The Spectrum of Kidney Disorders in Children Infected with COVID-19: A Retrospective Cohort Study

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ABSTRACT

Background. The COVID-19 pandemic, caused by the SARS-CoV-2 virus, has impacted various organ systems, including the kidneys, in adults and children. While acute kidney injury (AKI) is well-documented in adults with COVID-19, there is limited data on kidney involvement in pediatric patients, especially in resource-limited settings like the Philippines. This study explores the spectrum of kidney diseases in children infected with COVID-19.

Objective. The study aims to characterize the incidence and types of kidney dysfunction in pediatric COVID-19 patients, identify associated risk factors, and evaluate patient outcomes, including the need for renal replacement therapy (RRT) and mortality rates.

Methods. This retrospective cohort study analyzed pediatric patients diagnosed with SARS-CoV-2 infection via RT-PCR, admitted to the Philippine General Hospital from March 2020 to April 2023. Patients with prior kidney disease were excluded. Data on demographic characteristics, clinical status, comorbidities, and laboratory findings were collected. Kidney dysfunction was defined as AKI, proteinuria, hematuria, or glucosuria. Associations between kidney dysfunction, COVID-19 severity, and patient outcomes were analyzed using logistic regression.

Results. Of the 316 pediatric COVID-19 patients included, 47.78% (151) had kidney involvement, most commonly hematuria (28.48%), proteinuria (26.27%), and AKI (14.60%). Severe and critical COVID-19 were significantly associated with kidney dysfunction, while comorbidities such as oncologic/hematologic conditions decreased the odds of proteinuria and glucosuria. AKI was associated with hypertension, fever, and severe COVID-19. Mortality was 12.03%, with AKI and critical COVID-19 being significant risk factors.

Conclusion. Kidney dysfunction is common in pediatric COVID-19 cases, particularly in severe disease. AKI was strongly associated with worse outcomes, including mortality. Early detection and management of kidney involvement are essential to improving prognosis in pediatric COVID-19 patients.

Keywords: COVID-19, acute kidney injury, hematuria, proteinuria, children, glucosuria

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INTRODUCTION

The novel coronavirus disease (COVID-19) emerged as a global health crisis in December 2019, quickly escalating into a pandemic. COVID-19, caused by the SARS-CoV-2 virus, has profoundly affected health systems worldwide, leading to millions of infections and deaths. The World Health Organization (WHO) declared COVID-19 a public health emergency of international concern (PHEIC) in March 2020, a status maintained until May 2023. While adults, particularly males with comorbidities, were more prone to severe disease manifestations such as acute respiratory distress syndrome (ARDS) and multiple organ failure, children generally

experienced milder symptoms such as fever, cough, vomiting, diarrhea, and sore throat.[1] Nevertheless, the pediatric population has not been immune to the complications of COVID-19. Children at risk of mortality and severe COVID-19 include extremes of ages and those with cardiac disease, pulmonary disease, and obesity. Severe cases were also found among those with elevated serum C-reactive protein, D-dimer, and in those who developed Multisystem Inflammatory Syndrome in Children (MIS-C).[2] A local study identified the presence of a congenital anomaly, lung disease, and elevated procalcitonin as risk factors for severe disease.[3]

Although SARS-CoV-2 mainly affects the respiratory system, causing pneumonia, it can also impact various organ systems, including the kidneys, myocardium, intestines, hepatobiliary system, and central nervous system.[4] Kidney involvement remains an important extra-pulmonary manifestation, which has a critical impact on the prognosis and mortality in COVID-19 cases.[5]

Acute kidney injury (AKI) is one of the significant complications observed in adults with severe COVID-19, contributing to increased mortality, especially among those requiring kidney replacement therapy (KRT). The average incidence of AKI, as reported in adult patients with SARS-CoV-2, has been between 5.1 and 29%.[6] It is also attributed to comorbidities like hypertension, type 2 diabetes mellitus, cardiac failure, chronic kidney disease, and other chronic diseases in adults, which are almost non-existent in children.

However, children with comorbidities like congenital heart diseases and some urological disorders and post-kidney transplant recipients infected with SARS-CoV-2 have higher chances of kidney involvement and complications.

The pathophysiology of AKI in COVID-19 is multifactorial, involving direct viral damage to renal cells, systemic blood flow disturbances, and a prothrombotic environment that increases the risk of thrombotic microangiopathy.[7] While these mechanisms have been extensively characterized in adult populations, the incidence, clinical spectrum, and underlying pathophysiology of kidney involvement in pediatric COVID-19 cases remain incompletely understood. Preliminary reports suggest that children infected with SARS-CoV-2 may exhibit renal abnormalities such as proteinuria, hematuria, and evidence of tubular injury. However, comprehensive epidemiologic and mechanistic data in this age group are limited. Understanding the kidney effects of COVID-19 in children is essential because early detection and treatment can significantly impact health outcomes.

In the Philippines, over 470,000 COVID-19 cases in children, with over 1,500 deaths, were recorded during the same period. The Philippine General Hospital (PGH) has been at the forefront of managing COVID-19 cases in the Philippines, providing a unique opportunity to study the disease's impact on children in a resource-limited setting. A study of 448 pediatric patients with COVID-19 in this institution reported 22 patients (4.9%) with kidney injury.[3] No local data on the incidence of AKI and the possible manifestations of kidney dysfunction have been reported in the pediatric population. Although the pandemic has passed, COVID-19 has remained endemic, with newer subvariants, such as the JN.1, identified in September 2023 and the FLiRT subvariants in April 2024.

This study provides a comprehensive characterization of renal involvement among pediatric patients admitted with COVID-19 at the PGH. It details the incidence and spectrum of kidney dysfunction, including AKI, proteinuria, hematuria, and glucosuria. Furthermore, the study identifies clinical and laboratory risk factors associated with these renal complications. It evaluates patient outcomes, such as the requirement for kidney replacement therapy (KRT) and overall survival rates. Mortality rates within the cohort were also analyzed, along with associated predictors of poor outcomes. The findings provide valuable insights into the renal sequelae of COVID-19 in children and may inform future clinical guidelines for managing pediatric COVID-19, particularly within the local healthcare context.

METHODS

Study Design

This was a single-center retrospective cohort study conducted at the PGH from March 2020 until April 2023. It included patients under 19 years of age with SARS-CoV-2 infection confirmed by real-time reverse transcriptase polymerase chain reaction (RT-PCR) assay.

A list of pediatric patients diagnosed with COVID-19 was obtained from the PGH Pediatric Infectious Disease Service census. The corresponding case numbers were noted and used as a reference to retrieve the charts from the PGH Medical Records. Only confirmed COVID-19 patients with positive SARS-CoV-2 RT-PCR from samples collected from the upper (pharyngeal swabs, nasal swabs, nasopharyngeal secretions) and/or lower airways (sputum, airway secretions, bronchoalveolar lavage fluid) were included in this study. The RT-PCR tests were done at a national reference laboratory, a subnational reference laboratory, and/or Department of Health (DOH)-certified laboratory testing facilities. Patients were excluded if urinalysis is unavailable or if there was a pre-existing diagnosis of kidney disease.

COVID-19 cases were diagnosed and classified according to the existing guidelines set out by the Pediatric Infectious Disease Society of the Philippines, which were available at the time of the patient's admission.[8-10]

The exposure variables used were demographic characteristics, age and sex, clinical characteristics (i.e., COVID-19 severity, COVID-19 vaccination, anthropometrics, vital signs, presence of MIS-C, and comorbidities), diagnostic tests (i.e., laboratory tests), and the year of admission (as a surrogate marker for the prevalent SARS-CoV-2 serotypes of that year).

Data Collection

Demographic and clinical data were collected for all patients, including age, sex, anthropometric measurements (expressed as Z-scores), vital signs, pre-existing comorbidities, COVID-19 vaccination status, duration of hospitalization, clinical severity, and outcomes—both patient (recovery or death) and renal (presence of acute kidney injury and need for dialysis).

Laboratory parameters assessed included urinalysis, serum blood urea nitrogen, creatinine, electrolytes (sodium, potassium, chloride, calcium, magnesium, phosphorus), uric acid, albumin, arterial blood gas analysis, and complete blood count.

The primary outcome was kidney dysfunction, defined as Acute Kidney Injury (AKI), proteinuria, hematuria, and glucosuria. AKI was classified according to the Kidney Disease Improving Global Outcomes (KDIGO) 2012 Clinical Practice Guideline for Acute Kidney Injury I.[11] Glomerular Filtration Rate (GFR) (ml/min/1.73m^2) was estimated using the modified Schwartz formula.[12] Proteinuria was defined as a urinalysis/urine dipstick result of +1 to +4. Hematuria was defined as more than 5 red blood cells per high-power field. Normoglycemic glucosuria, used as a surrogate marker for tubular involvement, was defined as urine glucose of +1 to +4. Additional indicators of tubular dysfunction, such as normal anion gap metabolic acidosis and electrolyte abnormalities, were also recorded. Secondary outcomes included death or recovery, length of hospital stay, and renal recovery or requirement for dialysis on discharge.

