Title page:

Title: Intensive care needs and short-term outcome of Multisystem Inflammatory Syndrome in Children (MIS-C): Experience from North India.

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Abstract:

Objectives: To describe the intensive care needs and outcome of Multisystem Inflammatory Syndrome in Children (MIS-C). **Methodology:** This retrospective study was conducted in the Pediatric Emergency and Intensive Care Units and COVID-19 hospital of a tertiary care teaching and referral hospital in North India over a period of 5 months (September 2020-January 2021). Clinical details, laboratory investigations, intensive care needs, treatment, and short-term outcome were recorded. **Results:** Forty children with median (IQR) age of 7 (5-10) years were enrolled. The common clinical features were fever (97.5%), mucocutaneous involvement (80%), abdominal (72.5%) and respiratory (50%) symptoms. Shock was noted in 80% children. Most cases (85%) required PICU admission where they received nasal prong oxygen (40%), non-invasive (22.5%) and invasive (22.5%) ventilation, and vasoactive drug support (72.5%). The confirmation of SARS-CoV-2 exposure was noted in the form of positive serology (66.7%), RT PCR (10%), and contact with SARS-CoV-2 positive case (12.5%). The common echocardiographic findings included myocardial dysfunction (ejection fraction <55%) (72.5%), and coronary artery dilatation or aneurysm (22.5%). The immunomodulatory treatment included IVIG (2 gm/kg) (100%) and steroids (methylprednisolone 10-30 mg/kg/day for 3-5 days) (85%). Aspirin was used in 80% and heparin (low molecular weight) in 7.5% cases. Two children died (5%) and median duration of PICU and hospital stay in survivors were 5 (2-8) and 7 (4-9) days, respectively. Children with shock showed higher total leucocyte count and higher rates of myocardial dysfunction. **Conclusion:** Cardiovascular involvement and shock are predominant features in severe disease. Early diagnosis may be challenging given the overlapping features with other diagnoses. A high index of suspicion is warranted in children with constellation of fever, mucocutaneous, GI and cardiovascular involvement alongwith evidence of systemic inflammation and recent or concurrent SARS-CoV-2 infection.

The short-term outcome is good with appropriate organ support therapies and immunomodulation.

Keywords: COVID-19; Critically ill children; Hyperinflammation; Intravenous Immunoglobulin; Mechanical Ventilation; MIS-C, Myocarditis, PICU; PIMS-TS, SARS-CoV-2; Steroids.

Introduction:

Healthcare systems globally have been severely burdened by the coronavirus disease 2019 (COVID-19) pandemic.[1-6] The disease has been severe in adults typically occurring in the 2nd week of illness coinciding with increase in inflammatory markers and decrease in viral load. The aberrant and dysregulated innate and adaptive immune response is thought to be the cause of host tissue damage.[7-11] On the other hand, children were less frequently and less severely affected, especially in the early part of the pandemic.[1-3, 12] Severe and critical disease was reported in only 5.8% in a study from China.[12]

The first report of severe disease in children temporally associated with COVID-19 came from the United Kingdom (UK) in late April 2020 in a cluster of eight previously healthy children who presented with fever, shock, and hyperinflammation. This constellation was labelled as pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS).[13] Thereafter, multiple reports of PIMS-TS, multisystem inflammatory syndrome in children (MIS-C), Kawasaki disease (KD), Kawasaki-like syndrome, or toxic shock syndrome (TSS) were increasingly reported from other countries as well.[13-36] However, only <100 cases of PIMS-TS or MIS-C have been reported from India till date.[37-40]

In order to reduce the morbidity and mortality associated with MIS-C, it is important to study the disease spectrum, clinical features, evolution, treatment and outcome. The sicker cohort in particular needs to be studied for its PICU needs, complications, and outcome. More importantly since the clinical features of MISC closely mimics other common PICU admissions like TSS and tropical infections. it is important to raise awareness about this condition to facilitate early diagnosis and prompt treatment. In view of limited data from India, we planned this study to describe the clinical characteristics, intensive care needs, and short-term outcome of children with MIS-C.

