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RESEARCH

# Severe pertussis infections in pediatric intensive care units: a multicenter study

Nihal Akçay[1] · Demet Tosun[1] · İlyas Bingöl[1] · İbrahim Bingöl[2] · Agop Çıtak[2] · Süleyman Bayraktar[3] · Mehmet Emin Menentoğlu[4] · Esra Şevketoğlu[4] · Mey Talip[5] · Nazlı Umman Serin[5] · Ceren Bilgül[6] · Ülkem Koçoğlu Barlas[7] · Leyla Telhan[8] · Ebru Şahin[9] · Feyza İnceköy Girgin[10] · Mehmet Arda Kılınç[11] · Burcu Bursal[12] · Canan Baydemir[13]

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## Abstract

This study aims to evaluate the clinical course of critical pertussis illness to the pediatric intensive care unit in Istanbul. The study was conducted as a multicenter, retrospective study between January 1, 2023, and December 31, 2023. Cases with positive polymerase chain reaction testing for *Bordetella pertussis* of nasopharyngeal swab samples within the first 24 h of pediatric intensive care unit admission were recorded. We divided the patients into exchange blood transfusion group and non-exchange blood transfusion group, comparing related factors and clinical characteristics among each group. A total of 50 children with severe pertussis were enrolled in the study, including 29 males (58%), with a median age of 9.14 weeks (range, 7.29–15.3 weeks). The mortality rate for severe pertussis was 8%. Exchange blood transfusion was performed in eight patients (16%). There were no significant differences between patients who received exchange blood transfusion and those who did not in terms of age, male gender, gestational age, birth weight, comorbidities, presenting symptoms, duration of cough, prior antibiotic use, vaccination status, coinfections, PICU length of stay, or mortality ($p > 0.05$). Children who underwent exchange blood transfusion had significantly higher white blood cell (WBC) counts, lymphocyte counts, neutrophil counts, and C-reactive protein (CRP) levels compared to those who did not receive the procedure ($p < 0.05$). Pulmonary hypertension was observed in 50% of the children who received exchange blood transfusion, while it was present in only 11.8% of those who did not undergo the procedure ($p < 0.05$). Additionally, patients who received exchange blood transfusion had higher incidences of respiratory failure, cardiac failure or arrest, inotrope requirement, and mechanical ventilation compared to those who did not receive the transfusion ($p < 0.05$). *Conclusions*: Pertussis can lead to severe complications and mortality in critically ill infants. Most severe pertussis occurred in young, unimmunized infants. Children admitted with pertussis with high CRP level, high WBC and lymphocyte, and cardiac and respiratory failure can need exchange blood transfusion.

**What is Known:**

- *Pertussis is a highly contagious respiratory infection caused by Bordetella pertussis, which primarily affects infants. Despite vaccination efforts, pertussis remains a significant cause of morbidity and mortality in infants, particularly those too young to be fully vaccinated.*

**What is New:**

- *In pertussis, exchange blood transfusion may be considered in cases of severe pulmonary hypertension or cardiogenic shock, as indicated by echocardiographic findings, in conjunction with leukocytosis observed on laboratory tests.*

**Keywords** Children · Critical care · Exchange blood transfusion · Severe pertussis

## Introduction

Pertussis, commonly referred to as whooping cough, remains a significant public health challenge, despite being a vaccine-preventable disease [1]. This highly contagious respiratory illness, caused by *Bordetella pertussis*, predominantly

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Extended author information available on the last page of the article

affects infants and young children, often leading to severe morbidity and mortality [2]. Other *Bordetella species* such as *Bordetella parapertussis*, *Bordetella holmesii*, and *Bordetella bronchiseptica*, which can also cause pertussis-like syndromes. However, these species generally lead to milder clinical manifestations. While the introduction of effective vaccines in the mid-twentieth century dramatically reduced the global incidence of pertussis, outbreaks continue to occur, even in high-income countries. Pertussis is a disease observed worldwide without being restricted to a specific geographic location. Although it does not show a clear seasonal pattern, it peaks during autumn months, particularly in regions with low vaccination coverage, and exhibits periodic epidemics every 3 to 5 years [3]. These resurgences are attributed to factors such as waning immunity from acellular vaccines, antigenic shifts in circulating strains, and improved diagnostic capabilities that enhance detection [4].

The coronavirus disease 2019 (COVID-19) pandemic has disrupted routine vaccination schedules, leading to a decline in immunization rates. However, as COVID-19 restrictions have eased, vaccination rates have rebounded, and modeling studies predict an increase in morbidity and mortality from vaccine-preventable diseases. In addition, restrictions during the COVID-19 pandemic had a temporary reduction in the incidence of many infectious diseases [5].

Pertussis, an endemic disease globally, experiences cyclical outbreaks every 3 to 5 years, even in areas with high vaccination coverage. Following a period of reduced incidence during the COVID-19 pandemic, more than 25,000 pertussis cases were reported in Europe in 2023. The European Centre for Disease Prevention and Control (ECDC) has reported an increase in pertussis cases compared to pre-pandemic levels, potentially linked to diminished circulation of the pathogen during the pandemic and suboptimal vaccine uptake in certain populations [6]. Similarly, data from the Centers for Disease Control and Prevention (CDC) in 2023 indicate that the number of pertussis cases in the USA has approximately doubled compared to the previous year [7].

