

Research Article

Pediatric Parapneumonic Effusion and Empyema Cases After Relaxation of COVID-19 Pandemic Restrictions in Türkiye

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Abstract

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Aim: To compare the frequency, demographic, clinical, radiological and treatment characteristics of pediatric cases with a diagnosis of Parapneumonic Effusion (PPE)/empyema in the winter and spring of 2022-2023 after the strict restrictions of COVID-19 Pandemic lifted up, with the PPE/empyema cases hospitalized in the winter and autumn months of 2021-2022 during the continuation of COVID-19 Pandemic restrictions.

Materials and Methods: Pediatric cases with a diagnosis of PPE/empyema in the winter and spring of 2021-2022 (during the restrictions continuation; the controlled normalization period in Türkiye) and winter and spring of 2022-2023 (after the lifting up all restrictions) were included and compared in this study. Demographic, clinical, radiological and treatments of patients were discussed.

Results: In the study group, a total of 58 patients with PPE/empyema were included, with 15 in the 2021-2022 group and 43 in the 2022-2023 group. Although the number of PPE/empyema cases were more in 2022-2023 than 2021-2022 group there was no statistically significant difference between the frequencies of PPE/empyema cases ($p=0.588$). Additionally, there were no statistically significant differences in the demographic, clinical, laboratory and outcomes of patients between the two groups.

Conclusion: The number of PPE/empyema cases increased through the end of COVID-19 Pandemic with the ease of health-care restrictions together with immunity debt which children acquired during pandemic lockdown periods. Our study is the first to document the increased PPE/ empyema cases hospitalized in the post-pandemic period from a single center. Multicenter studies with larger numbers of patients are needed.

Keywords: Parapneumonic Effusion; COVID-19; Pandemic; Empyema Cases

Introduction

The strict public health measures implemented during the COVID-19 pandemic have caused changes in the epidemic patterns of many infectious diseases. Implementation of these measures resulted in low incidences of influenza, respiratory syncytial virus, pneumococcus, enterovirus and parainfluenza infections [1]. The lack of exposure to various microorganisms in children during the COVID-19 pandemic lockdown caused a paucity in their immunity that lead to susceptibility to infectious diseases, the so-called "immunity debt" [2]. Towards the end of COVID-19 pandemic immunity debt together with removal of strict restriction measures lead to off-season resurgence of respiratory infections in several countries.

In our country, the strict public health restrictions were followed until 1st July, 2021 [3]. During the 2021-2022 school year, controlled normalization period was continuing and face-to-face education started on September 6, 2021, for 5 days a week. Mask wearing was mandatory for both teachers and children in schools at that time. Additionally, teachers not been vaccinated with

any of the vaccines against SARS-CoV-2 were required to undergo weekly nasopharyngeal PCR tests [4]. After the lifting up of all restrictive measures by July 1st, 2022; the 2022-2023 school year began allowing children and teachers to attend their classes without masks. The removal of these restrictions resulted in more pulmonary infections and more parapneumonic effusion (PPE)/ empyema cases we observed.

PPEs are the most significant complications leading to mortality and morbidity caused by lower respiratory infections [5]. While some PPEs can be resolved with antibiotic therapy alone, others may require drainage due to failure of resolution, resulting in complicated PPE called empyema [6]. PPEs and empyema not only prolong hospital stays but also increase mortality rates [7]. Despite the significant reduction in mortality observed through appropriate antibiotic use, along with repeated therapeutic thoracentesis, closed-chest drainage, fibrinolytic treatment, Video-Assisted Thoracoscopic Surgery (VATS) and open thorotomy procedures for draining pleural effusion, there is no complete consensus on the treatment approach for parapneumonic effusions [8].

In this study, we aimed to evaluate the epidemiological, clinical, laboratory and radiological characteristics of children presenting to our hospital with PPE/empyema during the two consecutive winter and autumn seasons of COVID-19 pandemic. We hope that the data we obtained would contribute to the monitoring and treatment of parapneumonic effusions and empyema, a commonly observed complication in children.

