

Acute Kidney Injury in COVID-19 Pediatric Patients: Analysis of the Virtual Pediatric Systems Data

Isabelle Mawby¹, Ronith Chakraborty^{2,3}, Sidharth Kumar Sethi⁴, Kashin Mathur³, Shefali Mahesh², Michael Forbes⁵, and Rupesh Raina^{2,3}



¹ Department of Medicine, Northeast Ohio Medical University, Rootstown, OH

² Department of Nephrology, Akron Children's Hospital, Akron, OH

³ Department of Nephrology, Akron Nephrology Associates/ Cleveland Clinic Akron General Medical Center, Akron, OH

⁴ Pediatric Nephrology & Pediatric Kidney Transplantation, Kidney and Urology Institute, Medanta, The Medicity Hospital, Gurgaon, India

⁵ Department of Pediatrics, Akron Children's Hospital, Akron, OH



Introduction

- Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is responsible for the 2019 novel coronavirus disease pandemic (COVID-19). According to The World Health Organization, the pandemic has affected almost 60 million people worldwide [1].
- Despite vast research about the adult population, there has been little data collected on acute kidney injury (AKI) epidemiology, associated risk factors, treatments, and mortality in pediatric COVID-19 patients admitted to the ICU.
- AKI is a severe complication of COVID-19 among children and adolescents. Therefore, advancing understanding of this disease is crucial to further developing treatment and preventative care strategies to reduce morbidity and mortality.

Objectives

- Assess AKI incidence among COVID-19 pediatric patients in the pediatric ICU within North America using Virtual Pediatric Systems (VPS) data.
- Assess AKI associated risk factors, treatments such as KRT, and associated mortality rates among COVID-19 pediatric patients within North America using the VPS data.

Methodology

- Design:** This is a retrospective study of COVID-19 pediatric patients (age ≤ 21 years) in the pediatric ICU within North America using the VPS COVID-19 database between January 1, 2020 and June 30, 2021.
- Study Population:** Only male and female patients aged ≤ 21 years old with an AKI diagnosis, positive status for current or recent SARS-CoV2 infection via RT-PCR, serology, or antigen test, and ICU admission were selected for analysis.
- Study Variables:** Patient demographics (age, sex, race (White, Black, Hispanic, Asian/Pacific Islander, etc.), diagnosis (primary and secondary), lab order/results (hematology and chemistry tests), image order/results, respiratory support modality, kidney replacement therapy modality, medications, interventions and procedures, PELOD, PRISM-3, PIM-2, PIM3, discharge status, length of stay, and mortality.
- Data Collection & Analysis:** Data regarding pediatric patients under the age of 21 with a primary diagnosis of COVID-19 and AKI diagnosis was recorded. Data analysis followed. All the variables were tested for normality using Kolmogorov-Smirnov test. Categorical variables were summarized as frequencies and percentages, while continuous variables were summarized as medians and inter-quartile range. Univariate analysis was carried out to assess the unadjusted relationship between the variables / different outcomes in the two groups. The multivariate linear or logistic regression was conducted to assess the association of different outcomes in the two groups after adjusting for confounding factors.

Results

- A total of 2,546 COVID+ patients were included in the analysis.
- Among the 2,546 patients, 10.8% (n=274) had a diagnosis of AKI.
- Significantly higher continuous and categorical outcomes in the AKI subset compared to the non-AKI cohort included:
 - Length of stay at the hospital (LOS) [9.04 (5.11- 16.66) vs. 5.09 (2.58 – 9.94) days].
 - PIM 2 probability of death [1.20 (0.86 – 3.83) vs. 0.96 (0.79 – 1.72)]
 - PIM 3 probability of death [0.98 (0.72 – 2.93) vs. 0.78 (0.69 – 1.26)]
 - Mortality [crude OR (95% CI): 5.01 (2.89 – 8.70)]
 - Airway and respiratory support [1.63 (1.27 – 2.10)]
 - Cardio-respiratory support [3.57 (1.55– 8.23)]
 - Kidney support [12.52 (5.30 – 29.58)]
 - Vascular Access [4.84 (3.70 – 6.32)]
- Clinical lab values which were higher in the AKI subset compared to the non-AKI cohort are reported as 'median (IQR)' and include: white blood cells, count, serum potassium, blood urea nitrogen, creatinine, eGFR, and serum glucose. pH and bicarbonate levels were significantly lower in the AKI subset compared to the non-AKI cohort.
- Associated co-morbidities with AKI (as compared with the non-AKI cohort) according to the VPS database included:
 - Respiratory [64.2% vs. 55.3%; p=0.005]
 - Cardiovascular [58.8% vs. 31.7%; p<0.001]
 - Endocrinal [29.6% vs. 17.1%; p<0.001]
 - Hematological [45.3% vs. 22.6%; p<0.001]

Figure 1. Association of Different Categorical Outcomes Among AKI patients Across Different AKI stages