The management of pertussis is primarily supportive and includes oxygen therapy, suctioning, adequate hydration, and avoidance of respiratory irritants. In cases where the disease persists, parenteral nutrition may be required. First-line antibiotics for pertussis include erythromycin, azithromycin, and clarithromycin. Corticosteroids have not shown consistent benefits in mitigating the severity or duration of the illness but may be considered for critically ill infants. Beta-2 agonists, pertussis immune globulin, cough suppressants, and antihistamines have not proven effective. In cases of leukocytosis with lymphocytosis, exchange blood transfusion (EBT) therapy may be considered [8]. Death in young infants with severe pertussis is typically linked to profound leukocytosis with lymphocytosis, refractory pulmonary hypertension (PH), and cardiogenic shock [9].

The management of severe pertussis is primarily supportive and may involve mechanical ventilation, inhalation of nitric oxide (NO), exchange blood transfusion, and, in severe cases, extracorporeal membrane oxygenation (ECMO).

Exchange blood transfusion has been reported to enhance outcomes in patients with severe pertussis who experience life-threatening complications that persist despite aggressive therapeutic interventions [9].

Given these developments, this study aimed to assess the clinical course of pertussis in pediatric intensive care units (PICUs). The primary objective was to determine the incidence of *Bordetella pertussis* positive cases admitted to PICUs over the past year. The secondary objectives were to evaluate the clinical and laboratory presentations, treatment strategies, and disease progression in these patients.

## Materials and methods

### Study population

This multicenter retrospective study was conducted across 11 pediatric intensive care units (PICUs) in İstanbul, Türkiye. The study included all children diagnosed with pertussis and admitted to these PICUs between January 1, 2023, and December 31, 2023. Pertussis diagnosis was confirmed via polymerase chain reaction (PCR) testing. Only laboratory-confirmed cases were included in the analysis. Children under 18 years of age who required PICU care and had a confirmed pertussis diagnosis were eligible for inclusion. Suspected cases with negative PCR results, despite clinical evidence, were not included. Because of PCR, sensitivity is highest within the first 3 weeks of symptom onset.

### Data collection

Data were collected retrospectively from medical records at each participating center using standardized case report forms. For each case, demographic information, gestational age, comorbidities, immunization status, clinical presentation, date of symptom onset, admission diagnosis, illness duration, vital signs, laboratory test results, concurrent infections, complications, need for oxygen supplementation (non-invasive and invasive methods), therapy, length of hospital stay (LOS), and mortality were recorded.

The severity of pediatric acute respiratory distress syndrome (pARDS) was categorized as mild, moderate, or severe, based on the Second Pediatric Acute Lung Injury Consensus Conference criteria [10]. All patients underwent echocardiographic evaluation by a pediatric cardiologist. Pulmonary hypertension was diagnosed in accordance with pediatric pulmonary arterial hypertension guidelines [11].

There is no global consensus on the definitive criteria that determine when EBT should be indicated in cases of severe pertussis [9]. Participating centers decided on EBT based on their own experience. We categorized the patients into two groups based on whether they received EBT group or non-EBT group and subsequently compared relevant factors and clinical characteristics between these groups. The rationale for this grouping was to evaluate disease severity and examine the effect of EBT.

### Respiratory pathogen panel

The samples were processed using the Bio-Speedy kit (Bioeksen, Turkey) and analyzed using the multiplex real-time PCR method on the CFX96 Touch device (Bio-Rad Laboratories, Mannheim, Germany). This test is capable of detecting and differentiating *Legionella pneumophila*, human bocavirus, human adenovirus, *Bordetella pertussis*, *Chlamydia pneumoniae*, human coronavirus OC43, human coronavirus NL63, human coronavirus HKU1, human coronavirus 229E, human metapneumovirus, human rhino/enteroviruses, influenza A, influenza B, *Mycoplasma pneumoniae*, parainfluenza 1, 2, 3, and 4, respiratory syncytial virus A/B, severe acute respiratory syndrome coronavirus 2, human parechovirus, *Haemophilus influenzae*, and *Streptococcus pneumoniae*. The results were provided qualitatively.

### Statistical analysis

Statistical analysis was performed with IBM SPSS for Windows version 29.0 (IBM Corp., Armonk, NY, USA) statistical software package. Continuous variables were summarized as median (25–75 p). Categorical variables were expressed as frequencies and percentages. Comparisons between two groups were made using Fisher's exact Chi-square test, Yates' Chi-square test and Monte Carlo Chi-square test for categorical variables, and the Mann–Whitney *U* test for continuous variables. A $p$-value of $< 0.05$ was considered statistically significant.

### Ethical considerations

This study was approved by the Ethics Committee of Health Science University, Kanuni Sultan Süleyman Research and training hospital (KAEK/2024.01.18). Institutional review board approval was obtained from each participating hospital in accordance with local ethical regulations. Due to the retrospective nature of the study, informed consent was waived. The study was performed according to the ethical guidelines of the Declaration of Helsinki.

