Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(1), 3395-3401 | ISSN:2251-6727

A case series describing multisystem inflammatory syndrome associated with acute renal injury in pediatric sars-cov-19 infection.

Dr. Sagar Parida [1], Dr Aparna Aradhana [2], Dr Braja Kishore Behera [3], Dr. Dillip Kumar Dash [4], Dr Pawan Prakash[5], Dr Suchismita Panda [6]

1. Assistant Professor, Department of Pediatrics,IMS & SUM Hospital,Bhubaneswar, Odisha, India
2. Assistant Professor, Department of Pediatrics,IMS & SUM Hospital,Bhubaneswar, Odisha, India
3. Associate Professor, Department of Pediatrics,IMS & SUM Hospital,Bhubaneswar, Odisha, India
4. Professor, Department of Pediatrics,IMS & SUM Hospital,Bhubaneswar, Odisha, India
5. Post graduate, Department of Pediatrics,IMS & SUM Hospital,Bhubaneswar, Odisha, India
6. Assistant Professor, Department of Pediatrics,IMS & SUM Hospital,Bhubaneswar, Odisha, India

Corresponding Author:Dr.Suchismita Panda

Received: 15 November 2023 Revised: 11 December 2023 Accepted: 20 January 2024

KEYWORDS
COVID-19; Kawasaki disease, multisystem inflammatory syndrome, SARS-CoV-2.AKI

ABSTRACT
BACKGROUND: MIS-C (Multisystem inflammatory syndrome in children), is seen post COVID-19 infection with variable patho-physiology and symptoms. Acute kidney injury (AKI) is found to be a common feature in primary COVID-19 infections in adults, but it's presentation in MIS-C has been rarely described & studied. We first described the 2019 novel coronavirus infection in 10 children occurring in Odisha areas in India. The coronavirus diseases in children are usually mild and epidemiological exposure is a key clue to recognize paediatric case. Prolonged virus shedding is observed in respiratory tract and faeces at the convalescent stage [1]. We present a series of 8 critically ill children with multisystem inflammatory syndrome with AKI. Key findings of this syndrome include fever, diarrhoea, shock, and variable presence of rash, conjunctivitis, extremity oedema, mucous membrane changes with acute kidney injury.

CASE PRESENTATIONS

AKI was defined according to the 2012 Kidney Disease Improving Global Outcomes (KDIGO) classification which is applicable to both adult and paediatric age group (2,3). Due to the difficulty in urine output measurement, patients were classified on the basis of serum creatinine alone, as detailed in **(Table 1).** Important contributing factors to AKI were noted. Exposure to nephrotoxic medications commonly used in our hospital (i.e., aminoglycosides, vancomycin, acyclovir, nonsteroidal anti-inflammatory drugs, iodine-based contrast for imaging, and calcineurin inhibitors), hypotension requiring vasopressors were important contributing factors. echocardiographic findings of decreased left ventricular systolic function were also recorded. Two time points were recorded: time to peak creatinine (day of hospitalization) as well as time to recovery (days) defined as return to baseline/nadir creatinine. The presence of significant proteinuria was defined as +2 protein (100 mg/dl) on urinalysis. Patients for whom certain data were unavailable or missing were excluded from analysis regarding that factor.

Table 1. Kidney Disease Improving Global Outcomes classification Kidney Disease Improving Global Outcomes

Stage	Serum Creatinine
1	1.5–1.9 times baseline or 0.3-mg/dl increase
2	2.0–2.9 times baseline
3	3 3.0 times baseline or increase in serum creatinine to 4.0 mg/dl or initiation of RRT or decrease in eGFR to 35 ml/min per 1.73 m2 (in patients over 18 yr

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(1), 3395-3401 | ISSN:2251-6727

Table.2 clinicaTable -2 features among 2019-nCoV infected children

Clinical Characteristics	Patient 1	Patient 2	Patient 3	Patient 3	Patient 4	Patient 5	Patient6	Patient 7	Patient 8
Duration of fever (> 4 days)	+	+	+	+	+	+	+	+	+
Cough	-	+		+	-	-	+	-	+
Diarrhoea	+		+	+	+	+	+	+	-
Peak of fever (°F)	101.8 F	103.4	102.6	104,3	103.6	103.2	103.9	103.8	101.9
Sneezing	+			+	+		+		+
Sore throat	+	-	-	-	-	-	-	+	-+
Stuffy nose	+						+		
Rhinorrhoea	+	+		+	+	+	-	-	+
Dyspnoea	+	+	-	+	+	+	+	+	-

