RESEARCH PAPER

Multisystem Inflammatory Syndrome in Children (MIS-C) Associated With COVID-19 – Single-Center Experience

Poovazhagi Varadarajan,[1] S Elilarasi,[2] Ritchie Sharon Solomon,[3] Seenivasan Subramani,[1] Ramesh Subramanian,[1] Nisha Rangabashyam,[1] Gomathy Srividya[1]

[1]Department of Pediatric Intensive Care, Institute of Child Health and Hospital for Children, Chennai, Tamil Nadu.
[2]Department of Pediatric Pulmonology, Institute of Child Health and Hospital for Children, Chennai, Tamil Nadu.
[3]Department of Pediatric Cardiology, Institute of Child Health and Hospital for Children, Chennai, Tamil Nadu.

Correspondence to:
Dr Poovazhagi Varadarajan,
HOD and Professor,
Department of Pediatric Intensive Care, Institute of Child Health and Hospital for Children, Chennai, Tamil Nadu.
poomuthu@gmail.com
Received: June 29, 2022;
Initial review: August 3, 2022;
Accepted: March 2, 2023.

Objectives: To describe the clinical presentation, phenotype and outcome of multisystem inflammatory syndrome in children (MIS-C) associated with coronavirus disease 2019 (COVID-19) from a tertiary care center in southern India. **Methods:** 257 children fulfilling the inclusion criteria of MIS-C were prospectively enrolled from June, 2020 to March, 2022. **Results:** Median (range) age at presentation was 6 year (35 day to 12 years). Presenting features were fever (98%), vomiting (75.8%), red eyes (63%), rashes (49%), pain abdomen (49%), shock (45.9%), lymphopenia (73%, thrombocytopenia (58.3%) and anemia (45%). 103 (39.7%) children required intensive care admission. Shock phenotype, Kawasaki-like phenotype and no specific phenotype were diagnosed in 45.9%, 44.4%, and 36.6% children, respectively. Left ventricular dysfunction (30.3%), acute kidney injury (13%), acute liver failure (17.4%), and hemophagolymphohistiocytosis (HLH) (13.6%) were the major system involvement in MIS-C. Mitral regurgitation (*P*=0.029), hyperechogenic coronaries (*P*=0.006), left ventricular dysfunction (*P*=0.001) and low ejection fraction (*P*=0.007) were significantly associated with shock. Overall mortality was 11.7%. **Conclusions:** Kawasaki-like and shock-like presentation were common in MIS-C. Coronary abnormalities were seen in 118 (45.9%) children. Children with acute kidney injury, HLH, need for mechanical ventilation, and echocardiogram evidence of mitral regurgitation in MIS-C have a poor outcome.

Keywords: *Coronary artery, Kawasaki disease, Outcome, Shock*.

Published online: March 10, 2023; **PII**: : S097475591600507

Coronavirus disease 2019 (COVID-19) in children is usually a mild disease, but the associated multisystem inflammatory syndrome in children (MIS-C) presenting with toxic shock syndrome or Kawasaki-like presentation is a severe manifestation. The reported incidence is uncertain, but it occurs in less than 1% of children with SARS-CoV-2 infection. Probable immune-mediated mechanisms have been suggested for this major post-infectious complication, which sometimes requires intensive care admission. The World Health Organization (WHO) has given the clinical definition of this new disease [1].

In India, there are limited studies on MIS-C. This study from a single center in southern India, describes the clinical presentation, phenotype, complications and outcome among children with MIS-C.

METHODS

We prospectively enrolled children admitted with MIS-C, from a pediatric tertiary care center in Chennai during June, 2020 to March, 2022. The study was approved by the institutional ethics committee, and informed written consent was obtained from the parents/legal guardians. Consecutive children aged 1 month to 12 years, diagnosed as MIS-C as per the WHO criteria [1], were included. Children referred as MIS-C from other centers and whose complete treatment details were not available, and children with acute COVID-19 were not enrolled.

Invited Commentary: Pages 347-49.

