

Original Article

Changing phenotypes of pediatric empyema in the COVID-19 era

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ABSTRACT

Background: This study aimed to investigate whether the disease phenotype of pleural effusion and empyema in children changed across the COVID-19 periods, by analyzing clinical, biochemical, and radiological parameters among culture negative pediatric patients.

Materials and Methods: A retrospective analysis of 147 pediatric patients treated for thoracic empyema between 2012 and 2025 was conducted. Patients with current or previous SARS-CoV-2 infection were excluded. Patients were stratified into four groups: pre-COVID (≤ 2019), pandemic (2020-2021), early post-COVID (2022), and late post-COVID (≥ 2023). Worsening of the disease phenotype was assessed by the presence of lung abscess and necrotizing pneumonia. Demographic data, pleural fluid biochemistry (pH, glucose, lactate dehydrogenase (LDH)), and radiological findings were reviewed and compared.

Results: The prevalence of empyema-associated lung abscesses showed a trend toward increase across periods, being higher during the pandemic (33.3%) and late post-COVID (15%) compared with the pre-COVID era (7.4%, $p = 0.054$). Necrotizing pneumonia also increased numerically, reaching 35% in the late post-COVID period. LDH levels were significantly higher in the escalation group (4614.54 ± 4504.62 U/L) compared with the non-escalation group (2493.74 ± 4415.49 U/L, $p = 0.015$). Oxygen requirement ($p = 0.020$), ICU admission ($p < 0.001$) and secondary intervention requirements differed significantly across periods ($p = 0.046$), with the highest rates observed in the early post-COVID group.

Conclusions: In SARS-CoV-2 negative pediatric patients, empyema presenting in the post-pandemic period was associated with increased respiratory support requirements. These findings may reflect pandemic-related alterations in disease behavior and support earlier consideration of treatment escalation.

Keywords: empyema, COVID-19 era, pediatrics

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Introduction

Empyema is defined as collection of purulent fluid within the pleural space [1]. Pleural effusions (PEf) and empyema (PEm) are common pleural complications of pediatric community acquired pneumonia (CAP) causing significant morbidity [2]. While pleural involvement occurs in approximately 1% of CAP cases, it may be observed in up to 40% of hospitalized patients [3].

Pleural effusions are classified into three distinct stages by the American Thoracic Society, based on disease progression and biochemical analysis of the pleural fluid. Stage 1, the exudative phase, occurs within the first 1 to 3 days and is characterized by a clear fluid collection with normal glucose levels, normal pH, and an absence of bacteria or significant cellular activity. Stage 2, the fibrinopurulent phase, can last up to 10 days and is marked by purulent effusion with high cellularity, bacterial presence, low glucose concentration, a pH below 7.2, and the formation of septae and loculations. Finally, Stage 3, the organizing phase, develops over 2 to 4 weeks; during this period, fibroblast proliferation leads to the formation of a fibrous peel and pleural thickening, which may significantly limit lung expansion [4,5].

Although most effusions resolve with appropriate treatment of pneumonia, progression to empyema remains a clinical challenge and may require interventions ranging from chest drainage to video-assisted thoracoscopic surgery (VATS) [3].

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was declared a global pandemic by the World Health Organization in March 2020, leading to profound changes in healthcare systems worldwide [6]. Public health measures such as social distancing and mask use led to reductions in respiratory infections including influenza and invasive bacterial diseases [7,8]. In parallel, changes in healthcare-seeking behavior, including a decline in emergency department visits during its early phases were reported [9].

These pandemic-related shifts have raised questions about potential changes in the clinical presentation and severity of pediatric empyema.

The aim of this study was to evaluate temporal changes in the clinical, biochemical, and radiological

characteristics of pediatric pleural effusion and empyema across different COVID-19 periods, and to identify factors associated with disease severity and the treatment escalation in culture negative children.

Materials and Methods

This retrospective, single-center study was conducted in the Department of Pediatric Surgery at a tertiary referral hospital. 147 pediatric patients aged 1-18 years who were treated for pleural effusion and empyema between January 2012 and January 2025 were included.