Materials and Methods

This study was conducted retrospectively in a single center with pediatric patients (under the age of 18) diagnosed with parapneumonic effusion and empyema who were admitted to the hospital. All patients were hospitalized between October 1st, 2021 and May 31st, 2023 at the Children's Infectious Diseases Service of Bursa Medical Faculty City Practice and Research Hospital, which is a tertiary care hospital. The study was approved by the local ethics committee (Approval Number: 2019-KAEK-140 2023-8/3). Written informed consent was obtained from all parents or legal guardians before inclusion in the study. The diagnosis of parapneumonic effusion and empyema was made based on the patient's history, physical examination, radiological evidence of pleural fluid, and/or evaluation of the pleural fluid obtained by thoracentesis according to Light criteria [9]. Patients or legal guardians who refused to participate in the study and/or those with insufficient information in their hospital records were excluded from the study. Patients diagnosed with PPE and empyema included in our study were categorized as Group 1 if they were diagnosed between October 1st, 2021 and May 31st, 2022. Patients diagnosed between October 1st, 2022 and May 31st, 2023, were considered as Group 2.

Data Collection

The records of all patients were examined in terms of age, gender, pre-admission complaints and durations, history of comorbid diseases, use of antibiotics and the presence of risk factors for Parapneumonic Effusion (PPE)/empyema. Symptoms and signs of PPE and empyema, vital signs (respiratory and heart rates, blood pressure and oxygen saturation) and other physical examination findings were evaluated. Complete blood count, liver-kidney function tests, albumin, Erythrocyte Sedimentation Rate (ESR), C-Reactive Protein (CRP) and procalcitonin results obtained from all PPE and empyema patients at the time of admission were recorded from their files. From the pleural fluids obtained by thoracentesis; total leukocyte count, protein, glucose, lactate dehydrogenase, albumin, gram staining results and thoracentesis culture results which grew on specific and non-specific media, as well as simultaneous blood culture results, were recorded. During the follow-up of the patients; posteroanterior-lateral and decubitus lung X-ray findings, thoracic ultrasound and if any, thoracic CT findings were recorded from the files. In addition, oxygen support, admission to the Pediatric Intensive Care Unit (PICU) for mechanical ventilation need, presence of closed-chest tube drainage, antibiotic treatments, fibrinolytic treatment and their outcomes were evaluated.

Statistical Analysis

The characteristic data were presented as n (%) for categorical variables and, when appropriate, as mean \pm SD or median (minimum-maximum values) for continuous variables. Chi-square tests or Fisher's exact tests were used for comparing categorical variables. In the presence of parametric test conditions to assess differences between two groups, independent T-tests were used and when the conditions could not be met, the Mann-Whitney U test was used. All tests were two-tailed, p-values <0.05 were considered statistically significant and Bonferroni correction was applied when appropriate. Statistical analyses were performed using SPSS version 22.0 (SPSS Inc., Chicago, IL, USA).

Results

Characteristics of the Study Group

In our study, which included 58 pediatric patients admitted with the diagnosis of PPE/empyema the median age was 75 months (min-max, 4-210 months) and 62% of the patients were male. There were 15 patients in Group 1 and 43 patients in Group 2. No statistically significant difference was found according to the frequency of PPE/empyema cases between the two groups ($p=0.588$). While 93% of the patients presented with fever, 62% had cough and 50% had difficulty in breathing upon hospital admission. One or more comorbid conditions were observed in 13 (22%) of our patients. Of these patients; four were CP-epilepsy, two Down Syndrome, one Menkes disease, one dilated cardiomyopathy, one selective Ig M deficiency, one hypotonic infant, one hydrocephaly with VP shunt, one with right renal agenesis, one with ASD. Detailed baseline characteristics and laboratory results of all patients are listed in Table 1. No significant differences were found between the two groups in terms of demographic characteristics, symptoms, signs and laboratory results ($p > 0.05$).

Radiological Characteristics

In 42 cases (73%) included in our study, pleural effusion was detected on the chest X-ray taken in the AP-lateral and decubitus position at the time of admission. Thoracic Ultrasound (USG) was performed in 51 patients (88%). Isolated pleural effusion was most commonly reported in the patients (63%), with varying proportions of associated consolidated parenchymal areas and atelectasis. Thoracic CT was performed in 28 cases (48%) and the combination of pleural effusion and consolidation (71%) was the most frequently reported condition. Detailed radiological characteristics of the study patients in both groups are presented in Table 2. There was no statistically significant difference between the two groups.