## Results

During the study period, 6601 children admitted to 11 PICUs in Istanbul were identified in the hospital registry. Of these, 50 (0.76%) were diagnosed with pertussis. The median age of the patients was 9 weeks (7–16.5). Most were young infants 1–4 months of age ($n = 39$; 78%) (Fig. 1A). The majority of patients (58%) were male, and 78% were term. Most patients (84%) had a birth weight greater than 2500 g. As shown in Fig. 1B, most were unvaccinated (70%) for pertussis. Thirty percent of the patients had been vaccinated against pertussis at least once. The number of pertussis cases admitted to PICUs in Istanbul by month is shown in Fig. 1C.

Passive exposure to cigarette smoke in the household was reported in 28% of patients. Overall, 10 (20%) children had known comorbidity. The underlying diseases were wheezy infant in 2 (4%) and type 1 diabetes mellitus in 1 (2%), west syndrome in 1 (2%), ventricular septal defect in 1 (2%), spinal muscular atrophy type 1 in 1 (2%), bronchopulmonary dysplasia in 1 (2%), severe laryngomalacia in 1 (2%), and congenital human cytomegalovirus infection in 1 (2%) case. Household contacts with pertussis were reported in 4% of cases, and 62% of patients had visited a healthcare setting prior to the onset of pertussis symptoms. Among the cases, 12 (24%) received antibiotics before admission to the PICUs. In our study, we used the respiratory pathogen panel to detect viral and bacterial coinfections. Co-infections were present in 28% of cases, with viral infections being the most common (Table 1).

The most common clinical feature among the patients included respiratory distress (90%), paroxysmal cough (82%), and decrease in feeding ability (58%). Seizure and fever were less common, occurring in 8% and 22% of cases. The median duration of cough was 6.5 days (3–9.5). Vital signs and laboratory results of the patients are shown in Table 2. Chest X-rays were abnormal in 84% of patients, with interstitial findings being the most common. Echocardiographic findings revealed pulmonary hypertension of varying degrees in 18% of cases. Specifically, mild PH was observed in 4 patients (8%), moderate PH in 2 patients (4%), and severe PH in 3 patients (6%), while the remaining 37 patients (74%) had no evidence of PH. Other complications included pneumonia (82%), respiratory failure (68%), cardiac failure and cardiac arrest (10%), septic shock (4%), pleural effusion (4%), macrophage activation syndrome (4%), acute renal failure (2%), and rhabdomyolysis (2%). Pediatric acute respiratory distress syndrome (PARDS) was diagnosed in 12 patients (24%). Of these ARDS patients, 7 patients had mild ARDS, 1 patient had moderate ARDS, and 4 patients had severe ARDS.