+ = Present, - = Absent

Table 3. Management of the AKI patients

Clinical Characteristics		Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8
Bed location	General ward	-	-	+	-	-	-	-	+
	ICU	+	+	-	+	+	+	+	-
Vasopressors		+	-	-	+	+	-	+	-
Mechanical ventilation		+			+			+	
Dialysis		+	-	-	+	-	-	-	-
Treatment Steroids		+	+	-	+	+	+	+	-
Remdesivir		+	+	+	-	+	-	-	-

+ = Present, - = Absent

Table 4. Demographics and laboratory profile of patients with multisystem inflammatory syndrome in children with AKI

Variables	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8
Age	11y 3m	14y	9y 6m	5y 4m	6y 8m	5y 2m	9y 1m	5y 3m
Sex Boys(M) Girls(F)	F	F	F	M	M	M	F	M
Residence URBAN(U) RURAL(R)	U	U	U	U	R	U	R	U
Contact with index case directly Present(P) Absent(A)	P	P	P	A	P	P	A	P
Exposure setting Household(H) Community (C)	H	C	H	H	C	H	H	H
LV systolic dysfunction	P	P	A	A	P	P	P	A
Lymphopenia Defined as <1500/mm3	P	P	P	A	A	P	P	P
BMI>85th percentile	P	P	P	P	A	P	P	P
Peak ferritin, ng/ml Median (range)	600	760	336	156	436	656	786	146
Peak D-dimer, mg/L	2.8	3.2	2.9	2.6	2.2	1.8	2.4	2.5
Peak CRP, mg/L	21	66	28	26	34	9	6	18
Significant proteinuria Defined as >2 on dipstick	P	P	P	P	P	P	P	P

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(1), 3395-3401 | ISSN:2251-6727

Case 1

An eleven year three-month-old female child with k/c/o seizure disorder diagnosed at 1 years of age, presented with a complain of high-grade fever for 4 days, history of multiple episodes of seizure and 2 episodes of vomiting without blood and bile since past 3 days. The child had no other significant past medical history. In emergency department the child was found to be febrile (101.8 F), tachycardic (138bpm), hypotensive (84/58 mm Hg), with a respiratory rate of 30/minute and Spo2 of 95% in room air. In view of hypotension and low pulse volume normal saline bolus @20ml/kg was given. On examination, patchy maculopapular rash over face and trunk were seen. Patient was admitted to PICU, kept NPO, started on IV fluids, empirical antibiotics and anti-epileptics. Covid-19 RTPCR was negative. Initial laboratory investigations showed deranged LFT with urea of 106mg/dl & creatinine of 3.36 mg/dl, which was consistent with acute kidney injury. USG KUB shows bilateral acute medical renal disease. Dialysis was given for 2 times in view of AKI. Serum electrolytes having hyponatremia & hypokalemia for which correction was given. Repeat serum electrolytes were within normal limits. The child was negative for scrub typhus, dengue fever, typhoid and malaria. Inflammatory markers like-CRP, D-DIMER, S. Ferritin were elevated. Suspecting MIS-C, Covid antibodies were sent which was positive. Echocardiogram showed mild LV dysfunction which became normal before discharge. The child was started on IV immunoglobulin (IVIG) @2gm/kg, followed by IV methylprednisolone. The child gradually improved. maculopapular rash resolved, febrile episodes showed decreasing trend along with the decreased inflammatory markers and improved RFT (urea: 88mg/dl, creatinine: 1mg/dl). The child was discharged on day 9 of hospitalisation with aspirin prophylaxis and is advised for follow up.

Case 2

A 14-year-old female with no chronic medical conditions presented with a 6-day history of fever, cough, Dyspnoea, rhinorrhoea, headache and diarrhoea. Her blood pressure was 79/39 mm Hg. Laboratory findings at the admission included elevated inflammatory markers, hyperferritinemia, and acute kidney injury (raised urea and creatinine with acute medical renal disease in USG). Nasopharyngeal SARSCoV-2 polymerase chain reaction (PCR) testing was negative. Chest radiography shows bilateral pulmonary infiltrates, and 2D ECHO demonstrated moderately diminished left ventricular (LV) function (Table 4). She was intubated and mechanically ventilated and started on vasoactive infusions. SARS-CoV-2 PCR testing from tracheal aspirates were negative on 2 repeat samples. Vancomycin and doxycycline were started empirically for concern of toxic shock syndrome or rickettsial disease in view of skin rash and thrombocytopenia. Over the time she had intermittent fevers and developed severe thrombocytopenia and mild coagulopathy. Her fever resolved on day 6. She was weaned off vasoactive infusions and was extubated on HD 8. Her final echocardiogram demonstrated normal biventricular systolic function before discharge. SARS-CoV-2 immunoglobulin G (IgG) testing was positive

