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Prevalence of Pulmonary Embolism in COVID-19 Positive Critically Ill Children

OBJECTIVES: To investigate the prevalence of pulmonary embolism (PE) in children admitted to critical care diagnosed with COVID-19 infection.

DESIGN: Retrospective database study.

SETTING: Data reported to the Virtual Pediatric Systems, 2018–2021.

PATIENTS: Patients 28 days to younger than 18 years old, admitted to a PICU with either PE or COVID-19 diagnoses.

INTERVENTIONS: None.

MEASUREMENTS AND MAIN RESULTS: Among the PE-positive subgroups, from January 2020 to December 2021, 78 patients (14%) had an acute COVID-19 infection. The prevalence of PE pre-pandemic period (2018–2019) was 0.19% and for pandemic period (2020–2021) was 0.26% ($p < 0.001$). During the pandemic period, the prevalence of PE for COVID-negative patients was 0.21% and for COVID-positive patients was 1.01% ($p < 0.001$). The result shows that the chance to develop PE for COVID-positive patients is 4.8 times that for COVID-negative patients during the pandemic. In the subgroup of the PE-positive patients, 55.1% were Black or African American in the COVID-positive group and 19% in the COVID-negative group ($p < 0.001$). A multivariable logistic regression showed that race was an independent risk factor for COVID in PE-positive patients.

CONCLUSIONS: Our study demonstrates a significant increase in the prevalence of PE among pediatric patients admitted to PICUs during the COVID-19 pandemic compared with pre-pandemic. Our study indicates that COVID-positive patients are 4.8 times more likely to develop PE than COVID-negative patients. Additionally, the study highlights substantial racial disparities in the prevalence of PE, with Black or African American patients being disproportionately affected.

KEYWORDS: COVID-19; pulmonary embolism; racial disparities

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COVID-19 has had a profound global impact with both immediate and long-term effects on health. Disease presentation includes pulmonary symptoms, systemic inflammation, gastrointestinal, and cardiovascular complications (1). One prominent effect is developing a hypercoagulable state (2–5). In adult patients diagnosed with COVID-19, there is an increased frequency of thrombotic events, particularly pulmonary embolism (PE) (6). Systematic reviews suggest that the frequency of PE in COVID-19-positive adults is 10.5–17.9%, with an increase in patients admitted to intensive care (range, 24.7–48.6%) (5, 6).

In pediatric patients, PE is infrequent but associated with substantial morbidity and mortality (2, 7). During the COVID-19 pandemic (from March 2020 to January 2022), Kompaniyets et al (8) found that hospitalized and non-hospitalized children 0–17 years old with previous COVID-19 infection had higher rates of PE (hazard ratio = 2.01) compared with children without. A

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KEY POINTS

Question: What is the prevalence of pulmonary embolism (PE) in critically ill children with COVID-19?

Findings: PE prevalence increased from 0.19% pre-pandemic to 0.26% during the pandemic. COVID-19-positive children were 4.8 times more likely to develop PE than their COVID-negative counterparts. Black or African American children were disproportionately affected (55.1% in PE-positive COVID-19 cases).

Meanings: The findings highlight an increased risk of PE in critically ill COVID-19-positive children and underscore significant racial disparities, necessitating further research and targeted interventions.



RESEARCH IN CONTEXT

- This article examines pulmonary embolism (PE) prevalence in COVID-19-positive children admitted to pediatric intensive care.
- PE is rare in children but increased in those infected with COVID-19.
- Our study also revealed significant racial disparities in the rates of PE among COVID-19-positive pediatric patients admitted to pediatric intensive care.

retrospective cohort study using electronic health record data of patients under 18 years old showed that 1.2% (8/693) of hospitalized COVID-19 patients were diagnosed with PE, with 37.5% requiring critical care services (9).

This study aims to investigate the association of COVID-19 infection with the prevalence of PE in children requiring admission to a PICU. We hypothesize that the prevalence of PE will be higher in patients admitted to the PICU who are COVID-19 positive than those who are COVID-19 negative. Our secondary aim is to assess patient characteristics, focusing on race, to determine if the disparities reported in other studies involving hospitalized children with COVID-19 are observed in those diagnosed with PE in the PICU (10, 11).

METHODS

Using the Virtual Pediatric Systems (VPS) database (VPS LLC, Los Angeles, CA), we retrospectively analyzed the data of 127 PICUs worldwide during the COVID-19 pandemic (2020–2021) compared with a pre-COVID-19 baseline (2018–2019). The VPS database collects real-time data, documenting admission characteristics, severity of illness scores, critical care interventions, diagnosis codes during admission, and hospitalization and outcomes. We included patients 28 days to younger than 18 years old, admitted to

PICU, with a diagnosis of either PE or COVID-19 (*International Classification of Diseases*, 10th Edition [ICD-10]: I2699 or U07.1). We gathered demographical data, including sex and race, respiratory support, body mass index, and outcome. We also reviewed other available diagnoses to evaluate for other hypercoagulable states as a cause of PE. The institutional review board of the University of Maryland reviewed the study, determined it to be nonhuman subject research, and waived consent.