Data Analysis

Descriptive statistics were used to summarize the demographic and clinical characteristics of Filipino children with COVID-19 admitted to the PGH from 2020 to 2023. Numerical variables were reported as medians with interquartile ranges, while categorical variables were presented as frequencies and percentages. Patients were categorized based on the presence or absence of kidney dysfunction. The cumulative incidence of renal manifestations was expressed as a point estimate with a 95% confidence interval.

Associations between clinical factors and kidney dysfunction or mortality were assessed using multivariable logistic regression, while factors associated with AKI recovery were analyzed using univariable logistic regression. Statistical analyses were performed using Stata 17. Missing data were not replaced or imputed. The Shapiro-Wilk test was used to assess the normality of numerical variables. Statistical significance was set at a two-sided alpha level of 0.05.

Ethical Considerations

This study was approved by the University of the Philippines - Manila Research Ethics Board (UPMREB) panel and adhered to the ethical considerations and principles set out in relevant guidelines, including the Data Privacy Act of 2012, Declaration of Helsinki, WHO guidelines, International Conference on Harmonization-Good Clinical Practice, and National Ethical Guidelines for Health and Health-Related Research (NEGHHR, 2017). Each case was given a code, and no identifiers were recorded in the case report forms or the manuscript. There are no conflicts of interest among the primary investigator's financial, familial, or proprietary considerations. The study has no direct benefit or risk to the participants.

RESULTS

From March 2020 to April 2023, a total of 715 patients were diagnosed with COVID-19 at the PGH. Of these, 647 cases were confirmed by RT-PCR. Urinalysis results were available for 352, and 36 with pre-existing kidney disease were excluded. The final study cohort consisted of 316 pediatric patients with confirmed COVID-19 and available urinalysis data.

The most represented age groups were the 1-5 years and the 11-15 years, each comprising 25.6% of the cohort. This was followed by the <1-year age group (17.1%) and the 6-10- and 16-18-year age groups, both at 15.8%. Kidney involvement was prevalent among patients aged 11-15 years (24.5%). The majority of the study population was male (55.38%). Nutritional assessment revealed that 40% of the patients were stunted; 37.03% were underweight, and 7.91% were overweight (Table 1).

Upon admission, 14.56% presented with fever; 66.45% exhibited tachycardia, 22.47% had hypertension, and 6.96% were hypotensive. Regarding disease severity, 103 (32.59%) were asymptomatic and admitted for unrelated conditions, 97 cases (30.70%) had mild disease, 51 cases (16.14%) were classified as severe, and 31 cases (9.81%) as critical. Kidney involvement was observed in 64.71% with severe disease and 61.29% of those with critical illness.

Approximately 80% of the admitted patients with COVID-19 had at least one comorbidity. The most common underlying conditions were oncologic and hematologic disorders (21.27%), followed by neurologic (14.92%), infectious (10.16%), surgical (8.57%), cardiac (7.94%%), and congenital anomalies (5.08%). Most patients (98.41%) were unvaccinated against COVID-19. Multisystem inflammatory syndrome (MIS-C) developed in 11 patients (3.48%). The median length of hospital stay was 14 days; 233 cases (73.73%) were hospitalized for more than 1 week, while 83 cases (26.26%) were admitted for less than a week.

Table 2 summarizes the laboratory findings. Aside from the expected difference in urinalysis findings between those with and without kidney baseline laboratory findings were otherwise comparable between groups.

Of the 316 patients included in the study, 151 (47.78%) exhibited kidney involvement/dysfunction, while 165 (52.22%) had no evidence of kidney dysfunction. The most common kidney dysfunctions based on cumulative incidence were hematuria (28.48%, n=90), proteinuria (26.27%, n=83),

acute kidney injury (14.60%, n=46), and glucosuria (8.86%, n=28) (Table 3). Among patients with AKI, 3 (6.52%) underwent dialysis (two received hemodialysis, and one received peritoneal dialysis). An additional 9 cases with AKI requiring dialysis died before the procedure could be initiated, resulting in 12 patients (26.08%) who received dialysis. Among those with kidney involvement, 90 had at least +1 proteinuria (59.60%), 83 had hematuria (54.96%), and 28 had glucosuria (18.54%).

Among this cohort, notable renal presentations included one case of new-onset nephrotic syndrome (NS) associated with COVID-19 and three cases of acute glomerulonephritis. Two of the cases with acute glomerulonephritis presented with a rapidly progressive course, necessitating pulse intravenous methylprednisolone therapy.

Multivariable logistic regression analysis identified COVID-19 severity as a significant predictor of kidney dysfunction. Patients with severe disease had increased odds of developing renal complications compared to asymptomatic cases (Table 4A). Hematuria was significantly associated with both sex and disease severity; male patients had 46% lower odds of hematuria compared to females, and those

Table 1. Clinical profile and outcomes of Filipino children with COVID-19 infection in the Philippine General Hospital (PGH) from 2020 to 2023

	Patients, n = 316	With kidney involvement, n = 151	Without kidney involvement, n = 165
	Frequency (%); Median (IQR)		
Age (years)			
<1	54 (17.09%)	27 (17.88%)	27 (16.36%)
1-5	81 (25.63%)	30 (19.87%)	51 (30.91%)
6-10	50 (15.82%)	31 (20.53%)	19 (11.52%)
11-15	81 (25.63%)	37 (24.50%)	44 (26.67%)
16-18	50 (15.82%)	26 (17.22%)	24 (14.55%)
Sex			
Male	175 (55.38%)	79 (52.32%)	96 (58.18%)
Female	141 (44.62%)	72 (47.68%)	69 (41.82%)
Anthropometrics			
Weight			
Normal for age	174 (55.06%)	78 (51.66%)	96 (58.18%)
Underweight	117 (37.03%)	60 (39.74%)	57 (34.55%)
Overweight	25 (7.91%)	13 (8.61%)	12 (7.27%)
Height [n=315]			
Normal for age	190 (60.00%)	89 (58.28%)	101 (61.59%)
Stunted	126 (40.00%)	63 (41.72%)	63 (38.41%)
Vitals Signs			
Blood Pressure			
Normotensive	223 (70.57%)	100 (66.23%)	123 (74.55%)
Hypotensive	22 (6.96%)	10 (6.62%)	12 (7.27%)
Hypertensive	71 (22.47%)	41 (27.15%)	30 (18.18%)
Heart Rate [n=314]			
Normal Rate	104 (32.91%)	49 (32.24%)	55 (33.54%)
Bradycardia	2 (0.63%)	0	2 (1.22%)
Tachycardia	210 (66.45%)	103 (67.76%)	107 (65.24%)
Temperature			
Afebrile	270 (85.44%)	124 (82.12%)	146 (88.48%)
Febrile	46 (14.56%)	27 (17.88%)	19 (11.52%)
Comorbid Conditions [n=315]			
None	65 (20.32%)	31 (19.87%)	34 (20.73%)
Neurologic	47 (14.92%)	27 (17.88%)	20 (12.20%)
Cardiac	25 (7.94%)	10 (6.62%)	15 (9.15%)
Oncologic/Hematologic	67 (21.27%)	23 (15.23%)	44 (26.83%)
Congenital	16 (5.08%)	9 (5.96%)	7 (4.27%)
Pulmonary	4 (1.27%)	3 (1.99%)	1 (0.61%)
Infectious	32 (10.16%)	19 (12.58%)	13 (7.93%)
Surgical	27 (8.57%)	15 (9.93%)	12 (7.32%)
Others	33 (10.48%)	15 (9.93%)	18 (10.98%)

Table 1. Clinical profile and outcomes of Filipino children with COVID-19 infection in the Philippine General Hospital (PGH) from 2020 to 2023 *(continued)*

	Patients, n = 316	With kidney involvement, n = 151	Without kidney involvement, n = 165
	Frequency (%); Median (IQR)		
COVID-19 Severity			
Asymptomatic	103 (32.59%)	45 (29.80%)	58 (35.15%)
Mild	97 (30.70%)	38 (25.17%)	59 (35.76%)
Moderate	34 (10.76%)	16 (10.60%)	18 (10.91%)
Severe	51 (16.14%)	33 (21.85%)	18 (10.91%)
Critical	31 (9.81%)	19 (12.58%)	12 (7.27%)
COVID-19 Vaccine			
None	311 (98.41%)	151 (99.34%)	160 (97.56%)
Complete	5 (1.59%)	1 (0.66%)	4 (2.44%)
MIS-C			
Yes	11 (3.48%)	5 (3.31%)	6 (3.64%)
No	305 (96.52%)	146 (96.69%)	159 (96.36%)
Year Diagnosed			
2020	18 (5.70%)	7 (4.64%)	11 (6.67%)
2021	210 (66.46%)	102 (67.55%)	108 (65.45%)
2022/2023	88 (27.85%)	42 (27.81%)	46 (27.88%)
Patient Outcome			
Length of hospital stay, days	14 (20)	14 (21)	12 (19)
Recovery	278 (87.97%)	122 (80.79%)	156 (94.55%)
Death	38 (12.03%)	29 (19.21%)	9 (5.45%)

Table 2. Laboratory findings of Filipino children with COVID-19 infection in the PGH from 2020 to 2023

