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Risk factors and mortality in children with severe pertussis: the role of exchange transfusion in a PICU

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Abstract

Objective Although multiple risk factors have been reported for adverse outcomes in children with severe pertussis, their predictive values and the benefits of interventions such as exchange transfusion remain poorly understood. Therefore, we aimed to comprehensively evaluate the risk factors associated with mortality in children with severe pertussis and assess the potential benefits of exchange transfusion therapy.

Methods A retrospective analysis of 170 pertussis patients admitted to the Pediatric Intensive Care Unit (PICU) between January 2018 and June 2024 was performed.

Results Among the 170 patients, 38 (22.35%) died. The death group exhibited significantly higher white blood cell (WBC) counts (67.31 vs. 28.41 × 10^9/L, $P < 0.001$), neutrophils (29.95 vs. 11.61 × 10^9/L, $P < 0.001$), and C-reactive protein (CRP) (29 vs. 8 mg/L, $P < 0.001$). Additionally, sepsis (39.47% vs. 9.09%, $P < 0.001$), shock (63.16% vs. 6.06%, $P < 0.001$), ARDS (23.68% vs. 2.27%, $P < 0.001$), and acute kidney injury (21.05% vs. 0.76%, $P < 0.001$) were more prevalent in the death group. ROC analysis showed that WBC counts had a predictive value for mortality (AUC = 0.75, sensitivity = 0.78, specificity = 0.68), with an optimal cutoff of 48.58 × 10^9/L.

Conclusion High WBC counts are significantly correlated with increased mortality risk in severe pertussis children, with a threshold of 48.58 × 10^9/L marking high risk. Although exchange transfusion can reduce WBC counts and improve symptoms, its benefit is limited in patients with severe secondary infections, necessitating tailored treatment strategies.

Keywords Pertussis, Risk factors, Exchange transfusion, Children, Mortality, PICU

Introduction

Pertussis is an acute infectious respiratory disease caused by *Bordetella pertussis* and is one of the top ten leading causes of death in children under the age of one worldwide. The infection rate is highest in infants, particularly those under 6 months of age, with the majority of deaths occurring in infants under 3 months. It is estimated that up to 400,000 pertussis-related deaths occur annually, with 90% of these deaths happening in developing countries [1–3]. Severe pertussis is a common cause of hospitalization in infants, accompanied by a high risk of mortality, placing a significant burden on healthcare systems [4, 5]. Many studies [6–8] have indicated that high white blood cell (WBC) counts are a risk factor for death in patients with pertussis, and some case reports [9–11] and studies [12, 13] begun to explore interventions such as exchange transfusions to address this issue.

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However, case reports and current research sample sizes— with the largest being 23 [14]—still lack strong persuasive power, making it difficult to draw consistent conclusions. Furthermore, discrepancies exist among studies regarding the specific WBC counts thresholds for predicting death and survival, indicating that our understanding of this important biomarker remains insufficient.

To further investigate the risk factors for mortality in severe pertussis, establish the optimal predictive value of high WBC counts in this condition, and evaluate the potential for improving prognosis through exchange transfusion therapy, we plan to conduct a larger case–control study with a more systematic design, aimed at validating and exploring effective intervention strategies.

Methods

Study design

Retrospective analysis of clinical data and prognostic outcomes of pertussis patients admitted to the Pediatric Intensive Care Unit (PICU) of Chongqing Medical University Children's Hospital from January 2018 to June 2024. The Institutional Review Committee of Chongqing Medical University Children's Hospital has approved this study. The informed consent was waived due to the retrospective design.

The diagnosis of pertussis was based on clinical manifestations and laboratory test results (positive PCR for *Bordetella pertussis*). Patients were identified by retrieving discharge diagnosis data from electronic medical databases. The inclusion criteria include patients admitted to the pediatric intensive care unit (PICU) due to severe pertussis. Excluded patients with severe underlying diseases (leukemia, liver failure, etc.) and those who originally had severe infections and pertussis infection was not the initial infection.

Data quality control and management

The data for this study were retrieved from the hospital's data center and collected using Excel spreadsheets. A dedicated personnel member managed the data, which were stored on a secure computer. Strict quality control measures were implemented to ensure data accuracy and completeness.

Data collection and definition of variables

Demographic and clinical data were collected, including age, gender, diagnosis(AKI,Acute kidney injury; ARDS, Acute respiratory distress syndrome;PH,pulmonary arterial hypertension; epilepsy, hypoproteinemia;sepsis; shock; respiratory failure; myocardial injury; hepatic injury) as well as the highest white blood cell count (WBC) before treatment (including lymphocyte absolute value, monocyte absolute value, neutrophil absolute value), platelet count (PLT), C-reactive protein (CRP), procalcitonin (PCT),alanine transaminase (ALT),bilirubin, creatinine, and laboratory tests for other respiratory pathogen infections. Laboratory specimens are taken upon admission. The WBC from the last test taken during hospitalization were also collected.