Pleural Fluid and Culture Results

Pleural effusion was observed bilaterally in 23 cases (40%), only on the left side in 23 cases (40%) and only on the right side in 12 cases (21%). The median value of pleural effusion fluid volume was reported as 17 mm (min-max, 5-100 mm). Among all the cases 20 (34%) were diagnosed with empyema and pleural fluid samples were obtained. There was no significant difference in pleural fluid sample results between Group 1 and Group 2 ($p > 0.05$). Cultures were positive in 3 out of 17 pleural fluid samples (18%). The cultured organisms were reported as *Staphylococcus aureus*, *Streptococcus pneumoniae* and *Streptococcus pyogenes* in individual patients. Blood cultures were taken in 32 cases (55%). Positive cultures were detected in a total of four patients (12%), all in Group 2; with one case each of *Acinetobacter baumannii*, *Streptococcus pneumoniae*, *Streptococcus mitis* and *Staphylococcus epidermidis* (Table 3).

Clinical Outcomes and Treatments

The median length of hospital stay of the cases was 11 days (min-max, 3-61 days). Intensive Care Unit (ICU) admission was required for 21 cases (36%), with a median duration of 7 days (min-max, 1-58 days) in the ICU. The most preferred antibiotic treatment protocol in the patient groups included in our study was a combination of 3rd generation cephalosporin + vancomycin, accounting for 43% of all cases. This was followed by the combination of 3rd generation cephalosporin + clindamycin (24%). Chest tube placement was performed in 16 (36%) cases. Intrapleural fibrinolytic therapy was administered in 13 patients (22%). Alteplase of 2 to 5 mg in 25 to 100 ml normal saline with a dwell time of 4 hours followed by drainage was used for intrapleural fibrinolytic treatment. This protocol was given 3 consecutive days. Detailed clinical characteristics of the patients are presented in Table 4. No significant differences were observed in the clinical characteristics and treatment modalities of the study patients when compared by periods ($p > 0.05$).

Variables	Total (n=58)	Grup 1* (n=15)	Grup 2** (n=43)	P-value
Demographics				
Age (months), median (min-max)	75(4-210)	48(6-201)	84(4-210)	0.053 ^a
Gender				
Girls, n (%)	22 (38%)	3 (20%)	19 (44%)	0.096 ^b
Boys n, (%)	36 (62%)	12 (80%)	24 (56%)	
Comorbidity, n (%)	13 (22%)	4 (26%)	9 (21%)	0.448 ^b
Antibiotic use before admission, n (%)	40 (69%)	8 (53%)	32 (74%)	0.194 ^b
Signs and symptoms, n (%)				
Fever (body temperature>37.3°C)	54 (93%)	13 (87%)	41 (95%)	0.273 ^b

Cough	36 (62%)	7 (47%)	29 (67%)	0.153 ^b
Dyspnea/ortophea	29 (50%)	9 (60%)	20 (47%)	0.368 ^b
Chest pain	19 (33%)	3 (20%)	16 (37%)	0.185 ^b
Vomiting	5 (9%)	0 (0%)	5 (12%)	0.210 ^b
Laboratory findings, median (min-max)	Total (n=58)	Grup 1* (n=15)	Grup 2** (n=43)	<i>P-value</i>
White blood cells (10 ³ /μL)	15.41 (4.84-59.70)	18.77 (7.68-58.28)	12.48 (4.84-59.70)	0.224 ^a
Absolute neutrophil count (10 ³ /μL)	9.80 (1.15-48.17)	11.6 (1.18-48.17)	9.52 (1.15-46.91)	0.472 ^a
Hemoglobin (g/dL)	SD11.36 (±1.53)	11.02 (±1.72)	11.48 (±1.47)	0.451 ^c
Platelet count (10 ³ /μL)	368 (±171)	421 (±225)	349 (±147)	0.648 ^c
Total protein(g/L)	63.4(±9.5)	60.3(±2.8)	63.9(±10.2)	0.069 ^c
Albumin (g/L)	36.9(±6.0)	37.1(±5.7)	36.8(±6.2)	0.994 ^c
C-reactive protein (mg/L)	64(0.3-462)	88 (2.1-382.5)	46 (0.3-462.0)	0.283 ^a
Procalcitonin (ng/mL)	0.33 (0.00-100.00)	0.73 (0.04-54.86)	0.20 (0.00-100.00)	0.314 ^a
Erythrocyte sedimentation rate (mm/h)	40(±21.9)	45.(±21.9)	40 (±22.4)	0,648 ^c
Data are presented as median (minimum-maximum values) or number (%).				
*Patients diagnosed between October 1 st 2021 - May 31 st , 2022				
**Patients diagnosed between October 1 st 2022 - May 31 st , 2023				
a: Mann Whitney-U test, b: Chi-square test, and c: Independent Samples T-test				