	Patients, n = 316	With kidney involvement, n = 151	Without kidney involvement, n = 165
	Frequency (%); Median (IQR)		
Urinalysis			
Proteinuria	83 (26.27%)	83 (54.96%)	0 (0%)
Hematuria	90 (28.48%)	90 (59.60%)	0 (0%)
Glucosuria	28 (8.86%)	28 (18.54%)	0 (0%)
Serum Chemistry			
Blood Urea Nitrogen (mmol/L) [n=303]	4.3 (3.3)	5.0 (5.6)	3.5 (2.3)
Creatinine (umol/L) [n=309]	38 (24)	44.5 (38.5)	32 (17)
Sodium (mmol/L) [n=303]	136 (7)	137 (9)	136 (6)
Potassium (mmol/L) [n=303]	4.2 (1.0)	4.2 (1.0)	4.2 (0.9)
Chloride (mmol/L) [n=300]	103 (8)	102 (10)	103 (7)
Calcium (mmol/L) [n=294]	2.26 (0.32)	2.24 (0.35)	2.29 (0.31)
Magnesium (mmol/L) [n=260]	0.87 (0.17)	0.91 (0.21)	0.87 (0.15)
Phosphorus (mmol/L) [n=112]	1.42 (0.63)	1.49 (0.63)	1.36 (0.64)
Arterial Blood Gas			
Serum pH [n=202]	7.42 (0.12)	7.42 (0.13)	7.42 (0.10)
Serum Bicarbonate [n=202]	18.75 (6.8)	17.9 (7.9)	19.6 (5.8)
Complete Blood Count			
Hemoglobin (g/dL) [n=315]	118 (40)	118 (34)	117.5 (46.5)
White Blood Cell Count (10^9/L) [n=315]	12.2 (9.4)	13.4 (11.2)	11 (8.65)
Neutrophils [n=315]	55 (72)	56 (79.1)	52.5 (65.5)
Lymphocytes [n=315]	14 (27)	11 (23)	16 (30)
Platelet Count (10^9/L) [n=312]	290.5 (244)	311 (275)	274 (208)

Table 3. Kidney manifestations of COVID-19 in Filipino children in the PGH from 2020 to 2023

	Cumulative incidence	95% CI
Acute kidney injury	14.60%	10.89, 18.99
Hematuria	28.48%	23.57, 33.80
Proteinuria	26.27%	21.50, 31.48
Glucosuria	8.86%	5.97, 12.55

with moderate COVID-19 had 72% lower odds compared to asymptomatic patients (Table 4B). Proteinuria was also significantly associated with disease severity, with severe cases showing a 162% increase in odds compared to asymptomatic patients (Table 4C). Additionally, patients with oncologic or hematologic comorbidity have significantly reduced odds of developing both proteinuria and glucosuria (Table 4C and 4D).

Multivariable regression analysis identified hypertension, fever, and COVID-19 severity as significant risk fac-

Table 4A. Factors associated with kidney dysfunction among Filipino children with COVID-19 infection

Factors	Univariable			Multivariable		
	OR	95% CI	*p*-value	Adj. OR	95% CI	*p*-value
Age (years)						
<1	Reference			Reference		
1-5	0.59	0.29, 1.18	0.137	0.66	0.29, 1.54	0.340
6-10	1.63	0.75, 3.56	0.220	2.23	0.86, 5.80	0.099
11-15	0.84	0.42, 1.68	0.622	1.13	0.49, 2.62	0.774
16-18	1.08	0.50, 2.34	0.838	1.60	0.63, 4.08	0.327
Male	0.79	0.51, 1.23	0.295	1.60	0.63, 4.08	0.327
Weight						
Normal for age	Reference			Reference		
Underweight	1.30	0.81, 2.07	0.280	1.27	0.64, 2.52	0.489
Overweight	1.33	0.58, 3.09	0.502	1.44	0.55, 3.73	0.457
Stunted	1.15	0.73, 1.80	0.550	0.70	0.35, 1.38	0.304
Blood Pressure						
Normotensive	Reference			Reference		
Hypotensive	1.03	0.43, 2.47	0.956	1.67	0.62, 4.52	0.309
Hypertensive	1.68	0.98, 2.88	0.059	1.81	0.95, 3.46	0.073
Tachycardia	1.13	0.70, 1.81	0.623	1.12	0.64, 1.93	0.696
Febrile	1.67	0.89, 3.15	0.111	1.85	0.89, 3.84	0.099
Comorbidity						
None	Reference			Reference		
Neurologic	1.53	0.72, 3.27	0.272	1.07	0.45, 2.58	0.874
Cardiac	0.76	0.30, 1.93	0.558	0.77	0.27, 2.20	0.624
Oncologic/Hematologic	0.59	0.29, 1.20	0.145	0.46	0.20, 1.04	0.063
Congenital	1.46	0.48, 4.39	0.504	1.38	0.38, 5.03	0.629
Pulmonary	3.40	0.34, 34.45	0.300	3.17	0.28, 35.69	0.349
Infectious	1.66	0.70, 3.91	0.250	1.59	0.62, 4.10	0.336
Surgical	1.42	0.57, 3.50	0.450	1.20	0.44, 3.31	0.721
Others	0.94	0.41, 2.19	0.894	0.91	0.35, 2.36	0.848
COVID-19 Severity						
Asymptomatic	Reference			Reference		
Mild	0.83	0.47, 1.46	0.517	0.76	0.40, 1.45	0.408
Moderate	1.15	0.53, 2.49	0.732	1.21	0.51, 2.85	0.668
Severe	2.36	1.18, 4.73	0.015	2.37	1.06, 5.28	0.035
Critical	2.04	0.90, 4.64	0.089	2.31	0.89, 5.98	0.083
Complete COVID-19 Vaccination	0.52	0.17, 1.55	0.240	0.56	0.17, 1.81	0.334
MIS-C	0.91	0.27, 3.04	0.875	0.58	0.14, 2.41	0.454
Year Diagnosed						
2020	Reference			Reference		
2021	1.48	0.55, 3.98	0.432	1.24	0.42, 3.66	0.701
2022/2023	1.43	0.51, 4.04	0.495	1.33	0.40, 4.43	0.648

Table 4B. Factors associated with hematuria among Filipino children with COVID-19 infection

Factors	Univariable			Multivariable		
	OR	95% CI	*p*-value	Adj. OR	95% CI	*p*-value
Age (years)						
<1	Reference			Reference		
1-5	0.63	0.29, 1.39	0.254	0.58	0.23, 1.49	0.259
6-10	1.02	0.44, 2.36	0.967	0.92	0.33, 2.55	0.877
11-15	1.40	0.67, 2.92	0.374	1.71	0.69, 4.22	0.247
16-18	0.75	0.31, 1.80	0.518	0.93	0.33, 2.65	0.894
Male	0.69	0.42, 1.13	0.144	0.57	0.33, 0.98	0.044
Weight						
Normal for age	Reference			Reference		
Underweight	1.27	0.76, 2.14	0.360	1.37	0.66, 2.84	0.392
Overweight	1.61	0.67, 3.90	0.290	2.28	0.86, 6.05	0.100
Stunted	1.07	0.65, 1.75	0.799	0.89	0.43, 1.85	0.762
Blood Pressure						
Normotensive	Reference			Reference		
Hypotensive	0.58	0.19, 1.77	0.337	0.85	0.25, 2.84	0.788
Hypertensive	1.33	0.75, 2.35	0.334	1.70	0.86, 3.37	0.127
Tachycardia	0.94	0.56, 1.58	0.809	0.87	0.48, 1.58	0.645
Febrile	1.41	0.73, 2.74	0.307	1.34	0.64, 2.83	0.441
Comorbidity						
None	Reference			Reference		
Neurologic	1.22	0.55, 2.74	0.626	1.21	0.47, 3.14	0.687
Cardiac	0.75	0.26, 2.17	0.592	0.88	0.27, 2.86	0.836
Oncologic/Hematologic	0.81	0.37, 1.74	0.581	0.86	0.36, 2.08	0.746
Congenital	1.84	0.60, 5.67	0.287	1.86	0.50, 6.90	0.353
Pulmonary	-	-	-	-	-	-
Infectious	1.42	0.58, 3.48	0.441	1.44	0.54, 3.85	0.467
Surgical	0.68	0.24, 1.94	0.468	0.46	0.15, 1.44	0.180
Others	0.64	0.24, 1.72	0.374	0.56	0.19, 1.67	0.301
COVID-19 Severity						
Asymptomatic	Reference			Reference		
Mild	0.81	0.44, 1.50	0.507	0.83	0.42, 1.66	0.604
Moderate	0.38	0.14, 1.08	0.069	0.28	0.09, 0.84	0.023
Severe	1.21	0.60, 2.46	0.598	1.21	0.54, 2.71	0.651
Critical	0.91	0.38, 2.19	0.829	0.57	0.20, 1.60	0.286
Complete COVID-19 Vaccination	0.79	0.26, 2.37	0.672	0.68	0.20, 2.39	0.553
MIS-C	1.46	0.42, 5.10	0.558	2.15	0.51, 9.15	0.298
Year Diagnosed						
2020	Reference			Reference		
2021	1.47	0.46, 4.63	0.514	1.58	0.46, 5.47	0.467
2022/2023	1.31	0.39, 4.38	0.659	1.43	0.37, 5.55	0.602

tors for AKI. Specifically, moderate and critical COVID-19 had markedly increased odds of developing AKI by 303% and 613%, respectively, compared to asymptomatic patients. In contrast, the presence of neurologic comorbidities was associated with decreased odds of developing AKI (Table 4E).

