.3±1.1	0.573
Male n(%)	10 (71.4)	53 (72.6)	0.580
Alkalic n(%)	9 (64.3)	33 (45.2)	0.214
Malignancy n(%)	5 (35.7)	22 (30.1)	0.450
Hypertension n(%)	7 (50.0)	28 (38.4)	0.300
Diabetes mellitus n(%)	5 (35.7)	13 (17.8)	0.126
Heart failure n(%)	8 (57.1)	9 (12.3)	0.001
Unilateral fluid n(%)	12 (85.7)	59 (80.8)	0.500
Current/exsmoker n(%)	10 (71.4)	44 (60.3)	0.152

Compared to patients with other conditions (e.g., heart failure, malignancy), those diagnosed with pneumonia had higher pleural fluid protein levels (p=0.032), a higher proportion of males (p=0.013), and a greater likelihood of exudative effusion (p<0.001) (Table 3). When comparing malignancy to other causes, the HCO_3 level (p=0.001) and total protein level (p=0.036) were higher in the malignancy group (Table 4).

Table 3. Comparison of pleural fluid properties according to etiology (pneumonia vs others)

	Pneumonia (n=31)	Others (n=56)	p
Age, yr (mean±sd)	65.7±15.6	66.9±13.6	0.346
pH (mean±sd)	7.34±0.2	7.42±0.1	0.062
pCO2, mmHg (mean±sd)	45.1±18.7	41.1±17.7	0.163
pO2, mmHg (mean±sd)	113.8±31.8	123.0±31.0	0.197
hCO3, (mmol/L) (mean±sd)	25.5±6.2	26.8±5.8	0.153
Total protein, (g/L) (mean±sd)	35.8±14.3	28.1±17.1	0.032
LDH, (U/L) (mean±sd)	633.5±1199.3	518.5±872.2	0.399
Albumin, (g/L) (mean±sd)	21.1±5.5	22.5±7.1	0.305
White blood cell (mean±sd)	1.1±1.1	1.5±1.1	0.287
Male n(%)	28 (87.5)	35 (63.6)	0.013
Alkalic n(%)	13 (40.6)	29 (52.7)	0.099
Hypertension n(%)	12 (37.5)	23 (41.8)	0.434
Diabetes mellitus n(%)	7 (21.9)	11 (20.0)	0.521
Exudative n(%)	32 (100)	41 (74.5)	<0.001
Unilateral fluid n(%)	27 (84.4)	44 (80.0)	0.419
Current/exsmoker n(%)	23 (71.9)	31 (56.4)	0.223

Table 4. Comparison of malignant and non-malignant pleural effusions

	Malignant (n=27)	Others (n=60)	p
Age, yr (mean±sd)	65.3±8.3	67.0±16.3	0.603
pH (mean±sd)	7.42±0.1	7.38±0.2	0.324
pCO2, mmHg (mean±sd)	40.9±7.9	43.3±18.9	0.530
pO2, mmHg (mean±sd)	120.8±29.2	119.2±32.6	0.827
hCO3, (mmol/L) (mean±sd)	28.6±4.7	23.7±5.7	0.001
Total protein, (g/L) (mean±sd)	36.8±11.1	28.4±17.7	0.036
LDH, (U/L) (mean±sd)	335.8±308.2	649.8±1158.2	0.205
Albumin, (g/L) (mean±sd)	21.9±7.4	16.1±9.5	0.009
Male n(%)	20(74.1)	43 (71.7)	0.517
Alkalic n(%)	15 (55.6)	27 (45.0)	0.565
Hypertension n(%)	8 (29.6)	27 (45.0)	0.132
Diabetes mellitus n(%)	7 (25.9)	11 (18.3)	0.296
Exudative n(%)	22 (81.5)	51 (85.0)	0.450
Unilateral fluid n(%)	19 (70.4)	52 (86.7)	0.067
Current/exsmoker n(%)	17 (63.0)	37 (61.7)	0.725

Discussion

This study provides a comprehensive analysis of pleural fluid gas characteristics in patients with various pulmonary diseases, highlighting their potential diagnostic implications. Our findings underscore the significance of pleural fluid gas analysis as an adjunct to traditional pleural fluid evaluations. In our study, it was found that patients with pneumonia had pleural fluid with higher protein levels, and a greater likelihood of exudative effusion compared to other groups. Additionally, malignancy group had pleural fluid with higher protien leveles and HCO3 levels.

The observation that patients with transudative pleural effusions were older and had higher pH, lower LDH levels, albumin levels and total protein levels aligns with existing literature. Transudative effusions are often associated with systemic conditions like heart failure, which predominantly affects older populations. The elevated biochemical markers in transudative effusions reflect the underlying pathophysiology, where systemic factors lead to fluid accumulation without significant local inflammation. In addition to pleural fluid gas analysis, the evaluation of hematological and biochemical parameters such as C-reactive protein (CRP), mean platelet volume (MPV), and platelet count has been shown to aid in differentiating exudative from transudative effusions. These parameters, when used alongside traditional criteria, may enhance diagnostic accuracy in determining the etiology of pleural effusions (19).