Methodology:

This retrospective study was conducted in the Pediatric Emergency, Pediatric Intensive Care Unit (PICU), and COVID-19 hospital of a tertiary care teaching and referral hospital in North India from 1st September 2020 to 31st January 2021. Data of 40 children between 3 months to 12 years with diagnosis of MIS-C was retrieved from the admission files and patient electronic database and recorded on a pre-designed study proforma. The study protocol was approved by the Institute Ethics Committee and the final manuscript was approved by the Departmental Review Board.

The details included age, gender, underlying co-morbidity (obesity, congenital cardiac disease, chronic lung disease, neurological disease, neuromuscular disorder, or any other), presenting complaints, duration of illness, and pre-referral treatment. The evidence of recent or concurrent SARS-CoV-2 infection (SARS-CoV-2 antibody, RT-PCR, and contact/epidemiological link in 2-6 weeks prior) were also noted. The laboratory details included complete blood count, renal function tests, liver function tests, coagulation profile, C-reactive proteins (CRP), procalcitonin, ferritin, fibrinogen, D-dimer, lactate dehydrogenase (LDH), creatine kinase (CK)-MB, troponin, N-terminal pro B-type natriuretic peptide (NT-proBNP), cultures, chest radiograph, electrocardiogram, echocardiography (left ventricular ejection fraction, coronary artery abnormality, pericardial effusion), and computed tomography (CT) chest, if done. All organ system dysfunction in form of myocardial dysfunction, shock, coagulopathy, liver dysfunction, CNS dysfunction, and acute kidney injury (AKI) were also recorded. The treatment details including PICU admission, oxygen supplementation, continuous positive airway pressure (CPAP), high flow nasal cannula (HFNC), non-invasive ventilation (NIV) or invasive ventilation, fluid resuscitation, vasoactive drugs, renal replacement therapy (RRT), antibiotics, antivirals, intravenous immunoglobulin (IVIG),

steroids, and immunomodulators were recorded. The final outcomes including mortality, length of PICU and hospital stay were recorded.

The diagnosis of MIS-C was made on the basis of case definition given by the WHO (https://www.who.int/news-room/commentaries/detail/multisystem-inflammatory-syndrome-in-children-and-adolescents-with-covid-19). The diagnosis of recent or current COVID-19 was confirmed by nasopharyngeal swab (NPS) reverse transcriptase polymerase chain reaction (RT-PCR) for SARS-CoV-2 or SARS-CoV-2 serology. For SARS-CoV-2 RT-PCR, the NPS was collected as per standard procedure and transported in viral transport medium (VTM) under cold chain to the dedicated laboratory. The SARS-CoV-2 RT-PCR was done using Q-line Molecular RT-PCR Kit (POCT Services, Lucknow, India) or VIRALDTECT Multiplex RT-PCR Kit (Genes2Me Pvt. Ltd., Gurgaon, India) targeting envelope nucleoprotein and RNA-dependent RNA Polymerase Genes. The amplification was done using BIO-RAD CFX96 Real-time PCR Machine (California, USA). The SARS-CoV-2 antibody testing was done by enzyme-linked immunosorbent assay (ELISA) as per the standards of the manufacturer of the kits used [EUROIMMUN Anti-SARS-CoV-2 ELISA (IgG), Seekamp, Lübeck]. We followed recent guidelines and protocols in managing children with MIS-C.[41, 42]

The definitions for various laboratory parameters included: hyponatremia as serum sodium <135 meq/L, lymphopenia as absolute lymphocyte count <3000/cumm for infants and <1000/cumm for older children, thrombocytopenia as platelet count <1,50,000/cumm, elevated CRP >10 mg/dl, elevated procalcitonin >0.2 ng/ml, elevated ferritin >500 ng/ml, elevated D-dimer >500 ng/ml, elevated fibrinogen >4 gm/L, and elevated NT-proBNP as >125 pg/ml. The myocardial dysfunction was defined as left ventricular ejection fraction (LVEF) <55%. The coronary artery dilatation or aneurysm was defined as coronary artery diameter ≥2.5 z score and giant aneurysm as ≥10 z score or >8 mm.