The overall mortality was 12.03% (n=38), with 76.31% (n=29) of these deaths occurring in patients with kidney involvement/dysfunction. Multivariable logistic regression analysis identified several factors significantly associated with increased mortality (Table 5). These included the presence of AKI (OR 7.36, CI 2.14- 25.29), hypotension (OR 8.56, CI 1.75- 41.79), oncologic//hematologic comorbidity (OR 35.39, CI 4.45- 283.16), congenital anomalies (OR 20.10, CI 1.78- 227.45), and critical COVID severity (OR 15.51, CI 3.16- 76.03), all with p<0.05.

Univariate analysis also revealed significant associations between mortality and several electrolyte abnormalities. Patients with hyponatremia (OR 3.06, CI 1.45-6.45), hypernatremia (OR 5.91, CI 1.78-19.58), hyperkalemia (OR 5.29, CI 2.01-13.95), and hypermagnesemia (OR 6.01, CI 2.49-14.51) have increased odds of death (p<0.05).

Table 4C. Factors associated with proteinuria among Filipino children with COVID-19 infection

Factors	Univariable			Multivariable		
	OR	95% CI	*p*-value	Adj. OR	95% CI	*p*-value
Age (years)						
<1	Reference			Reference		
1-5	0.41	0.18, 0.96	0.041	0.45	0.17, 1.18	0.105
6-10	1.58	0.70, 3.57	0.268	2.27	0.83, 6.26	0.112
11-15	0.78	0.36, 1.69	0.525	0.94	0.37, 2.40	0.895
16-18	1.02	0.44, 2.36	0.967	1.33	0.47, 3.77	0.589
Male	1.00	0.61, 1.66	0.993	0.92	0.52, 1.63	0.780
Weight						
Normal for age	Reference			Reference		
Underweight	1.08	0.64, 1.83	0.778	1.14	0.53, 2.46	0.730
Overweight	0.91	0.34, 2.41	0.842	0.75	0.24, 2.31	0.620
Stunted	0.99	0.59, 1.65	0.958	0.73	0.34, 1.61	0.440
Blood Pressure						
Normotensive	Reference			Reference		
Hypotensive	0.90	0.32, 2.55	0.840	1.34	0.42, 4.23	0.618
Hypertensive	1.46	0.82, 2.62	0.200	1.69	0.84, 3.43	0.144
Tachycardia	0.91	0.54, 1.56	0.744	1.01	0.54, 1.87	0.980
Febrile	1.44	0.73, 2.82	0.292	1.67	0.75, 3.70	0.207
Comorbidity						
None	Reference			Reference		
Neurologic	0.88	0.37, 2.06	0.761	0.58	0.22, 1.58	0.288
Cardiac	0.81	0.28, 2.35	0.694	0.88	0.28, 2.82	0.834
Oncologic/Hematologic	0.40	0.16, 0.96	0.041	0.36	0.13, 0.97	0.044
Congenital	1.16	0.35, 3.82	0.805	0.93	0.24, 3.65	0.913
Pulmonary	0.85	0.08, 8.74	0.893	0.62	0.05, 7.45	0.705
Infectious	1.53	0.62, 3.77	0.352	1.61	0.59, 4.39	0.349
Surgical	1.50	0.58, 3.90	0.402	1.52	0.52, 4.47	0.448
Others	1.11	0.44, 2.79	0.823	1.25	0.44, 3.57	0.671
COVID-19 Severity						
Asymptomatic	Reference			Reference		
Mild	0.96	0.49, 1.88	0.908	0.87	0.41, 1.87	0.729
Moderate	1.07	0.43, 2.68	0.885	1.27	0.47, 3.46	0.639
Severe	2.24	1.08, 4.65	0.030	2.62	1.11, 6.19	0.028
Critical	1.91	0.80, 4.56	0.144	2.78	0.99, 7.84	0.053
Complete COVID-19 Vaccination	-	-	-	-	-	-
MIS-C	1.05	0.27, 4.07	0.938	0.62	0.13, 3.07	0.561
Year Diagnosed						
2020	Reference			Reference		
2021	0.99	0.34, 2.91	0.988	0.62	0.19, 1.98	0.416
2022/2023	0.76	0.24, 2.40	0.646	0.47	0.12, 1.79	0.271

Among the patients who died, nine cases had multiorgan failure and hypotension/shock, necessitating dialysis, but this could not be performed due to profound hemodynamic instability. Notably, none of the patients with AKI who survived were discharged on dialysis. Of the 11 cases with MISC-C, two deaths were recorded. The median length of hospital stay was similar between patients with and without kidney dysfunction was similar, at 14 and 12 days, respectively.

DISCUSSION

This retrospective cohort study analyzed 316 pediatric patients with RT-PCR-confirmed COVID-19 admitted at a tertiary referral center between March 2020 and April 2023, focusing on the epidemiology and spectrum of kidney dysfunction, including AKI, hematuria, proteinuria, and glucosuria. Consistent with the known ability of SARS-CoV-2 to infect all age groups, the majority of cases in this cohort were observed in children aged 1-5 years and 11-15 years. This age distribution aligns with findings from the

Table 4D. Factors associated with glucosuria among Filipino children with COVID-19 infection

Factors	Univariable			Multivariable		
	OR	95% CI	*p*-value	Adj. OR	95% CI	*p*-value
Age (years)						
<1	Reference			Reference		
1-5	1.56	0.46, 5.36	0.478	2.01	0.46, 8.80	0.354
6-10	1.70	0.45, 6.43	0.431	2.89	0.59, 14.20	0.191
11-15	1.00	0.27, 3.72	>0.999	1.61	0.37, 7.12	0.528
16-18	0.80	0.17, 3.76	0.775	0.68	0.11, 4.31	0.686
Male	0.67	0.31, 1.47	0.321	0.89	0.36, 2.23	0.811
Weight						
Normal for age	Reference			Reference		
Underweight	1.69	0.74, 3.84	0.212	2.28	0.66, 7.92	0.194
Overweight	1.84	0.48, 7.04	0.373	1.72	0.35, 8.39	0.504
Stunted	1.33	0.61, 2.91	0.489	0.92	0.28, 3.03	0.891
Blood Pressure						
Normotensive	Reference			Reference		
Hypotensive	1.70	0.46, 6.15	0.428	2.24	0.50, 10.04	0.291
Hypertensive	0.99	0.38, 2.59	0.985	0.58	0.17, 1.91	0.370
Tachycardia	1.87	0.73, 4.77	0.189	2.22	0.76, 6.49	0.146
Febrile	0.98	0.32, 2.96	0.966	0.97	0.25, 3.70	0.959
Comorbidity						
None	Reference			Reference		
Neurologic	1.19	0.37, 3.81	0.767	0.55	0.14, 2.19	0.394
Cardiac	0.71	0.14, 3.67	0.681	0.40	0.06, 2.63	0.338
Oncologic/Hematologic	0.12	0.01, 1.03	0.054	0.05	0.01, 0.49	0.010
Congenital	-	-	-	-	-	-
Pulmonary	2.71	0.25, 29.78	0.414	0.04	0.18, 35.08	0.491
Infectious	0.84	0.20, 3.50	0.813	0.57	0.12, 2.77	0.485
Surgical	-	-	-	-	-	-
Others	2.61	0.85, 7.97	0.093	2.52	0.71, 8.93	0.153
COVID-19 Severity						
Asymptomatic	Reference			Reference		
Mild	0.94	0.35, 2.54	0.901	0.72	0.23, 2.25	0.568
Moderate	0.65	0.13, 3.18	0.598	0.49	0.09, 2.76	0.421
Severe	1.39	0.47, 4.15	0.552	0.67	0.18, 2.47	0.544
Critical	1.12	0.28, 4.42	0.872	0.70	0.14, 3.46	0.662
Complete COVID-19 Vaccination	-	-	-	-	-	-
MIS-C	1.03	0.13, 8.35	0.978	0.87	0.09, 8.74	0.907
Year Diagnosed						
2020	Reference			Reference		
2021	0.66	0.14, 3.13	0.600	0.85	0.15, 4.91	0.853
2022/2023	1.03	0.20, 5.13	0.975	3.87	0.54, 27.68	0.178

SALVACION Registry, a large-scale cohort study involving 3,221 Filipino children with COVID-19.[13] Notably, most cases of kidney dysfunction occurred in the 11-15 age group. However, the overall cohort was predominantly composed of children aged 10 and below (~59%). A slight male predominance was also observed among the affected patients. There is limited literature on the kidney manifestations of COVID-19 in adults and children. In one pediatric study, the median age of children was 6 years (IQR, 3- 10), with a slight male predominance (55.3%).[14]

In the Philippines, the pediatric COVID-19 vaccination program for ages 12-17 was only implemented in October 2021, followed by vaccination for ages 5-11 in February 2022. As a result, most of the children in this study had no vaccination against COVID-19, with only five patients receiving complete vaccination. Four of these patients, who completed the primary series, were either asymptomatic or had mild cases, except for one patient with lymphoma who had critical COVID-19 with myocarditis.