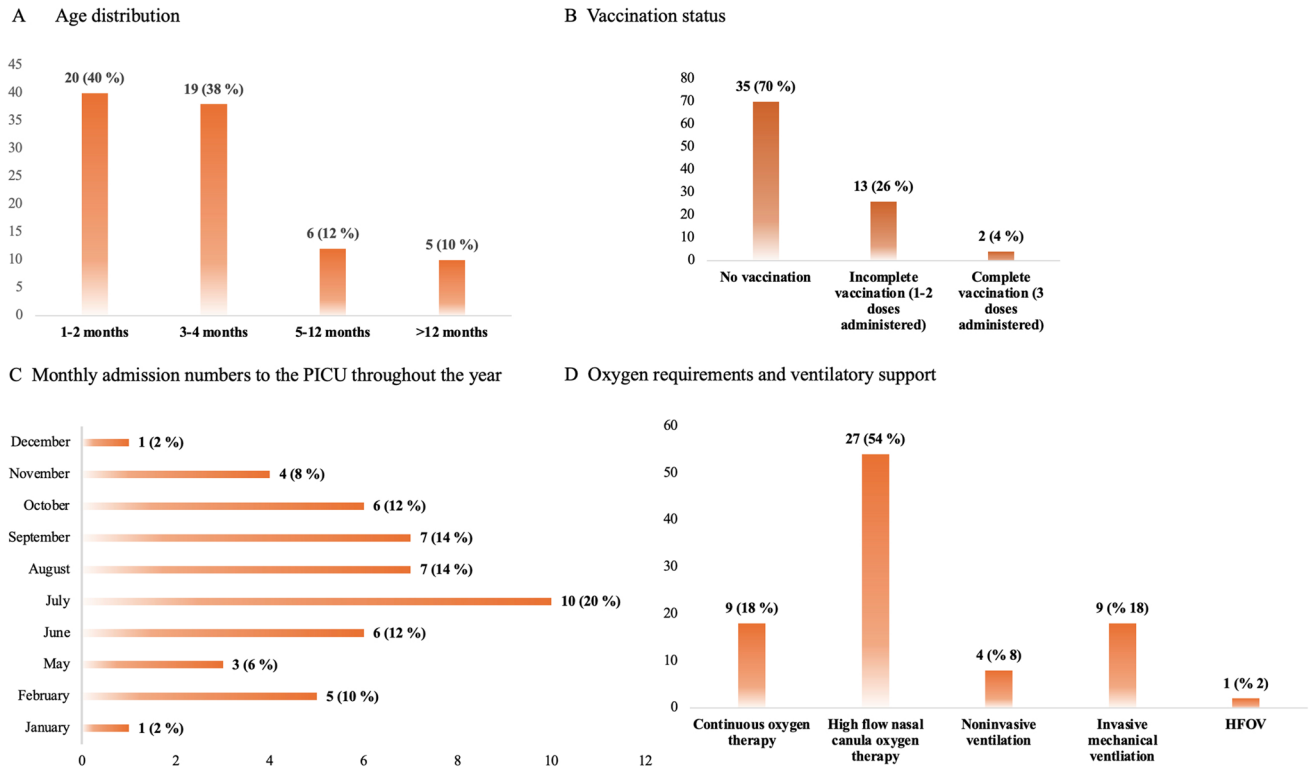


**Fig. 1** Characteristics of pertussis cases, 1 January2023–31 December 2023 ($n=50$)

**Table 1** Pathogen coinfections associated with *B. pertussis* infection ($n=14$)

| Pathogens | *n* |
|---|---|
| One-coinfection | **7** |
| *H. influenzae* | 2 |
| HRV | 1 |
| HMPV | 1 |
| ADV | 1 |
| SARS-CoV-2 | 1 |
| CMV | 1 |
| Two-coinfections | **4** |
| HRV, EV | 4 |
| Three-coinfections | **2** |
| PIV III, RSV, *H. influenzae* | 1 |
| HRV, EV, *H. influenzae* | 1 |
| Four-coinfections | **1** |
| HRV, EV, ADV, *S. pneumoniae* | 1 |

*ADV* adenovirus, *CMV* human cytomegalovirus, *EV* enterovirus, *HMPV* human metapneumovirus, *HRV* human rhinovirus, PIV parainfluenza, *H. influenzae Haemophilus influenzae*, *RSV* respiratory syncytial virus, *S. pneumoniae Streptococcus pneumoniae*, *SARS-CoV-2* severe acute respiratory syndrome coronavirus 2

The most commonly used antibiotic therapy was azithromycin (62%), followed by clarithromycin (36%). Methylprednisolone at a dose of 2 mg/kg was administered to 21 patients (42%), while intravenous immunoglobulin (IVIG) was given to 4 patients (8%). Inotropic support was required for 8 patients (16%), and renal replacement therapy (RRT) was provided to 2 patients (4%). Exchange blood transfusion was performed in a single session for 5 patients (10%) and in two sessions for 3 patients (6%). High-flow nasal cannula (HFNC) was the most frequently used respiratory support (54%), followed by invasive mechanical ventilation (18%), non-invasive mechanical ventilation (8%), and high-frequency oscillatory ventilation (2%) (Fig. 1D). No patients required extracorporeal membrane oxygenation (ECMO). The median duration of ventilatory support was 10.5 days, and the median pediatric intensive care unit (PICU) stay was 5.5 days. Of the 50 patients, 92% (46) improved or were cured, while 8% (4) succumbed to the illness.

The epidemiological data, clinical manifestations, laboratory findings, radiological findings, treatment, and outcomes were compared between EBT and non-EBT and are shown in Table 2. There was no statistically significant difference between the two groups in terms of age, gender, gestational age, birth weight, comorbidity, vaccination status, antibiotic use before admission, coinfection, and manifestations (all $p>0.05$). Respiratory rate was statistically higher in the

**Table 2** Epidemiological data, clinical manifestations, laboratory findings, radiological findings, treatment, and outcomes of pertussis patients

