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ORIGINAL ARTICLE

Acute kidney injury in critically ill children with COVID-19 and MIS-C

Hasan Özen[1] · Ayşen Durak Aslan[2] · Burak Balaban[1] · Oktay Perk[3] · Hacer Uçmak[1] · Serhan Özcan[3] · Anar Gurbanov[1] · Emel Uyar[3] · Fevzi Kahveci[1] · Emrah Gün[1] · Ali Kansu Tehci[4] · Serhat Emeksiz[3] · Tanıl Kendirli[1]

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Abstract

Background This study's objective was to investigate the incidence of acute kidney injury (AKI) in children with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and multisystem inflammatory syndrome (MIS-C) and to report our clinical experience.

Methods Acute COVID-19 and MIS-C-diagnosed patients observed in two pediatric intensive care units (PICUs) between 2019 and 2021 were examined for AKI and retrospectively compared to children with AKI.

Results The study comprised 163 children, of whom 98 (60.1%) were diagnosed with acute COVID-19 and 65 (39.9%) with MIS-C. AKI was observed in 40 (40.8%) of the acute COVID-19 patients and 18 (27.7%) of the MIS-C patients. Low calcium level and hypotension were linked with AKI at initial presentation (OR: 0.56, 95% CI: 0.369–0.560, $p = 0.006$ and OR: 3.64, 95% CI: 1.885–7.152, $p = 0.001$, respectively). A history of nephrotoxic medication usage played an essential role in the development of AKI in patients who acquired AKI after hospitalization ($p = 0.001$, odds ratio: 9.32, confidence interval: 3.106–27.973). In clinical practice, individuals with respiratory distress and cough had a high chance of having AKI (OR: 4.47, 95% confidence interval: 2.25–8,892 and OR: 3.48, 95% confidence interval: 1.76–6.88). AKI patients had a greater demand for respiratory assistance and a longer period of stay in the PICU.

Conclusions AKI in the COVID-19 and MIS-C patient groups is related with increased mortality and extended hospitalization, according to the findings. These statistics imply that identifying and preventing risk factors is necessary.

Keywords SARS-CoV-2 · Multisystem inflammatory syndrome · Acute kidney injury · Pediatric intensive care

Introduction

Coronavirus disease-2 (COVID-19), caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-19), has been a worldwide pandemic since 2019, with significant health and other consequences. As of July 1, 2022, 222 countries have been hit by the COVID-19 pandemic, with 550 million positive cases and 6.3 million deaths [1, 2]. As the epidemic continues, the pathophysiology of COVID-19, its consequences, and its accompanying diseases have become increasingly evident. Acute kidney injury (AKI) is an adverse prognostic factor documented in 25% of adult patients with COVID-19 infection. This syndrome is prevalent in the elderly and those with comorbidities [2, 3].

In late April 2020, clinicians in the UK first characterized the clinical picture known as a multisystem inflammatory syndrome in children (MIS-C). It has been observed that previously healthy children and adolescents frequently appear with a severe inflammatory syndrome defined by fever, cardiovascular, gastrointestinal, skin, kidney, neurological, and respiratory system fever 4–6 weeks after COVID-19 infection [4]. The syndrome was quickly found in the USA, and as of December 4, 2020, the Centers for Disease Control and Prevention (CDC) has identified 1288 individuals. The CDC recommends hospitalization for MIS-C and multiple organ involvement, defined as

✉ Hasan Özen
ozen87@hotmail.com

1 Department of Pediatric Intensive Care, Faculty of Medicine, Ankara University School of Medicine, Ankara, Turkey

2 Department of Pediatrics, Ankara University School of Medicine, Ankara, Turkey

3 Department of Pediatric Intensive Care Unit, Department of Pediatrics, Ministry of Health, Ankara City Hospital, Ankara, Turkey

