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Serum calcium and mortality in pediatric pneumonia patients admitted to the PICU: a retrospective cohort study

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This study investigates serum calcium's prognostic value in pediatric pneumonia, focusing on its correlation with PICU mortality, to enhance understanding and treatment approaches in this field. Data from 414 pediatric pneumonia patients (2010–2019) admitted to the intensive care units at the Children's Hospital, Zhejiang University School of Medicine were analyzed. The study utilized restricted cubic spline analysis, Cox proportional hazard regression, and Kaplan–Meier survival curve analysis to assess the relationship between serum calcium levels at admission and PICU mortality risk. After adjusting for multivariate factors, for each 1 mmol/dL increase in serum calcium, the risk of mortality decreased by 24% (HR: 0.76, 95% CI 0.67–0.87). Among the three levels of serum calcium groups, higher serum calcium levels were linked to a 63% reduction in the mortality rate compared to lower levels (HR: 0.37, 95% CI 0.16–0.84). The cumulative hazard estimates of mortality significantly differed across serum calcium groups (log-rank *P* = 0.032). This association was consistent across diverse subgroups (*P* for interaction > 0.05). Higher serum calcium levels are associated with decreased PICU mortality in pediatric pneumonia, highlighting its potential as a prognostic marker.

Keywords Calcium, Mortality, Pediatric, Pneumonia

Pneumonia, an acute lower respiratory tract inflammation, continues to be a leading cause of child mortality worldwide. Annually, it claims the lives of over 2 million individuals, with nearly 30% of these cases occurring in children under the age of 5[1–3]. While the period from 2000 to 2015 witnessed a decline in pneumonia-related child fatalities, attributed to advancements in vaccination and public health measures, it continues to pose a significant health threat, especially to children with underlying conditions such as immunodeficiency, airway hyperreactivity, or cardiovascular issues[3–5].

Calcium, a multifaceted intracellular messenger, plays a vital role in various biological processes including gene expression, cell proliferation, and cell death[6]. It is crucial in both healthy cellular functions and in the pathology of diseases like pneumonia. The role of calcium in the mechanisms of pneumonia is particularly complex. During cellular infection, calcium facilitates the apoptotic elimination of pathogens as part of the host defense mechanism[7]. Concurrently, it can be exploited by viruses to enhance their replication and invasion capabilities, notably in coronavirus infections, where alterations in calcium homeostasis are closely linked to viral spread and activation of inflammatory responses in the host[7–9].

Calcium's regulation of the immune system's response to infection is crucial, and its dysregulation can exacerbate illness. Recent studies indicate that calcium disturbances are prevalent in various clinical contexts, including pediatric sepsis[10], traumatic injury[11], childhood diarrhea[12], adult cardiovascular disease[13,14], acute kidney injury[15], and all-cause mortality among inpatients[16], particularly with hypocalcemia,as observed in COVID-19 pneumonia patients[17]. However, the specific role and mechanisms of calcium in pediatric pneumonia, especially its association with the mortality rate of pediatric pneumonia patients, remain under-explored.

Thus, this study aims to delve into whether there is an association between serum calcium levels at admission and the PICU mortality of pediatric pneumonia patients. By comprehensively understanding this relationship, we aspire to offer new perspectives on the disease progression and prognosis of pneumonia patients. We anticipate

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that this research will not only enrich our understanding of the relationship between calcium and pneumonia but also provide substantial support for future clinical practices and treatment decisions, thereby contributing to the improvement of treatment outcomes and survival rates for pneumonia patients.

Results

Baseline characteristics of study subjects

We enrolled a total of 414 patients, with an average age of 22.9 ± 33.6 months. Male patients constituted 42.0% of the total study cohort. The overall PICU mortality was 11.1%. Table 1 presents the baseline characteristics of patients grouped according to serum calcium levels. The group with higher serum calcium exhibited higher levels of hemoglobin, albumin, cholesterol, serum sodium, serum potassium, and monocytes, and these differences were statistically significant ($P < 0.05$). Conversely, this group showed lower levels of lactate dehydrogenase (LDH) and aspartate aminotransferase (AST), as well as a lower PICU mortality rate. However, there were no statistically significant differences in terms of gender, oxygen saturation, blood urea nitrogen (BUN), gamma-glutamyl transferase (GGT) (Table 1).