Statistical analysis:

Appropriate data entry and statistical analysis was performed on Microsoft Excel 2010 (Microsoft, Redmond, WA) and SPSS software version 20 (SPSS, Inc, Chicago, IL). Descriptive statistics [median, interquartile range (IQR), number, and percentages] was used to describe the data variables. Children with and without shock were compared by using Chi-Square Test or Fisher Exact test for categorical variables and Mann-Whitney U test for continuous variables. The p-value <0.05 was considered significant.

Results:

Forty children with MIS-C were admitted during the study period. The month wise distribution is given in Figure 1; the highest number of cases were admitted in the month of October 2020 (n=11). The median (IQR) age of the enrolled subjects was 7 (5-10) years and 65% (n=26) were boys. The median (IQR) duration of symptoms before hospitalisation was 6 (5-7) days and most common clinical features were fever (97.5%); mucocutaneous (80%) including rash (72.5%), conjunctival injection (60%), oral mucosal changes (27.5%), and extremity changes (17.5%); abdominal (72.5%) including abdominal pain (57.5%), vomiting (50), and diarrhea (30%); and respiratory (50%) including rapid breathing (40%) and cough (25%). Four (10%) cases had hemorrhagic non-purulent conjunctivitis (Figure 2a and 2b). Other features recorded were pallor (45.9%), hepatomegaly (27.5%), musculoskeletal symptoms (10%) in form of myalgia, and seizures (2.5%). The median (IQR) Glasgow Coma Scale at admission was 15 (14-15). Majority (62.5%) of children were hospitalised prior to referral to our centre where they received fluid boluses and vasoactive drugs (15% each). The evidence of SARS-CoV-2 infection was noted in form of positive SARS-CoV-2 antibodies in 66.7% (20/30) cases and positive SARS-CoV-2 RT PCR in 10% cases. The history of exposure to a SARS-CoV-2 case was there in 12.5% cases (Table 1).

Table 2 elaborates the laboratory abnormalities and echocardiographic findings in these children. The common laboratory abnormalities were elevated NT-proBNP (100%), CRP (95%), D-dimer (92.5%), ferritin (90%), fibrinogen (87.5%), and procalcitonin (80%); lymphopenia (65%); and thrombocytopenia (50%). The IL-1 was measured in only 2 children and was elevated in both (68 and 1188 pg/ml). Among survivors, the levels of inflammatory markers showed decreasing trend with treatment (along with clinical improvement) and normalized at the time of discharge. Two (5%) cases had transient arrhythmias (junctional rhythm in one case during acute illness and sinus tachycardia with ST elevation in inferior leads

in one case 2 weeks after discharge) which recovered spontaneously. Two children (5%) developed peripheral gangrene of bilateral toes during admission which resolved at the time of discharge (Figure 2c and 2d). All cases underwent echocardiography. The common echocardiographic findings were LVEF <55% (72.5%), coronary artery dilatation or aneurysm (22.5%), and giant coronary aneurysm (2.5%). None had pericardial effusion. At discharge, residual myocardial dysfunction was noted in 15% (n=6) cases.

Majority (85%) of the cases required PICU admission. The highest level of respiratory support received were nasal prong oxygen (40%), non-invasive ventilation (22.5%), invasive ventilation (22.5%), and HFNC (2.5%). Shock was present in 80% cases out of which 81.2% required fluid bolus/es and 90.6% (72.5% of total cohort, 29/40) required vasoactive drug support for a median duration of 81 (48-120) hours with highest median VIS score being 20 (10-53). Not all children with shock received fluid boluses in view of suspected myocardial dysfunction. Acute kidney injury was seen in 45% cases but none required RRT. All cases received IVIG soon after admission in dose of 2 gm/kg over 12-24 hours. Only one child (2.5%) required an additional dose of IVIG for non-improvement after first dose IVIG and steroids. Steroids were used in 85% cases, the most common steroid being methylprednisolone (82.5%) in dose of 10 mg/kg/day (75.3%) for 3-5 days followed by oral prednisolone for 4-6 weeks. The methylprednisolone was usually started at dose of 10 mg/kg/day and if there was no improvement in next 24-48, the dose was increased to 20 or 30 mg/kg/day. Steroid and IVIG (combined) was used in 85% cases. Aspirin was started in 80% cases in a dose of 3 mg/kg/day (maximum daily dose 75 mg) for a minimum of 4 weeks. The anticoagulation (low molecular weight heparin) was used in 7.5% cases (including 2 cases with peripheral gangrene). The median length of PICU and hospital stay were 5 (2-8) days and 7 (4-9) days, respectively. Two (5%) children died due to refractory shock within 24 hours of admission (Table 4).