4 Department of Pediatrics, Ministry of Health, Ankara City Hospital, Ankara, Turkey

prolonged fever and laboratory markers of inflammation accompanied by evidence of severe disease (e.g., cardiac, gastrointestinal, renal, rheumatological, dermatological, and neurological) [5]. The criterion of being 21 years old and interacting with a confirmed or suspected COVID-19 patient was approved for the children's age group. Individuals may exhibit any or all of Kawasaki disease symptoms [4, 6]. The most prevalent cardiovascular system involvement in MIS-C is the left ventricle and shock malfunction [6, 7]. Several investigations have highlighted the occurrence of AKI in this subgroup of infants with MIS-C [8, 9]. In a systematic evaluation of 662 individuals diagnosed with MIS-C, 16.3% developed AKI; however, the criteria for AKI varied among health centers [9]. Although there are preliminary data on the occurrence of AKI in pediatric patients with acute COVID-19 and MIS-C, the incidence, related clinical characteristics, and short-term outcomes still need to be better understood.

In this study, we sought to quantify acute kidney injury (AKI) incidence in children diagnosed with COVID-19 and MIS-C to evaluate the demographic, clinical, and outcome characteristics of individuals with identified AKI.

Materials and methods

This retrospective study was conducted on patients with COVID-19 and MIS-C diagnoses who were followed in pediatric intensive care units (PICUs) at two centers between 2019 and 2021. The Ethics Committee of the Ankara University Faculty of Medicine, referenced by number 2022/206, granted approval.

Criteria for inclusion and patient descriptions

ICU admission for COVID-19

Patients who presented with evidence of acute respiratory tract infection or had a positive PCR result for COVID-19 in preoperative nasopharyngeal or endotracheal swab samples were considered acute COVID-19 patients. Patients with a positive or negative initial swab result followed by a positive retest were determined to be infected.

MIS-C patients

Our diagnostic criteria are the MIS-C diagnostic criteria as established by the CDC guideline [10]

Criteria of exclusion

We excluded COVID-19-positive individuals with insufficient data and emergency department patients with positive swab who did not require hospitalization. Thus, we referred to patients with acute COVID-19 as "ICU admission for COVID-19." In addition, we excluded patients with a history of chronic kidney disease stages III to V.

Patient hospitalization criteria

- Hypotension and requirement for inotrope support
- Cardiac dysfunction
- Need for respiratory or oxygen support
- Absence of isolated spaces in the infection services
- Positive preoperative COVID PCR result

Primary outcome and definition of AKI

The incidence of AKI was the direct result of the study. The 2012 Kidney Disease: Improving Global Outcomes (KDIGO) classification defines AKI [11]. Using the Schwartz algorithm for reverse computation [12], glomerular filtration rate (GFR) values were determined.

Secondary outcomes and treatment methods

The secondary outcomes were demographic and clinical variables linked with AKI. The following factors were assessed: demographic characteristics, symptoms, and coexisting conditions. In addition, serum electrolytes, creatinine, blood urea nitrogen, albumin, D-dimer, inflammatory markers, and hematological parameters were assessed as laboratory tests. Monitoring information, such as vasoactive medication use and exposure to nephrotoxic medications, was also obtained. Due to a lack of data, the vasoactive inotrope score (VIS) was examined at a single center. Patients with MIS-C were treated per the New York treatment guidance guide [13]. In critically ill children with COVID-19 and MIS-C, we computed GFR due to correct and increased treatment doses and decreased nephrotoxicity due to correct and increased drug doses.

Residual kidney injury

Residual kidney injury at discharge consists of the following kidney outcomes: (1) the need for dialysis at discharge among patients who developed and survived AKI 3D (stage 3, receiving dialysis); and (2) improvement of kidney function at discharge among patients who developed and survived AKI (both AKI 1–3 [stage 1–3, not receiving dialysis] and AKI 3D).

Statistical analysis

Acute COVID-19 and MIS-C characterized the essential demographic and clinical features. Depending on the

normality distribution, continuous variables are described by the mean (SD) or the median (min-max). Frequencies and ratios were reported for categorical variables. The Mann-Whitney *U* test, chi-square test, and Student *T*-test were utilized to compare the essential characteristics of AKI and non-AKI COVID-19 and MIS-C patients.

