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Research Article

COVID 19: Is it Really Over? To Study Clinical Profile and Outcome of Multisystem Inflammatory Syndrome in Children (MIS-C) Associated with COVID-19 Infection Even after 2 Years of Pandemic: A Single-Center Observational Study from a Private Hospital in Raipur, C.G

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Abstract

Aim: To study the clinical profile and outcome in children admitted in pediatric ICU.

Objective: 1. To study the present scenario and presentation of MISC after 2 years of pandemic, 2. Treatment and outcome of pediatric patient admitted in ICU.

Material and methods: This prospective observational study was done in a tertiary care hospital located in Raipur, the capital of Chhattisgarh over a period of 12 months from July 2023 to June 2024. Eighteen children below 12 years of age who satisfied the WHO diagnostic criteria for MIS-C were included in the study. Clinical parameters were recorded at admission. Relevant laboratory investigations, radiological studies, and outcome were documented.

Observation: The most commonly affected age group was 6-12 years with a female predominance. COVID RTPCR was negative in all patients. Most cases presented 2-6 weeks after the onset of acute infection. Breathing difficulty, Lethargy, vomiting, abdominal pain, cough, and cold are common symptoms of MIS-C syndrome in children and the common signs were rash, conjunctival congestion, hypotension, tachycardia, tachypnea, and hypoxemia. CNS system was the commonly affected followed by the gastrointestinal, cardiac, hepatic, and renal systems. IVIg and steroids was the mainstay of therapy used in 95% of patients. Mortality was 15%. Cases responded well to IVIg and steroids.

Conclusion: Even after 2 years of covid pandemic there is a vast percentage of children's having MIS-C infections, Overall, the short-term outcome was favorable with treatment from IVIg and steroid combine. There is a strong need to follow up of all children's having COVID 19 infection.

Background

Multisystem inflammatory syndrome in children (MIS-C) was first identified in April 2020 by doctors at children's hospitals in the United States and the United Kingdom. The condition has also been called pediatric inflammatory multisystem syndrome (PIMS) [1,2].

Tough in the initial days of pandemic it was found that children had milder disease compared to adults, a unique, severe inflammatory disease which resembled Kawasaki disease (KD) was reported from May 2020 onwards in many children who recovered from COVID-19 infection [3-5]. Since this condition had a striking temporal association with SARS CoV-2 infection, it was later designated as multisystem inflammatory syndrome in children (MIS-C) associated with COVID-19 infection. This potentially life-threatening complication of COVID-19 infection may occur during or after recovery in symptomatic as well as asymptomatic children. Spectrum of MIS-C may range from mild disease to severe involvement including shock, multiorgan dysfunction, coagulopathy, respiratory failure, myocardial dysfunction, and encephalopathy.

The existing treatment guidelines for MIS-C in children are extrapolated from guidelines to treat Kawasaki disease, since both these conditions have significant overlapping features.

After 2 years of COVID-19 Pandemic there is still prevalence of MIS-C in children. Considering the relative paucity of data, there is an urgent need to study the clinical profile and outcomes of MIS-C based on the current treatment guidelines, so that evidence-based modifications, if required, can be done [6-9].

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Methods

This observational study was done in a tertiary care hospital located in Raipur over a period of 12 months from July 2023 to June 2024. This study was done to find out the clinical presentation, laboratory abnormalities, and outcomes of children admitted with MIS-C associated with COVID-19 infection. All children below 12 years fulfilling the WHO diagnostic criteria for MIS-C syndrome were enrolled in the study. Children suffering from chronic disorders like congenital or acquired heart diseases, asthma, bronchiectasis, chronic liver disease, chronic kidney disease, genetic disorders, IEM (inborn errors of metabolism), and neurodevelopmental disorders were excluded from the study.

After initial stabilization, detailed clinical history was obtained and documented. Clinical examination findings and results of laboratory and imaging tests were recorded. Cases were managed as per the existing guidelines for the management of MIS-C syndrome. Investigations to rule out common tropical infections like malaria smear and/or rapid test, dengue serology, WIDAL test, and scrub typhus serology were also performed. The treatment modalities given, response to treatment, the entire course at hospital, and outcome were documented [10].

Statistical analysis

Data was collected with Microsoft Excel and analysis was done using EpiInfo Version 7.2.4. The categorical variables were summarized as frequency and percentage. The continuous variables were summarized as mean and standard deviation. The association between categorical variables was assessed using chi-square. p-value < 0.05 was considered statistically significant.