Children with shock had significantly higher rates of myocardial dysfunction (p=0.02), higher total leukocyte count (p=0.048), and higher proportion of them received steroids (p=0.009). Although children with shock were relatively younger; had lower ejection fraction, platelet count, and fibrinogen levels; higher ferritin, D-dimer, pro-BNP, CRP, and procalcitonin levels; higher proportion needed PICU care; and had longer PICU and hospital stay, the difference in these parameters was not statistically significant (Table 5).

Discussion

We describe the largest cohort of critically ill children with MIS-C from North India with respect to their clinical and laboratory characteristics, intensive care needs, and outcome. As opposed to COVID 19 which was less in frequency and severity in children, MIS-C tends to be more severe. It is postulated to be a post-SARS-CoV-2 phenomenon, characterised by multiple organ dysfunction (gastrointestinal, mucocutaneous, and cardiovascular) and a critical course secondary to immune-mediated injury, hyperinflammation, and hypercytokinemia.[11, 14, 16] Unlike in children with acute COVID-19, the involvement of respiratory system is less frequent. A post viral hypothesis is supported by lower rates of SARS-CoV-2 RT-PCR positivity and higher rates of SARS-CoV-2 positive serology,[14-17, 36] a finding that was observed in our cohort too. Furthermore, the peak incidence of MIS-C is reported to occur about 2-6 weeks after the COVID-19 peak.[14-17, 31, 43] We observed a similar trend; in India the cases of COVID-19 peaked in mid-September 2020 and maximum number of MIS-C cases were admitted in the month of October. The dramatic improvement in myocardial dysfunction and decrease in inflammatory markers following administration of IVIG and/or steroids reinforces the post viral hypothesis.[17, 25, 36, 41, 42]

Early diagnosis of MIS-C can be challenging given the overlapping features with other diseases. Symptoms mimicking GI infection, acute abdomen, or inflammatory bowel disease attributed to vasculitis induced bowel wall edema or ischemia, cardiac dysfunction and/or shock, mesenteric lymphadenitis, and mesenteric inflammation have been reported.[14, 16-27, 29, 31, 35, 36. 44] Similarly, the neurological manifestations (seizure, encephalopathy, meningismus, headache) although uncommon in our cohort (2.5%) have also been reported previously in children with MIS-C (10-55%).[35-37, 40] Kawasaki Disease, TSS, macrophage activation syndrome (MAS), or hemophagocytic lymphohistiocytosis (HLH) are the other close differential diagnoses.[16, 17] Older age group (7-10 years), more GI, respiratory and

cardiovascular system (shock, LV dysfunction) involvement, marked hyper-inflammation (elevated CRP, procalcitonin, ferritin, lymphopenia, and thrombocytopenia), and higher need for organ support therapies (vasoactive drugs and mechanical ventilation) differentiates MIS-C from KD.[11, 13, 14, 16, 17, 21, 31]

Diagnosis of MIS-C warrants a high index of suspicion. Any child with history of SARS-CoV-2 infection (asymptomatic or symptomatic), 2-6 weeks prior to the symptom onset, presenting with constellation of fever, mucocutaneous features, GI symptoms, and shock should alert pediatricians towards this entity. Broadly, the diagnosis of MIS-C requires presence of fever, severe illness requiring hospitalization with ≥1 organ dysfunction, elevated markers of inflammation, evidence of current or recent SARS-CoV2-2 infection (positive SARS-CoV-2 RT PCR or serology or epidemiological contact), and exclusion of other alternative etiologies.[14, 16, 17, 35, 45]