Patients diagnosed with isolated parapneumonic pleural effusion or empyema were eligible for inclusion. Only patients with community-acquired pneumonia-related pleural disease were included. Patients with evidence of current or previous SARS-CoV-2 infection were excluded from the study. Cases with pleural effusion secondary to neonatal pneumonia, trauma, malignancy, postoperative causes, or non-pneumonic etiologies were also excluded.

Pleural effusion and empyema were diagnosed based on clinical presentation, radiological findings, and pleural fluid analysis. Pleural effusions were classified as exudative according to Light's criteria, defined by the presence of one or more of the following: a pleural fluid-to-serum protein ratio > 0.5 , a pleural fluid-to-serum lactate dehydrogenase (LDH) ratio > 0.6 , or pleural fluid LDH levels greater than two-thirds of the upper limit of normal serum LDH [10]. Empyema was defined as the presence of purulent pleural fluid and/or pleural fluid with biochemical characteristics consistent with infection.

Patients were categorized into four groups according to the period of admission in relation to the COVID-19 pandemic: pre-COVID period (≤ 2019), pandemic period (2020-2021), early post-COVID period (2022), and late post-COVID period (≥ 2023).

Disease severity was defined by the requirement for intensive care admission, supplemental oxygen support, treatment escalation, and the presence of lung abscess or necrotizing pneumonia. Treatment escalation was defined as the requirement for secondary invasive interventions following initial management, including additional chest tube insertion, video-assisted thoracoscopic surgery (VATS), or thoracotomy with decortication, excluding planned intrapleural fibrinolytic therapy as part of first-line management.

Demographic data, clinical characteristics, laboratory findings, radiological features, treatment modalities, and outcomes were retrospectively collected from hospital medical records and the institutional electronic database. Collected demographic variables included age and sex. Clinical data comprised symptom duration, laterality of pleural disease, respiratory support requirements (supplemental oxygen and ICU admission), and length of hospital stay.

Laboratory data included pleural fluid biochemical parameters obtained at the time of thoracentesis, including pH, glucose, lactate dehydrogenase (LDH), and leukocyte count. Radiological evaluation was performed using chest radiography and thoracic ultrasonography in all patients, with computed tomography reserved for selected cases to assess disease severity, loculations, lung abscess formation, or necrotizing pneumonia.

Treatment-related data included initial management strategy (chest tube drainage with or without intrapleural fibrinolytic therapy), the need for secondary interventions, and the type of surgical procedures performed. Outcome measures included treatment escalation requirements and duration of hospitalization. Culture-negative status was defined as the absence of bacterial growth in pleural fluid and blood cultures obtained prior to antibiotic modification. Most patients had received empirical antibiotic therapy before referral, which may have reduced culture yield.

This study was approved by the Ethics Committee of Health and Science University Dr. Behcet Uz Pediatric Diseases and Surgery Training and Research Hospital (12.03.2026/ GOA-303) and it was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards, and informed consent was obtained from all patients.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics software. Continuous variables were presented as mean \pm standard deviation or median (minimum–maximum), depending on data distribution. Categorical variables were expressed as frequencies and percentages. Normality of continuous variables was assessed

using the Shapiro-Wilk test. Comparisons between two groups were performed using the Student's t-test for normally distributed variables and the Mann-Whitney U test for non-normally distributed variables. Comparisons among multiple groups were conducted using the Kruskal-Wallis test for continuous variables and the Pearson chi-square test or Fisher's exact test for categorical variables, as appropriate. A p value < 0.05 was considered statistically significant.

Results

A total of 147 pediatric patients were included in the analysis. The mean age was 6.96 ± 4.72 years. Of the patients, 87 (59.2%) were male. Pleural involvement was located in the right hemithorax in 69 patients (46.9%), in the left hemithorax in 68 patients (46.3%), and was bilateral in 10 patients (6.8%). Patients were grouped according to the period of admission as pre-COVID (≤ 2019), pandemic (2020–2021), early post-COVID (2022), and late post-COVID (≥ 2023) (Table 1).