A logistic regression analysis was done on the variables associated with AKI (for both acute COVID-19 and MIS-C). The arguments related to the dependent variable (AKI existence) in the logistic regression analysis with a single variable have been included in the logistic regression model with multiple variables. $P = 0.05$ was chosen as the significance level, and SPSS version 26 was utilized for analysis.

Results

The study includes 163 children. There were 98 (60.1%) ICU admissions for COVID-19 and 65 (39.9%) MIS-C diagnoses. The median age of the patients was 10 years (0.16–18.0). A total of 101 (62%) patients were male, while 62 (38%) were girls. AKI developed in 35.6% ($n = 58/163$) of all patients. In Figure 1, patient numbers are presented as flowcharts for stages 1, 2, and 3 based on the distribution of patients within patient categories and KDIGO criteria.

Acute COVID-19

The median age of ICU-admitted children with COVID-19 was 9.0 (0.16–18.0) years, and 66.3% were male. AKI developed in 40 patients (40.8%), including 65% in stage 1, 15% in stage 2, and 20% in stage 3 compared to KDIGO. Two patients developing AKI needed continuous kidney replacement therapy (CKRT) (5%). In the acute COVID-19 group, there was no significant difference in age, gender, or BMI z scores between the AKI and non-AKI groups. In the AKI group, the PICU length of stay was longer than 5.0 (1.0–600.0) days ($p = 0.007$) to 8.5 (1.0–57.0) days. There was a statistically significant difference between the developed and non-developed groups regarding mortality ($p = 0.001$). The developing group required significantly greater noninvasive ventilation (NIV) and invasive mechanical ventilation (IMV) support ($p = 0.003$ and $p = 0.001$, respectively). Those who experienced AKI had a calcium level at hospital admission that was statistically substantially lower (8.2 (5.4–9.7) to 8.3 (7.4–13.4), $p = 0.012$).

Multisystem inflammatory syndrome in children

The median age of MIS-C patients was 10 (1.5–17.0) years, and 55.4% were male. AKI developed in 18 patients (27.7%), and 31% of all AKI patients in the overall population satisfied the diagnostic criteria for MIS-C. A total of 89.2% of MIS-C patients reported fever as their most common application complaint. At a ratio of 72.3%, gastrointestinal issues placed second, while rash accounted for 49.2%. According to the KDIGO phase system, 33.3% of these patients were in stage 1, 22.2% were in stage 2, and 44.4% were in stage 3. The AKI group had higher white blood cell