| Characteristics | Non-EBT $n=42$ | EBT $n=8$ | Total $n=50$ | $p$ value |
|---|---|---|---|---|
| Age, week, median (IQR) | 9 (7−15) | 8 (6.5−15) | 9 (7−16.5) | 0.543 |
| Male gender, *n* (%) | 25 (59.5) | 4 (50) | 29 (58) | 0.625 |
| Gestational age, week, *n* (%) | | | | 0.121 |
| > 37 | 31 (73.8) | 8 (100) | 39 (78) | |
| 32–36 + 6 | 10 (23.8) | 0 | 10 (20) | |
| 28–31 + 6 | 1 (2.3) | 0 | 1 (2) | |
| Birth weight, g, median (IQR) | | | | 0.207 |
| > 2500 | 34 (80.9) | 8 (100) | 42 (84) | |
| 1500–2499 | 7 (16.6) | 0 | 7 (14) | |
| 1000–1499 | 1 (2.3) | 0 | 1 (2) | |
| Comorbidities, *n* (%) | 9 (21.4) | 1 (12.5) | 10 (20) | 0.572 |
| Cough duration before admission(days) median (IQR) | 5.5 (3−9.5) | 7 (2.75−8.75) | 6.5 (3−9.5) | 0.862 |
| Received antibiotics before admission, *n* (%) | 10 (23.8) | 2 (25) | 12 (24) | 0.944 |
| Household contacts history, *n* (%) | 2 (4.7) | 0 | 2 (4) | 0.538 |
| Pertussis vaccination status, *n* (%) | | | | 0.381 |
| Non-vaccinated (0 dose) | 31 (73.8) | 4 (50) | 35 (70) | |
| Incompletely vaccinated (1 dose or 2 doses) | 9 (21.4) | 4 (50) | 13 (23) | |
| Completely vaccinated (3 doses) | 2 (4.7) | 0 | 2 (4) | |
| Coinfections, *n* (%) | 11 (26.1) | 3 (37.5) | 14 (28) | 0.524 |
| Manifestations, *n* (%) | | | | |
| Paroxysmal cough | 41 (97.6) | 8 (100) | 49 (98) | 0.667 |
| Post-tussive vomiting | 14 (33.3) | 5 (62.5) | 19 (38) | 0.124 |
| Apnea | 11 (26.1) | 4 (50) | 15 (30) | 0.185 |
| Cyanosis | 15 (35.7) | 4 (50) | 19 (38) | 0.456 |
| Fever | 10 (23.8) | 1 (12.5) | 11 (22) | 0.489 |
| Decrease in feeding ability | 24 (57.1) | 5 (62.5) | 29 (58) | 0.784 |
| Nasal congestion, rhinorrhea | 21 (50) | 5 (62.5) | 26 (52) | 0.526 |
| Facial flushing and/or cyanosis during coughing | 20 (47.6) | 5 (62.5) | 25 (50) | 0.451 |
| Respiratory distress | 38 (90.4) | 7 (87.5) | 45 (90) | 0.802 |
| Seizure | 2 (4.76) | 2 (25) | 4 (8) | 0.055 |
| Enteritis | 12 (28.5) | 1 (12.5) | 13 (26) | 0.352 |
| Vital and clinical signs | | | | |
| Heart rate (beats/min), median (IQR) | 140 (123–150) | 142 (132–154) | 140 (125–150) | 0.559 |
| Respiratory rate (breaths/min), median (IQR) | 42 (36–50) | 68 (58–72) | 44 (38–56) | **0.001** |
| SBP (mm Hg), median (IQR) | 84 (74–90) | 88 (76.5–92) | 85 (75–90) | 0.350 |
| DBP (mm Hg), median (IQR) | 49 (42–56) | 48 (45.8–60.5) | 49 (43–59) | 0.588 |
| $sPO_2$ (%), median (IQR) | 96 (93–98) | 93.5 (92.8–99.3) | 95 (93–99) | 0.775 |
| Crackles, *n* (%) | 23 (54.7) | 7 (87.5) | 30 (60) | 0.086 |
| Wheezing, *n* (%) | 17 (40.4) | 6 (75) | 23 (46) | 0.075 |
| Laboratory values, median (IQR) | | | | |
| White blood cell count ($10^3$/μL) | 18.8 (13.5–38.7) | 37.7 (28.1–58.8) | 22.8 (14.4–42.1) | **0.013** |
| Lymphocyte count, ($10^3$/μL) | 11.8 (7.0–20.2) | 23.9 (14.4–35) | 12.5 (8.5–24.8) | **0.034** |
| Neutrophil count, ($10^3$/μL) | 6.30 (4.0–9.35) | 16.5 (12.0–20.7) | 7.88 (4.3–10.5) | **0.003** |
| Platelet count, ($10^3$/μL) | 499 (392–623) | 505 (389–625) | 499 (392–625) | 0.979 |
| Hemoglobin, (g/dL) | 10.1 (9.7–10.8) | 10.5 (9.6–10.9) | 10.2 (9.7–10.8) | 0.652 |
| Hematocrit (%) | 30.8 (28.8–33.8) | 32.7 (30–34.9) | 30.9 (29–34.1) | 0.321 |
| ALT (U/L) | 23 (14.9–31) | 14.5 (9.75–19) | 23 (14–30.3) | 0.085 |
| AST (U/L) | 32.5 (24.9–40.8) | 28.5 (23–32) | 32 (24.2–39.8) | 0.334 |
| Urea (mg/dL) | 10 (7–21) | 12.5 (9.7–20.6) | 10.5 (7.48–21) | 0.289 |
| Creatinine (mg/dL) | 0.25 (0.20–0.30) | 0.25 (0.18–0.30) | 0.25 (0.19–0.3) | 0.874 |

**Table 2** (continued)

| Characteristics | Non-EBT $n=42$ | EBT $n=8$ | Total $n=50$ | $p$ value |
|---|---|---|---|---|
| Sodium (mEq/L) | 138 (135–140) | 138 (136–142) | 138 (135–140) | 0.549 |
| Potassium (mEq/L) | 4.85 (4.1–5.21) | 4.9 (4.69–5.35) | 4.85 (4.18–5.27) | 0.368 |
| Calcium (mg/dL) | 9.61 (9–9.98) | 9.6 (8.97–10.2) | 9.61 (9–10) | 0.874 |
| Creatine kinase (U/L) | 96 (66.8–119) | 110 (88.8–156) | 98.5 (70–127) | 0.254 |
| Lactate dehydrogenase (U/L) | 327 (280–410) | 374 (313–436) | 336 (280–430) | 0.398 |
| C-reactive protein (mg/L) | 1 (0.46–6.9) | 4.69 (3.2–14) | 1.04 (0.6–7.54) | **0.032** |
| Procalcitonin (ng/mL) | 0.2 (0.09–0.53) | 0.22 (0.09–0.34) | 0.2 (0.09–0.5) | 0.932 |
| Troponin (ng/mL) | 5.3 (0.02–24) | 12.3 (7.1–16.5) | 9.71 (0.06–23.6) | 0.508 |
| Ferritin (ng/mL) | 299 (205–544) | 513 (464–3715) | 358 (218–552) | 0.158 |
| Fibrinogen (mg/dL) | 247 (215–392) | 269 (227–331) | 247 (217–348) | 0.725 |
| Prothrombin time (s) | 14.4 (13.2–15.9) | 13.9 (13.2–15.3) | 14.3 (13.2–15.9) | 0.743 |
| APTT (s) | 30.9 (28–34.3) | 30.1 (27.8–32.3) | 30.6 (28–34.3) | 0.851 |
| Pro-BNP (pg/mL) | 729 (325–14,339) | 253 (180–1313) | 625 (234–1313) | 0.476 |