Majority of the affected children in our cohort had shock, and required PICU admission, close monitoring and organ support therapies (vasoactive support and mechanical ventilation). It has been reported in literature that 65-88% of children with MIS-C require PICU admission[14-17, 36, 46] as was the case in most of our children. Shock in children with MIS-C is multifactorial contributed by myocardial dysfunction, vasoplegia, and vasculitis.[25] Although we did not identify any clinical or laboratory variable that could significantly predict the development of shock, we found that a significant proportion of children with shock had higher leucocyte count and myocardial dysfunction. The patterns of myocardial involvement described in MIS-C include LEVF <55% (50-70% children), myocarditis (50-80%), coronary artery dilatation or aneurysm (6-20%), and residual myocardial dysfunction at discharge (2-18%).[14, 15, 35, 36, 47, 48] The type of myocardial involvement seen in our cohort was similar.

The biomarkers of hyperinflammation and organ dysfunction should be monitored closely in critically ill children as they help both in diagnosis and in monitoring the therapeutic

response. Majority of children in the index study had elevated markers of inflammation (CRP, procalcitonin, fibrinogen, ferritin, D-dimer), lymphopenia, and thrombocytopenia, similar to previously published reports[14, 15, 35, 36, 47] and showed an improvement following treatment.

The major goals of treatment of MIS-C include control of systemic inflammation, organ support, and decrease the risk of long-term sequelae.[49] The intensive care needs reported in literature are: non-invasive (13-31%) or invasive (19-37%) ventilation, vasoactive drugs (53-73%), and renal replacement therapy (1-4%). The targeted therapies used in children were IVIG (74-89%), and steroids (40-65%). The antiplatelet agent (aspirin) and anticoagulation were used in 30-78% and 25-77% children, respectively. Although there has been a great variation in the use of immunomodulatory treatments for MIS-C, we had put in place an evidenced based protocol which we followed uniformly for all children.[41, 42, 50] We used IVIG in all cases with MIS-C and added steroids in those with moderate to severe illness and/or shock. There is some evidence to suggest that combination of IVIG and methylprednisolone as against IVIG alone was associated with rapid resolution of fever; lower treatment failure, lesser need for second-line therapy, and hemodynamic support; faster recovery of myocardial function; and shorter duration of PICU stay.[51, 52]

Despite the multisystemic involvement and shock, the mortality in our cohort was low highlighting the importance of timely diagnosis, organ support and immunomodulatory therapies. The two deaths that occurred in our cohort, was due to refractory shock and occurred within 24 hours of admission further underscoring the importance of early recognition, resuscitation (fluids and vasoactive drugs), and targeted immunomodulation preferably at first contact healthcare facility.

The strengths of this study are that it reports the largest critically ill cohort of MIS-C from India focussing on their intensive care needs and outcome. All the children were managed using uniform guidelines and protocols. The study however suffers from the inherent

limitations of a single centre retrospective analysis. The SARS-CoV-2 serology could not be performed in all the children. A long-term follow-up to evaluate for persistent myocardial dysfunction and coronary artery abnormalities would have made the data more robust.

Conclusion:

MIS-C is a severe multisystemic manifestation of SARS-CoV-2 infection in children. Cardiovascular involvement and shock are predominant features in severe disease. Early diagnosis may be difficult given the overlapping features with other diagnoses. A high index of suspicion is warranted in children with constellation of fever, mucocutaneous, GI and cardiovascular involvement alongwith evidence of systemic inflammation and recent or concurrent SARS-CoV-2 infection. The short-term outcome is good with appropriate organ support therapies and immunomodulation (IVIG and/or steroids).

Figure legends:

Figure 1: Month-wise and cumulative distribution of children with admitted with MIS-C.

Figure 2: Hemorrhagic non-purulent conjunctivitis in 2 children (a and b) and bilateral peripheral gangrene involving toes in 1 child (c and d).

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Table 1: Clinical characteristics in children with MIS-C.