All patients included in the study were confirmed to be negative for SARS-CoV-2 infection at the time of diagnosis. Microbiological evaluation of pleural fluid and thoracic cultures revealed no growth of Mycobacterium tuberculosis or other specific pathogenic microorganisms. No significant comorbid condition was identified in the majority of patients. Symptom duration prior to hospital admission did not differ significantly across the COVID-19 periods ($p = 0.188$). The mean duration of symptoms was 10.1 ± 13.2 days in the pre-COVID period, 8.8 ± 5.6 days during the pandemic, 6.0 ± 3.7 days in the early post-COVID period, and 7.8 ± 7.4 days in the late post-COVID period.

Comparisons according to treatment escalation status are summarized in Table 2. Pleural fluid LDH levels were significantly higher in the escalation group (4614.54 ± 4504.62 U/L) compared with the non-escalation group (2493.74 ± 4415.49 U/L, $p = 0.015$). No statistically significant differences were observed between the two groups with respect to pleural fluid pH or glucose levels ($p > 0.05$). Similarly, the presence of empyema-associated lung abscess, necrotizing pneumonia, and pleural effusion volume did not differ significantly between patients with and without treatment escalation ($p > 0.05$).

Comparisons according to intrapleural fibrinolytic treatment success are summarized in Table 3. Pleural fluid biochemical parameters, including pH, lactate dehydrogenase (LDH), and glucose levels, were comparable between patients with successful and unsuccessful fibrinolytic therapy ($p > 0.05$). Similarly, the presence of empyema-associated lung abscess, necrotizing pneumonia, and the volume of pleural effusion did not differ significantly between patients with successful and unsuccessful fibrinolytic treatment ($p > 0.05$). No pleural fluid or radiological parameter was found to be significantly associated with fibrinolytic treatment success (Table 3).

Comparisons of secondary treatment requirements, fibrinolytic therapy outcomes, disease severity, and length of hospital stay across the COVID-19 periods are summarized in Table 4. The requirement for secondary treatment escalation differed significantly between the COVID-19 periods ($p = 0.046$). Secondary intervention was most frequently required in the early post-COVID period, while no patients required secondary treatment during the pandemic period. The requirement for supplemental oxygen differed significantly across the COVID-19 periods ($p = 0.020$), with higher proportions observed during the pandemic and post-COVID periods compared with the pre-COVID period. Similarly, ICU admission rates varied significantly between periods ($p < 0.001$), being most frequent in the early and late post-COVID groups. The rates of specific secondary interventions, including thoracoscopic debridement and thoracotomy with decortication, did not differ significantly across periods ($p > 0.05$). Similarly, the distribution of other secondary interventions was comparable between groups. The success

rates of intrapleural fibrinolytic therapy did not differ significantly among the COVID-19 periods ($p > 0.05$), although a higher proportion of successful outcomes was observed in the early post-COVID period. Lung abscess formation was more frequently observed during the pandemic period compared with the pre-COVID period ($p = 0.054$). Although necrotizing pneumonia was more commonly observed during the pandemic and late post-COVID periods, this difference did not reach statistical significance ($p > 0.05$). The overall length of hospital stay did not differ significantly across the COVID-19 periods ($p > 0.05$).

Table 1. Baseline demographic characteristics of pediatric patients with parapneumonic pleural effusion and empyema, including distribution according to COVID-19 periods (n=147).

	value
Number of patients	147
Age (years), mean \pm SD	6.96 \pm 4.72
Sex, n (%)	
Male	87 (59.2)
Female	60 (40.8)
Side of pleural involvement, n (%)	
Right	69 (46.9)
Left	68 (46.3)
Bilateral	10 (6.8)
COVID-19 period of admission, n (%)	
Pre-COVID (≤ 2019)	81 (55.1)
Pandemic (2020–2021)	12 (8.2)
Early post-COVID (2022)	14 (9.5)
Late post-COVID (≥ 2023)	40 (27.2)
<i>Values are presented as mean \pm standard deviation or number (percentage), as appropriate</i>	

Table 2. Comparison of pleural fluid characteristics, lung abscess, necrotizing pneumonia, and pleural effusion volume according to treatment escalation status (n=147).