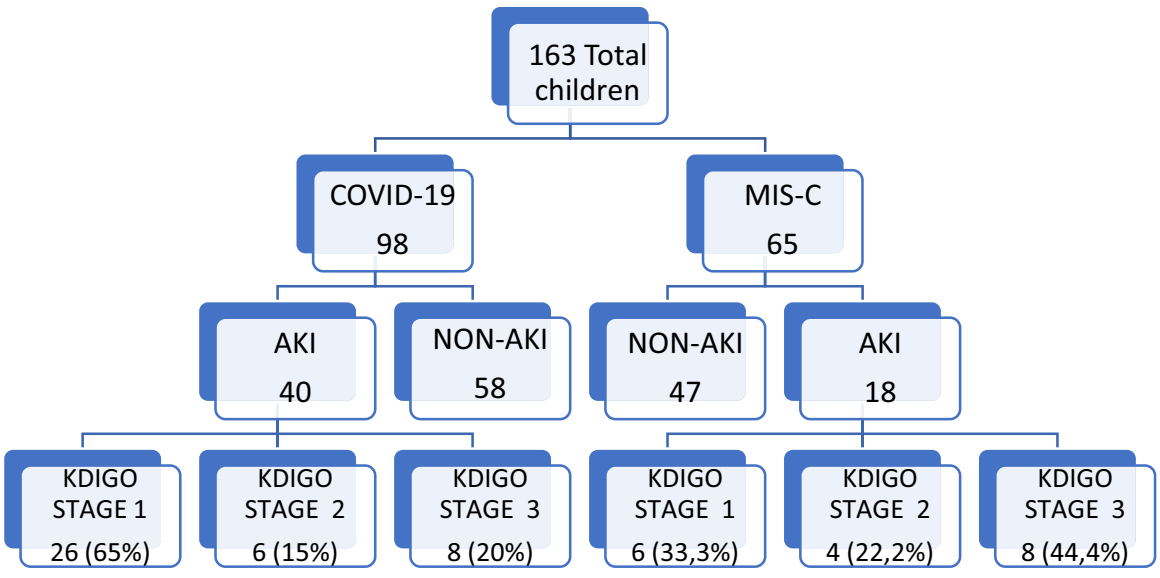

Fig. 1 Flowchart of study population. Acute kidney injury (AKI) was staged by Kidney Disease: Improving Global Outcomes (KDIGO) criteria. COVID-19, coronavirus disease 2019; MIS-C, multisystem inflammatory syndrome in children

(WBC) count (14.2 ± 3.7 to 9.3 ± 4.4, $p = 0.003$) and lactate dehydrogenase (LDH) values (309.0 (227.0–789.0) to 282.0 (187.0–358.0), $p = 0.025$) (Table 2).

Tables 1 and 2 list the admission characteristics and laboratory values of patients with MIS-C and acute COVID.

Baseline demographic and clinical characteristics associated with AKI

There was no difference in age, gender, or body mass index (BMI) z scores between patients with AKI and those without the condition. AKI was present in 16 of 58 AKI patients at the time of application; these patients were 50% in stage 2 and 50% in stage 3 relative to the KDIGO phase. AKI developed during PICU admission in 16 (61.5%) of the 26 patients classified as stages 2–3.

Of the application complaints, fever was the most prevalent (81%) complaint. The ratio of gastrointestinal issues ranked second at 52.8%. Other application complaints were altered consciousness at 19.0%, cough at 35.0%, rash at 26.4%, myalgia at 28.8%, and respiratory distress at 24.2%. Cough, respiratory distress, and altered levels of consciousness were statistically significant in the group with AKI compared to the group without AKI. In clinical practice, individuals with respiratory distress and cough had a high chance of having AKI (OR: 4.47, 95% confidence interval: 2.25–8.892 and OR: 3.48, 95% confidence interval: 1.76–6.88).

At the moment of application, a low calcium level and the presence of hypotension were linked to AKI (OR: 0.56, 95% CI: 0.369–0.560, $p = 0.006$ and OR: 3.64, 95% CI: 1.885–7.152, $p = 0.001$, respectively) (Table 3). In 38 (90.4%) of the patients who developed AKI, a history of nephrotoxic medication usage was present (NSAID, vancomycin, amikacin, colystin, furosemide). The use of nephrotoxic medications in patients with AKI is linked with the development of AKI ($p = 0.001$, odds ratio: 9.32, confidence interval: 3.106–27.973).

Clinical course and patient outcomes

The length of stay in pediatric intensive care units was greater from 5.0 (1.0–60.0) days to 8.0 (1.0–57.0) days ($p = 0.001$) in the AKI groups. The overall cohort mortality rate was 8.5% ($n = 12/163$), while mortality in the AKI group was significantly higher ($n = 12/58$ (20.7%) to $n = 2/105$ (1.9%), $p = 0.001$). In the MIS-C group, two patients were lost, and two of the patients experienced AKI. AKI patients with residual kidney injury at discharge constituted 6.8% of the group.

One hundred and two patients (62.6%) were treated with intravenous immune globulin (IVIG), 97 (59.5%) with methylprednisolone, 79 (48.5%) with pulse steroid, 46 (28.2%) with favipiravir, 35 (21.5%) with anakinra, 9 (5.5%) with remdesivir, and 7 (4.3%) with tocilizumab.