Imaging results were categorized into pneumonia, atelectasis, and lung consolidation. The treatment needs of patients during hospitalization were divided into use of vasoactive drugs, albumin, hormones, intravenous immune globulin (IVIG), extracorporeal membrane oxygenation (ECMO), ventilator, high frequency ventilation, invasive ventilation, exchange Transfusion (Double Blood Volume, a procedure where the patient's blood volume is replaced with donor blood). The primary focus of this study was to evaluate the frequency of mortality at any point.

Statistical analysis

This study used R 4.4.1 statistical analysis software, where the continuous data with skewed distribution was represented by M (IQR), and the rank sum test of two independent samples was used; The classified data is represented by n (%) and Chi-squared or Fisher's exact probability method is used. The difference between groups is considered statistically significant with $P < 0.05$. Patients are divided into Survivors group or Death group based on outcomes and Without or With groups based on whether they had exchange transfusion.

Results

A total of 170 children were included in this study (Table 1), with 132 (77.65%) survivors and 38 (22.35%) deaths.

Compared to survivors, the Death group had significantly higher WBC counts (67.31 vs. 28.41 $\times 10^9$/L, $P < 0.001$), lymphocytes (24.47 vs. 14.62 $\times 10^9$/L, $P = 0.034$), neutrophils (29.95 vs. 11.61 $\times 10^9$/L, $P < 0.001$), monocytes (2.90 vs. 1.23 $\times 10^9$/L, $P < 0.001$), and CRP levels (29 vs. 8 mg/L, $P < 0.001$). The PCT (0.22 vs. 0.11 ng/mL, $P < 0.001$) and bilirubin (9.30 vs. 6.00 μmol/L, $P = 0.035$) were also higher in the Death group, while PLT was lower (524 vs. 584 $\times 10^9$/L, $P = 0.021$).

The incidence of sepsis (39.47% vs. 9.09%, $P < 0.001$), shock (63.16% vs. 6.06%, $P < 0.001$), ARDS (23.68% vs. 2.27%, $P < 0.001$), and AKI (21.05% vs. 0.76%, $P < 0.001$) was significantly higher in the Death group. Regarding treatment, the Death group had a higher proportion of vasoactive drug use (92.11% vs. 47.73%, $P < 0.001$), albumin administration (92.11% vs. 67.42%, $P < 0.001$), ECMO support (7.89% vs. 0%, $P = 0.010$), and exchange transfusion (42.11% vs. 17.42%, $P = 0.001$). However, IVIG use

Table 1 Characteristics of patients according to outcome

Variables	Total ($n = 170$)	Survivors ($n = 132$)	Death ($n = 38$)	*P*
Age (day), M (IQR)	84 (49, 151)	84 (50, 161)	83 (48, 146)	0.599
Gender (male), n(%)	90 (52.94)	74 (56.06)	16 (42.11)	0.129
Immunization, n(%)	76 (44.71)	59 (44.70)	17 (44.74)	0.997
WBC ($\times 10^9$/l),M (IQR)	32.77 (17.68, 58.25)	28.41 (16.01, 47.36)	67.31 (29.31, 92.76)	<.001
Lymphocytic absolute value, M (IQR)	15.18 (7.68, 27.20)	14.62 (7.22, 24.04)	24.47 (9.79, 32.10)	0.034
Neutrophils absolute value, M (IQR)	13.62 (7.20, 23.83)	11.61 (6.37, 19.13)	29.95 (14.52, 49.94)	<.001
Monocytes absolute value, M (IQR)	1.44 (0.73, 2.80)	1.23 (0.70, 2.15)	2.90 (1.25, 4.87)	<.001
PLT ($\times 10^9$/l), M (IQR)	565 (466, 708)	584 (481, 715)	524 (330, 666)	0.021
CRP (mg/l), M (IQR)	8 (8, 22)	8 (8, 14)	29 (8, 45)	<.001
PCT (ng/ml), M (IQR)	0.11 (0.07, 0.31)	0.10 (0.07, 0.18)	0.22 (0.11, 0.63)	<.001
Bilirubin (μmol/l), M (IQR)	6.50 (2.00, 13.68)	6.00 (1.90, 12.07)	9.30 (4.20, 21.92)	0.035
Creatinine (μmol/l), M (IQR)	21.50 (17.52, 25.48)	21.00 (17.90, 25.20)	22.20 (16.00, 26.30)	0.830
ALT (U/L), M (IQR)	34.00 (23.85, 47.00)	33.15 (23.60, 46.00)	37.70 (26.10, 53.85)	0.205
PCO_2(mmHg), M (IQR)	43.30 (37.00, 52.00)	43.00 (37.00, 49.60)	50.75 (40.25, 56.90)	0.050
PO_2(mmHg), M (IQR)	86.40 (65.03, 118.50)	86.60 (65.07, 111.25)	85.00 (65.25, 148.00)	0.440
PH, n(%)	18 (10.59)	16 (12.12)	2 (5.26)	0.362
Epilepsy, n(%)	8 (4.71)	7 (5.30)	1 (2.63)	0.802
Hypoproteinemia, n(%)	74 (43.53)	58 (43.94)	16 (42.11)	0.841
Sepsis, n(%)	27 (15.88)	12 (9.09)	15 (39.47)	<.001
Shock, n(%)	32 (18.82)	8 (6.06)	24 (63.16)	<.001
Respiratory failure, n(%)	164 (96.47)	128 (96.97)	36 (94.74)	0.874
ARDS, n(%)	12 (7.06)	3 (2.27)	9 (23.68)	<.001
Myocardial injury, n(%)	50 (29.41)	35 (26.52)	15 (39.47)	0.122
Hepatic injury, n(%)	34 (20.00)	24 (18.18)	10 (26.32)	0.269
AKI, n(%)	9 (5.29)	1 (0.76)	8 (21.05)	<.001
Other respiratory pathogen infections[a], n(%)	129 (75.88)	97 (73.48)	32 (84.21)	0.173
Pneumonia, n(%)	165 (97.06)	127 (96.21)	38 (100.00)	0.501
Atelectasis, n(%)	66 (38.82)	54 (40.91)	12 (31.58)	0.298
Lung consolidation, n(%)	121 (71.18)	92 (69.70)	29 (76.32)	0.427
Vasoactive drugs, n(%)	98 (57.65)	63 (47.73)	35 (92.11)	<.001
Albumin, n(%)	124 (72.94)	89 (67.42)	35 (92.11)	0.003
Hormones, n(%)	98 (57.65)	78 (59.09)	20 (52.63)	0.478
IVIG, n(%)	110 (64.71)	91 (68.94)	19 (50.00)	0.031
ECMO, n(%)	3 (1.76)	0 (0.00)	3 (7.89)	0.010
Ventilator, n(%)	155 (91.18)	117 (88.64)	38 (100.00)	0.064
High frequency ventilation, n(%)	11 (6.47)	7 (5.30)	4 (10.53)	0.436
Invasive ventilation, n(%)	142 (83.53)	107 (81.06)	35 (92.11)	0.106
Exchange transfusion, n(%)	39 (22.94)	23 (17.42)	16 (42.11)	0.001