SARS-CoV-2 generally results in milder diseases in children compared to adults, though a subset of children

Table 4E. Factors associated with AKI among Filipino children with COVID-19 infection

Factors	Univariable			Multivariable		
	OR	95% CI	*p*-value	Adj. OR	95% CI	*p*-value
Age (years)						
<1	Reference			Reference		
1-5	0.31	0.11, 0.91	0.032	0.32	0.09, 1.14	0.078
6-10	0.98	0.37, 2.55	0.963	1.56	0.45, 5.45	0.487
11-15	0.56	0.22, 1.43	0.223	0.82	0.25, 2.74	0.751
16-18	0.86	0.32, 2.28	0.759	1.56	0.44, 5.63	0.493
Male	1.18	0.63, 2.22	0.610	1.18	0.56, 2.50	0.659
Weight						
Normal for age	Reference			Reference		
Underweight	0.94	0.48, 1.84	0.852	0.69	0.26, 1.82	0.457
Overweight	1.48	0.51, 4.30	0.472	1.16	0,31, 4.31	0.825
Stunted	1.06	0.56, 2.00	0.860	1.01	0.37, 2.74	0.990
Blood Pressure						
Normotensive	Reference			Reference		
Hypotensive	1.68	0.53, 5.33	0.383	3.39	0.88, 12.97	0.075
Hypertensive	2.19	1.10, 4.38	0.026	3.06	1.28, 7.32	0.012
Tachycardia	0.90	0.47, 1.74	0.756	0.73	0.33, 1.62	0.435
Febrile	1.80	0.82, 3.94	0.142	3.20	1.18, 8.72	0.023
Comorbidity						
None	Reference			Reference		
Neurologic	0.36	0.11, 1.20	0.970	0.23	0.06, 0.89	0.033
Cardiac	0.98	0.31, 3.11	0.974	1.48	0.38, 5.76	0.571
Oncologic//Hematologic	0.47	0.17, 1.26	0.131	0.34	0.10, 1.13	0.079
Congenital	0.56	0.11, 2.78	0.479	0.44	0.07, 2.85	0.390
Pulmonary	1.31	0.13, 13.63	0.822	2.85	0.22, 37.19	0.425
Infectious	1.10	0.39, 3.10	0.859	1.03	0.30, 3.49	0,962
Surgical	0.31	0.07, 1.50	0.146	0.23	0.04, 1.36	0.105
Others	0.70	0.23, 2.17	0.537	0.57	0.15, 2.13	0.404
COVID-19 Severity						
Asymptomatic	Reference			Reference		
Mild	1.21	0.47, 3.13	0.688	1.33	0.47, 3.79	0.591
Moderate	3.76	1.35, 10.47	0.011	4.03	1.26, 12.89	0.019
Severe	2.24	0.83, 6.04	0.112	2.36	0.72, 7.76	0.156
Critical	4.27	1.52, 12.02	0.006	7.13	1.96, 26.00	0.003
Complete COVID-19 Vaccination	-	-	-	-	-	-
MIS-C	0.58	0.07, 4.61	0.603	0.15	0.01, 1.64	0.120
Year Diagnosed						
2020	Reference			Reference		
2021	3.19	0.41, 24.78	0.268	2.35	0.27, 20.57	0.440
2022/2023	2.68	0.33, 22.07	0.358	2.88	0.02, 23.31	0.488

may still develop severe or even critical illnesses. The clinical spectrum of COVID-19 in children ranges from asymptomatic to critical illness, with severity classified according to the guidelines from the Pediatric Infectious Disease Society of the Philippines. The cases are classified as asymptomatic, mild, moderate, severe, or critical disease. In this study, the majority of cases were asymptomatic and mild, 63.29% overall. In these cases, 54.97% had kidney involvement, consistent with previous reports.[15] Many of these asymptomatic and mild cases were admitted for unrelated conditions and were detected incidentally through RT-PCR screening upon admission. Common reasons for admission include trauma, acute abdomen, burn, chemotherapy, seizures, diabetic ketoacidosis, and blood transfusion, among other reasons. Notably, 20% of admitted patients had no underlying comorbidities.

At the start of the pandemic, on March 30, 2020, PGH was designated as a COVID-19 referral center. As a result, severe and critical COVID-19 patients from other hospitals were prioritized and managed over patients with other illnesses. In this study, patients with severe and critical COVID-19 made up 25.95% of total admissions, with 63.41%

of them having kidney dysfunction. Most patients had co-morbidities and underlying conditions, especially oncologic/hematologic, neurologic, infectious (such as tuberculosis and dengue), and other conditions. The SALVACION Registry also showed that the top comorbidities among children with COVID-19 in the country were oncologic/hematologic, neurologic/developmental, pulmonary, surgical, cardiac, obesity, and kidney disease. Co-infections reported in this registry include sepsis, dengue fever, nosocomial pneumonia, tuberculosis, and urinary tract infection. Previous studies also indicated that having multiple comorbidities and being unvaccinated were risk factors for developing severe COVID-19, which aligns with our findings.[16]

The most common kidney dysfunctions based on cumulative incidence in this study were hematuria (28.48%), proteinuria (26.27%), acute kidney injury (14.60%), and

Table 5. Factors associated with mortality

Factors	Univariable			Multivariable		
	OR	95% CI	*p*-value	Adj. OR	95% CI	*p*-value
Kidney dysfunction						
Acute kidney injury	5.18	2.44, 10.96	<0.001	7.36	2.14, 25.29	0.002
Proteinuria	2.95	1.47, 5.91	0.002	1.55	0.49, 4.83	0.454
Hematuria	2.58	1.29, 5.14	0.007	2.17	0.62, 7.56	0.225
Glucosuria	1.25	0.41, 3.81	0.701	1.41	0.31, 6.36	0.658
Pyuria	2.16	1.09, 4.29	0.027	1.59	0.51, 4.98	0.426
Age (years)						
<1	Reference			Reference		
1-5	0.62	0.23, 1.69	0.355	0.79	0.17, 3.79	0.772
6-10	0.56	0.17, 1.79	0.324	0.91	0.13, 6.36	0.928
11-15	0.79	0.30, 2.05	0.621	1.39	0.27, 7.03	0.694
16-18	0.43	0.12, 1.51	0.191	0.37	0.05, 2.75	0.333
Male	1.12	0.57, 2.23	0.740	1.89	0.67, 5.36	0.231
Weight						
Normal for age	Reference			Reference		
Underweight	1.68	0.83, 3.41	0.152	1.12	0.26, 4.87	0.878
Overweight	1.26	0.34, 4.65	0.729	0.33	0.03, 3.27	0.343
Stunted	1.49	0.75, 2.97	0.255	2.97	0.61, 14.40	0.176
Blood Pressure						
Normotensive	Reference			Reference		
Hypotensive	5.31	1.92, 14.71	0.001	8.56	1.75, 41.79	0.008
Hypertensive	2.55	1.18, 5.52	0.017	2.32	0.73, 7.38	0.155
Tachycardia	1.36	0.63, 2.92	0.435	1.13	0.36, 3.58	0.834
Febrile	2.40	1.08, 5.36	0.032	2.94	0.88, 9.78	0.079
Comorbidity						
None	Reference			Reference		
Neurologic	2.98	0.70, 12.58	0.138	2.66	0.33, 21.11	0.356
Cardiac	2.77	0.52, 14.77	0.232	7.96	0.80, 78.85	0.076
Oncologic/Hematologic	4.90	1.32, 18.10	0.017	35.39	4.45, 283.16	0.001
Congenital	9.24	1.93, 44.37	0.005	20.10	1.78, 227.45	0.015
Infectious	1.36	0.21, 8.55	0.746	4.21	0.40, 44.21	0.231
Others	4.52	1.05, 19.42	0.043	26.56	2.67, 264.05	0.005
COVID-19 Severity						
Asymptomatic	Reference			Reference		
Mild	0.65	0.20, 2.05	0.457	0.36	0.07, 1.77	0.206
Moderate	0.74	0.15, 3.68	0.715	0.54	0.07, 4.02	0.545
Severe	2.90	1.07, 7.87	0.037	2.20	0.52, 9.23	0.283
Critical	8.58	3.11, 23.66	<0.001	15.51	3.16, 76.03	0.001
MIS-C	1.66	0.35, 7.99	0.527	0.36	0.02, 5.55	0.466
Year Diagnosed						
2020	Reference			Reference		
2021	1.08	0.23, 4.98	0.920	0.16	0.02, 1.19	0.073
2022/2023	1.14	0.23, 5.66	0.870	0.15	0.01, 1.51	0.106