Variable	No escalation (n=127)	Escalation (n=20)	Z / χ^2	p
pH	7.24 \pm 0.58	7.23 \pm 0.78	-0.708	0.474
LDH (U/L)	2493.74 \pm 4415.49	4614.54 \pm 4504.62	-2.425	0.015
Glucose (mg/dL)	42.96 \pm 84.37	40.14 \pm 38.44	-1.056	0.291
Lung abscess, n (%)	14 (11.0)	3 (15.0)	—	0.705*
Necrotizing pneumonia, n (%)	34 (26.8)	8 (40.0)	0.904	0.342
Pleural effusion greater than half of hemithorax, n (%)	67 (52.8)	12 (60.0)	0.131	0.717
<i>Mann-Whitney U test for continuous variables; Pearson chi-square or Fisher's exact test for categorical variables, as appropriate. *Fisher's exact test.</i>				

Table 3. Comparison of pleural fluid characteristics, lung abscess, necrotizing pneumonia, and pleural effusion volume according to intrapleural fibrinolytic treatment success (n=61).

	Unsuccessful (n=3)	Successful (n=58)	Z / χ^2	p
pH	7.60 ± 0.82	7.27 ± 0.70	0.212	0.845
LDH (U/L)	1171.33 ± 892.34	2917.09 ± 3864.52	-0.579	0.574
Glucose (mg/dL)	18.0 ± 19.7	36.98 ± 32.92	-0.545	0.603
Lung abscess, n (%)	2 (66.7)	10 (17.2)	—	1.000*
Necrotizing pneumonia, n (%)	2 (66.7)	19 (32.8)	—	1.000*
Pleural effusion > half hemithorax, n (%)	2 (66.7)	40 (69.0)	—	1.000*

*Fisher's exact test. Mann-Whitney U test and Fisher's exact test, as appropriate.

Table 4. Comparison of secondary treatment requirements, fibrinolytic therapy success, disease severity, respiratory support, and length of hospital stay across COVID-19 periods (n=147).

	Pre-COVID (n=81)	Pandemic (n=12)	Early post-COVID (n=14)	Late post-COVID (n=40)	χ^2 / H	p
Secondary treatment required, n (%)	14 (17.3)	0 (0)	4 (28.6)	2 (5.0)	8.010	0.046
Thoracoscopic debridement, n (%)	1 (1.2)	0 (0)	1 (7.1)	0 (0)	4.215	0.239
Thoracotomy with decortication, n (%)	8 (9.9)	0 (0)	2 (14.3)	1 (2.5)	4.011	0.260
Other secondary interventions, n (%)	5 (6.2)	0 (0)	1 (7.1)	1 (2.5)	1.582	0.664
Fibrinolytic therapy successful, n (%)	27 (33.3)	5 (41.7)	9 (64.3)	19 (47.5)	5.813	0.121
Lung abscess, n (%)	6 (7.4)	4 (33.3)	1 (7.1)	6 (15.0)	7.658	0.054
Necrotizing pneumonia, n (%)	20 (24.7)	5 (41.7)	3 (21.4)	14 (35.0)	2.766	0.429
Oxygen requirement, n (%)	33 (40.7)	8 (66.7)	9 (64.3)	27 (67.5)	9.843	0.020
ICU admission, n (%)	30 (37.0)	7 (58.3)	11 (78.6)	30 (75.0)	19.873	<0.001
Length of hospital stay (days), mean ± SD	27.59 ± 20.49†	20.75 ± 15.74	26.36 ± 10.26	24.05 ± 20.75	5.650	0.130

Values are presented as number (percentage) or mean ± standard deviation. Pearson chi-square test was used for categorical variables and Kruskal-Wallis test for length of stay.

Discussion

In this retrospective cohort study, we evaluated changes in the clinical phenotype of pediatric parapneumonic pleural effusion and empyema across different COVID-19 periods.

The most notable finding of our study was the increased need for respiratory support, including supplemental oxygen and ICU admission, in the post-COVID era. Interestingly, this increase was not accompanied by a statistically significant rise in structural complications such as lung abscess or necrotizing pneumonia. Therefore, the post-pandemic shift in our cohort appears to reflect greater respiratory burden rather than increased destructive pulmonary involvement.