ALT Alanine transaminase, *AKI* Acute kidney injury, *ARDS* Acute respiratory distress syndrome, *CRP* C-reactive protein, *ECMO* Extracorporeal membrane oxygenation, *IQR* Interquartile range, *IVIG* Intravenous immune globulin, *M* Median, *PCT* Procalcitonin, PCO_2 Partial pressure of carbon dioxide, PO_2 Oxygen partial pressure, *PLT* Platelet, *PH* Pulmonary arterial hypertension, *WBC* White blood cells

[a] Other respiratory pathogen infections include the following pathogens: *Adenovirus, Epstein-Barr Virus, Bocavirus, Parainfluenza Virus, Coronavirus, Respiratory Syncytial Virus, Influenza Virus, Acinetobacter baumannii, Citrobacter freundii, Enterobacter cloacae, Escherichia coli, Klebsiella pneumoniae, Streptococcus pneumoniae, Haemophilus influenzae, Staphylococcus aureus, Moraxella catarrhalis, Enterobacter aerogenes, Serratia marcescens, Leminospira nodosa, Methicillin-Resistant Staphylococcus aureus, Elizabethkingia meningoseptica, Klebsiella oxytoca, Achromobacter xylosoxidans, Pseudomonas aeruginosa, Lysinibacillus sphaericus, Candida albicans, Chlamydia pneumoniae, Mycoplasma pneumoniae, Chlamydia, Chlamydia trachomatis*, and others

was lower in the Death group (50.00% vs. 68.94%, $P=$ 0.031).

Patients who underwent exchange transfusion had higher WBC counts (66.12 vs. 25.42 $\times 10^9$/L, $P<$ 0.001), lymphocytes (28.22 vs. 12.11 $\times 10^9$/L, $P<$ 0.001), neutrophils (27.57 vs. 10.26 $\times 10^9$/L, $P<$ 0.001), monocytes (2.84 vs. 1.09 $\times 10^9$/L, $P<$ 0.001), and CRP (18 vs. 8 mg/L, $P=$ 0.001), as well as a higher incidence of shock (48.72% vs. 9.92%, $P<$ 0.001) and increased mortality (41.03% vs. 16.79%, $P=$ 0.001) compared to those without exchange transfusion (Table 2).

Among patients who received exchange transfusion, the Death group had significantly higher WBC counts (80.06 vs. 62.40 $\times 10^9$/L, $P=$ 0.017), neutrophils (42.75 vs. 22.47 $\times 10^9$/L, $P<$ 0.001), monocytes (2.90 vs. 1.23 $\times 10^9$/L, $P<$ 0.001), and CRP (32 vs. 8 mg/L, $P=$ 0.019), whereas lymphocyte levels showed no significant difference ($P=0.944$). And there also had a higher proportion of sepsis patients (31.25% vs. 4.35%, $P=$ 0.033), shock patients (48.72% vs. 9.92%, $P<$ 0.001) and more vasoactive drugs (74.36% vs. 52.67%, $P=$ 0.016) use. In addition, the PO2 of the Death group (87.05 vs. 65.10 mmHg, $P=$ 0.009) was higher than that of the Survivors group (Table 3).