Table 5. Factors associated with mortality *(continued)*

Factors	Univariable			Multivariable		
	OR	95% CI	*p*-value	Adj. OR	95% CI	*p*-value
Serum Chemistry						
Blood Urea Nitrogen	1.05	1.01, 1.09	0.018			
Creatinine	1.00	1.00, 1.01	0.140			
Sodium						
Normal	Reference					
Hyponatremia	3.06	1.45, 6.45	0.003			
Hypernatremia	5.91	1.78, 19.58	0.004			
Potassium						
Normal	Reference					
Hypokalemia	1.71	0.68, 4.25	0.252			
Hyperkalemia	5.29	2.01, 13.95	0.001			
Chloride						
Normal	Reference					
Hypochloremia	2.40	1.00, 5.73	0.050			
Hyperchloremia	1.76	0.77, 4.01	0.180			
Calcium						
Normal	Reference					
Hypocalcemia	2.72	1.35, 5.49	0.005			
Hypercalcemia	0.54	0.07, 4.29	0.560			
Magnesium						
Normal	Reference					
Hypomagnesemia	2.32	0.61, 8.89	0.219			
Hypermagnesemia	6.01	2.49, 14.51	<0.001			
Phosphorus						
Normal	Reference					
Hypophosphatemia	2.64	0.83, 8.40	0.100			
Hyperphosphatemia	1.32	0.32, 5.39	0.699			
Arterial Blood Gas						
Serum pH	0.16	0.01, 2.76	0.208			
Serum Bicarbonate	0.99	0.93, 1.05	0.795			
Metabolic Acidosis	1.29	0.55, 3.02	0.552			
Complete Blood Count						
Hemoglobin	1.00	0.99, 1.01	0.934			
White Blood Cell Count	1.00	0.99, 1.02	0.666			
Neutrophils	1.00	0.99, 1.01	0.897			
Lymphocytes	0.99	0.97, 1.01	0.267			
Platelet Count	1.00	1.00, 1.00	0.165			

glucosuria (8.86%). While adult studies reported the prevalence of hematuria (27-53%), proteinuria (36-66%), and oliguria (10%), data in children remain limited.[17,18] In a study by Stewart et al. involving 52 pediatric patients, hematuria and proteinuria were observed in 30% and 23%, respectively. Additionally, 30% of the cohort had AKI, which they defined as serum creatinine values 50% above the upper limit of the reference range.[19] Another study with 47 children with confirmed or suspected COVID-19 found that 27.7% of children had elevated serum creatinine, 78.8% eGFR below 90 25.5% had eGFR below 60 ml/min/1.73m^2. Additionally, 27.7%microscopic hematuria and/or proteinuria.[20]

Emerging evidence indicates that SARS-CoV-2 can lead to both glomerular and tubular damage in the kidneys. In our cohort, we identified one case of new-onset nephrotic syndrome and three cases of acute glomerulonephritis associated with COVID-19, two of which had a rapidly progressive course requiring pulse methylprednisolone therapy. One of these cases has been previously published.[21]

To characterize renal involvement, we used hematuria and proteinuria as markers of glomerular involvement, normoglycemic glucosuria as a marker for possible tubular involvement, and AKI as a marker for both glomerular and tubular dysfunction. Additionally, the presence of normal anion gap metabolic acidosis and electrolyte abnormalities, such as hypokalemia, supported evidence of tubular involvement. Among 39 patients with metabolic acidosis, five had normal anion gap acidosis, two of whom also had glucosuria, and one with associated hypokalemia. Adult studies have similarly reported glomerular manifestations such as

proteinuria and hematuria detected via urine dipstick tests, with or without concomitant elevated creatinine levels. Kidney biopsy findings revealed a range of glomerular pathologies, including collapsing glomerulopathy (characterized by podocyte hypertrophy compressing glomerular tufts) as well as endothelial injury, and thrombotic microangiopathy.[22] In a study by Sharma et al., all ten hospitalized patients with severe COVID-19 and AKI demonstrated varying degrees of acute tubular necrosis.[23] Other adult studies have reported AKI and nephrotic-range proteinuria, with kidney biopsies showing minimal change disease, membranous glomerulopathy, crescentic lupus nephritis, and anti-GBM nephritis.[24]

Various forms of kidney involvement have also been reported in pediatric populations with COVID-19. One report described two adolescent males who developed acute glomerulonephritis with rapidly progressive kidney failure requiring hemodialysis and corticosteroid therapy. Histopathologic findings revealed acute necrotizing glomerulonephritis with tubular injury in both cases, and diffuse glomerulosclerosis in one.[25] This is comparable to one of our patients who presented with rapidly progressive glomerulonephritis and responded well to treatment with intravenous methylprednisolone followed by oral prednisone. Kidney biopsy in this case revealed diffuse proliferative glomerulonephritis with focal crescent formation and thin basement membrane nephropathy.[21]

Additionally, three separate reports have documented new-onset nephrotic syndrome (NS) as a primary extrapulmonary manifestation of COVID-19 in children.[26,27] The clinical presentation of COVID-19–associated NS was similar to that observed in NS triggered by other viral infections.

Mechanisms of Kidney Injury in COVID-19

Several mechanisms have been proposed to explain kidney injury in the context of COVID-19. SARS-CoV-2 uses its surface spike (S) protein to bind to the angiotensin-converting enzyme 2 (ACE2) receptor on host cells, with viral entry facilitated by transmembrane protease serine 2 (TMPRSS2). This interaction allows for direct viral invasion and cytopathic effects, particularly targeting renal tubular cells and podocytes. The kidneys express high levels of ACE2 and TMPRSS2, especially in proximal tubular cells and podocytes, making these structures vulnerable to viral injury.[28]

Post-mortem studies have provided histopathologic evidence of this mechanism. In one study involving 26 patients who died from COVID-19–associated AKI, light microscopy revealed extensive tubular damage. In contrast, electron microscopy demonstrated viral particles within the epithelial lining of tubules and podocytes, supporting direct viral cytotoxicity.[29] Injury to the proximal tubules may result in urinary losses of glucose, phosphate, uric acid, amino acids, and bicarbonate.

In our cohort, normoglycemic glucosuria—observed in 8.86% of patients—served as a surrogate marker for tubular dysfunction, particularly in the absence of other diagnostic tests. Additional indicators included normal anion gap metabolic acidosis and electrolyte abnormalities such as hypokalemia. Among 39 patients with metabolic acidosis, five had normal anion gap acidosis; two of these also had glucosuria, and one had concurrent hypokalemia.

Adult studies have further demonstrated glomerular involvement, with proteinuria and hematuria frequently detected via urine dipstick, sometimes in the absence of elevated serum creatinine. Renal biopsies have revealed a range of glomerular pathologies, including collapsing glomerulopathy, endothelial injury, and thrombotic microangiopathy.[22] Additional reports have documented AKI and nephrotic-range proteinuria, with histologic findings such as minimal change disease, membranous glomerulopathy, crescentic lupus nephritis, and anti-glomerular basement membrane (anti-GBM) nephritis.[24]

Beyond direct viral effects, kidney injury may also result from immune dysregulation. SARS-CoV-2 can trigger macrophage infiltration and complement activation (C3a, C5b-9), leading to inflammation and tissue fibrosis. Post-mortem biopsies in adult patients have shown deposition of complement components C1q, C3, and C5b-9 in renal tissue, indicating complement-mediated injury.[30,31] Furthermore, disruption of the ACE2/Ang-(1–7)/Mas receptor axis contributes to renin-angiotensin-aldosterone system (RAAS) imbalance, resulting in hypovolemia, vasoconstriction, a procoagulant state, and microvascular injury.

Acute kidney injury (AKI) may also arise from systemic inflammatory responses, including cytokine storm and lung-kidney crosstalk in patients with multiorgan dysfunction. Elevated interleukin-6 levels, particularly in children with acute respiratory distress syndrome (ARDS), have been implicated in renal inflammation, vascular leakage, third-space fluid loss, and shock.[32] Additionally, aggressive mechanical ventilation may exacerbate kidney injury through oxygen toxicity, endothelial damage, and systemic inflammation.[33] The use of nephrotoxic agents, including antivirals and antibiotics administered during COVID-19 treatment, may further contribute to or worsen AKI.

Risk Factors for Kidney Dysfunction and Acute Kidney Injury

This study identified several potential risk factors associated with kidney dysfunction in pediatric patients with COVID-19, including hematuria, proteinuria, and glucosuria—markers of glomerular and tubular involvement. To date, few studies have specifically examined risk factors for these manifestations, with most available literature focusing on AKI in adult and pediatric populations.

In our cohort, severe COVID-19 was the only factor significantly associated with an increased risk of overall kidney dysfunction, likely due to its strong association with AKI. Severe disease also significantly increased the risk of proteinuria. Interestingly, male sex and moderate COVID-19

were associated with lower odds of developing hematuria. Additionally, patients with oncologic or hematologic comorbidities were less likely to develop proteinuria and glucosuria—findings not previously reported and warranting further investigation.

Risk factors for AKI identified in this study included hypertension, fever, and moderate to critical COVID-19. Prolonged fever can lead to fluid loss, increasing the risk of pre-renal AKI. Hypertension may both cause and result from AKI, driven by sympathetic overactivity, RAAS activation, and fluid overload. Septic shock, present in all patients with critical COVID-19, is a known factor contributing to both pre-renal and intrinsic AKI. Co-infections, such as bacterial pneumonia and COVID-19 pneumonia, were seen in 72.22% of patients with severe or critical disease and AKI, potentially adding to ischemic renal injury.