Variables	Total (n = 414)	Q1 ≤ 21.9 (n = 137)	22.0 ≤ Q2 ≤ 23.5 (n = 136)	Q3 ≥ 23.6 (n = 141)	*P* value
Serum Calcium (mmol/dL)	22.6 ± 2.1	20.3 ± 1.7	22.7 ± 0.5	24.7 ± 0.8	< 0.001
Gender, n (%)					0.081
Male	174 (42.0)	47 (34.3)	63 (46.3)	64 (45.4)	
Female	240 (58.0)	90 (65.7)	73 (53.7)	77 (54.6)	
Age (month)	7.0 (2.0, 22.0)	16.0 (4.0, 48.0)	6.0 (3.0, 21.2)	4.0 (2.0, 10.0)	< 0.001
Hemoglobin (g/L)	107.1 ± 19.7	101.9 ± 21.7	107.6 ± 18.7	112.0 ± 17.1	< 0.001
RDW (CV%)	14.7 ± 2.3	14.8 ± 2.4	14.4 ± 1.8	14.7 ± 2.6	0.422
White blood cell (10^9/L)	10.1 (6.8, 14.5)	10.0 (6.0, 16.4)	8.4 (6.4, 12.4)	11.0 (8.7, 14.9)	0.004
Lymphocyte (10^9/L)	2.7 (1.6, 5.3)	2.1 (1.3, 3.9)	2.6 (1.5, 4.2)	4.4 (2.3, 6.8)	< 0.001
Neutrophil (10^9/L)	5.1 (2.9, 9.0)	6.8 (4.0, 10.7)	4.6 (2.4, 7.2)	4.6 (2.8, 7.8)	0.003
Monocyte (10^9/L)	0.6 (0.3, 1.0)	0.5 (0.2, 0.9)	0.5 (0.3, 0.8)	0.7 (0.4, 1.1)	0.008
Platelet (10^9/L)	316.0 (218.5, 404.5)	261.5 (166.8, 340.8)	297.0 (223.0, 378.0)	372.5 (291.2, 490.2)	< 0.001
CRP (g/L)	21.5 ± 30.7	32.1 ± 40.8	19.0 ± 26.2	12.2 ± 14.1	< 0.001
PH	7.3 ± 0.1	7.4 ± 0.1	7.3 ± 0.1	7.3 ± 0.1	0.868
Oxygen saturation (%)	89.4 ± 15.3	88.5 ± 14.0	90.2 ± 16.6	89.5 ± 15.3	0.674
Lactic acid (mmol/L)	1.9 (1.3, 2.9)	1.6 (1.2, 2.6)	1.9 (1.3, 2.6)	2.3 (1.6, 3.2)	< 0.001
ALT (U/L)	23.0 (16.0, 41.0)	27.0 (16.0, 54.0)	22.0 (16.0, 37.0)	22.0 (16.0, 35.5)	0.183
AST (U/L)	45.0 (33.0, 73.0)	56.5 (34.0, 99.5)	45.0 (32.0, 70.0)	41.0 (33.0, 53.0)	0.006
Albumin (g/L)	38.2 ± 6.0	33.1 ± 5.4	39.2 ± 4.3	42.1 ± 4.5	< 0.001
Cholesterol (mmol/L)	3.3 ± 1.1	2.9 ± 1.3	3.2 ± 0.9	3.7 ± 1.0	< 0.001
Sodium (mmol/L)	137.4 ± 4.9	136.3 ± 5.9	137.6 ± 4.9	138.4 ± 3.5	0.003
Potassium (mmol/L)	4.1 ± 0.7	3.8 ± 0.8	4.1 ± 0.6	4.3 ± 0.6	< 0.001
Chloride (mmol/L)	105.2 ± 5.6	105.8 ± 5.9	104.5 ± 5.0	105.3 ± 5.7	0.2
Triglycerides (mmol/L)	1.0 (0.7, 1.3)	1.1 (0.8, 1.4)	1.0 (0.7, 1.2)	1.0 (0.7, 1.3)	0.069
γ-GT (U/L)	26.0 (14.0, 53.0)	23.0 (13.0, 47.5)	27.0 (13.0, 62.2)	28.0 (14.0, 56.0)	0.511
LDH (U/L)	386.0 (302.5, 574.5)	527.5 (371.0, 898.2)	373.0 (288.0, 517.0)	335.5 (286.2, 397.8)	< 0.001
BUN (mmol/L)	3.3 (2.4, 4.9)	3.4 (2.2, 5.6)	3.3 (2.7, 4.3)	3.1 (2.3, 4.6)	0.465
Creatinine (umol/L)	42.1 ± 17.3	47.1 ± 25.8	40.0 ± 10.1	39.1 ± 9.6	< 0.001
Glu (mmol/L)	7.0 ± 3.2	7.3 ± 3.4	7.3 ± 3.8	6.3 ± 2.4	0.038
Bacteremia (%)					0.069
NO	233 (56.3)	88 (64.2)	70 (51.5)	75 (53.2)	
YES	181 (43.7)	49 (35.8)	66 (48.5)	66 (46.8)	
PICU mortality, n (%)					0.029
NO	368 (88.9)	114 (83.2)	123 (90.4)	131 (92.9)	
YES	46 (11.1)	23 (16.8)	13 (9.6)	10 (7.1)	