Case 3

Case 3 A 9-year 6-month-old female with no chronic medical conditions presented with fever, diarrhoea, and pain abdomen. Laboratory findings were notable for elevated inflammatory markers with deranged RFT in the line of AKI (Tables 1). An abdominal computed tomography (CT) scan demonstrated B/L acute medical renal disease. She was admitted to PICU for apparent hypovolemic shock from secretory diarrhoea. Her lowest documented blood pressure within 24 hours of her PICU admission was 92/50 mm Hg. SARS-CoV-2 nasopharyngeal PCR was positive. On 3rd day she developed conjunctivitis, and mucosal changes (fissured lips and strawberry tongue). An echocardiogram showed no coronary artery abnormalities and normal cardiac function. in view of AKI patient underwent Dialysis for once. On day 6 her fever resolved. She was managed supportively with furosemide, weaned off from other supportive measures by day 7, and was discharged home on day 8.

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(1), 3395-3401 | ISSN:2251-6727

Case 4

Case 4 A 5-year 4month-old male with no chronic medical conditions presented with a 4-day history of fever, morbilliform rash, emesis and diarrhoea. Her lowest documented blood pressure within 24 hours of admission was 76/54 mm Hg. Notable laboratory findings included elevated inflammatory markers, thrombocytopenia, deranged RFT and significant proteinuria and haematuria (Tables 1 and 4). SARS-CoV-2 PCR testing was positive. His chest radiograph demonstrated parabronchial thickening with B/L patchy infiltrates. He was admitted to the PICU due to hypotension and concern for shock. 2D echo showed no abnormalities. He was started on epinephrine and milrinone infusions and was intubated. Given this constellation of findings all necessary investigations were send and kept at PICU with invasive ventilation under ionotropic support. Due to ongoing fevers, elevated inflammatory markers, thrombocytopenia antibiotics was upgraded along with antifungals also started. He was weaned off epinephrine on day 9, extubated on day 10, Her fever resolved on day 11. He was transferred to the inpatient care area on day 13 and discharged home on day 15

Case 5

A 6-year-8-month-old male with no chronic medical conditions presented with a 7-day history of fever, abdominal pain, diarrhoea and emesis. She was initially admitted to an outside facility and all other symptomatic treatment was started. Her lowest documented blood pressure within the 24 hours of admission was 86/58 mm Hg. Notable laboratory findings on admission included elevated inflammatory markers, hypoalbuminemia, and elevated urea and creatinine (Tables 1 and 4). SARS-CoV-2 nasopharyngeal PCR was positive with high cycle threshold (39.17) at our institution. Her echocardiogram demonstrated moderate LV dilation with diminished systolic shortening. Dobutamine and epinephrine were added for cardiac support. On next day child develops decreased urination Given this constellation of findings, she received all the supportive treatment in the line of AKI. Over next few days child's kidney and cardiac functions improved and discharged without any sequelae.

Case 6

A 5-year 2-month-old male with no chronic medical conditions presented with a 5-day history of fever, cough, diarrhoea and bilateral conjunctivitis with mild respiratory distress. She was admitted and necessary symptomatic treatment was started. Her lowest documented blood pressure within 24 hours of admission was 72/54 mm Hg. Notable laboratory findings on admission included elevated inflammatory markers (serum ferritin, CRP and D -dimer) along with significant proteinuria (Tables 1 and 4). SARS-CoV-2 nasopharyngeal PCR was positive. Her chest radiograph demonstrated a prominent cardiac silhouette and B/L mild patchy opacities. Her echocardiogram demonstrated mild diminished LV function and no coronary artery abnormalities. She was started on dopamine and epinephrine for cardiac support. She did not require mechanical ventilation but was tachypnoeic on admission. She was also started on low-dose aspirin. She was weaned off inotropic support on day 6, and her fever resolved day 5. Her mental status and tachypnoea improved and planned for discharge. A follow-up echocardiogram done on day 8 showed mild LV dilation, normal biventricular function and no coronary artery dilation. She was discharged home on day 13.

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(1), 3395-3401 | ISSN:2251-6727

Case 7

A 9-year 1 month-old female with no chronic medical conditions presented with fever, cough, diarrhoea, sore throat and dyspnoea. Laboratory findings were notable for elevated inflammatory markers (Tables 1 and 4). Chest x ray suggest B/L patchy opacities. SARS-CoV-2 nasopharyngeal PCR testing was positive. She was admitted to the PICU for apparent hypovolemic shock from secretory diarrhoea with respiratory distress kept under ventilator support. Her lowest documented blood pressure within 24 hours of her PICU admission was 94/60 mm Hg. An echocardiogram showed mild LV dysfunction. Routine urine reports show significant proteinuria and haematuria. D-dimer and all other inflammatory markers were elevated. She received symptomatic treatment in the line of AKI, pneumonia with cardiac failure. On day 6, her fever resolved and weaned off from ventilator with significant improvement of cardiac and renal functions. Discharged on day 10 without any sequalae.