In 75.8% of the AKI patients, the fluid overload has improved. CKRT was administered to 19% of patients developing AKI ($n = 11/58$), and existing antibiotics were adjusted for 24% of patients with AKI. The necessity for respiratory assistance in the group with AKI was statistically significant (for MV; $n = 21/58$ (36.2%) to $n = 8/105$ (7.6%), $n = 29/58$ (50%) to $n = 17/105$ 1 (16.2%) ($p = 0.001$)).

Discussion

In December 2019, when COVID-19 first emerged, children were less susceptible to this disease than adults. Due to the growing demand for intensive care and dialysis in the adult case series, pediatric nephrologists and the intensive care unit were mobilized for this patient population. During the pandemic, a clinical picture known as MIS-C was identified, which was supposed to affect children less severely; one of the major organ uptakes of this was the kidneys. The world is undergoing the largest epidemic in the past century, and there has been a great deal of new information concerning it. Whether the AKI that developed in COVID-19 is one of the target organs of the virus or the hypoxia induced by COVID-19, these aspects of the cytoid storm are still not well understood. Although AKI appears to be a directly damaged organ during inflammation in MIS-C patients, it is regarded as a crucial factor in the development of the mortality and shock table [2].

This study consisted of 163 individuals in two PICUs who were diagnosed with COVID-19 or MIS-C. AKI is prevalent in 35.5% of the cohort, 27.6% of the COVID-19 group, and 40.8% of the MIS-C group. In a trial involving 89 individuals, 21% developed AKI [14]. In another study conducted by Stewart and colleagues, involving 52 patients, the incidence of AKI was 29% [15]. The incidence of AKI is estimated to range from 15 to 73% by case series [9, 15, 16]. We believe this wide range of hospitalization in the prevalence of AKI in the literature is a result of the various definitions employed and the heterogeneity of patients. Literature suggests that the incidence of AKI in children with MIS-C which is characterized by hypovolemia, cardiac dysfunction, and severe inflammation is higher than in children with acute COVID-19. This analysis validated the literature-based AKI prognosis but did not support the MIS-C prognosis to AKI, indicating the presence of other risk variables and the possibility of distinct pathogenesis. In addition, the prevalence of comorbid status was more significant in our COVID-19 patient cohort ($n = 58/95$ (59.2%), $n = 6/65$ (9.0%)). Our MIS-C group was healthier and had higher kidney reserves as a result.

Table 1 Admission characteristics and laboratory values by acute COVID-19 and COVID-19-associated MIS-C