Table 1. Baseline clinical and demographic characteristics of pediatric pneumonia patients. ALT, glutamic pyruvic transaminase; AST, glutamic oxaloacetic transaminase; LDH, lactate dehydrogenase; RDW, red cell distribution width, PH, arterial blood gas pH, γ-GT, gamma-glutamyl transpeptidase; BUN, blood urine nitrogen, Glu, blood glucose. *P* values were obtained through one-way ANOVA analysis for continuous variables and chi-square test for categorical variables.

Association between serum calcium and PICU mortality

Association between serum calcium and PICU mortality smooth curve fitting revealed a significant linear relationship between serum calcium levels and the risk of PICU mortality (non-linearity $P = 0.734$, Supplementary Fig. S1). This analysis employed a restricted cubic spline model adjusted for multiple variables. The curve demonstrates that as the level of serum calcium increases, the risk of mortality shows a downward trend, indicating that higher serum calcium levels are associated with a reduced risk of mortality during PICU stay.

Univariate analysis indicated a significant correlation between serum calcium and PICU mortality (HR 0.81, 95% CI: 0.73–0.89, $P < 0.001$, Supplementary Table 1). In the multivariate model, higher serum calcium levels were associated with a decreased risk PICU mortality in pneumonia patients. In the fully adjusted model, for every 1 mmol/dL increase in serum calcium, the risk of mortality significantly decreased by 24% (HR: 0.76, 95% CI: 0.67–0.87). Analysis of serum calcium as a categorical variable, compared to the lowest tertile group (T1), the middle tertile group (T2) had a 42% reduced risk of mortality (HR: 0.58, 95% CI: 0.27–1.26), while the highest tertile group (T3) had a hazard ratio of 0.37 (95% CI: 0.16–0.86) (Table 2). Furthermore, Kaplan–Meier estimates of the cumulative incidence of PICU mortality are presented in Fig. 1, with a statistically significant difference observed in the log-rank test ($P = 0.032$).

The results of sensitivity analyses

The correlation between serum calcium and PICU mortality remained consistent across different subgroups and was not influenced by factors such as age, gender, serum albumin levels, oxygen saturation, or the occurrence of bacteremia ($P > 0.05$, Fig. 2). This association underscores the independence of serum calcium as a predictive factor for PICU mortality.

In sensitivity analyses that included individuals who died within two days of PICU admission, the results remained similar (see Supplementary Table 2). In the fully adjusted Cox regression model, for every 1 mmol/dL increase in serum calcium, the risk of mortality significantly decreased by 23% (HR: 0.77, 95% CI 0.67–0.87). Additionally, multiple imputations were performed including the 278 patients with missing serum calcium values, and the results remained consistent, as shown in Supplementary Table 3. Furthermore, we handled missing data with multiple imputations. After adjusting for multiple covariates, the fundamental results remained unchanged (see Supplementary Fig. 2). Moreover, to evaluate the influence of unmeasured confounding, E-values (with their lower 95% confidence intervals) were calculated (Supplementary Fig. 3). Unmeasured variables were related to both serum calcium and mortality by HRs of two-fold; weaker confounding did not alter these associations. These findings affirm the robustness and reliability of our research results.

Discussion

In two pediatric intensive care unit studies, 84% of patients exhibited electrolyte imbalances, with hypocalcemia being the most common at 57.6%. The mortality rate for hypocalcemic patients was significantly higher at 28.3%, compared to 7.5% for those with normal calcium levels, indicating that hypocalcemia is common in critically ill pediatric patients and is associated with a higher mortality rate[18,19]. The research conducted explored the significant relationship between serum calcium levels and PICU mortality in pediatric pneumonia patients. Findings indicated that patients with higher serum calcium levels (22.0–23.5 mmol/dL) had a significantly reduced PICU mortality risk by 42% compared to those with lower levels (below 21.9 mmol/dL), and this risk reduction was even greater, at 63%, for levels above 23.6 mmol/dL. Subgroup analysis confirmed the consistency of this association across different clinical subgroups, emphasizing the importance of monitoring and managing serum calcium levels in pediatric pneumonia.