Table 1: Demographic, clinical features and laboratory findings of pediatric patients.

Chest X-ray	Total	Group 1*	Group2**
	(n=58)	(n=15)	(n=43)
Pleural Effusion+Consolidation	37 (64%)	13 (87%)	24 (56%)
Pleural Effusion+Consolidation+Atelectasis	5 (9%)	1 (7 %)	4 (9%)
Consolidation	16(28)	1 (7%)	15 (35%)
Chest Ultrasound Results	Total	Group 1*	Group2**
	(n=51)	(n=12)	(n=39)
Pleural Effusion	32(63%)	7(58%)	25(64%)
Pleural Effusion-Consolidation	15(29%)	4(33%)	11(28%)
Pleural Effusion +Consolidation+ Atelectasis	4(8%)	1(8%)	3(8%)
Chest Computed Tomography (CT) Result	Total	Group1*	Group2**
	(n=28)	(n=11)	(n=17)
Pleural Effusion-Consolidation	20 (71%)	9 (82%)	11 (65%)
Pleural Effusion +Consolidation+ Atelectasis	7 (25%)	2 (18%)	5 (29%)
Pleural Effusion+Atelectasis	1 (4%)	0 (0%)	1 (6%)
Data are presented as number n (%).			
*Patients diagnosed between October 1 st 2021 - May 31 st , 2022			
**Patients diagnosed between October 1 st 2022 - May 31 st , 2023			

Table 2: Radiological features of pediatric patients on chest X-ray, chest ultrasonography and chest Tomography.

Variables	Total (n=20)	Grup 1* (n=5)	Grup 2** (n=15)	<i>P-value</i>
Pleural fluid analysis				
WBC(10 ⁹ /L)	1.239 (0.064-25.658)	1.640 (0.064-18.476)	1.184(0.098-25.658)	0.885 ^a
PMN (%)	52.96 (±23.16)	32.80 (±10.40)	58.87 (±21.73)	0.352 ^b
Glucose(mg/dl)	59(±36)	31(±36)	63(±35)	0.843 ^b
Protein(mg/dl)	43(±10)	46(±2)	42(±11)	0.053 ^b
LDH (IU/L)	681(143-5395)	4620(591-5395)	603(143-2630)	0.093 ^a

Albumin(g/L)	25.6(±4.6)	27.5(±1.7)	25.0(±5.1)	0.375 ^b
Pleural Fluid Location and Depth	Total (n=58)	Grup 1* (n=15)	Grup 2** (n=43)	P-value
Pleural effusion location, n (%)				0.677 ^c
Bilateral	23(40)	7(47)	16(37)	
Right	12(21)	2(13)	10(23)	
Left	23(40)	6(40)	17(39)	
Pleural effusion depth (mm)	17(5-100)	17(5-26)	15(5-100)	0.913 ^a
Blood culture				
Blood culture results	32(55)	9 (60)	23(53)	0.456 ^c
No growth	28(87)	9(100)	19(83)	
<i>Acinetobacter baumannii</i>	1(3)	0(0)	1(4)	
<i>Streptococcus mitis</i> / <i>Streptococcus oralis</i>	1(3)	0(0)	1(4)	
<i>Staphylococcus epidermidis</i>	1(3)	0(0)	1(4)	
<i>Streptococcus pneumoniae</i>	1(3)	0(0)	1(4)	
<p>Data are presented as median (minimum-maximum values), mean (std. deviation) and number (%).</p> <p>*Pediatric patients with PPE/ empyema between October 1st 2021 - May 31st, 2022</p> <p>**Pediatric patients with PPE/ empyema between October 1st 2022 - May 31st, 2023</p> <p>NA: not applicable.</p> <p>WBC:White blood cells</p> <p>PMN:Polymorph Nuclear Neutrophil</p> <p>LDH:Lactate Dehydrogenase</p> <p>a: Mann Whitney-U test; b: Independent Samples T test; c: Chi-square test</p>				

Table 3: Results of pleural fluid analysis, location, depth and blood culture features of patients.