In inflammatory events, phagocytic activity results in acid accumulation, leading to a decrease in pH (8). In pleural effusions caused by tuberculosis or other microorganisms, pH is consequently low. In patients with pneumonia, pleural fluid analysis revealed distinct characteristics compared to those with other underlying conditions. Pneumonia-associated effusions exhibited lower pH, higher pCO2, and lower

HCO3 levels, indicating a more acidic environment and altered gas exchange within the pleural space. Various studies in the literature have shown that in infectious conditions like tuberculosis, pH decreases, while in malignancies, pH remains above 7.30 (10,20,21). The pCO2 measured in pleural fluid, like pH, is significant in diagnosing infectious diseases (11,22). However, our study found that the pH in pneumonia patients was not significantly lower compared to other conditions. This discrepancy may be due to the timing of pleural fluid sampling, as pH levels can fluctuate depending on the stage of infection and treatment status. Additionally, variations in host immune response and bacterial virulence could influence the extent of acid production within the pleural space.

In parapneumonic effusion, the presence of diffuse inflammation of the pleural membrane decreases free gas exchange between blood and pleural fluid through the inflamed membrane. As a result, the pH of parapneumonic effusion is lower than normal because CO2 in the pleural fluid cannot diffuse freely. Sobhey et al. (10) attributed the reduction in pleural fluid pH to the buildup of glucose metabolism byproducts, specifically CO2 and lactic acid. In our study, pCO2 levels in patients diagnosed with pneumonia were found to be higher than the normal range. However, when compared to other etiologies, this difference was not statistically significant. One possible explanation is the substantial proportion of cancer patients in the non-pneumonia group, which may have influenced the overall results. Malignant effusions are typically associated with less pronounced metabolic activity and a relatively stable pleural environment, potentially mitigating differences in pCO2 levels. Additionally, variations in disease severity and the timing of pleural fluid sampling could have contributed to the observed findings. Notably, approximately one-fourth of pneumonia cases in our cohort were diagnosed as empyema, a condition characterized by intense inflammation and purulent fluid accumulation. Among the 31 patients with pneumonia, 8 cases (25.8%) were diagnosed with empyema based on clinical and radiological findings. In these patients, the pleural fluid was characterized by a purulent appearance, markedly low pH, and elevated pCO_2 levels. Given that empyema represents a severe inflammatory process within the pleural space, it is expected to cause significant alterations in pleural fluid gas parameters. The presence of empyema in this subgroup likely contributed to the overall acid-base imbalance observed in the pneumonia cohort. Furthermore, when evaluating the clinical significance of pleural gas parameters, it is important to consider such complicating factors, as they may distort the interpretation of results. Therefore, future studies should aim to separately analyze uncomplicated parapneumonic effusions and empyema cases to better elucidate their respective gas profile characteristics. These factors highlight the complexity of pleural fluid acid-base balance and suggest that multiple mechanisms influence pH and gas exchange in different pathological conditions.

Some studies have highlighted that pleural fluid pCO2 levels may be lower and pO2 levels higher in malignant diseases (10). However, in our study, there were no statistically significant differences in pleural fluid pH, pCO2, or pO2 levels between malignant diseases and other conditions. Although there were no statistically significant differences in pleural fluid gas characteristics between patients with malignancy and those with other causes, identifying malignancy through pathological examination of pleural fluid remains crucial. The ability to diagnose malignancy from pleural fluid highlights the importance of careful cytological evaluation, in addition to biochemical and gas analyses.

Our findings align with previous reports suggesting that the pleural fluid pH and gas parameters are not solely disease-specific but are also influenced by pleural integrity and the inflammatory environment (10–12). While empyema exhibits markedly low pH due to intense neutrophilic infiltration and diffuse pleural inflammation, malignant and transudative effusions may retain near-normal pH levels owing to preserved regions of healthy pleura that allow for effective gas exchange (10,11). Interestingly, post-pleurodesis malignant effusions demonstrate lower pH despite a lower WBC count, likely due to fibrosis-induced impairment of gas diffusion rather than cellular inflammation (10) . Additionally, the technical reliability of blood gas analyzers for pleural pH and pCO_2 assessment has been validated, although anaerobic sample handling remains essential to avoid artificial pH elevation (11). These insights emphasize the combined importance of pleural pathophysiology and sample handling in interpreting pleural fluid gas analysis.

HCO3 is another parameter that can be analyzed in pleural fluid. In the study by Sohbey and Naglaa, it was reported that HCO3 levels were the lowest in malignant diseases and the highest in empyema. In our study, due to the limited number of patients, a direct comparison of all groups was not feasible. Contrary to the findings of Sobhey and Naglaa (10), in our study, HCO3 levels were found to be higher in malignant patients compared to other diseases.

Despite the valuable findings, this study has limitations, including its retrospective design and the relatively small sample size. Additionally, investigating the role of other gas parameters, such as oxygen and carbon dioxide levels, in different stages of pulmonary diseases could provide a deeper understanding of the pathophysiological processes at play.

Conclusion

In conclusion, pleural fluid gas analysis, when combined with traditional biochemical and cytological evaluations, offers a robust approach for diagnosing and understanding the underlying causes of pleural effusions. The distinct gas characteristics associated with different pulmonary diseases highlight the potential of this method in clinical practice, ultimately improving patient outcomes through more accurate diagnosis and targeted treatments. It is important to note that the interpretation of pleural fluid gas analysis results should be done in conjunction with other diagnostic tests, such as imaging studies and clinical examination.

Ethical Approval: *The study protocol was approved by the Institutional Review Board (IRB) of Akdeniz University (06.03.2025/225). All procedures were conducted in accordance with the Declaration of Helsinki and local regulations. Patient confidentiality was maintained throughout the study.*

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