In our study involving pediatric pneumonia patients in the PICU, serum calcium levels emerged as an independent prognostic factor for mortality, aligning with findings from other studies[10,20–24]. Notably, research by Yan et al. on sepsis and multiple myeloma, along with Yang et al.'s comprehensive cohort analysis, identified non-linear relationships[21,22]. Specifically, in sepsis patients, a decline in serum calcium below 9.0 mg/dL significantly increased mortality risk[20]. In contrast, for multiple myeloma patients, optimal survival correlated with serum calcium levels around 8.40 mg/dL, with both higher and lower levels indicating increased mortality[22]. Yang's extensive cohort studies in UK Biobank and NHANES also discovered a U-shaped correlation between albumin-adjusted calcium levels and all-cause or cardiovascular mortality, with linear association observed in

Variable	n.event%	Crude HR (95% CI)	*P* value	Adjusted HR (95% CI)	*P* value
Serum calcium (mmol/dL)	46 (11.1)	0.81 (0.73–0.89)	< 0.001	0.76 (0.67–0.87)	0.002
Serum calcium tertiles					
T1 (≤ 21.9mmol/dL)	23 (16.8)	1 (Ref)		1 (Ref)	
T2 (22.0–23.5mmol/dL)	13 (9.6)	0.61 (0.31–1.21)	0.164	0.58 (0.27–1.26)	0.181
T3 (> 23.6mmol/dL)	10 (7.1)	0.42 (0.2–0.88)	0.026	0.37 (0.16–0.86)	0.03

Table 2. Cox Regression analysis of the association between serum calcium levels and PICU mortality in in pediatric pneumonia. T, tertiles; HR, hazard ratio; CI, confidence interval; Ref, reference. Adjusted Model: adjusted for age, sex, WBC (white blood cell count), bacteremia, arterial blood gas (ABG) pH, lactate levels, oxygen saturation, serum potassium, serum sodium, blood urea nitrogen and the use of inotropes.

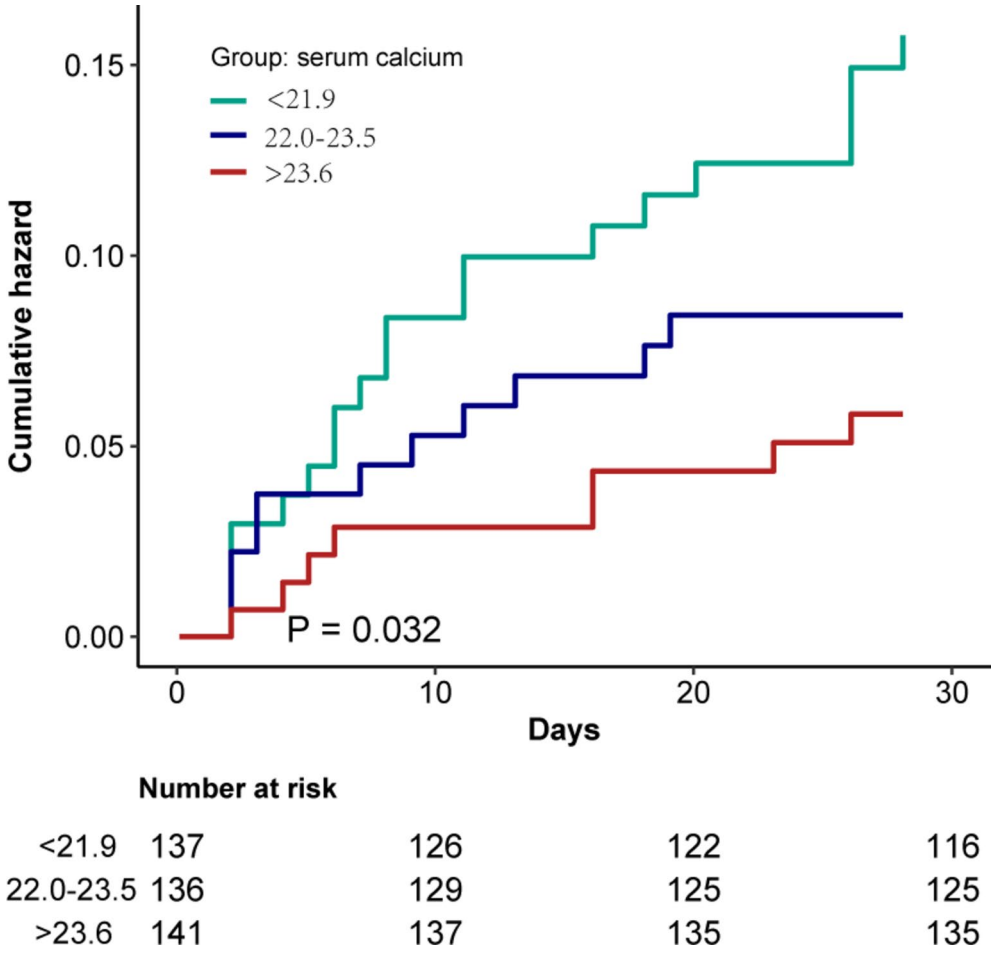

Figure 1. Cumulative incidence of PICU mortality by serum calcium levels in pediatric pneumonia patients.

cancer mortality[21]. Our findings, consistent with these studies, establish a direct relationship between serum calcium and mortality, underscoring the clinical importance of monitoring and managing serum calcium levels.