*ET* exchange blood transfusion, *IQR* interquartile range, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, $SpO_2$ peripheral capillary oxygen saturation, *WBC* white blood cell, *ALT* alanine aminotransferase, *AST* aspartate aminotransferase, *APTT* activated partial thromboplastin time, *pro-BNP* B-type natriuretic peptide, *BE* base excess, *ARDS* acute respiratory distress syndrome, *AKI* acute kidney injury, *ECMO* extracorporeal membrane oxygenation, *IVIG* intravenous immunoglobulin, *HFOV* high-frequency oscillatory ventilation, *PICU* pediatric intensive care unit, *CRP* C-reactive protein, $pCO_2$ partial pressure of carbon dioxide

EBT group ($p<0.05$). There was no significant difference in other vital signs, crackles, and wheezing (all $p>0.05$). The white blood cell count, lymphocyte count, neutrophil count, and the C-reactive protein were statistically higher in the EBT group (all $p<0.05$). There was no significant difference in other laboratory findings (all $p>0.05$). Respiratory failure, cardiac failure and cardiac arrest, pulmonary hypertension, inotrope requirement, IVIG used, pARDS, and mechanical ventilation requirement were statistically higher in the EBT group. There was no statistical difference between the two groups in terms of lengths of hospital stay, lengths of intensive care unit stay, and mortality. A detailed summary of EBT (+) cases is presented in Table 3.

## Discussion

Here, we present data on an ongoing pertussis outbreak in Istanbul, from January up to December 2023, affecting children. This study offers critical insights into the clinical characteristics and outcomes of pertussis patients admitted to pediatric intensive care units (PICUs) in Istanbul, Turkey.

The extensive adoption of pertussis vaccination has resulted in a notable reduction in both the incidence and mortality of the disease. Nevertheless, recent years have witnessed a gradual increase in the global incidence of pertussis. Pertussis is common worldwide, with an increase every 3–5 years. Also, pertussis increases in the European Union (EU) during the summer months [12]. Hitz et al. observed a *B. pertussis* seasonality with the highest number of positive samples in the months from June until September in Germany [13]. Summer peak of the pertussis seen in our study was similar to the EU (Fig. 1C). The European Centre for Disease Prevention and Control has reported that the low level of pertussis activity during COVID-19 pandemic in the EU may have increased the proportion of the population susceptible to pertussis and may be partly responsible for the increase observed in 2023 [12].

Pertussis can affect individuals of all ages, but it is most common among infants and young children. Infants tend to experience more severe disease [14]. The children included in this study were admitted with severe pertussis patients in PICU, with a median average age of 9 weeks. In this study, 70% of the children were not vaccinated against pertussis, and 78% were infants younger than 4 months. In Turkey, the pertussis vaccine is administered as a pentavalent combination vaccine of diphtheria, tetanus, pertussis, polio, and *Haemophilus influenzae type b* (DTaP-IPV/Hib) at 2, 4, 6, and 18 months of age. Also, the national vaccination schedule includes a booster dose at 48 months, delivered as a tetravalent combination vaccine (DTaP -IPA) [15]. Our study shows that nearly half of the patients experienced onset of pertussis under 2 months, and the proportion of unvaccinated infants was quite high.

Although laboratory testing is not always necessary to diagnose pertussis, it is often performed to confirm the diagnosis, particularly when contact prophylaxis is needed or for public health considerations (e.g., in outbreak settings). Laboratory testing is beneficial, especially in patients without an exposure history. However, we emphasize that laboratory confirmation should not delay the initiation of treatment. PCR is an important tool for the diagnosis of pertussis.