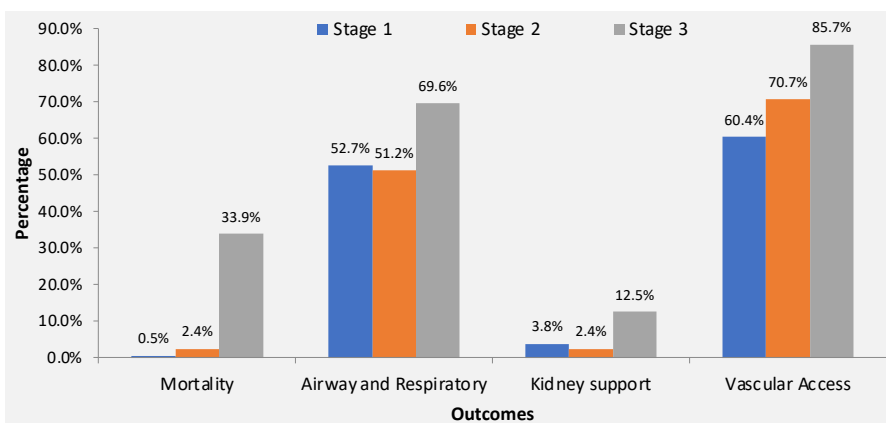


Figure 1 identifies differences in categorical outcomes across AKI stages 1, 2, and 3 based upon Kidney Disease Improving Global Outcomes (KDIGO) staging guidelines.

Figure 2. Association of Different Continuous Outcomes Among AKI Patients Across Different AKI Stage

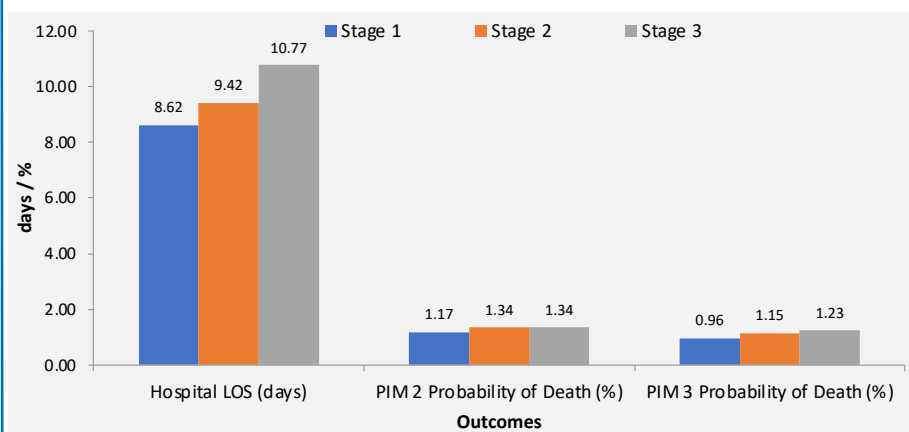


Figure 2 identifies differences in continuous outcomes across AKI stages 1, 2, and 3 based upon KDIGO staging guidelines.

Discussion

- Overall, based on our results, AKI among children with COVID-19 has been shown to be associated with an increased risk of mortality and disease complication.
- Among 2,546 COVID-19+ children, 10.8% of patients developed AKI. This coincides with the incidence reported by Derespina et al. in a study at New York City PICUs; Among 70 children admitted, 12.9% developed AKI [2].
- Separate studies from Saudi Arabia, Iran, England, and France found much higher incidences of AKI at 21%, 22%, 29%, 19% and 70% respectively [3, 4, 5, 6, 7]
- Contrarily, studies from Italy, Spain, and two from China all reported AKI incidences significantly lower at 1.2%, 0.8%, 1.3%, and of 2.7% respectively [8, 9, 10, 11]
- What is Unique About COVID-19 in Children?**
- The most common clinical features of COVID-19 among children include fever, dry cough, and pneumonia, along with an increasing prevalence of multisystem dysfunction [5].
- Within the 2,546 pediatric COVID-19 cohort from the VPS data from North American PICU's, several additional organ systems were reportedly involved including 49.3% of patients with respiratory symptoms, 33.1% with circulatory symptoms, 21.6% with digestive/excretory symptom, 17.6% with hematologic symptoms, 12.3% with neurologic symptoms, and 11.7% with kidney/urinary symptom.
- Children tend to have less severe disease than adults. This may be due to:
 - More active innate immune response [12].
 - Generally overprotected by parents [12].
 - Fewer outdoor activities [12].
 - Undertake less international travel [12].
 - Fewer comorbidities [12].
 - Biochemically, ACE2 demographics differ from its distribution, maturation, and function – ultimately affecting its association with the receptor binding domain of the COVID-19 spike protein and reducing susceptibility and severity [12,13]

Conclusion

- Although COVID-19 in the pediatric population tends to present more favorably, renal involvement, including AKI, among the pediatric COVID-19 patient population may be considered a negative prognostic factor with respect to patient outcomes.

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