In the ROC curve analysis, WBC counts demonstrated a predictive value for mortality, with an AUC of 0.75 (95% CI: 0.64–0.85). The optimal cutoff value was 48.58 $\times 10^9$/L, yielding an accuracy of 0.76, sensitivity of 0.78, and specificity of 0.68 (Fig. 1 Diagnostic Performance of WBC: ROC Curve Analysis for Mortality Prediction).

Univariate analysis identified sepsis (OR $=6.52$, 95% CI: 2.70–15.73, $P<$ 0.001) and shock (OR $=26.57$, 95% CI: 10.05–70.26, $P<$ 0.001) as significant predictors of mortality (Table 4). In the multivariate model, both remained significant, with sepsis (OR $=3.79$, 95% CI: 1.21–11.91, $P=$ 0.023) and shock (OR $=13.88$, 95% CI: 4.72–40.82, $P<$ 0.001). WBC counts also remained a significant predictor (OR $=1.02$, 95% CI: 1.01–1.04, $P<$ 0.001).

Table 5 displayed the highest WBC levels recorded prior to treatment and the results of the final test for all patients categorized into Survivors and Death groups who underwent exchange transfusion. Supplementary Table 1 provided clinical characteristics of patients who received ECMO treatment in comparison to those who did not.

Discussion

We conducted a retrospective analysis of children with severe pertussis admitted to the PICU over the past 6 years. Our results revealed that sepsis, shock, and elevated WBC counts significantly increased the risk of adverse outcomes. In addition, patients receiving exchange transfusion had more severe conditions with higher mortality; among these patients, the proportions of sepsis and shock—as well as elevated WBC counts—were significantly greater in those who died. WBC counts also demonstrated good predictive ability for distinguishing between death and survival (AUC of 0.76, 95% CI: 0.69–0.82) with an optimal cutoff value of 48.58.

The present study identified a mortality rate of 22% (38/170). This mortality rate is somewhat higher compared to other reports. One study reported a mortality of 14% among 49 children with pertussis in intensive care, while a 2021 study noted 13 deaths among 38 ICU admissions [15, 16]. These differences may be attributable to variations in patient populations, clinical settings, or treatment protocols.

One of the central findings of our study is the association between elevated WBC counts and mortality. Consistent with previous reports, the WBC counts in the death group were significantly higher than those in survivors [17]. Specifically, WBC counts of $\geq 30 \times 10\text{^}9$/L or $\geq 50 \times 10\text{^}9$/L were significantly associated with mortality, and when the WBC count exceeded $70 \times 10\text{^}9$/L, the odds ratio for mortality soared to 230.66 [15, 18, 19]. In our study, ROC curve analysis identified an optimal cutoff value of $48.58 \times 10\text{^}9$/L (AUC $=0.76$, 95% CI: 0.69–0.82). Differences in thresholds among studies may be attributed to variations in population age (this study mainly focused on infants under 3 months) or differences in the timing of treatment.

Secondary infections also emerged as a critical factor in our cohort. We observed that patients in the death group not only had higher neutrophil counts and CRP levels, but also a greater incidence of sepsis compared to survivors. Similar findings have been reported by other researchers [20, 21]. Even after exchange transfusion—which effectively reduced overall WBC counts—the persistence of elevated inflammatory markers suggests that secondary infections may continue to drive adverse outcomes. This is further supported by the high rate of respiratory infections (up to 75.88% in our cohort) and comparable findings in other studies [22].

Exchange transfusion therapy for severe pertussis patients is based on theoretical foundations. Some researchers suggest that an increase in white blood cell counts may impair pulmonary microcirculation, leading to pulmonary arterial hypertension, heart failure, and hypoxemia [23, 24]. However, Winter et al. pointed out that pertussis toxin might cause more extensive and destructive damage to cardiac and respiratory functions by inhibiting key Gi protein signaling pathways in the heart and lungs [6]. They proposed that leukocytosis may simply be a marker of severe pertussis toxin (PT)-related disease rather than a direct cause of death, yet exchange transfusion could still be beneficial by reducing