Continuous variables were reported as means (SDs), and categorical variables were reported as frequencies (percentages). The chi-square tests were conducted to compare the prevalence of PE between the pre-pandemic period (2018–2019) and the pandemic years (2020–2021). Additionally, these tests assessed the association between PE and COVID-19 status within the pandemic years (2020–2021). The characteristics of the PE-positive subjects were compared between those who were COVID-positive and those who were COVID-negative. Logistic regression models were used to examine the possible impacts of characteristics of subjects to COVID-19. All analyses were performed using SAS (v. 9.4; SAS Institute, Cary, NC) with a type I error of 0.05.

RESULTS

In total, 488,298 admissions from January 2018 to December 2021 were evaluated. Between 2018 and 2019 (pre-pandemic), 502 patients were diagnosed with PE out of 267,901 patients admitted to the ICU (**Fig. 1**). Between 2020 and 2021 (pandemic), 577 patients were diagnosed with PE out of 220,397

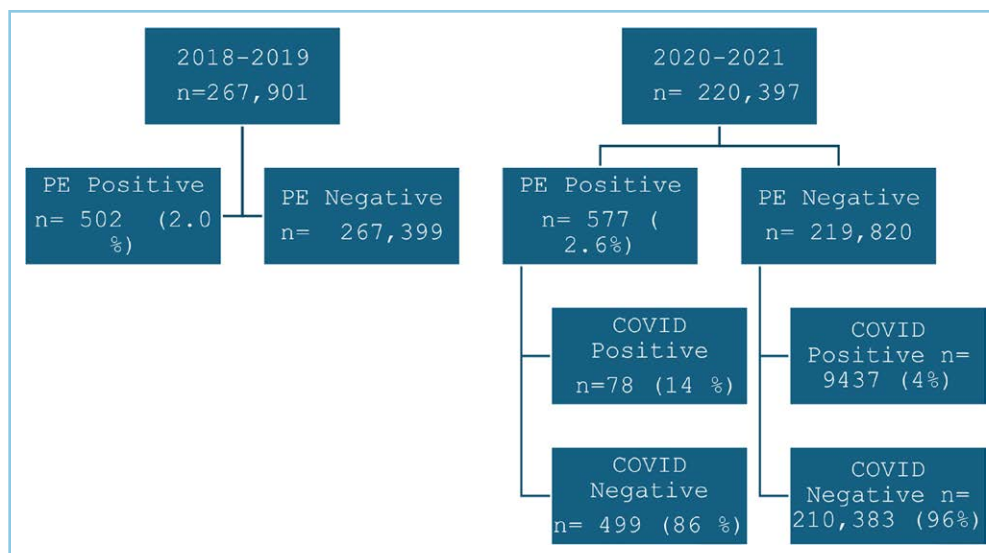


Figure 1. Flowchart of patient's distribution. PE = pulmonary embolism.



AT THE BEDSIDE

- Patients who were COVID-19 positive were 4.8 times more likely to develop PE than those who were COVID-19 negative during the pandemic.
- These findings underscore the need for vigilance for hypercoagulable states in critically ill children with COVID-19, especially in Black or African American children.
- Optimal management of coagulopathy in COVID-19 remains an area of ongoing research.

patients admitted to the PICU (Fig. 1). Among the PE-positive subgroups from January 2020 to December 2021 (pandemic), 78 patients (14%) had an acute COVID-19 infection, while 499 patients (86%) were COVID-19-negative (Fig. 1 and **Table 1**). The prevalence of PE pre-pandemic period (2018–2019) was 0.19% and for pandemic period (2020–2021) was 0.26% ($p < 0.001$). During the pandemic period, the prevalence of PE for COVID-negative patients was 0.21% and for COVID-positive patients was 1.01% ($p < 0.001$). The result shows that the chance to develop PE for COVID-positive patients is 4.8 times that for COVID-negative patients during the pandemic. In the subgroup of the PE-positive patients, 55.1% were Black or African American in the COVID-positive

group and 19% in the COVID-negative group ($p < 0.001$). No statistical difference was found in the PE-positive subgroup between the COVID-19 positive and COVID-19 negative patients on age, hospital length of stay, Pediatric Risk of Mortality (PRISM) score, or mortality. A multivariable logistic regression showed that race was an independent risk factor for COVID-19 in PE-positive patients, regardless of age,

sex, PRISM scores, and hospital stay. Compared with White people, Black or African Americans had an increased risk of developing COVID-19 (odds ratio, 5.20; 95% CI, 2.91–9.28; $p < 0.0001$).

