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This suggests that SARS-CoV-2 is associated with an increased risk of PARDS, but not severe PARDS, in children with respiratory failure compared with several other common respiratory viruses. Additional data could help better assess the impact and contribute to our understanding of the pathophysiology of respiratory virus infections in critically ill children.

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The author declares no conflicts of interest.

References

1. Derespina KR, Kaushik S, Plichta A, Conway EE Jr, Bercow A, Choi J, et al. Clinical manifestations and outcomes of critically ill children and adolescents with coronavirus disease 2019 in New York City. *J Pediatr* 2020;226:55-63.e2.
2. Ravindranath TM, Gomez A, Harwayne-Gidansky I, Connors TJ, Neill N, Levin B, et al. Pediatric acute respiratory distress syndrome associated with human metapneumovirus and respiratory syncytial virus. *Pediatr Pulmonol* 2018;53:929-35.
3. Smith ME, Wilson PT. Human rhinovirus/enterovirus in pediatric acute respiratory distress syndrome. *J Pediatr Intensive Care* 2020;9:81-6.
4. Baird JS, Buet A, Hymes SR, Ravindranath TM, Zackai S, Cannon JM, et al. Comparing the clinical severity of the first versus second wave of 2009 Influenza A (H1N1) in a New York City pediatric healthcare facility. *Pediatr Crit Care Med* 2012;13:375-80.

Reply



To the Editor:

The acute respiratory distress syndrome (ARDS) was originally described by Ashbaugh et al in 1967 as a syndrome of acute onset of tachypnea, hypoxemia, and loss of lung compliance.¹ In 2015, the Pediatric Acute Lung Injury Consensus Conference introduced a definition of ARDS specific for pediatric patients (PARDS) that includes invasive and noninvasive mechanical ventilation and uses invasive and noninvasive markers of oxygenation to diagnose and classify the severity of PARDS.²

Dr Baird astutely observes that in pediatric patients with respiratory failure because of infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (coronavirus disease 2019 [COVID-19]), the incidence of PARDS is significantly higher than previously reported for patients with respiratory syncytial virus, human metapneumovirus, human rhinovirus/enterovirus infections, and pandemic 2009 H1N1 influenza A. Baird points out further that the incidence of severe PARDS because of SARS-CoV-2 infection

appears similar to that reported for human metapneumovirus, pandemic 2009 H1N1 influenza A, and respiratory syncytial virus.

The increased incidence of PARDS correlates with an increased intubation rate in COVID-19 that we observed compared with other respiratory viruses. We pointed out that this may be due, at least in part, to an early recommendation to limit use of noninvasive ventilation because of the risk of aerosolization of the virus. Thus, limited use of noninvasive positive pressure ventilation may have led to higher rates of endotracheal intubation and invasive mechanical ventilation, thus, explaining, to some extent, the higher rate of PARDS seen with COVID-19 compared with that observed with other viral infections.

Whether or not pulmonary infection with SARS-CoV-2 results in a unique or different pathophysiologic state than other respiratory viruses is yet to be elucidated. Relatively well preserved pulmonary compliance in COVID-19 ARDS has been reported by others^{3,4} and observed by us. This high compliance type of ARDS may represent a very early stage or possible differences in the pathophysiology of ARDS in COVID-19 compared with that caused by other viral illnesses.

In addition, a substantial proportion of patients with PARDS in our study met criteria for severe sepsis and required vasoactive support, thus, indicating increased severity of illness. The presence of sepsis may be an additional risk factor for the development of PARDS and need for mechanical ventilation in this group, perhaps explaining the higher rate of PARDS in this cohort.

It is also worthy of note, though not explanatory, that the average age in our study cohort of patients who developed ARDS was 14 years, significantly higher than the average ages in the other virus studies noted by Baird, which were approximately 4-5 years.⁵

Although COVID-19 appears to confer a higher risk of PARDS in pediatric patients, mortality seems to be lower than that reported in the literature for PARDS of various etiologies; 28-day mortality in our cohort was 2.9%, whereas 90-day mortality in patients with PARDS has been reported at 17%.⁶ Further characterization of the pathophysiology of PARDS in COVID-19 may help explain this difference in mortality. Longer term follow-up and larger sample size will be paramount to determining the true mortality and morbidity associated with development of PARDS in children with COVID-19.

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References

1. Ashbaugh DG, Bigelow DB, Petty TL, Levine BE. Acute respiratory distress in adults. *Lancet* 1967;2:319-23.
2. Pediatric Acute Lung Injury Consensus Conference Group. Pediatric acute respiratory distress syndrome: consensus recommendations from the pediatric acute lung injury consensus conference. *Pediatr Crit Care Med* 2015;6:428-39.
3. Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, Castelli A, et al. COVID-19 Lombardy ICU Network. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy Region, Italy. *JAMA* 2020;323:1574-81.
4. Gattinoni L, Coppola S, Cressoni M, Busana M, Rossi S, Chiumello D. COVID-19 does not lead to a "typical" acute respiratory distress syndrome. *Am J Respir Crit Care Med* 2020;201:1299-300.
5. Baird JS, Buet A, Hymes SR, Ravindranath TM, Zackai S, Cannon JM, et al. Comparing the clinical severity of the first versus second wave of 2009 Influenza A (H1N1) in a New York City pediatric healthcare facility. *Pediatr Crit Care Med* 2012;13:375-80.
6. Khemani RG, Smith L, Lopez-Fernandez YM, Kwok J, Morzov R, Klein MJ, et al. Paediatric acute respiratory distress syndrome incidence and epidemiology (PARDIE): an international, observational study. *Lancet Respir Med* 2019;7:115-28.