**Table 3** Clinical characteristics and outcomes of pertussis patients in undergoing exchange blood transfusion therapy

| Characteristics | Case 1 | Case 2 | Case 3 | Case 4 | Case 5 | Case 6 | Case 7 | Case 8 |
|---|---|---|---|---|---|---|---|---|
| Gender | Female | Male | Male | Male | Female | Male | Female | Female |
| Age (weeks) | 11 | 4.3 | 28.4 | 200.6 | 8 | 5.4 | 8.7 | 6.9 |
| Birth status | Full term | Full term | Full term | Full term | Full term | Full term | Full term | Full term |
| Birth weight (g) | 2800 | 3500 | 3300 | 4500 | 3200 | 2500 | 2900 | 3600 |
| Presenting symptoms | Fever. Cough. Dyspnea. Apnea. Decreased oral intake | Cough. Dyspnea. Apnea. Decreased oral intake | Cough. Dyspnea. Apnea | Cough. Dyspnea. Apnea. Decreased oral intake | Cough. Dyspnea. Apnea. Decreased oral intake | Cough. Dyspnea. Apnea. Decreased oral intake | Cough. Dyspnea. Apnea. Decreased oral intake | Cough. Post-tussive vomiting. Enteritis |
| Peak WBC ($\times 10^3$/ml) | 103.01 | 72.3 | 58.45 | 78.87 | 24.59 | 36.40 | 60.50 | 75.10 |
| Peak lymphocyte | 48.8 | 48.0 | 31.13 | 63.00 | 15.90 | 10.15 | 23.90 | 36.50 |
| Pulmonary hypertension | Severe | Mild | None | - | Severe | Severe | None | None |
| Chest X-ray | Bilateral consolidation | Bilateral consolidation | Bilateral consolidation | Consolidation on upper right lung | Consolidation on upper right lung | Bilateral consolidation | Bilateral consolidation | Bilateral consolidation |
| Combined pathogen | None | None | None | *Human rhino / enterovirus. Adenovirus. S. pneumonia* | *Human rhino / enterovirus* | *Severe acute respiratory syndrome coronavirus 2* | None | None |
| Maximum parameters of mechanical ventilation (PIP/PEEP) ($cmH_2O$) | 20/8 | 36/12 | *High flow nasal canula* | *High flow nasal canula* | 20/5 | 23/8,5 | 31/10 | NIV (EPAP: 7 IPAP:14) |
| CRRT | Yes | None | None | None | None | None | None | None |
| Time of hospital stay (day] | 50 | 2 | 25 | 19 | 18 | 1 | 23 | 42 |
| Exchange sessions | Single | Double | Single | Single | Single | Single | Double | Double |
| Outcome | Recovered | Died | Recovered | Recovered | Recovered | Died | Recovered | Recovered |

*AST* aspartate aminotransferase, *ALT* alanine aminotransferase, *WBC* white blood cell count, *CRRT* continuous renal replacement therapy, *PIP* peak inspiratory pressure, *PEEP* positive end-expiratory pressure, *NIV* non-invasive mechanical ventilation

*Tests not performed on the patient

PCR provides faster and more sensitive results compared to culture. However, careful specimen collection and transport are critical to ensure that healthcare providers obtain reliable diagnostic results that accurately inform patient diagnosis [16]. In our study, PCR testing was utilized; however, the sensitivity of this method decreases during or after the paroxysmal stage and after antibiotic therapy has been initiated. Serologic tests could not be performed due to resource limitations. Nasopharyngeal samples were sent to the Ministry of Health Laboratory, where bacterial culture was also conducted. Despite these efforts, our study was limited to the diagnosis of *B. pertussis* via PCR, and other *Bordetella species*, such as *B. parapertussis*, were not systematically investigated. Other *Bordetella species*, including *Bordetella parapertussis*, *Bordetella bronchiseptica*, and *Bordetella holmesii*, may cause clinical syndromes similar to pertussis, but they are generally less severe. These species were not targeted in our diagnostic approach, representing a limitation of our study.

Infants critically ill with pertussis encompass those presenting with apnea, seizures, or pneumonia that is complicated by respiratory failure, pulmonary hypertension, and/or cardiac failure. Complicated pneumonia is typically associated with a white blood cell count of ≥ 30,000 cells/μL [17]. Pneumonia complicated by refractory hypoxemia, pulmonary hypertension, and/or cardiac failure is frequently associated with severe leukocytosis and carries a mortality rate of up to 80%. In young infants with pertussis, a white blood cell count (WBC) of ≥ 30,000 cells/μL correlates with increased disease severity and mortality [15]. Based on experiences from the California outbreak, some infectious disease experts recommend ET for infants under 4 months of age who exhibit any of the following criteria: WBC count ≥ 25,000 cells/μL with a lymphocyte count ≥ 12,000 cells/μL, and one or more of the following conditions: cardiogenic shock, pulmonary hypertension, organ failure (e.g., renal failure). Alternatively, ET may be considered in cases where the total WBC count is ≥ 48,000 cells/μL with a lymphocyte count ≥ 15,000 cells/μL, or if the total WBC count is ≥ 30,000 cells/μL with a lymphocyte count ≥ 15,000 cells/μL and the rate of rise is ≥ 50% over 24 h. Additional indications for ET include a consistently elevated pulse rate (> 170 beats/minute), a consistently high respiratory rate (> 70 breaths/minute), and oxygen saturation levels below 80% [18]. In our study, we performed ET on 8 patients diagnosed with severe pertussis. WBC median value was 37.700 cells/μL, and lymphocyte median value was 23.900 cells/μL in our patients. All patients had pneumonia and respiratory failure, while 4 patients had heart failure and pulmonary hypertension. Two of our patients died despite ET.

The mortality rate observed in our study is consistent with recent data from the Collaborative Pediatric Critical Care Research Network Critical Pertussis Study, which reported similar mortality rates among critically ill pertussis patients across multiple centers [19]. This alignment underscores the grave impact of pertussis, especially in infants who may lack adequate immune protection. Our results echo Straney et al. [20], who documented significant resource utilization in critically ill pertussis patients, reinforcing the necessity for effective prevention strategies to reduce healthcare strain.

Identified risk factors such as abnormal echocardiographic findings and cardiac dysfunction emphasize the critical importance of monitoring for cardiac complications in pertussis patients, as supported by previous research. Our findings are also consistent with recent work by Poeta et al. [21], which described a pertussis outbreak in neonates and young infants in Italy, highlighting the vulnerability of this age group and the potential for severe outcomes.