Characteristics	**Total cases, n=40**
Age in years, median (IQR) Range (years)	7 (5-10) 2-12
Male gender, n (%)	26 (65)
Comorbidity, n (%) Congenital acyanotic heart disease, n (%) Chronic renal failure, n (%)	2 (5) 1 (2.5) 1 (2.5)
Duration of illness in days, median (IQR)	6 (5-7)
Clinical features	
Fever, n (%)	39 (97.5)
Mucocutaneous features, n (%) Rash, n (%) Conjunctival injection, n (%) Oral mucosal changes, n (%) Peripheral extremity changes, n (%) Cervical lymphadenopathy, n (%)	32 (80) 29 (72.5) 24 (60) 11 (27.5) 7 (17.5) 2 (5)
Abdominal symptoms, n (%) Pain abdomen, n (%) Vomiting, n (%) Diarrhoea, n (%)	29 (72.5) 23 (57.5) 20 (50) 12 (30)
Respiratory symptoms, n (%) Rapid breathing Cough	20 (50) 12 (40) 10 (25)
Pallor, n (%)	17 (42.5)
Hepatomegaly, n (%)	11 (27.5)
Musculoskeletal symptoms, n (%)	4 (10)
Neurological symptoms, n (%)	1 (2.5)
Admission GCS, median (IQR)	15 (14-15)
Pre-referral admission, n (%) Received fluid boluses, n (%) Received vasoactive drugs, n (%)	25 (62.5) 6 (15) 6 (15)
Confirmation of exposure Positive SARS-CoV-2 antibody, n (%) Positive SARS-CoV-2 RT-PCR, n (%) Contact with positive case of SARS-CoV-2, n (%)	 20/30 (66.7) 4 (10) 5 (12.5)

Table 2: Laboratory characteristics and echocardiographic findings in children with MIS-C.

Characteristics	**Total cases, n=40**
Lymphopenia, n (%)	26 (65)
Thrombocytopenia, n (%)	20 (50)
Elevated CRP, n (%)	38 (95)
Elevated procalcitonin, n (%)	34 (80)
Elevated ferritin, n (%)	36 (90)
Elevated D-dimer, n (%)	37 (92.5)
Elevated fibrinogen, n (%)	35 (87.5)
Elevated NT-proBNP, n (%)	40 (100)
Elevated CK-MB, n (%)	29 (72.5)
Elevated troponin, (%)	26 (65)
Hypoalbuminemia, n (%)	27 (67.5)
Elevated transaminases, n (%)	19 (47.5)
Elevated LDH, n (%)	27 (67.5)
Hyponatremia, n (%)	24 (60)
Echocardiography performed	40 (100)
Ejection fraction at admission, median (IQR)	45 (36-50)
Myocardial dysfunction or left ventricular ejection fraction <55%, n (%)	29 (72.5)
Coronary artery dilatation or aneurysm, n (%)	9 (22.5)
Coronary giant aneurysm, n (%)	1 (2.5)
Residual myocardial dysfunction at discharge, n (%)	6 (15)

Table 3: Laboratory parameters at admission in children with MIS-C.

Characteristics*	Total cases, n=40
Hemoglobin (gm%)	10 (9-11.7)
Total leukocyte count (per mm^3)	10250 (5000-16250)
Absolute neutrophil count (per mm^3)	8256 (3713-13248)
Absolute lymphocyte count (per mm^3)	1467 (800-2760)
Platelet count (per mm^3)	140000 (70000-210000)
Prothrombin time (seconds)	15 (13-188)
International normalization ratio	1 (1-1)
Activated partial thromboplastin time (seconds)	35 (30-38)
Ferritin (ng/ml)	1089 (525-2000)
Fibrinogen (gm/L)	4 (3-4)
LDH (U/L)	347 (281-380)
D-dimer (ng/ml)	1135 (888-2751)
CK-MB (mg/dl)	29 (21-46.5)
NT-proBNP (pg/ml)	9494 (828-21651)
Troponin (IU/L)	84 (47-1058)
IL-6 (n=1) (pg/ml)	68
Lactate (mmol/L)	3 (2-4)
CRP (mg/dl)	124 (21-204)
Procalcitonin (ng/ml)	13 (1-26.75)
Sodium (meq/L)	134 (131-136)
Potasium (meq/L)	4 (4-5)
Urea (mg/dl)	29.5 (23-69)
Creatinine (mg/dl)	0.2(0.1-1.0)
AST (IU/L)	44 (27-120)
ALT (IU/L)	56 (29-106)
Total protein (gm/dl)	6 (5-7)
Serum Albumin (gm/dl)	2 (2-3)

*All values in median (IQR)

Table 4: Intensive care needs, treatment details, and outcome in children with MIS-C.