DISCUSSION

Our study aimed to investigate the prevalence of PE associated with COVID-19 infection in pediatric patients requiring admission to a PICU. The findings indicate an increase in the prevalence of PE in pediatric patients admitted to a PICU during the COVID-19 pandemic compared with pre-pandemic years. Specifically, the prevalence of PE was 0.19% in the pre-COVID years (2018–2019) and increased to 0.26% during the COVID-19 pandemic years (2020–2021). Furthermore, patients who were COVID-19 positive were 4.8 times more likely to develop PE than those who were COVID-19 negative during the pandemic. Our results align with previous studies in adult and pediatric populations demonstrating an increased risk of thrombotic events, mainly PE, associated with COVID-19 infection. The hypercoagulable and inflammatory state induced by COVID-19 contributes to this increased risk, as suggested by various studies (2–5). Given gaps in our data, aside from age, which was not statistically significant, we were unable to evaluate the presence of additional risk factors for thromboembolic events, such as the presence of malignancy, central venous catheter, obesity, or mechanical ventilation, which were noted in other studies (12, 13). The higher

TABLE 1.
Demographics

2020–2021	<i>n</i> = 577	COVID-19 (Negative), <i>n</i> = 499	COVID-19 (Positive), <i>n</i> = 78	<i>p</i>
Gender, <i>n</i> (%)				0.257
Male	247 (42.8)	209 (41.9)	38 (48.7)	
Female	330 (57.2)	290 (58.1)	40 (51.3)	
Age, <i>n</i> (%)				0.350
28 d to < 12 yr	79	89 (17.8)	7 (8.9)	
12–18 yr	481	410 (82.2)	71 (91.0)	
Race, <i>n</i> (%)				< 0.001
Caucasian	266 (46.1)	244 (48.9)	22 (28.2)	
African American	140 (24.3)	97 (19.4)	43 (55.1)	
Other	171 (29.6)	158 (31.7)	13 (16.7)	
Pediatric Risk of Mortality score(s), <i>n</i> (%)				0.750
≤ 9	495 (85.8)	429 (85.8)	66 (84.6)	
> 9	82 (14.2)	70 (14.0)	12 (15.4)	
Outcome, <i>n</i> (%)				0.286
Survived	547 (94.8)	475 (95.2)	72 (92.3)	
Deceased	30 (5.2)	24 (4.8)	6 (7.7)	

frequency of PE in COVID-19-positive pediatric patients underscores the need for heightened vigilance and early diagnostic measures in this population, particularly in critical care settings and in patients with risk factors, as mentioned by Cohen et al (12).

Notably, our study also revealed significant racial disparities in the rates of PE among COVID-positive pediatric patients. A majority of the PE-positive and COVID-positive patients were Black or African American (55.1%). A multivariable logistic regression showed that in PE-positive patients, Black or African Americans had an increased risk of developing COVID-19 (odds ratio, 5.20; 95% CI, 2.91–9.28; $p < 0.0001$). This finding highlights the potential impact of racial disparities on health outcomes during the COVID-19 pandemic, consistent with other studies that have reported similar disparities in COVID-19 infection rates and disease severity (10, 11). A review of the pediatric COVID-19 hospitalization data from 14 states found that hospitalization rates were higher for Black or African American and Hispanic children with COVID-19 than they were for White children (10, 14). In addition, the rates of comorbid conditions were

higher in Black or African American and Hispanic than in White children (10). Racial disparities in COVID-19 infection rates and disease severity may have contributed to the rise in PE cases. Further research is necessary to understand the factors driving these disparities and to develop strategies to address them.

The study has several strengths, including using an extensive multicenter database (VPS) that allowed for comprehensive data collection and analysis. The real-time documentation of admission characteristics, severity of illness scores, critical care interventions, and diagnosis codes by trained analysts at each site ensured the accuracy and reliability of our data. However, there are also limitations to consider. The retrospective nature of the study limits the ability to establish causality. Additionally, reliance on ICD-10 codes for identifying PE and COVID-19 cases may have led to underreporting or misclassifying some cases and the inability to assess the severity of either diagnosis. Third, the diagnosis relied on the ICD-10 code, and patients may not have had a COVID-19 diagnosis or positive test result, resulting in misclassification. Another limitation

is increased screening, given the known association of PE in COVID patients from the adult data, which could have contributed to more cases.

In conclusion, our study demonstrates a significant increase in the prevalence of PE among pediatric patients admitted to PICUs during the COVID-19 pandemic, with COVID-19-positive patients being 4.8 times more likely to develop PE than those who were COVID-19-negative. The study findings also highlight substantial racial disparities in the prevalence of PE, indicating a need for further research to understand the underlying factors contributing to these disparities and to develop targeted strategies for addressing them. Enhanced awareness and early diagnostic measures are crucial for improving outcomes in pediatric patients at risk of PE, especially in the context of COVID-19.

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Virtual Pediatric Systems (VPS), LLC, provided VPS data. The VPS Research Committee has reviewed this article.

The authors have disclosed that they do not have any potential conflicts of interest.

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