Diagnosis	Total (n=58)	Grup 1* (n=15)	Grup 2** (n=43)	P-value
Total	58 (100)	15 (100)	43 (100)	0.933 ^c
Parapneumonic Effusion	38(66)	10 (67)	28 (65)	0.588 ^c
Empyema	20(34)	5(33)	15(35)	0.536 ^c
Outcomes				
Total duration of hospitalization, day	11 (3-61)	10 (5-41)	11 (3-61)	0.663 ^a
Intensive care requirement (%)	921 (36)	8 (53)	13(30)	0.109 ^c
Total duration in intensive care unit,days	7(1-58)	6(1-18)	9(2-58)	0.363 ^a
Chest tube insertion, n (%)	20(34)	5(3)	15(35)	0.723 ^c
O2 support	30(51)	8(53)	22(51)	0.562 ^c
Invasive mechanical ventilation	8(13)	3(20)	5(11)	0.414 ^c
Non-invasive mechanical ventilation	6(10)	2(13)	4(9)	0.643 ^c
Reservoired mask oxygenation	16(27)	3(20)	13(30)	0.445 ^c
Treatments, (%)	Total (n=58)	Grup 1* n=15)	Grup 2** (n=43)	P-value
Antibiotics	58 (100)	15 (100)	43 (100)	NA
Cephalosporins	7(12)	2(13)	5(12)	
Meropenem	4(7)	2(13)	2(5)	
Meropenem+ Vancomycin	4(7)	1(7)	3(7)	
Cephalosporins+ Vancomycin	25(43)	8(53)	17(40)	
Cephalosporins+ Clindamycin	14(24)	1(7)	13(30)	
Cephalosporins+Vancomycin+Metronidazole	4(7)	1(7)	3(7)	
Intrapleural fibrinolytic treatment	13(22)	5(33)	8(19)	0.204 ^c

Data are presented as median (minimum-maximum values) , mean (std.deviation) and number (%).

*Patients diagnosed between October 1st 2021 - May 31st, 2022

**Patients diagnosed between October 1st 2022 - May 31st, 2023

NA: not applicable.

a: Mann Whitney-U test; b Independent Samples T test; c: Chi-square test

Table 4: Results of diagnosis, outcomes and treatment of patients.

Discussion

Prolonged reduction of exposure to many viruses and bacteria during COVID-19 Pandemic period resulted in a lack of immune stimulation against various bacteria and viruses called as immunity debt. This entity lead to expansion of the “naive” population to these pathogens and to the decline of herd immunity, making children more vulnerable to these infections. Bertran, et al., reported the children’s IPD incidence declined by 50% in year 2020 but increased in 2021 after lifting up COVID-19 public health restrictions [10]. They also reported that 2021 children’s IPD incidence was higher than that during the same period in pre-pandemic years 2017-2019. Perniciaro, et al., reported that the IPD levels returned to and even exceeded seasonal levels in spring and summer of 2021 in Germany, although striking declines in 2020 was seen as a result of Non Pharmaceutical Interventions (NPIs) taken to be protected from being infected by SARS-CoV-2 [11]. The rates of RSV and influenza associated hospitalizations of infants and children in late-2022 were higher than those during the same period in 2010-2020 [12]. Many other articles reported that the annual numbers of many community-acquired viral and bacterial infections decreased in 2020 compared to previous years. However, after the second half of 2021 and following 2 years, regardless of COVID-19 disease, these infections increased to the annual predicted numbers even higher [1,13-15].