Diarrhea, a common symptom in pediatric COVID-19, was observed in 15.21% of patients with AKI and in 70% of those with moderate COVID-19 and AKI. Gastrointestinal losses from diarrhea and vomiting can lead to hypovolemia and pre-renal AKI. A previous study involving 66 pediatric patients with moderate to severe COVID-19 identified the use of vasoactive/inotropic agents and gastrointestinal symptoms as independent risk factors for AKI.[34] Although the use of vasoactive agents was not explicitly analyzed in our study, nearly all patients with septic shock required such interventions.

In contrast, a recent systematic review of adult patients with COVID-19 identified a broader range of risk factors for AKI, including older age, male sex, obesity, Black race, invasive ventilation, use of diuretics, steroids, and vasopressors, as well as comorbidities such as hypertension, heart failure, chronic kidney disease, ARDS, and diabetes.[35]

Recent investigations on MIS-C underscore the notable prevalence of AKI in affected patients. Toraih et al. reported a 41% incidence of AKI in a meta-analysis of 15 studies, while another meta-analysis found a pooled AKI rate of 20% in MIS-C patients.[36] However, our study did not demonstrate a statistically significant association between MIS-C and AKI and other forms of kidney dysfunction. To account for the influence of circulating SARS-CoV-2 variants, we used year of admission as a surrogate marker; no correlation was observed between variant prevalence and kidney involvement.

In this study, the overall mortality rate was 12.03%, with 76.31% of deaths associated with kidney dysfunction. Multivariable logistic regression analysis identified AKI, hypotension, oncologic/hematologic comorbidities, congenital comorbidities, and critical COVID-19 severity as significant predictors of mortality. AKI is recognized as an adverse prognostic indicator in both adults and children.[37] Among COVID-positive pediatric patients, the incidence of AKI was 30.51%, yet only 0.56% of these patients received KRT. The overall mortality in this subgroup was 2.55%.

Univariable analysis revealed that electrolyte imbalances significantly increased the risk of death, with hyponatremia, hypernatremia, hyperkalemia, and hypermagnesemia showing strong associations. These findings are consistent with previous studies demonstrating that such imbalances are linked to adverse clinical outcomes in patients with COVID-19.[38-41] Hyponatremia has been associated with increased odds of mortality, ICU admission, assisted ventilation, and longer hospital stays, often resulting from SIADH, adrenal insufficiency, or hypovolemia. Hypernatremia is linked to higher mortality, longer hospital stay, and greater need for ventilatory and intensive care support, with older age compounding poor outcomes. Hyperkalemia is linked to higher in-hospital mortality, increased ICU admissions, longer hospital stay, and higher healthcare costs. Hypermagnesemia is associated with higher incidence of shock, respiratory failure, AKI, and reduced 30-day survival, with mortality risk further exacerbated by vasopressor use and elevated CRP. These findings underscore the importance of early recognition and management of electrolyte disturbances to improve clinical outcomes in children with COVID-19.

Limitations

This study has several limitations. As a retroactive, single-center analysis, it is subject to inherent biases and limited generalizability. Missing data during chart review may have contributed to incomplete findings. More specific diagnostic tests, such as red blood cell morphology in urine microscopy, would better distinguish glomerular from non-glomerular hematuria. Additionally, quantitative measures of proteinuria, such as 24-hour urine total protein and urine protein-creatinine ratio, would enhance diagnostic precision. Imaging studies, such as Kidneys, Ureters, and Bladder (KUB) ultrasound could have identified structural abnormalities. Additionally, the study was restricted to data collected during admission and did not include follow-up and long-term renal and patient outcomes.

CONCLUSION

The study underscores the high prevalence and clinical significance of kidney involvement in children with COVID-19, including hematuria, proteinuria, acute kidney injury (AKI), and glucosuria. Severe COVID-19 substantially increases the risk of kidney dysfunction and proteinuria. Key factors associated with AKI include hypertension, fever, and disease severity, particularly in moderate to critical cases. AKI was strongly linked to higher mortality, alongside critical COVID-19, hypotension, and comorbid conditions such as congenital anomalies and oncologic/hematologic diseases. Electrolyte imbalances, such as hyponatremia, hypernatremia, hyperkalemia, and hypermagnesemia, were also significantly tied to increased mortality risk. These findings highlight the urgent need for early detection and management of kidney complications in pediatric COVID-19 patients. Timely interventions, especially in severe cases, are essential to improve survival and reduce mortality.

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Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

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REFERENCES

1. Mansourian M, Ghandi Y, Habibi D, Mehrabi S. COVID-19 infection in children: A systematic review and meta-analysis of clinical features and laboratory findings. Arch Pediatr. 2021 Apr;28(3):242–8. doi: 10.1016/j.arcped.2020.12.008. PMID: 33483192; PMCID: PMC7794595.
2. Shi Q, Wang Z, Liu J, Wang X, Zhou Q, Li Q, et al. Risk factors for poor prognosis in children and adolescents with COVID-19: A systematic review and meta-analysis. EClinicalMedicine. 2021 Nov;41:101-155. doi: 10.1016/j.eclinm.2021.101155. PMID: 34693233; PMCID: PMC8523335.
3. Reyes-Pagcatipunan MG, Isada PMD, Delos Reyes CA. Clinical and Laboratory Profile, Management and Outcome of Pediatric SARS-CoV-2 Infection Admitted at the Philippine General Hospital. Acta Med Philipp. 2024 Apr 30;58(7):14-26. doi: 10.47895/amp.v58i7.7717.
4. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA. 2020 Mar 17;323(11):1061-1069. doi: 10.1001/jama.2020.1585. Erratum in: JAMA. 2021 Mar 16;325(11):1113. doi: 10.1001/jama.2021.2336. PMID: 32031570; PMCID: PMC7042881.
5. Diao B, Wang C, Wang R, Feng Z, Zhang J, Yang H, et al. Human kidney is a target for novel severe acute respiratory syndrome coronavirus 2 infection. Nat Commun. 2021 May 4;12(1):2506. doi: 10.1038/s41467-021-22781-1. PMID: 33947851; PMCID: PMC8096808.
6. Cheng Y, Luo R, Wang K, Zhang M, Wang Z, Dong L, et al. Kidney disease is associated with in-hospital death of patients with COVID-19. Kidney Int. 2020 May;97(5):829-838. doi: 10.1016/j.kint.2020.03.005. PMID: 32247631; PMCID: PMC7110296.
7. Li H, Liu L, Zhang D, Xu J, Dai H, Tang N, et al. SARS-CoV-2 and viral sepsis: observations and hypotheses. Lancet. 2020 May 9;395(10235):1517-1520. doi: 10.1016/S0140-6736(20)30920-X. PMID: 32311318; PMCID: PMC7164875.
8. Philippine Pediatric Society, Pediatric Infectious Disease Society of the Philippines. Interim guidelines on the screening, assessment and clinical management of pediatric patients with suspected or confirmed coronavirus disease 2019 (COVID-19), Version 1 (30 March 2020) [Internet]. 2020 [cited 2022 Feb 25]. Available from: https://www.pidsphil.org/home/wp-content/uploads/2020/03/INTERIMGUIDELINES-ON-THE-SCREENING-ASSESSMENT-ANDCLINICAL.pdf.
9. Philippine Pediatric Society, Pediatric Infectious Disease Society of the Philippines. Interim guidelines on the screening, assessment and clinical management of pediatric patients with suspected or confirmed coronavirus Disease 2019 (COVID-19), Version 4 (06 February 2021) [Internet]. 2021 [cited 2023 Feb 25]. Available from: https://www.pidsphil.org/home/wp-content/uploads/2021/02/1613518307591635.pdf.
10. Philippine Pediatric Society, Pediatric Infectious Disease Society of the Philippines. Interim guidelines on the screening, assessment and clinical management of pediatric patients with suspected or confirmed coronavirus disease 2019 (COVID-19), Version 5 (8 January 2022) [Internet]. 2022 [cited 2023 Feb 25]. Available from: https://www.pidsphil.org/home/wp-content/uploads/2022/01/1641793296797384.pdf.
11. Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO clinical practice guideline for acute kidney injury. Kidney Int Suppl. 2012;2:1–138.
12. Schwartz GJ, Muñoz A, Schneider MF, Mak RH, Kaskel F, Warady BA, et al. New equations to estimate GFR in children with CKD. J Am Soc Nephrol. 2009 Mar;20(3):629-37. doi: 10.1681/ASN.2008030287. PMID: 19158356; PMCID: PMC2653687.
13. Philippine Pediatric Society. Salvacion: Surveillance and analysis of COVID-19 in children nationwide, case bulletin #5 March 31, 2022 [Internet]. 2022 [cited 2023 Feb 25]. Available from: http://www.pidsphil.org/.
14. Sorkhi H, Esmaeili Dooki M, Nikpour M, Mohammadi M, Mohammadpour-Mir A, Kiani M, et al. COVID-19 and renal involvement in children: a retrospective study. Caspian J Intern Med. 2022;13(Suppl 3):193-198. doi: 10.22088/cjim.13.0.193. PMID: 35872683; PMCID: PMC9272974.
15. Zimmermann P, Curtis N. Why is COVID-19 less severe in children? A review of the proposed mechanisms underlying the age-related difference in severity of SARS-CoV-2 infections. Arch Dis Child. 2021 Apr 21;106(5):429-439. doi: 10.1136/archdischild-2020-320338. PMID: 33262177.
16. Sun YK, Wang C, Lin PQ, Hu L, Ye J, Gao ZG, et al. Severe pediatric COVID-19: a review from the clinical and immunopathophysiological perspectives. World J Pediatr. 2024 Apr;20(4):307-324. doi: 10.1007/s12519-023-00790-y. PMID: 38321331; PMCID: PMC11052880.
17. Cheng Y, Luo R, Wang K, Zhang M, Wang Z, Dong L, et al. Kidney disease is associated with in-hospital death of patients with COVID-19. Kidney Int. 2020 May;97(5):829-838. doi: 10.1016/j.kint.2020.03.005. PMID: 32247631; PMCID: PMC7110296.
18. Li Z, Wu M, Yao J, Guo J, Liao X, Song S, et al. Caution on kidney dysfunctions of 2019-nCoV patients. medRxiv 2020. doi: 10.1101/2020.02.08.20021212.
19. Stewart DJ, Hartley JC, Johnson M, Marks SD, du Pré P, Stojanovic J. Renal dysfunction in hospitalised children with COVID-19. Lancet Child Adolesc Health. 2020 Aug;4(8):e28-e29. doi: 10.1016/S2352-4642(20)30178-4. PMID: 32553126; PMCID: PMC7295466
20. Sorkhi H, Esmaeili Dooki M, Nikpour M, Mohammadi M, Mohammadpour-Mir A, Kiani M, et al. COVID-19 and renal involvement in children: a retrospective study. Caspian J Intern Med. 2022;13(Suppl 3):193-198. doi: 10.22088/cjim.13.0.193. PMID: 35872683; PMCID: PMC9272974.
21. Flores VAG, Chicano S, Resontoc LP, Aragon EE. Diffuse proliferative glomerulonephritis in a patient with COVID-19 infection. BMJ Case Rep. 2023 Jan 5;16(1):e251962. doi: 10.1136/bcr-2022-251962. PMID: 36604108; PMCID: PMC9827186.
22. Akilesh S, Nast CC, Yamashita M, Henriksen K, Charu V, Troxell ML, et al. Multicenter Clinicopathologic Correlation of Kidney Biopsies Performed in COVID-19 Patients Presenting with Acute Kidney Injury or Proteinuria. Am J Kidney Dis. 2021 Jan;77(1):82-93.e1. doi: 10.1053/j.ajkd.2020.10.001. PMID: 33045255; PMCID: PMC7546949.
23. Sharma P, Uppal NN, Wanchoo R, Shah HH, Yang Y, Parikh R, et al. Northwell Nephrology COVID-19 Research Consortium. COVID-19-Associated Kidney Injury: A Case Series of Kidney Biopsy Findings. J Am Soc Nephrol. 2020 Sep;31(9):1948-1958. doi: 10.1681/ASN.2020050699. PMID: 32660970; PMCID: PMC7461689.
24. Kudose S, Batal I, Santoriello D, Xu K, Barasch J, Peleg Y, et al. Kidney Biopsy Findings in Patients with COVID-19. J Am Soc Nephrol. 2020 Sep;31(9):1959-1968. doi: 10.1681/ASN.2020060802. PMID: 32680910; PMCID: PMC7461665.