Under physiological conditions, unbound calcium inversely correlates with serum pH as calcium ions compete with hydrogen ions for binding sites on proteins such as albumin[25]. In trauma patients, lower blood calcium levels are associated with worsened acidosis, a condition prevalent in trauma and critically ill patients needing extensive blood transfusions[26,27]. Studies indicate a significant direct relationship between ionized calcium levels and arterial pH in trauma patients[27,28]. Our research underscores the independent association between serum calcium levels and in-mortality in pediatric pneumonia, even after adjusting for pH. Furthermore, research shows hypocalcemia is common in neonatal sepsis and significantly linked to higher mortality[10]. While our study did not specifically identify sepsis patients, we adjusted for blood culture results in our model. These findings emphasize the importance of serum calcium in assessing the prognosis of severe pediatric diseases, confirming its stable relationship with mortality across different clinical contexts in pediatric pneumonia. In a study conducted within an intensive care unit, the relationship between serum calcium levels and arterial blood pressure was analyzed. It was found that ionized calcium levels were directly associated with arterial blood pressure, and patients with hypocalcemia were more likely to require vasopressor support compared to those with normal calcium levels[29]. In our study, due to a significant number of missing blood pressure values, we could not analyze the impact of blood pressure on the relationship between serum calcium levels and PICU mortality in pediatric pneumonia patients. This limitation highlights an area for improvement in future research, where we aim to incorporate blood pressure data to provide a more comprehensive understanding of the factors influencing mortality in pediatric pneumonia cases.

Calcium disorders are common in clinical practice, especially in critically ill patients[30]. Hypocalcemia in critically ill patients is an independent risk factor for mortality, particularly in those requiring extensive blood transfusions. While the need to treat hypocalcemia is recognized, specific thresholds and parameters for its supplementation are still under research[31]. Overcorrection and the risks of hypercalcemia must also be considered. Moreover, studies indicate that intravenous calcium salts can significantly impact blood pressure and cardiac function in critically ill patients, especially in septic shock[32]. These findings emphasize the importance of monitoring and adjusting serum calcium levels in critical care management.

Based on data from a large teaching hospital, this retrospective cohort study delves into the relationship between serum calcium levels and PICU mortality rates among pediatric pneumonia patients. With strict