Table 2 Characteristics of patients according to outcome

Variables	Total ($n=170$)	Without ($n=131$)	With ($n=39$)	*P*
Age (day), M (IQR)	84 (49, 151)	85 (48, 141)	71 (51, 192)	0.732
Gender (male), n(%)	90 (52.94)	73 (55.73)	17 (43.59)	0.183
Immunization, n(%)	76 (44.71)	59 (45.04)	17 (43.59)	0.873
WBC ($\times 10^9$/l),M (IQR)	32.77 (17.68, 58.25)	25.42 (15.38, 42.33)	66.12 (55.26, 83.10)	<.001
Lymphocytic absolute value, M (IQR)	15.18 (7.68, 27.20)	12.11 (6.14, 21.66)	28.22 (23.40, 37.78)	<.001
Neutrophils absolute value, M (IQR)	13.62 (7.20, 23.83)	10.26 (6.29, 16.92)	27.57 (20.33, 39.46)	<.001
Monocytes absolute value, M (IQR)	1.44 (0.73, 2.80)	1.09 (0.66, 1.94)	2.84 (2.12, 4.57)	<.001
PLT ($\times 10^9$/l), M (IQR)	565(466, 708)	548 (446, 690)	620 (527, 743)	0.064
CRP (mg/l), M (IQR)	8 (8, 22)	8 (8, 15)	18 (8, 34)	0.001
PCT (ng/ml), M (IQR)	0.11 (0.07, 0.31)	0.11 (0.07, 0.30)	0.13 (0.08, 0.33)	0.278
Bilirubin (μmol/l), M (IQR)	6.50 (2.00, 13.68)	7.00 (2.00, 13.55)	6.30 (3.00, 13.15)	0.956
Creatinine (μmol/l), M (IQR)	21.50 (17.52, 25.48)	22.00 (18.00, 25.75)	21.00 (16.00, 25.20)	0.162
ALT (U/L), M (IQR)	34.00 (23.85, 47.00)	35.60 (26.25, 48.15)	30.60 (19.50, 42.70)	0.029
PCO_2(mmHg), M (IQR)	43.30 (37.00, 52.00)	43.00 (36.50, 50.25)	49.00 (40.40, 55.05)	0.03
PO_2(mmHg), M (IQR)	86.40 (65.03, 118.50)	89.10 (67.35, 124.50)	78.20 (61.50, 97.20)	0.142
PH, n(%)	18 (10.59)	15 (11.45)	3 (7.69)	0.709
Epilepsy, n(%)	8 (4.71)	5 (3.82)	3 (7.69)	0.567
Hypoproteinemia, n(%)	74 (43.53)	58 (44.27)	16 (41.03)	0.719
Sepsis, n(%)	27 (15.88)	21 (16.03)	6 (15.38)	0.923
Shock, n(%)	32 (18.82)	13 (9.92)	19 (48.72)	<.001
Respiratory failure, n(%)	164 (96.47)	127 (96.95)	37 (94.87)	0.903
ARDS, n(%)	12 (7.06)	9 (6.87)	3 (7.69)	1.000
Myocardial injury, n(%)	50 (29.41)	34 (25.95)	16 (41.03)	0.070
ECMO, n(%)	3 (1.76)	3 (2.29)	0 (0.00)	1.000
Hepatic injury, n(%)	34 (20.00)	29 (22.14)	5 (12.82)	0.202
AKI, n(%)	9 (5.29)	6 (4.58)	3 (7.69)	0.723
Other respiratory pathogen infections[a], n(%)	129 (75.88)	100 (76.34)	29 (74.36)	0.800
Pneumonia, n(%)	165 (97.06)	128 (97.71)	37 (94.87)	0.703
Atelectasis, n(%)	66 (38.82)	54 (41.22)	12 (30.77)	0.240
Lung consolidation, n(%)	121 (71.18)	90 (68.70)	31 (79.49)	0.192
Vasoactive drugs, n(%)	98 (57.65)	69 (52.67)	29 (74.36)	0.016
Albumin, n(%)	124 (72.94)	86 (65.65)	38 (97.44)	<.001
Hormones, n(%)	98 (57.65)	78 (59.54)	20 (51.28)	0.359
IVIG, n(%)	110 (64.71)	86 (65.65)	24 (61.54)	0.637
Ventilator, n(%)	155 (91.18)	117 (89.31)	38 (97.44)	0.212
High frequency ventilation, n(%)	11 (6.47)	6 (4.58)	5 (12.82)	0.143
Invasive ventilation, n(%)	142 (83.53)	106 (80.92)	36 (92.31)	0.092
Mortality,n (%)	38 (22.35)	22 (16.79)	16 (41.03)	0.001

ALT Alanine transaminase, *AKI* Acute kidney injury, *ARDS* Acute respiratory distress syndrome, *CRP* C-reactive protein, *ECMO* Extracorporeal membrane oxygenation, *IQR* Interquartile range, *IVIG* Intravenous immune globulin, *M* Median, *PCT* Procalcitonin, PCO_2 Partial pressure of carbon dioxide, PO_2 Oxygen partial pressure, *PLT* Platelet, *PH* Pulmonary arterial hypertension, *WBC* White blood cells

[a] Other respiratory pathogen infections include the following pathogens: *Adenovirus, Epstein-Barr Virus, Bocavirus, Parainfluenza Virus, Coronavirus, Respiratory Syncytial Virus, Influenza Virus, Acinetobacter baumannii, Citrobacter freundii, Enterobacter cloacae, Escherichia coli, Klebsiella pneumoniae, Streptococcus pneumoniae, Haemophilus influenzae, Staphylococcus aureus, Moraxella catarrhalis, Enterobacter aerogenes, Serratia marcescens, Leminospira nodosa, Methicillin-Resistant Staphylococcus aureus, Elizabethkingia meningoseptica, Klebsiella oxytoca, Achromobacter xylosoxidans, Pseudomonas aeruginosa, Lysinibacillus sphaericus, Candida albicans, Chlamydia pneumoniae, Mycoplasma pneumoniae, Chlamydia, Chlamydia trachomatis*, and others

circulating PT levels and thereby mitigating other potentially fatal effects.