Results

A total of 18 patients fulfilling the inclusion criteria were included in the study. The number of children less than 1 year, 1-5 years, and 6-12 years' age group were 1 (5.5%), 4 (22.2%), and 14 (72.2%) respectively. There were 6 boys (34%) and 12 girls (65%) in our study population. Seventy-three percent of children had a history of COVID-19 infection. Figure 1 shows the clinical spectrum of MIS-C in the descending order of incidence among children with MIS-C. The comparison of clinical symptoms and signs in various age groups are tabulated in Table 1. The prevalence of rash (p=0.03) and conjunctival congestion (p=0.021) was significantly higher in older children compared to infants. The mean and standard deviation of laboratory parameters and the distribution of abnormal laboratory and radiological investigations among study participants are described in Table 2. Leukocytosis and thrombocytopenia were commonly seen as hematological abnormalities in 47.3% and 31.5% of study population respectively. Elevated d-dimer, elevated PT-INR, and elevated aPTT were seen in 57%, 42%, and 21% cases respectively. The various treatment modalities received and outcome measures are described in Table 3. The proportion of children who received fluid bolus, inotropic support, renal replacement, and ventilation were 63.1%, 63%, 12%, and 52% respectively. Steroid and IVIg were used in 73.5% of study participants respectively. There were three deaths in our study population.

Discussion

Our knowledge about the epidemiology, pathogenesis, clinical spectrum, and associated laboratory abnormalities seen in MISC

Table 1: Comparison of clinical symptoms and signs in various age groups.

Item		Age group		
		< 1 year	1–5 years	6–12 years
		n = 1 (%)	*n* = 4 (%)	*n* = 14 (%)
Cough		1 (100)	3	10
Cold		1 (100)	3	8
Rash		0	2	4
Vomiting		1 (100)	2	4
Loose stool		0	1	2
Abdominal pain		0	2	2
Conjunctival congestion		1 (100)	2	8
Lethargy		1 (100)	3	8
Poor oral intake		1	4	12
Pulse rate	**Normal for age**		3	8
	Tachycardia	1	1	10
Blood pressure	**Normal**		2	6
	Hypotension	1	2	12
SpO2	**90–100%**		1	3
	81–89%	1	2	5
	< 80%		1	6
Respiratory rate	**Normal**		2	3
	Tachypnea	1	2	11

Table 2: Distribution of abnormal laboratory radiological investigations among study participants.

Investigations	Parameters	Frequency (*n* = 19)	Percentage
Laboratory investigation			
Hematology	Leucocytosis	9	47.3
	Elevated NLR (> 3.53)	4	21.5
	Thrombocytopenia	6	31.5
Inflammatory indicators	Elevated CRP (> 30 mg/l)	19	100
	Elevated ESR (> 40 mm/h)	9	47.3
	Elevated Ferritin (> 500 ng/mL)	11	57
	Elevated LDH (> 460 U/l)	4	21
Coagulation profile	Elevated D-dimer (> 0.5 µg/ml)	11	57
	Elevated INR (> 1.2)	8	42
	Elevated APTT (> 35 s)	4	21
Liver enzymes	SGPT (> 40 IU/l)	4	21
	SGOT (> 40 IU/l)	4	21
Kidney Function Test	Urea (> 40 mg/dl)	3	15.7
	Creatinine (> 1.1 mg/dl)	3	15.7
Radiological investigation			
Chest X-ray	Pleural effusion	2	10.5
	Pneumonia	12	63.1
Echocardiogram	Ventricular dysfunction	4	21
	Coronary artery abnormalities	2	10.5
	Small patent ductus arteriosus	1	5.6
	Pulmonary arterial hypertension	1	5.6
Ultrasound abdomen	Polyserositis	2	10.5
	Ascites	6	31.5
	Hemoperitonerum	1	5.2
	Mesenteric lymphadenopathy	2	10.5

NL ratio: Neutrophil–lymphocyte ratio; CRP: C-reactive Protein; ESR: Erythrocyte Sedimentation Rate; LDH: Lactate Dehydrogenase; PT: Prothrombin Time; INR: International Normalized Ratio; APTT: Activated Partial Thromboplastin Time; SGPT: Serum Glutamic Pyruvic Transaminase; SGOT: Serum Glutamic Oxaloacetic Transaminase

Table 3: Distribution of treatment modalities and outcome of study participants.

Parameters	Frequency ($n = 19$)	Percentage
Respiratory support		
Low-flow nasal oxygen (*LFO*)	1	5.2
High-flow nasal cannula (*HFNC*)	4	21.1
Non-invasive ventilation (NIV)	4	21.1
Mechanical ventilation	10	52
Treatment		
Fluid bolus	12	63.1
Steroids	14	73.6
IVIg	14	73.6
Aspirin	10	52
Inotropic support	12	63.1
Renal support	2	1.2
Outcome		
Death	3	15.7
Hospital stay (mean ± SD days)	8.7 ± 1.8	
ICU stay (mean ± SD days)	4.8 ± 1.5	

ICU: Intensive Care Unit

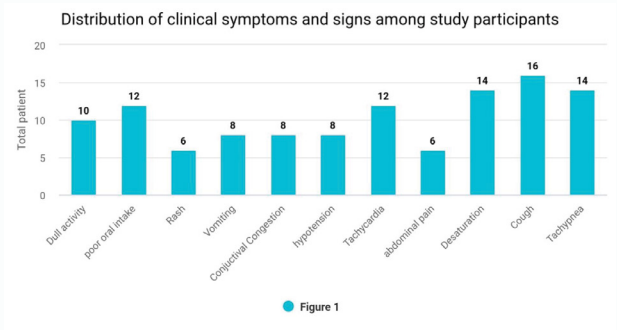

Figure 1: Distribution of clinical symptoms and signs among study participants.

syndrome is still evolving [7]. The diagnostic criteria of MISC are constantly revised with time as more evidence is being generated [7,10].