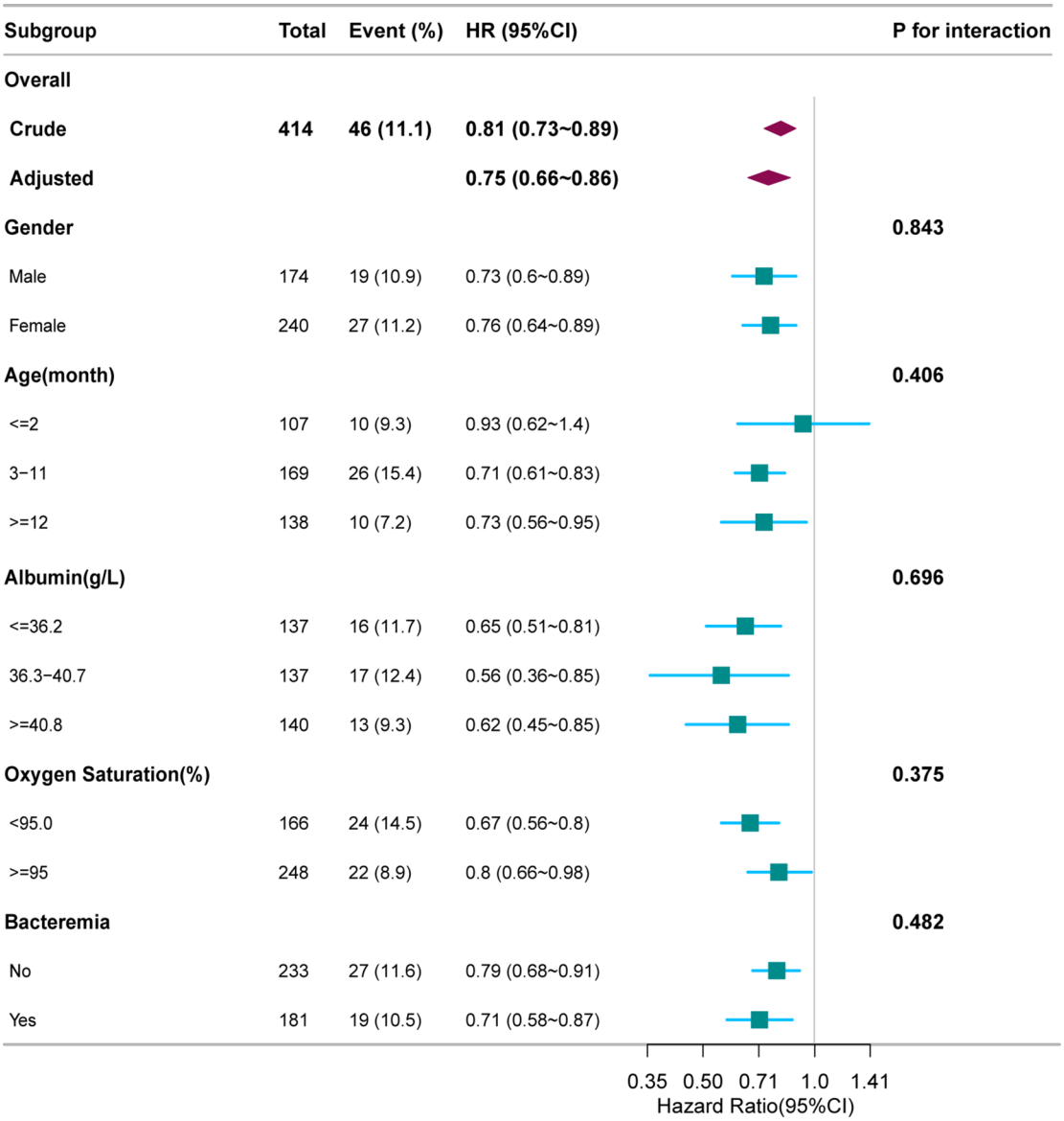

Figure 2. The correlation between serum calcium and PICU mortality remained consistent across different subgroups and was not influenced by factors such as age, gender, serum albumin levels, oxygen saturation and bateremia ($P > 0.05$). Except for stratification component itself, each stratification factor was adjusted for all other variables (age, sex, WBC, bacteremia, pH, lactate levels, oxygen saturation, serum potassium, serum sodium, blood urea nitrogen, and the use of inotropes).

inclusion and exclusion criteria and adjustments for key confounding factors like age, sex, white blood cell count (WBC), bacteremia, arterial blood gas pH, blood lactate, blood oxygen saturation, serum potassium, serum sodium,blood urea nitrogen, and the use of inotropes, the study's reliability and practicality are enhanced. Despite the study's authenticity and innovative therapeutic value, its small sample size and single-center nature require cautious interpretation. Additionally, unmeasured confounders, such as physiological severity indicators (e.g., organ failure and mechanical ventilation use), may also influence the results. Similar to studies like those conducted by Hui et al.[33], the role of calcium dysregulation and its duration in clinical outcomes is a future research target. Additionally, the lack of detailed classification of pneumonia types—such as community-acquired versus hospital-acquired or identification of specific pathogens—is a notable limitation. Nonetheless, this research lays the groundwork for future extensive, multicenter, prospective studies to validate and extend these findings.

Conclusion

This research emphasizes the crucial role of serum calcium as a predictor of PICU mortality in pediatric pneumonia cases. The study confirms that higher serum calcium correlates with reduced mortality risk, underscoring its potential as a key biomarker for severity assessment and prognosis in pediatric pneumonia. This insight is pivotal for clinical decision-making.

Materials and methods

PIC database

The PIC (Paediatric Intensive Care) database is a large, freely accessible resource containing de-identified health-related data of 12,881 pediatric patients hospitalized in the intensive care unit (ICU) of the Children's Hospital affiliated with Zhejiang University School of Medicine from 2010 to 2019 [34]. This project was authorized by the Institutional Review Board/Ethics Committee of the Children's Hospital, Zhejiang University School of Medicine (2019_IRB_052).

Clinical data collection

After completing registration with the Collaborative Institutional Training Initiative (CITI), access was granted to use the PIC database. All laboratory variables were obtained from the first blood sample drawn post-admission to the PICU. The clinical data collected included patient characteristics, vital signs, laboratory findings, and mortality outcomes.