Since Romano et al. published the first report in 2004 on severe pertussis patients receiving double-volume exchange transfusion, an increasing number of case reports and small-scale studies have focused on this therapeutic approach [25, 26]. Our data show that survivors undergoing exchange transfusion experienced a

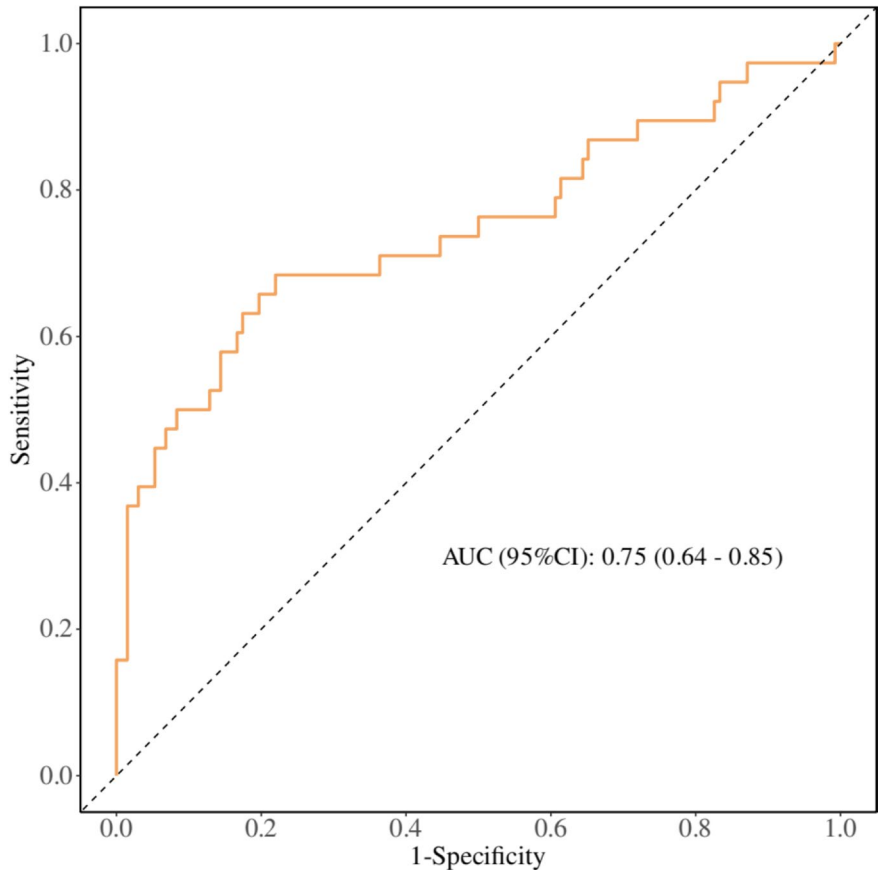
Table 3 Characteristics of exchange transfusion patients according to outcome

Variables	Total ($n=39$)	Survivors ($n=23$)	Deceased ($n=16$)	*P*
Age (day), M (IQR)	71 (51, 192)	94(54, 244)	63 (40, 94)	0.050
Gender (male), n(%)	22 (56.41)	11 (47.83)	11 (68.75)	0.325
Immunization, n(%)	17 (43.59)	12 (52.17)	5 (31.25)	0.325
WBC ($\times 10^9$/l),M (IQR)	66.12 (55.26, 83.10)	62.40 (50.43, 70.32)	80.06 (59.24, 92.89)	0.017
Lymphocytic absolute value, M (IQR)	28.22 (23.40, 37.78)	28.22 (22.88, 39.40)	27.41 (24.56, 34.91)	0.944
Neutrophils absolute value, M (IQR)	27.57 (20.33, 39.46)	22.47 (18.27, 31.67)	42.75 (28.19, 53.60)	<.001
Monocytes absolute value, M (IQR)	2.84 (2.12, 4.57)	2.45 (2.03, 3.98)	3.76 (2.27, 4.91)	0.199
PLT ($\times 10^9$/l), M (IQR)	620 (527, 743)	620 (547, 743)	655(508, 742)	0.989
CRP (mg/l), M (IQR)	18 (8, 34)	8 (8, 22)	32 (16, 44)	0.019
PCT (ng/ml), M (IQR)	0.13 (0.08, 0.33)	0.10 (0.07, 0.26)	0.16 (0.12, 0.34)	0.106
Bilirubin (μmol/l), M (IQR)	6.30 (3.00, 13.15)	6.00 (1.95, 9.60)	9.45 (4.60, 18.77)	0.153
ALT (U/L), M (IQR)	30.60 (19.50, 42.70)	32.20 (21.00, 48.80)	24.50 (18.75, 33.50)	0.145
Creatinine (μmol/l), M (IQR)	21.00 (16.00, 25.20)	21.00 (16.00, 23.45)	19.55 (14.00, 26.50)	0.864
PCO_2(mmHg), M (IQR)	49.00 (40.40, 55.05)	43.40 (39.60, 53.50)	51.85 (42.70, 59.62)	0.242
PO2(mmHg), M (IQR)	78.20 (61.50, 97.20)	65.10 (58.00, 88.95)	87.05 (73.07, 163.25)	0.009
PH, n(%)	3 (7.69)	2 (8.70)	1 (6.25)	1.000
Epilepsy, n(%)	3 (7.69)	2 (8.70)	1 (6.25)	1.000
Hypoproteinemia, n(%)	16 (41.03)	8 (34.78)	8 (50.00)	0.509
Sepsis, n(%)	6 (15.38)	1 (4.35)	5 (31.25)	0.033
Shock, n(%)	19 (48.72)	4 (17.39)	15 (93.75)	<.001
Respiratory failure, n(%)	37 (94.87)	23 (100.00)	14 (87.50)	0.162
ARDS, n(%)	3 (7.69)	0 (0.00)	3 (18.75)	0.061
Myocardial injury, n(%)	16 (41.03)	8 (34.78)	8 (50.00)	0.509
Hepatic injury, n(%)	5 (12.82)	3 (13.04)	2 (12.50)	1.000
AKI, n(%)	3 (7.69)	0 (0.00)	3 (18.75)	0.061
Other respiratory pathogen infections[a], n(%)	29 (74.36)	16 (69.57)	13 (81.25)	0.480
Atelectasis, n(%)	12 (30.77)	10 (43.48)	2 (12.50)	0.076
Lung consolidation, n(%)	31 (79.49)	19 (82.61)	12 (75.00)	0.694
Vasoactive drugs, n(%)	29 (74.36)	13 (56.52)	16 (100.00)	0.002
Albumin, n(%)	38 (97.44)	22 (95.65)	16 (100.00)	1.000
Hormones, n(%)	20 (51.28)	12 (52.17)	8 (50.00)	1.000
IVIG, n(%)	24 (61.54)	16 (69.57)	8 (50.00)	0.318
Ventilator, n(%)	38 (97.44)	22 (95.65)	16 (100.00)	1.000
High frequency ventilation, n(%)	5 (12.82)	2 (8.70)	3 (18.75)	0.631
Invasive ventilation, n(%)	36 (92.31)	21 (91.30)	15 (93.75)	1.000