Our study identified that the most commonly affected age group was 6 to 12 years accounting for more than 50% of the study population. This finding was in agreement with other similar published studies [9,11-14]. We also noticed that girls were affected more than boys (M:F ratio of 1:2.1). Similar finding was also seen in another study by Brundavanam Venkata Krishna Sai et al. (M:F ratio of 1:1.9 out of 78 cases) whereas most other studies showed male predisposition- Hoste et al. (M:F-1.4:1 out of 928 cases), Goldfred et al. (M:F-1.2:1 out of 570 cases), Sethy et al. (M:F-3.2:1 out of 21 cases), Kaushik et al. (M:F-1.6:1 out of 33 cases), and Sugunan et al. (M:F-1.9:1 out of 32 cases) [9,12-18].

Though COVID RT-PCR was done in all patients, none were found to be positive. COVID-19 antibody was positive in 19 (100%) children. fourteen (73.6%) children had a history of contact with COVID positive cases. Other studies have shown RT-PCR positive in 19% to 31% of cases [9,13,15]. In our population, we noted a 2-6-week lag period for MIS-C presentation following COVID-19 infection or contact with COVID-19 case.

The most common presentations were cough (84%), lethargy (52%), poor oral intake (63%), rash (31%), vomiting (42%) and conjunctival congestion (42%). The presence of rash and conjunctival congestion was proportionately higher with the increasing age of children. Gastrointestinal system involvement was seen in 42% of our study population which was lower than global data of 86% as reported by recent systematic reviews [14, 17].

Leukocytosis, high N/L ratio and thrombocytopenia were found in 47%, 21%, and 31% of patients respectively. C-Reactive protein (CRP) was elevated in 19 (100%) patients. 9 (48%) had elevated ESR [18]. Serum Ferritin, d-dimer, and LDH were elevated in 57%, 57%, and 21% respectively. In contrast, to the study done by Brundavanam Venkata Krishna Sai et al. [18] 21 percent of patients had biochemical evidence of hepatic dysfunction as evidenced by elevated SGOT, SGPT, or both. In our study, 15% of patients had renal dysfunction as evidenced by elevated serum urea or creatinine or both and 2 (10%) required hemodialysis. In a study by Williams et al. incidence of AKI was 35% and 2% required renal replacement therapy [17].

Hypoxemia was observed in 50% of patients at presentation out of which 40% had SpO2 below 80%. 60 percent of patients had abnormal chest radiograph. 10 (52%) children needed invasive mechanical ventilation. The need for invasive mechanical ventilation was ranging from 0 to 39% in published studies [8,9,15].

Sixty-three percent of children were hypotensive at presentation. In one study, the incidence of hypotension at admission was found to be 47% [13]. Cardiac involvement was found in a significant number of cases in our population. Incidence of myocardial systolic dysfunction was relatively less (21%) in our study compared to 63% in data from New York by Kaushik et al. [16]. 12 (63%) of children presented with shock which were fluid refractory requiring inotropes. Similar results were reported by Hoste et al. [14]. In studies from New York by Kaushik et al. 51% required vasopressor support [16].

Neurological involvement was seen in more than 50% of cases in some studies, in contrast to this Brundavanam Venkata Krishna Sai [20] et al shoes only 5.1% children that presented with seizure and altered sensorium.

Though IVIg, steroids, anticoagulation, and aspirin are the mainstay of therapy in MISC syndrome, there is limited evidence to support their use. Due to the striking similarities of this syndrome with Kawasaki disease, the same treatment is being recommended for MIS-C as well [7,14,17]. Our study group received IVIg as the first-line treatment followed by steroids, anticoagulation, and aspirin but we did not use biological agents. Seventy three percent of our patients received both IVIg and steroids. There is no evidence-based consensus for managing MIS-C syndrome which reinforces the immediate need for such studies.

The mean duration of hospital stay was 8.7 days. And mean duration of ICU stay was 4.8 days. Out of 19 children, 16 survived and 3 child (15%) died. one study from Odisha reported 9% mortality [13].

The main limitation of this study is the small sample size and lack of follow-up. Long-term follow-up can throw more light on chronic complications of MIS-C in children.

Conclusion

Fever, breathing difficulty, Lethargy, poor feeding, vomiting, abdominal pain, loose stools, cough, and cold are common symptoms of MIS-C syndrome in children and the common signs include rash, conjunctival congestion, hypotension, tachycardia, tachypnea, and hypoxemia. The incidence of rash and conjunctival congestion increased significantly with the increasing age of the child. The CNS system was the most commonly affected system in MIS-C followed by

the respiratory and cardiovascular systems. Cases responded well to IVIg and steroids. Overall, the short-term prognosis was good in our study population. Large scale multi-centric data on MIS-C is required to understand this novel complication of COVID-19 infection in children even after 2 years of pandemic being over.

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