Patient selection

For this study, individuals aged between 28 days and 18 years, who were definitively diagnosed with pneumonia, were included. The inclusion criteria were as follows: patients diagnosed with pneumonia during their ICU stay, defined by ICD-10 codes JB.900 and JB.901. Of the 828 patients initially identified from the PIC database (considering only their first ICU admission), 31 neonates under 28 days old, 105 patients who died within 2 days of admission to the ICU, and 278 patients with missing serum calcium data were excluded, leaving a total of 414 patients for this study (Fig. 3). However, a comparison between patients excluded due to missing serum calcium and those included in the study was conducted to ensure the robustness of our findings (Supplementary table 4).

Survival information was extracted from the 'Patients' table within the PIC database. Data related to hospitalization duration and time of death were obtained from the 'Admissions' table. Laboratory tests and microbiological cultures were gathered from the 'LabEvents' and 'MicrobiologyEvents' tables, respectively.

Outcome measurement

In the PIC database, within the 'Patients' section, PICU mortality was identified as the primary outcome measure. To ensure accurate inclusion of pneumonia patients, the study team confirmed pneumonia as the main diagnosis based on detailed symptoms and diagnoses recorded at admission and discharge. Consequently, pneumonia was established as the cause of death in the discharge diagnoses. The key outcome variable assessed in this research was the rate of PICU mortality, calculated from the date of PICU admission to the date of death.

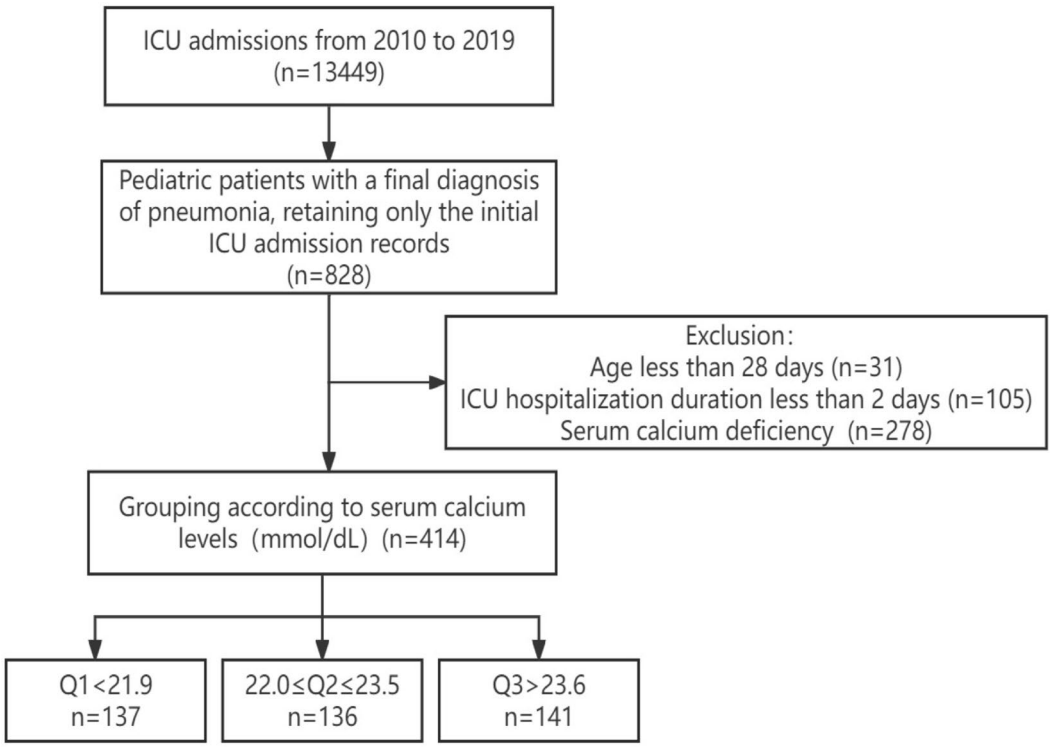

Figure 3. Patient selection flowchart for the pediatric pneumonia study.

Covariates

The selection of confounders inclusion were based on a combination of the results from univariate Cox regression analysis, previous literature reports[12,35], and covariate impact on the exposure-outcome association greater than 10%. The final model included the following covariates: age, sex, white blood cell count (WBC), bacteremia, arterial blood gas pH, blood lactate, blood oxygen saturation, serum potassium, serum sodium,blood urea nitrogen, and the use of inotropes.

Statistical analysis

Serum calcium levels, due to their minimal numerical variation, were amplified tenfold from their original values for analysis, with measurements presented in mmol/dL. Patients were stratified into three categories based on serum calcium levels (21.9 mmol/dL, 22.0–23.5 mmol/dL, and > 23.6 mmol/dL).