The use of multiplex PCR, which only detects *B. pertussis*, has been acknowledged as a major limitation of our study. *Bordetella parapertussis* and other *Bordetella species* could not be detected. The other limitations of our study include its retrospective design and potential sample size constraints, which may affect the generalizability of the findings. Future research should include larger, prospective studies to validate these findings and explore independent mortality risk factors in critically ill pertussis patients.

In conclusion, this study enhances the understanding of pertussis in critically ill children by identifying key risk factors and highlighting the disease's severity. Early diagnosis, aggressive management, and improved vaccination coverage are crucial for reducing the burden of pertussis and its associated mortality, especially in young infants and children. Our results contribute to the existing body of evidence on severe pertussis. We recommend that WBC and lymphocyte counts be closely monitored in patients with severe pertussis. If the patient is diagnosed with concomitant tachypnea, hypoxia, respiratory failure, heart failure, and/or pulmonary hypertension, exchange transfusion should be promptly initiated.

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**Authors' contributions** N.A, D.T, İ.B, B.B and C.B. wrote the main manuscript text. D.T. and İ.B prepared figure and tables. İ.B, A.Ç, S.B, M.E.M, E.Ş, M.T, N.U, C.B, U.K.B, L.T, E.Ş, M.A.K and F.İ.G collected the data in their own centers. All authors reviewed and approved the final manuscript.

**Data availability** No datasets were generated or analysed during the current study.

## Declarations

**Conflict of interest** The authors declare no competing interests.

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## Authors and Affiliations

**Nihal Akçay[1] · Demet Tosun[1] · İlyas Bingöl[1] · İbrahim Bingöl[2] · Agop Çıtak[2] · Süleyman Bayraktar[3] · Mehmet Emin Menentoğlu[4] · Esra Şevketoğlu[4] · Mey Talip[5] · Nazlı Umman Serin[5] · Ceren Bilgül[6] · Ülkem Koçoğlu Barlas[7] · Leyla Telhan[8] · Ebru Şahin[9] · Feyza İnceköy Girgin[10] · Mehmet Arda Kılınç[11] · Burcu Bursal[12] · Canan Baydemir[13]**

✉ Nihal Akçay
drnihalakcay@gmail.com

Demet Tosun
demettsn@gmail.com

İlyas Bingöl
drilyasbingol@hotmail.com

İbrahim Bingöl
ibrahimbingol@gmail.com

Agop Çıtak
agopcitak@hotmail.com

Süleyman Bayraktar
bsuleyman@hotmail.com

Mehmet Emin Menentoğlu
menentoglu@hotmail.com

Esra Şevketoğlu
caglaes@yahoo.com

Mey Talip
meytalip@gmail.com

Nazlı Umman Serin
nazliumman@hotmail.com

Ceren Bilgül
cerenbilgun@yahoo.com

Ülkem Koçoğlu Barlas
ulkemkocoglu@yahoo.com

Leyla Telhan
leylatelhan@gmail.com

Ebru Şahin
ebruguneysahin@hotmail.com

Feyza İnceköy Girgin
feyzagirgin@hotmail.com

Mehmet Arda Kılınç
makilinc@hotmail.com

Burcu Bursal
burcubursal@hotmail.com

Canan Baydemir
canandoruk@hotmail.com

[1] Department of Pediatric Intensive Care Unit, Kanuni Sultan Süleyman Training and Research Hospital, University of Health Sciences, Istanbul 34093, Turkey

[2] Department of Pediatric Intensive Care Unit, Acıbadem Atakent Hospital, Acıbadem University, Istanbul, Turkey

[3] Department of Pediatric Intensive Care Unit, Haseki Training and Research Hospital, University of Health Sciences, Istanbul, Turkey

[4] Department of Pediatric Intensive Care Unit, Bakırköy Dr. Sadi Konuk Training and Research Hospital, University of Health Sciences, Istanbul, Turkey

[5] Department of Pediatric Intensive Care Unit, Okmeydanı Cemil Taşçıoğlu Training and Research Hospital, University of Health Sciences, Istanbul, Turkey

[6] Department of Pediatric Intensive Care Unit, Faculty of Medicine, İstanbul University, Istanbul, Turkey

[7] Department of Pediatric Intensive Care Unit, Göztepe Prof. Dr. Süleyman Yalçın City Hospital, İstanbul Medeniyet University, Istanbul, Turkey

[8] Department of Pediatric Intensive Care Unit, İstanbul Medipol University, Istanbul, Turkey

[9] Department of Pediatric Intensive Care Unit, Sancaktepe Training and Research Hospital, University of Health Sciences, Istanbul, Turkey

[10] Department of Pediatric Intensive Care Unit, Pendik Training and Research Hospital, Marmara University, Istanbul, Turkey

[11] Department of Pediatric Intensive Care Unit, Başakşehir Çam Ve Sakura City Hospital, University of Health Sciences, Istanbul, Turkey

[12] Pediatric Infectious Diseases Clinic, Kanuni Sultan Suleyman Training and Research Hospital, University of Health Sciences, Istanbul, Turkey

[13] Department of Biostatistics and Medical Informatics, Faculty of Medicine, Kocaeli University, Kocaeli, Turkey