	ICU admission for acute COVID-19 (***N*** = 98)	ICU admission for COVID-19-associated MIS-C (***N*** = 65)	***p***
Age, years	9.0 (0.16–18.0)	10.0 (1.5–17.0)	0.421
Male	65 (66.3%)	36 (55.4%)	0.159
BMI	17.5 (8.3–40.9)	18.5 (13.3–30.47)	0.40
BMI z scores	0.53 (−6.2 to 4.65)	0.32 (−2.27 to 3.86)	0.69
Presence of comorbidity	58 (59.2%)	6 (9.2%)	< 0.001
Immune deficiency	10 (17.2%)	0	-
Cardiovascular disease	10 (17.2%)	0	-
Down syndrome	5 (8.7%)	2 (33.3%)	-
Diabetes mellitus	8 (13.8%)	2 (33.3%)	-
Asthma	5 (8.6%)	0	-
Other	20 (34.5%)	2 (33.3%)	-
Presenting symptoms, *n* (%)			
Fever	74 (75.5%)	58 (89.2%)	0.029*
Cough	46 (46.9%)	11 (16.9%)	< 0.001*
Respiratory distress	62 (63.3%)	10 (15.4%)	< 0.001*
Gastrointestinal	39 (39.8%)	47 (72.3%)	< 0.001*
Rash	11 (11.2%)	32 (49.2%)	< 0.001*
Myalgia	17 (17.3%)	30 (46.2%)	< 0.001*
Changes of consciousness	25 (25.8%)	6 (9.2%)	0.009*
Hypotension, VIS score	15.0 (5.0–60.0)	15.0 (5.0–83.0)	0.765
Respiratory support			
IMV	25 (25.5%)	4 (6.2%)	0.002*
NIV	39 (39.8%)	7 (10.8%)	< 0.001*
LOS PICU, days	6.5 (1.0–60.0)	5.0 (1.0–25.0)	0.074
Mortality	12 (12.2%)	2 (3.1%)	0.041*
Admission Cr	0.49 (0.02–10.93)	0.57 (0.13–6.56)	0.022**
Admission e-GFR	124.1 (4.93–314.29)	126.0 (11.96–300.0)	0.703
Sodium	137.0 (125.0–168.0)	134.0 (123.0–148.0)	< 0.001*
Potassium	4.23 ± 0.61	3.9 ± 0.75	0.002*
Bicarbonate	22.7 (5.4–32.9)	21.2 (10.1–30.8)	0.075
WBC	7.5 (0.99–37.34)	10.1 (1.89–37.32)	0.040*
HGB	11.8 (4.8–19.3)	12.0 (6.7–18.8)	0.379
Platelets	238,000 (7000–2,790,000)	176,000 (43,000–517,000)	0.002*
LDH	366.0 (154.0–4491.0)	300.5 (166.0–8341.0)	< 0.001*
Calcium	8.85 (5.4–13.4)	8.6 (7.3–9.9)	0.023*
Albumin	3.9 ± 0.62	3.6 ±0.56	< 0.001*
CRP	23.4 (0.0–298.3)	173.0 (1.2–428.5)	< 0.001
D-Dimer	570.0 (50.0–35,200)	3204.0 (103.0–17,700)	< 0.001*
Nephrotoxic medication (NSAID, vancomycin, amikacin, colystin, furosemide, etc.)	61 (62.2%)	45 (69.2%)	0.360

BMI, body mass index; *VIS*, vasoactive inotropic scores; *IMV*, invasive mechanical ventilation; *NIV*, non-invasive ventilation; *GFR*, glomerular filtration rate; *WBC*, white blood cell; *HGB*, hemoglobin; *LDH*, lactate dehydrogenase; *CRP*, C-reactive protein; *COVID-19*, coronavirus disease 2019; *MIS-C*; multisystem inflammatory syndrome in children

Categorized variables are presented with frequencies and ratios, comparing for AKI and non-AKI groups with chi-square testing

Continuous variables that do not have normal distribution are defined by median (min-max) and group comparisons are performed by the Mann-Whitney *U* test

Continuous variables with normal distribution mean (± SD) identified with and group comparisons with independent sample *T* test

*$p < 0.05$ was determined as the level of significance

Table 2 Admission characteristics and laboratory values by AKI diagnosis in acute COVID-19 and COVİD-19 associated MIS-C

MIS-C				COVID-19-associated MIS-C		
	AKI	Non-AKI	*p*	AKI	Non-AKI	*p*
Age, year	12.3 ± 4.7	9.4 ± 3.7	0.06	13.5 (1.0–18.0)	16.0 (1.0–18.0)	0.393
BMI	23.2 ± 4.7	17.1 ± 2.2	0.023*	19.0 ± 6.7	25.6 ± 10.4	0.287
BMI z scores	0.65 ± 1.18	0.18 ± 1.25	0.190	−0.35 ± 2.3	−0.01 ± 2.5	0.52
Admission Cr	1.09 (0.61–1.40)	0.5 (0.22–0.74)	< 0.001*	0.79 (0.22–10.93)	0.65 (0.32–1.07)	0.008*
Sodium	133.5 (123.0–139.0)	134.5(131.0–140.0)	0.369	136.6 ± 3.6	136.2 ± 2.9	0.206
Potassium	3.78 ± 0.87	3.65 ± 0.49	0.939	4.1 ± 0.53	3.9 ± 0.46	0.392
Bicarbonate	19.3 ± 2.9	20.1 ± 3.57	0.736	24.5 (5.6–30.0)	24.0 (5.4–29.4)	0.995
WBC	14.2 ± 3.7	9.3 ± 4.4	0.003*	7.5 (0.99–27.5	7.3 (1.2–37.325)	0.490
HGB	12.4 (7.5–15.4)	12.0 (8.1–18.6)	0.148	12.4 ± 3.48	13.1 ± 2.92	0.472
Thrombocyte	150 (113–200)	179 (43–517)	0.683	226 (32–599)	187 (102–699)	0.483
LDH	309.0 (227.0–789.0)	282.0 (187.0–358.0)	0.025*	468 (161–1931)	352 (176–626)	0.062
Calcium	8.1 ± 0.4	8.4 ± 0.65	0.517	8.2 (5.4–9.7)	8.3 (7.4–13.4)	0.012*
Albumin	3.47 ± 0.45	3.57 ± 0.53	0.245	3.7 ± 0.70	3.8 ± 0.76	0.544
CRP	217.7 ± 66.7	160.4 ± 90.7	0.160	43.7 (4.3–296.3)	41.9 (0.00–231.7)	0.153
D-Dimer	3200 (400–13,900)	3400 (170–17,700)	0.847	1610 (500–35,200)	966 (196–8960)	0.004*