For continuous variables exhibiting a normal distribution, the mean ± standard deviation was employed for representation, and one-way ANOVA tests were conducted for statistical analysis. In cases where continuous variables did not follow a normal distribution, the median and interquartile range were utilized for descriptive purposes, and the Kruskal–Wallis test was applied for comparative analysis. The chi-square test was used to examine differences in categorical variables. To maximize statistical efficiency and minimize bias, multiple imputations were performed for missing data. The relationship between serum calcium levels and the risk of PICU mortality was analyzed using restricted cubic splines. We applied a Cox proportional hazards model to calculate the hazard ratio (HR). Kaplan–Meier curves were plotted to illustrate outcomes across different groups, and the log-rank test was utilized for comparing cumulative mortality rates. The presence of potential multicollinearity was evaluated using the variance inflation factor (VIF), with a threshold of VIF ≥ 5 indicating significant multicollinearity. For the analysis, the final model was constructed with adjustments for age, sex, WBC (white blood cell count) , bacteremia, arterial blood gas (ABG) pH, lactate levels, oxygen saturation, serum potassium, serum sodium,blood urea nitrogen and the use of inotropes.

To ensure the robustness of the findings, several sensitivity analyses were conducted. Initially, to eliminate potential reverse causality, cases where patients died within the first two days of PICU admission were excluded from the primary analysis. For a comprehensive assessment, all 458 patients were included in a subsequent Cox regression analysis. Additionally, we analyzed 692 patients, including the 278 with missing serum calcium values, using multiple imputation.To address the missing values, a robust statistical approach was employed using multiple imputation with five replications, utilizing the chained equations method within the R MICE procedure. This method was selected to enhance the statistical integrity of the analysis and to minimize potential biases caused by missing data. The results from the five completed datasets were then analyzed for sensitivity, and the outcomes were pooled. Additionally, unmeasured confounders frequently arise in observational studies. To assess their impact on the primary findings, a formal sensitivity analysis was performed using the E-value algorithm. Significant multicollinearity was identified between albumin and serum calcium during the multicollinearity assessment. However, recognizing the importance of albumin in adjusting the model, sensitivity analyses were conducted to evaluate its potential impact on study outcomes, this included interaction analysis. These comprehensive measures reinforced the credibility of the results.

Subgroup analyses were carried out using a stratified Cox proportional hazards model, stratifying by gender, age (≤ 2 months, 3–11 months, ≥ 12 months), albumin levels (≤ 36.2 g/L, 36.3–40.7 g/L, ≥ 40.8 g/L), oxygen saturation (< 95%, ≥ 95%), and bacteremia outcomes. The likelihood ratio test was utilized to evaluate interactions between subgroups.

Our study adhered to the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines to ensure the rigor and comprehensiveness of our observational research.

Statistical analyses were conducted using R version 3.3.2 (http://www.R-project.org, R Foundation) and Free Statistics software version 1.7. A two-tailed P-value < 0.05 was considered statistically significant.

Data availability

The data used in this study are sourced from the publicly accessible Pediatric Intensive Care (PIC) database. This database contains de-identified health-related data of pediatric patients admitted to the ICU of Children's Hospital affiliated with Zhejiang University School of Medicine from 2010 to 2019. The database, comprising 12881 pediatric patients' records, is available at http://pic.nbscn.org//. Details on the specific dataset used, analytical methods, and results can be found within this paper and its supplementary materials. For further inquiries about data access and details, please contact the corresponding author.

Received: 22 January 2024; Accepted: 9 August 2024
Published online: 12 August 2024

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Acknowledgements

The authors would like to extend their heartfelt appreciation to the individuals responsible for developing and maintaining this database. Additionally, the authors would like to express their gratitude to the clinical scientist team and Dr. Jinbao Ma for their continuous support and valuable advice.

Author contributions

J.L.Z. played a pivotal role in the conception and design of the study, data acquisition, data analysis, interpretation of results, drafting the manuscript, and revising it critically for important intellectual content. M.H.L. significantly contributed to the study's design, data acquisition, analysis and interpretation, and was involved in drafting and revising the manuscript. D.Y. was involved in the study's design, data analysis, and interpretation of results. Y.Y.Zwas instrumental in the study's conception, design, data acquisition and analysis, interpretation of results, drafting the manuscript, and its revision. All authors have reviewed and approved the final version of the manuscript.

Funding

This study was supported by the Medical Key Laboratory Construction Project (No. ZDXK2021006).

Competing interests

The authors declare no competing interests.

Additional information

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1038/s41598-024-69885-4.

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