ALT Alanine transaminase, *AKI* Acute kidney injury, *ARDS* Acute respiratory distress syndrome, *CRP* C-reactive protein, *IQR* Interquartile range, *IVIG* Intravenous immune globulin, *M* Median, *PCT* Procalcitonin, PCO_2 Partial pressure of carbon dioxide, PO_2 Oxygen partial pressure, *PLT* Platelet, *PH* Pulmonary arterial hypertension, *WBC* White blood cells

[a] Other respiratory pathogen infections include the following pathogens: *Adenovirus, Epstein-Barr Virus, Bocavirus, Parainfluenza Virus, Coronavirus, Respiratory Syncytial Virus, Influenza Virus, Acinetobacter baumannii, Citrobacter freundii, Enterobacter cloacae, Escherichia coli, Klebsiella pneumoniae, Streptococcus pneumoniae, Haemophilus influenzae, Staphylococcus aureus, Moraxella catarrhalis, Enterobacter aerogenes, Serratia marcescens, Leminospira nodosa, Methicillin-Resistant Staphylococcus aureus, Elizabethkingia meningoseptica, Klebsiella oxytoca, Achromobacter xylosoxidans, Pseudomonas aeruginosa, Lysinibacillus sphaericus, Candida albicans, Chlamydia pneumoniae, Mycoplasma pneumoniae, Chlamydia, Chlamydia trachomatis*, and others

dramatic reduction in white blood cell counts (from a median of 62.40 ×10^9/L to 11.41 ×10^9/L), whereas the decrease was less pronounced in non-survivors (from 80.06 ×10^9/L to 45.43 ×10^9/L). Furthermore, the death group exhibited persistently elevated absolute neutrophil counts and CRP levels, suggesting that exchange transfusion may not fully address underlying risk factors such as secondary infections. These findings are consistent with previous reports [13, 20, 22]. A recent study reported that rapid proliferation



AUC (95%CI)	Accuracy (95%CI)	Sensitivity (95%CI)	Specificity (95%CI)	PPV (95%CI)	NPV (95%CI)	Cut off
0.75 (0.64-0.85)	0.76 (0.69-0.82)	0.78 (0.71 - 0.85)	0.68 (0.54 - 0.83)	0.90 (0.84 - 0.95)	0.47 (0.34 - 0.60)	48.58

Fig. 1 Diagnostic Performance of WBC: ROC Curve Analysis for Mortality Prediction

Table 4 Univariate and multivariate regression analysis

Variables	Univariate			Multivariate		
	β	*P*	OR (95%CI)	β	*P*	OR (95%CI)
Immunization	0	0.997	1.00 (0.48 ~ 2.07)			
PH	− 0.91	0.24	0.40 (0.09 ~ 1.84)			
Sepsis	1.88	<.001	6.52 (2.70 ~ 15.73)	1.33	0.023	3.79 (1.21 ~ 11.91)
Shock	3.28	<.001	26.57 (10.05 ~ 70.26)	2.63	<.001	13.88 (4.72 ~ 40.82)
Myocardial injury	0.59	0.125	1.81 (0.85 ~ 3.85)			
Age (day)	0	0.315	1.00 (1.00 ~ 1.00)			
WBC ($\times 10^9$/l)	0.04	<.001	1.04 (1.02 ~ 1.05)	0.02	0.029	1.02 (1.01 ~ 1.04)
PCO_2(mmHg)	0.03	0.049	1.03 (1.01 ~ 1.06)			