Recent reports have suggested that the COVID-19 pandemic altered the epidemiology of pleural infections. Chan et al. reported changes in microbiological

etiology during the pandemic period, including an increase in polymicrobial infections, although overall clinical outcomes such as ICU admission and mortality were not significantly different between pre- and post-pandemic periods [7]. In contrast to their findings, our cohort demonstrated a clear increase in respiratory support requirements without parallel changes in structural complication rates.

Moreover, delayed presentation may lead to more advanced-stage empyema (fibrinopurulent or organizing phases), in which simple drainage is insufficient and early surgical intervention becomes necessary [5]. Although delayed presentation has been proposed as a potential explanation in other cohorts, symptom duration did not differ significantly across periods in our study and it does not explain the increased respiratory support requirements observed in the post-pandemic group.

We observed significant differences in the rate of secondary treatment escalation across COVID-19 periods, while specific surgical modalities did not individually differ. Current literature continues to debate the optimal first-line approach in pediatric empyema. A recent meta-analysis comparing VATS and tube thoracostomy with fibrinolytics showed shorter length of stay and faster recovery with VATS, although overall outcomes were comparable [5,11].

In our cohort, although escalation rates differed across periods, overall length of hospital stay remained comparable. This aligns with evidence suggesting that hospital stay in empyema is influenced by multiple clinical variables and is difficult to predict reliably [12]. Thus, increased respiratory support requirements did not necessarily translate into prolonged hospitalization.

Pleural fluid LDH levels were significantly higher in patients requiring secondary intervention. This finding supports the concept that biochemical markers may reflect disease intensity and inflammatory burden. The American Thoracic Society staging system recognizes elevated LDH as characteristic of the fibrinopurulent phase [5]. However, recent data suggest that pleural fluid biochemical parameters alone may not consistently predict fibrinolytic failure [13]. In our study, while LDH was associated with treatment escalation, pleural fluid pH and glucose were not. This may indicate that LDH reflects overall inflammatory activity rather than specific microbiological characteristics. Larger studies are required to validate LDH as a practical risk stratification tool.

Although lung abscess showed a numerical increase in certain periods among our patients, the difference did not reach statistical significance. Necrotizing pneumonia rates were also comparable across periods. These findings suggest that the post-pandemic shift in our cohort was characterized more by increased respiratory compromise than by a measurable rise in destructive parenchymal complications [3].

The increased frequency of oxygen requirement and ICU admission in the post-pandemic period highlights the need for careful respiratory monitoring in pediatric empyema patients. From a clinical perspective, elevated pleural fluid LDH may serve as an early warning marker to identify patients at higher risk of treatment escalation, prompting closer monitoring and earlier consideration of invasive interventions.

Limitations of the Study

Several limitations should be considered about this study. First of all, its retrospective design and single center setting may limit the generalizability of the findings. Secondly, the relatively small sample size within certain subgroups may have reduced the statistical power of some comparisons. In particular, the limited number of patients in the unsuccessful fibrinolytic therapy group restricts the interpretability of subgroup analyses. Additionally, the predominantly culture-negative results precluded pathogen-specific analyses, thereby limiting insights into microbiological trends across the studied periods.

In conclusion, pediatric empyema in the post-COVID-19 period appears to present with increased respiratory support requirements, without a clearly demonstrated rise in structural pulmonary complications. Elevated pleural fluid LDH levels were associated with the need for secondary treatment escalation, suggesting a potential role as a clinical indicator of disease severity. Further large-scale, multicenter studies are warranted to validate these findings and to better elucidate the long-term impact of pandemic-related factors on the clinical phenotype of pediatric empyema.

Declaration of conflicting interests

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Ethics approval

This study was approved by the Ethics Committee of Health and Science University Dr. Behcet Uz Pediatric Diseases and Surgery Training and Research Hospital (12.03.2026/ GOA-303).

Authors' contribution

AEB: contributed to the study's concept, design, data collection or processing, analysis or interpretation, literature search, and writing. ADP: played a key role in the data collection or processing, analysis or interpretation, and writing of the manuscript. AS: involved in the study's concept, design, and final writing of the manuscript. All authors have read and approved the final version of the manuscript.

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