.

Case 8

A 5-year 3month-old male with no chronic medical conditions presented with history of fever for 6 days. morbilliform rash, conjunctivitis, diarrhoea, irritability, and nuchal rigidity. Her lowest documented blood pressure within 24 hours of admission was 65/32 mm Hg. Important laboratory findings included elevated inflammatory markers, thrombocytopenia, and deranged RFT in the line of AKI (Tables 1 and 4). Initial SARS-CoV-2 PCR testing was negative, but a repeat test on day 5 was positive. Her chest radiograph demonstrated peri bronchial thickening with patchy right lower lobe infiltrates. She was admitted to the PICU due to hypotension and concern for shock and found to have moderately diminished LV systolic function without coronary artery abnormalities. She was started on epinephrine and milrinone infusions and was intubated. Due to AKI child was treated conservatively with fluid restriction. A lumbar puncture was performed that was consistent with pyogenic meningitis with 68 white blood cells, of which 21% were neutrophils, 69% were lymphocytes, and 9% were monocytes. Cerebrospinal fluid (CSF) bacterial cultures were negative. Given this constellation of findings suggestive of meningitis, she received meropenem and vancomycin for 14 days. A head CT performed shows normal findings. She was weaned off epinephrine on day 7, extubated on day 8, and off milrinone on day 6. Her fever resolved on day 9 and She was transferred to the inpatient care area on day 10 and discharged home on day 11. SARS-CoV-2 IgG testing obtained was positive.

Discussion: Acute kidney injury reported in adult Covid-19 infection is more common than in children with MIS-C [(2,3).] The manifestation of COVID-19 infection in Pediatric age group is often of mild to moderate severity. It's rare to find critical Covid-19 cases in Paediatric population. The Pathogenesis of AKI in children with MIS-C is still unclear, though it is thought to be multifactorial. AKI in COVID-19 infection may be due to infection of renal parenchyma through ACE-2 proteins and micro vascular injury caused by cytokine storm [4] MIS-C is mostly a result of immune dysregulation causing greater Inflammation, which with cytokine mediated damage and hypotension can cause renal hypoperfusion, thus leading to AKI [5]. Available literatures suggest that acute kidney injury associated with MIS-C is generally mild and outcome is good with a shorter recovery period which is in contrast with AKI in primary Covid-19 infections. [6].

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(1), 3395-3401 | ISSN:2251-6727

Conclusion: Critical COVID -19 in Paediatric population is uncommon when compared to adult population. The prevalence of AKI in paediatric COVID-19 population is rare and the knowledge is limited. With such wide spectrum of presentation of Covid-19 infection, the diagnosis, management and prevention of Covid-19 outbreak in Pediatric population becomes difficult and needs global collaboration in understanding the SARS-CoV-2 infection in children.

References:

1. Souza TH, Nadal JA, Nogueira RJN, Pereira RM, Brandão MB. Clinical manifestations of children with COVID-19: a systematic review. Pediatr Pulmonol. 2020;55(8):1892–9.

2. Centers for Disease Control and Prevention: Multisystem Inf lammatory Syndrome (MIS-C): Health department–reported cases of Multisystem Inflammatory Syndrome (MIS-C) in the United States, 2020. Available at: https://www.cdc.gov/mis-c/ cases/index.html. Accessed December 16, 2020
3. Cheung EW, Zachariah P, Gorelik M, Boneparth A, Kernie SG, Orange JS, Milner JD: Multisystem inflammatory syndrome related to COVID-19 in previously healthy children and adolescents in New York City. JAMA 324: 294–296, 2020 https:// doi.org/10.1001/jama.2020.10374
4. Batlle D, Soler MJ, Sparks MA, Hiremath S, South AM, Welling PA, et al. Acute kidney injury in COVID-19: emerging evidence of a distinct pathophysiology. J Am Soc Nephrol. 2020;31(7):1380–3.
5. Powell TC, Powell SL, Allen BK, Griffin RL, Warnock DG, Wang HE: Association of inflammatory and endothelial cell activation biomarkers with acute kidney injury after sepsis. Springerplus 3: 207, 2014 https://doi.org/10.1186/2193-1801-3-207
6. Chen YT, Shao SC, Hsu CK, Wu IW, Hung MJ, Chen YC. Incidence of acute kidney injury in COVID-19 infection: a system- atic review and meta-analysis. Crit Care. 2020;24(1):346.