PCO_2 Partial pressure of carbon dioxide, *WBC* White blood cells, *OR* odds ratio, *CI* confidence interval

Table 5 Characteristics of patients after exchange transfusion according to outcome

Variables	Survivors ($n=23$)		Deceased ($n=16$)	
	Before treatment	last detection	Before treatment	last detection
WBC ($\times 10^9$/l),M (IQR)	62.40 (50.43, 70.32)	11.41 (10.05, 15.09)	80.06 (59.24, 92.89)	45.43 (26.12, 55.00)
Lymphocytic absolute value, M (IQR)	28.22 (22.88, 39.40)	6.11 (5.20, 8.67)	27.41 (24.56, 34.91)	15.36 (5.41, 18.37)
Monocytes absolute value, M (IQR)	2.45 (2.03, 3.98)	0.72 (0.56, 1.00)	3.76 (2.27, 4.91)	1.43 (0.82, 3.80)
Neutrophils absolute value, M (IQR)	22.47 (18.27, 31.67)	3.85 (2.41, 5.09)	42.75 (28.19, 53.60)	23.82 (18.75, 32.74)
PLT ($\times 10^9$/l), M (IQR)	620 (547, 743)	591 (476, 715)	655 (508, 742)	153 (68, 249)
CRP (mg/l), M (IQR)	8 (8, 22)	8(8, 8)	32 (16, 44)	37 (27, 68)

CRP C-reactive protein, *IQR* Interquartile range, *M* Median, *PCT* Procalcitonin, *WBC* White blood cells

of neutrophils during acute infection may exacerbate organ injury, which further explains the high neutrophil levels observed in the death group [14].

Shock was significantly more prevalent in death group, consistent with reports linking pertussis-associated pulmonary hypertension to low cardiac output and fatal circulatory collapse [18, 24]. Other complications, including AKI and ARDS, were significantly more frequent in the death group, suggesting that pertussis-associated organ dysfunction may contribute to fatal outcomes [27]. Moreover, blood gas analysis revealed significant differences in PCO_2 between groups, indicating that CO_2 retention might further impact prognosis. Although the higher PO_2 observed in the death group likely reflects the early use of high-concentration oxygen therapy, this phenomenon merits additional investigation.

Finally, while the death group had a younger median age compared to survivors and a lower proportion received IVIG therapy, the influence of these factors on patient outcomes remains to be fully elucidated. Given the limited evidence regarding IVIG in pertussis management [28], further studies are necessary to determine its potential therapeutic role.

Limitations

Although this study provides valuable data on the clinical characteristics and mortality risk factors of children with severe pertussis, there are also several limitations. The study is retrospective, relying on clinical records that may contain omissions or inconsistencies, which could affect the accuracy of the results. In addition, as a single-center study, the external generalizability of the findings is limited. Even though the overall sample size is relatively large (170 cases), some subgroup analyses, such as the comparison between the exchange transfusion group and the non-exchange transfusion group, involve smaller samples that may reduce statistical significance and increase random error. Furthermore, the data were collected from January 2018 to June 2024, and changes in disease prevalence patterns during this period might have influenced the results.

Conclusion

Our study highlights the complex nature of severe pertussis, where hyperleukocytosis, secondary infections, and multi-organ complications collectively contribute to mortality. Notably, high WBC counts are significantly correlated with the risk of death, with ROC curve analysis indicating that when WBC counts exceed 48.58×10^9/L, the risk of mortality increases significantly. This suggests that WBC counts can serve as a valuable clinical indicator for identifying high-risk children and guiding early intervention. Secondary infections play a critical role in disease progression, emphasizing the need for strengthened infection control and timely intervention. While exchange transfusion may be beneficial for some severe children, its efficacy varies, as some patients remain at risk of death despite treatment. Therefore, its use should be carefully evaluated based on individual clinical conditions, particularly in children with high WBC counts. Future research should focus on establishing standardized thresholds for treatment initiation and developing integrated management strategies to improve patient outcomes.

Supplementary Information

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Supplementary Material 1.

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Authors' contributions
JH, CL and FX designed, supervised and revised the paper. JH also contributed to the data collection, data analysis, literature search, table, figures design and writing. SC contributed to the data analysis, literature search and table, figures

revisions. YQ participated in the database management and statistical analysis. All authors read and approved the final manuscript.

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Data availability
Data available on request from the authors. The data that support the findings of this study are available from the corresponding author, upon reasonable request.

Declarations

Ethics approval and consent to participate
This study was approved by the Ethics Committee (Institutional Review Board of Children's Hospital of Chongqing Medical University). The ethical considerations for this study are based on the guidelines provided by the World Medical Association (WMA) and the International Committee on Medical Ethics and Safety (CIOMS).

Consent for publication
N/A.

Competing interests
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