25. Basiratnia M, Derakhshan D, Yeganeh BS, Derakhshan A. Acute necrotizing glomerulonephritis associated with COVID-19 infection: report of two pediatric cases. Pediatr Nephrol. 2021 Apr;36(4): 1019-1023. doi: 10.1007/s00467-021-04944-w. PMID: 33495896; PMCID: PMC7834948.
26. Shah SA, Carter HP. New-Onset Nephrotic Syndrome in a Child Associated With COVID-19 Infection. Front Pediatr. 2020 Aug 20;8:471. doi: 10.3389/fped.2020.00471. PMID: 32974243; PMCID: PMC7469478.
27. Takagi Y, Yoshihara S. New-onset pediatric idiopathic nephrotic syndrome secondary to COVID-19. Pediatr Nephrol. 2023 Jul;38(7):2495-2496. doi: 10.1007/s00467-023-05946-6. PMID: 36943466; PMCID: PMC10028311.
28. Pan XW, Xu D, Zhang H, Zhou W, Wang LH, Cui XG. Identification of a potential mechanism of acute kidney injury during the COVID-19 outbreak: a study based on single-cell transcriptome analysis. Intensive Care Med. 2020 Jun;46(6):1114-1116. doi: 10.1007/s00134-020-06026-1. PMID: 32236644; PMCID: PMC7106051.
29. Farkash EA, Wilson AM, Jentzen JM. Ultrastructural Evidence for Direct Renal Infection with SARS-CoV-2. J Am Soc Nephrol. 2020 Aug;31(8):1683-1687. doi: 10.1681/ASN.2020040432. Erratum in: J Am Soc Nephrol. 2020 Oct;31(10):2494. doi: 10.1681/ASN.2020081117. PMID: 32371536; PMCID: PMC7460898.
30. Wichmann D, Sperhake JP, Lütgehetmann M, Steurer S, Edler C, Heinemann A, et al. Autopsy Findings and Venous Thromboembolism in Patients With COVID-19: A Prospective Cohort Study. Ann Intern Med. 2020 Aug 18;173(4):268-277. doi: 10.7326/M20-2003. PMID: 32374815; PMCID: PMC7240772.
31. He W, Liu X, Hu B, Li D, Chen L, Li Y, et al. Mechanisms of SARS-CoV-2 Infection-Induced Kidney Injury: A Literature Review. Front Cell Infect Microbiol. 2022 Jun 14;12:838213. doi: 10.3389/fcimb.2022.838213. PMID: 35774397; PMCID: PMC9237415.
32. Ronco C, Reis T. Kidney involvement in COVID-19 and rationale for extracorporeal therapies. Nat Rev Nephrol. 2020 Jun;16(6): 308-310. doi: 10.1038/s41581-020-0284-7. PMID: 32273593; PMCID: PMC7144544.
33. Perico L, Benigni A, Casiraghi F, Ng LFP, Renia L, Remuzzi G. Immunity, endothelial injury and complement-induced coagulopathy in COVID-19. Nat Rev Nephrol. 2021 Jan;17(1):46-64. doi: 10.1038/s41581-020-00357-4. PMID: 33077917; PMCID: PMC7570423.
34. Durdevic M, Durdevic D, Riera MB, Nimkar A, Stan AC, Hasan A, et al. Progressive renal failure in patients with COVID-19 after initiating mechanical ventilation: A case series. Chest. 2020 Oct;158(4):A2629. doi: 10.1016/j.chest.2020.09.216. PMCID: PMC7548627.
35. Tastemel Ozturk T, Düzova A, Oygar PD, Baltu D, Ozcilingir Hakverdi P, Lacinel Gurlevik S, et al. Acute kidney injury in children with moderate-severe COVID-19 and multisystem inflammatory syndrome in children: a referral center experience. Pediatr Nephrol. 2024 Mar;39(3):867-877. doi: 10.1007/s00467-023-06125-3. PMID: 37676500.
36. Zhang J, Pang Q, Zhou T, Meng J, Dong X, Wang Z, Zhang A. Risk factors for acute kidney injury in COVID-19 patients: an updated systematic review and meta-analysis. Ren Fail. 2023 Dec; 45(1):2170809. doi: 10.1080/0886022X.2023.2170809. PMID: 37021610; PMCID: PMC10081062.
37. Tripathi AK, Pilania RK, Bhatt GC, Atlani M, Kumar A, Malik S. Acute kidney injury following multisystem inflammatory syndrome associated with SARS-CoV-2 infection in children: a systematic review and meta-analysis. Pediatr Nephrol. 2023 Feb;38(2):357-370. doi: 10.1007/s00467-022-05701-3. PMID: 35943577; PMCID: PMC9362633.
38. Stevens JS, Moses AA, Nickolas TL, Husain SA, Mohan S. Increased Mortality Associated with Hypermagnesemia in Severe COVID-19 Illness. Kidney360. 2021 May 17;2(7):1087-1094. doi: 10.34067/KID.0002592021. PMID: 35368359; PMCID: PMC8786084.
39. Khidir RJY, Ibrahim BAY, Adam MHM, Hassan RME, Fedail ASS, Abdulhamid RO, Mohamed SOO. Prevalence and outcomes of hyponatremia among COVID-19 patients: A systematic review and meta-analysis. Int J Health Sci (Qassim). 2022 Sep-Oct;16(5):69-84. PMID: 36101848; PMCID: PMC9441642.
40. Shrestha AB, Sapkota UH, Shrestha S, Aryal M, Chand S, Thapa S, et al. Association of hypernatremia with outcomes of COVID-19 patients: A protocol for systematic review and meta-analysis. Medicine (Baltimore). 2022 Dec 23;101(51):e32535. doi: 10.1097/MD.0000000000032535. PMID: 36595846; PMCID: PMC9794240.
41. Amin A, Moon R, Agiro A, Rosenthal N, Brown H, Legg R, et al. In-hospital mortality, length of stay, and hospitalization cost of COVID-19 patients with and without hyperkalemia. Am J Med Sci. 2022 Oct;364(4):444-453. doi: 10.1016/j.amjms.2022.04.029. PMID: 35490703; PMCID: PMC9050185.