BMI, body mass index; *WBC*, white blood cell; *HGB*, hemoglobin; *LDH*, lactate dehydrogenase; *CRP*, C-reactive protein; *COVID-19*, coronavirus disease 2019; *MIS-C*; multisystem inflammatory syndrome in children

Acute kidney injury (AKI) was staged by Kidney Disease: Improving Global Outcomes (KDIGO) criteria. Categorized variables are presented with frequencies and ratios, comparing for AKI and non-AKI groups with chi-square testing

Continuous variables that do not have normal distribution are defined by median (min-max) and group comparisons are performed by the Mann-Whitney *U* test

Continuous variables with normal distribution mean (± SD) identified with and group comparisons with independent sample *T* test. *$p < 0.05$ was determined as the level of significance

In our MIS-C group, the most common application complaints were fever, gastrointestinal symptoms, and rash. This was consistent with contemporary research [7, 8]. Recent findings have demonstrated the severity of MIS-C with a rise in PICU admission rates and the requirement for inotropic support and extracorporeal membrane oxygenation (ECMO) [8, 9, 13, 16-18]. The majority of MIS-C patients admitted to our PICU must be treated with inotropes and vasopressors. Although it was stated that MIS-C patients had fatality rates comparable to severe COVID-19 adults, our MIS-C groups had a considerably lower death rate than the COVID-19 group.

Without laboratory evidence of AKI, autopsy analyses of adult case series indicate signs of kidney injury. The AKI mechanism in COVID-19 and MIS-C remains unknown. Battle et al. [19] demonstrated a complex mechanism of AKI in SARS-CoV-2-infected patients. This damage may be the result of both direct infections of the kidney parenchyma by the virus via ACE-2 receptors and microvascular damage caused by cytokine production. In adult trials, AKI was related to elevated indicators of inflammation. Basalely et al. [20] published an additional investigation corroborating similar findings.

Increased WBC count, elevated C-reactive protein (CRP) level, and low albumin level were related to AKI in COVID-19 and MIS-C patients with acute infection. In our study, we were unable to find any evidence indicating an inflammatory mechanism for AKI. First, AKI was related to hypotension and the need for vasoactive inotropes in our patient population. Hypotension might contribute to AKI by reducing kidney perfusion. In addition, we discovered that respiratory distress was related to AKI, and acute lung injury may be connected with AKI in 16 of the 42 patients who acquired AKI during follow-up and who required mechanical ventilation. We report that 61.5% of children with severe AKI are admitted to intensive care with the condition. The fact that this disease and hypotension are linked to AKI suggests that this topic warrants more investigation. Fluid resuscitation and timing of inotropic therapy for optimization of cardiac function, the timing of anti-inflammatory medications, and indications for use are still concerns that need to be researched, particularly in the MIS-C patient population.