Characteristics	Total cases, n=40
Admitted to PICU, n (%)	34 (85)
Oxygen by nasal prongs, n (%)	16 (40)
Non-invasive ventilation, n (%) Duration of NIV in days, median (IQR)	9 (22.5) 2 (1.25-2.5)
Invasive ventilation, n (%) Duration of IMV in days, median (IQR)	9 (22.5) 2 (1-4)
HFNC, n (%) Duration of HFNC in days	1 (2.5) 4
Shock, n (%) Fluid bolus, n (%) Vasoactive drugs, n (%) Adrenaline, n (%) Milrinone, n (%) Noradrenaline, n (%) Vasopressin, n (%) Vasoactive Inotropic Score (VIS), median (IQR) Duration of vasoactives in hours, median (IQR)	32 (80) 26 (81.2) 29 (90.6) 19 (65.5) 18 (62.1) 16 (55.2) 1 (3.4) 20 (10-53) 81 (48-120)
Acute kidney injury, n (%) AKI stages (KDIGO) I, n (%) II, n (%) III, n (%)	18 (45) 7 (17.5) 8 (20) 3 (7.5)
Renal replacement therapy, n (%)	0
IVIG, n (%)	40 (100)
2nd dose IVIG, n (%)	1 (2.5)
Steroids, n (%) Steroids used: Methylprednisolone, n (%) Dexamethasone, n (%) Methylprednisolone dose: 10 mg/kg/day, n (%) 20 mg/kg/day, n (%) 30 mg/kg/day, n (%)	34 (85) 33 (82.5) 1 (2.5) 25 (75.7) 1 (3) 7 (21.2)
Steroids + IVIG, n (%)	34 (85)
PRBC Transfusion, n (%)	9 (22.5)
PC transfusion, n (%)	3 (7.5)
FFP transfusion, n (%)	1 (2.5)
Antiplatelets (Aspirin), n (%)	32 (80)
Anticoagulation (Heparin), n (%)	3 (7.5)
Duration of ED stay in hours, median (IQR)	12 (8-24)
Length of PICU stay in days, median (IQR)	5 (2-8)
Duration of hospital stay in days, median (IQR)	7 (4-9)
Mortality, n (%)	2 (5)

Table 5: Profile of children with MIS-C with or without shock.

Characteristics	With shock (n=32)	Without shock (n=8)	p
Age in years, median (IQR)	7 (4.2-9)	9 (6-11.5)	0.58
Positive SARS-CoV-2 antibody, n (%)	15 (46.9)	5 (62.5)	0.61
Ejection fraction at admission, median (IQR)	40 (30-45)	45 (40-50)	0.17
Myocardial dysfunction or left ventricular ejection fraction <55%, n (%)	26 (81.3)	3 (37.5)	**0.02**
Total leukocyte count (per mm^3)	11450 (6467-18300)	5990 (4050-9960)	**0.048**
Absolute neutrophil count (per mm^3)	5979 (1158-11720)	2758 (232-7443)	0.69
Absolute lymphocyte count (per mm^3)	1214 (215-2626)	673 (136-1137)	0.24
Platelet count (per mm^3)	145000 (75000-170000)	157000 (49750-216000)	0.42
Ferritin (ng/ml)	946 (262-2000)	646 (136-1959)	0.44
Fibrinogen (gm/L)	3 (2-4)	4 (4-5)	0.12
D-dimer (ng/ml)	1872 (1143-3191)	1099 (794-2355)	0.22
NT-proBNP (pg/ml)	12079 (4366-32056)	3488 (441-18533)	0.17
CRP (mg/dl)	218 (54-273)	107 (24-182)	0.69
Procalcitonin (ng/ml)	16 (4-24)	10 (2-18.5)	0.63
Serum sodium (meq/L)	134 (131-136)	134 (125-139)	0.75
Admitted to PICU, n (%)	29 (90.6%)	5 (62.5)	0.082
Invasive ventilation, n (%)	8 (25)	1 (12.5)	0.42
Steroids, n (%)	30 (93.7)	4 (50)	**0.009**
Length of PICU stay in days, median (IQR)	6 (4.2-7.8)	4.5 (2-8)	0.29
Duration of hospital stay in days, median (IQR)	7 (5.5-11)	6.5 (4-9)	0.81
Mortality, n (%)	2 (6.2)	0	0.48