Chan KF, et al., reported that there was a marked decline in the incidence of pleural empyema in children observed (pre-COVID-19, 18.4 ± 4.8 vs. post-COVID-19, 2.0 ± 2.9 cases per year, $p = 0.036$) in Hong Kong [16]. Their study included the pleural empyema cases from only January 2020 until June 2022 (until the beginning of summer in the northern hemisphere) and they had compared them to the empyema cases diagnosed between January 2015 and December 2019. Their study also comprised adult patients and the authors did not find any difference between pre and post-COVID-19 periods according to overall frequencies. In multivariate analysis, clinical outcomes for all ages (length of stay, ICU admission, intrapleural antifibrinolytic treatment, surgical intervention, death) were not significantly different in pre- and post-COVID-19 periods. Lee, et al., reported that non-COVID-19 pneumonia hospitalizations decreased 27% during the first year of the pandemic (1047 in 2020/2021 vs 1349 and 1433 in 2018/2019 and 2019/2020, respectively) then returned to prepandemic levels (1390 in 2021/2022) [17]. Alemayheu, et al., reported that in late 2022 they observed quite a large number of RSV hospitalizations at their centre, followed by higher rates of invasive group A streptococcal disease and pediatric CAP [18]. They concluded that after the pandemic, it was difficult to accurately predict respiratory viral circulation patterns or the future incidence or epidemiology of paediatric community-acquired pneumonia. In October 2022, we noticed a remarkable rise in cases diagnosed with PPE and empyema among the children admitted to our hospital. At that time, although COVID-19 Pandemic had lost its intensity, it was still on the agenda. However, mandatory mask-wearing requirement had been lifted up in schools in Turkiye and the respiratory infections were emerging to rise either due to climate change or the immunity debt children had achieved during COVID-19 Pandemic. At the end of the autumn 2023 there were a total of 43 children hospitalized with PPE, 15 of whom were empyema in our hospital. The previous winter and autumn season there were only 15 children hospitalized with PPE, 5 of whom were empyema. The total number of hospitalized PPE and empyema cases had increased about 3 times in 2022-2023 than 2021-2022 winter and autumn seasons, similar to the studies above mentioned. There was no statistically significant difference between the 2 consecutive seasons ($p=0.588$). Since Bursa City Hospital had started its services in July 2019, we did not have data of PPE/ empyema patients from years before the pandemic that we could make comparisons.

In the studies conducted by Segerer, et al. and Liese, et al., the median value of the Length of Stay in hospital (LOS) was 17 days and in the studies conducted by Langley, et al. and Alemayheu, et al., LOS was reported as 9 days for children with PPE/ empyema [8,18-20]. In our study, the median LOS in hospital was 11 days for all patients (10 days for Group 1 and 11 days for Group 2; with no statistically significant difference). Our results were similar to the studies above. Alemayheu, et al., reported that LOS in PICU was a median of 5 days for the 32% (35/109), drainage rate was reported as 74% (81/109) of children with PPE/Empyema [18]. Segerer, et al., reported that LOS in PICU was a median of 7 days for 58% (375/645) of total patients, drainage

rate was 55% (347/645) and fibrinolytic treatment was applied to 14% (89/645) of children with empyema [8]. Our results were similar to the studies by Alemayheu and Segerer for LOS in PICU and drainage rates. The rate of fibrinolytic treatment in our study was comparable to the study by Segerer, et al., (22% \pm 14%) [8].

To the best of our knowledge, this study is the first to report an increase in the frequency of PPE/empyema in pediatric patients towards the end of pandemic period in Türkiye. However, it has some limitations. This is a single center experience with limited numbers of patients. The number of microorganisms isolated in either pleural fluid cultures or blood cultures is very low in the study because 74% of the children have had used antibiotics before PPE/ empyema diagnosis [19,20].

Conclusion

The increased cases of PPE/ empyema cases in the 2022-2023 winter and autumn season, indirectly indicates that there was an increase in pneumonia cases among pediatric patients after the lifting up of pandemic restrictions. Although there was an increase in the number of pneumonia cases with pleural effusion, there was no significant statistical difference in the clinical course and length of hospitalization. Multicenter studies with larger numbers of PPE/ empyema cases are needed to document the impact of lifting up of restrictions on the frequency and characteristics of PPE/empyema cases towards the end of pandemic.

Conflict of Interest

The authors have declared no conflict of interest.

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