In adult publications, obesity has been linked to severe COVID-19 disease and AKI [21]. This may be related to an increase in obesity-related comorbidity, although our study did not notice this correlation. There was no significant

Table 3 Logistic regression analyses of baseline demographics and clinical variables associated with acute kidney injury in COVID-19 and COVID-19-associated MIS-C

Variable	Unadjusted OR (95% CI)	*p*
Age, years	0.959 (0.904–1.017)	0.164
BMI z scores	0.975 (0.926–1.026)	0.328
Diagnosis (MIS-C)	0.555 (0.282–1.092)	0.088
Albumin (g/L)	1.222 (0.723–2.066)	0.454
Calcium (mg/dL)	1.785 (1.178–2.707)	0.006*
LDH (U/L)	1.000 (1.000–1.001)	0.176
Na (mmol/L)	0.933 (0.869–1.002)	0.058
K (mmol/L)	0.740 (0.434–1.264)	0.271
D-Dimer (ng/mL)	1.000 (1.000–1.000)	0.098
Fibrinogen (g/L)	1.037 (0.850–1.266)	0.718
HCO_3	1.017 (0.951–1.088)	0.619
CRP (mg/L)	0.999 (0.996–1.003)	0.674
WBC ($\times 10^9$/L)	0.973 (0.925–1.024)	0.299
Respiratory distress	4.47 (2.25–8.892)	< 0.001*
Cough	3.48 (1.76–6.88)	< 0.001*
Hypotension	3.64 (1.854–7.152)	< 0.001*

[a]COVID-19 and COVID-19-associated MIS-C analyzed together as one group

BMI, body mass index; *LDH*, lactate dehydrogenase; *K*, potassium; HCO_3, bicarbonate; *CRP*, C-reactive protein; *WBC*, white blood cell

*$p < 0.05$ was determined as the level of significance

difference in BMI z scores between the group with AKI and the group without AKI.

Continuous kidney replacement therapy indications for acute COVID-19 and MIS-C are identical to those for non-COVID and non-MIS-C. The initial decision of CKRT should be based on a calculated risk-benefit ratio for both the patient and the healthcare provider. Lipton et al. reported that one of 26 MIS-C patients was treated with CKRT [22]. A total of 152 patients with MIS-C and COVID-19 diagnoses were included in another study by Basalely et al. [20]. Eight COVID-19 patients were diagnosed with AKI, and two patients had CKRT, whereas ten MIS-C patients were diagnosed with AKI, and none required CKRT. In our cohort, 11 AKI-developing patients required CKRT. Nine individuals had MIS-C, and 2 had COVID-19. Considering the other studies, we think having a high level of CKRT is because our centers receive referrals for critically ill patients.

Our work has a few limitations. First, this study included patients who were hospitalized in the PICU for other reasons but whose COVID-19 PCR test results were positive and who did not have COVID-19 symptoms. That resulted in significant heterogeneity among these patients. In the application, baseline exams were performed on COVID-19 and MIS-C patients, and during the data-collecting phase, a KDIGO classification based on creatinine values was performed. We did not have information regarding urine output. Regardless of these limitations, our research is the nation's largest (20 and 32 beds) in terms of COVID-19 and MIS-C patient count care. It has merit since it includes long-term data, such as 2 years of information from two centers with third-level intensive care.

Conclusion

The incidence of AKI in the MIS-C and COVID-19 pediatric population may increase due to the severity of the illnesses and the use of several medicines during admission and follow-up. AKI is a primary factor in determining a patient's level of criticality, fluid balance, length of stay in the intensive care unit, and mortality. It is vital to maintain normal blood pressure in developing AKI patients, to avoid fluid balance and nephrotoxic medications, and to regulate the amount of nephrotoxic medication according to GFR. In order to comprehend the pathophysiology and evaluate the efficacy and outcomes of treatments currently in use, multicentric and more advanced studies are required at this time.

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Declarations

Ethics approval Approval was obtained from the institutional review board.

Consent to participate Approval was obtained from the family of each participant.

Consent for publication Approval was obtained from the family of each participant.

Competing interests The authors declare no competing interests.

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