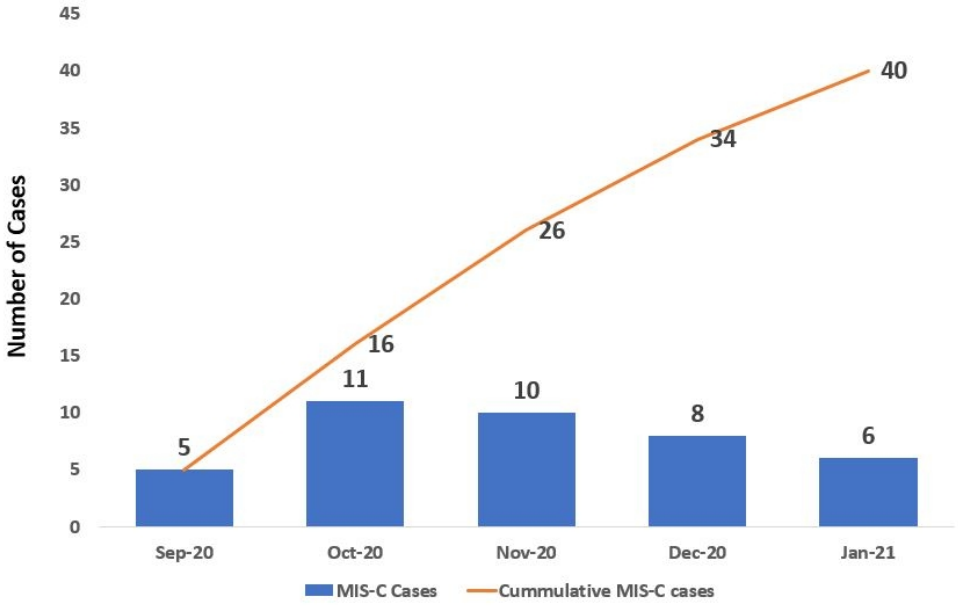

Figure 1: Month-wise and cumulative distribution of children admitted with MIS-C.

152x100mm (144 x 144 DPI)

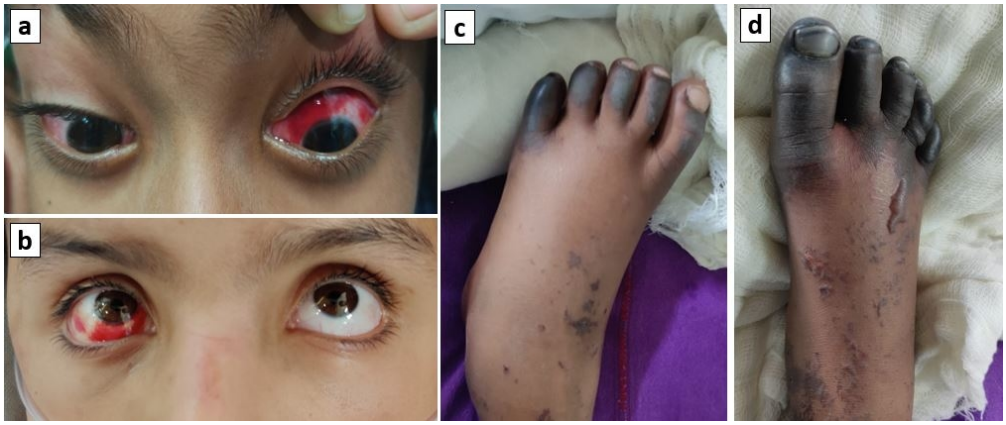

Figure 2: Hemorrhagic non-purulent conjunctivitis in 2 children (a and b) and bilateral peripheral gangrene involving toes in 1 child (c and d).

177x74mm (144 x 144 DPI)