Detailed history, clinical features, phenotype, laboratory investigations, complications and outcome were recorded. Clinical parameters like tachycardia, tachypnea and shock were defined as per Indian Academy of Pediatrics, Advanced Life Support guidelines [2]. Anemia was defined according to the WHO definition as hemoglobin <11 g/L up to 5 years, <11.5 g/L for 5 -11 years and <12 g/L for 12-14 years [3]. Thrombocytopenia was defined as platelet count $<150\times10^9$/L while thrombocytosis was platelet count $>450\times10^9$/L, and lymphopenia was defined as lymphocyte count $<3.0\times10^9$/L. Standard definitions

were used for complications like acute kidney injury (AKI) [4], acute liver failure (ALF) [5], hemophagocytic lymphohistiocytosis (HLH) [6], and pediatric acute respiratory distress syndrome (pARDS) [7]. On admission, children were evaluated for sepsis, common tropical infections and baseline laboratory workup including inflammatory markers like erythrocyte sedimentation rate, C-reactive protein, ferritin, liver enzymes, alongwith complete blood counts, electrolytes and renal parameters. Cardiac evaluation for all children was done by a qualified pediatric cardiologist using GE Vivid S6 ultrasound machine with phased array cardiac transducer. Coronary artery abnormalities were categorized as normal (*z* score <2), dilated (*z* score 2-2.5) or aneurysm (*z* score >2.5) and aneurysms were sub-categorized as small, medium and giant based on their *z* scores of 2.5-5, 5-10 and >10, respectively [8]. An ejection fraction less than 55% was considered left ventricular dysfunction [9]. Severe acute respiratory (SARS-CoV-2) IgG antibody test was performed with Indian Council of Medical Research (ICMR) approved assay kits as per the manufacturer's instructions, and titers more than 10 AU were considered reactive. All children were followed-up till discharge from the hospital, or death, in case of mortality.

Statistical analysis: All analyses were performed using Epi Info 7.0 and SPSS statistical software (version 20). Descriptive statistics were used to present the data. *P* value <0.05 was considered statistically significant. Multiple regression analysis was done to identify the risk factors for mortality.

RESULTS

Among the 312 children with acute febrile illness and features of multisystem inflammatory syndrome, 257 were included for the study. Children with sepsis (*n*=3), tropical infections like enteric fever (*n*=2), dengue (*n*=24), scrub typhus (*n*=18), leptospirosis (*n*=2) and other bacterial infections (*n*=2), and children who were treated outside with no details of therapy, were excluded (*n*=4).

Overall, we studied 257 children for their clinical and laboratory parameters and outcome. Of these,147 (57.2%) children had consulted elsewhere prior to attending our Institute and 110 children came directly for the first consult. Two children had received one dose of methylprednisolone prior to referral. Other children had received antipyretics, antibiotics, antiemetics, oral rehydration fluid and intravenous fluids. The median (IQR) age of the population was 6 (2-9) years and the male:female ratio was 1.19:1. Median (IQR) duration of illness was 5 (3-7) days. Twenty one children (8%) had documented COVID infection in the past, while 51 children (19.8%) had epidemiological link with COVID-19.

Table I Clinical and Laboratory Characteristics of Children With MIS-C (*N*=257)

Parameter	*Value*
Clinical features	
Fever at admission	252 (98.0)
Red eye	163 (63.4)
Red lips	98 (38.1)
Cracked lips	113 (43.9)
Rashes	127 (49.4)
Pain abdomen	128 (49.8)
Vomiting	195 (75.9)
Diarrhoea	137 (53.3)
Edema	114 (44.3)
Strawberry tongue	88 (34.2)
Altered sensorium	85 (33.1)
Breathlessness	61 (23.7)
Oliguria	47 (18.3)
Lymphadenopathy	32 (12.9)
Comorbid illness	39 (13.2)
Myalgia	27 (10.5)
Sore throat	20 (7.7)
Acute kidney injury	34 (13.2)
Acute liver failure	45 (17.5)
Peeling of skin	31 (12.1)
Seizures	21 (8.1)
Headache	19 (7.3)
Aneurysm of 1 coronary	45 (17.5)
Aneurysm of 2 coronaries	31 (12.1)
Aneurysm of 3 coronaries	24 (9.3)
Ascites	38 (15.4)
Laboratory parameters	
aPTT (s)[a]	30.2 (26.7-97)
International normalized ratio[a]	1.2 (1.05 -1.49)
Alanine aminotransferase (U/L)[a]	30 (17 -59)
Aspartate aminotransferase (U/L)[a]	38 (25 -78)
D-dimer (ng/mL)[a]	2.83 (1.23 -4.78)
C-reactive protein (mg/L)[a]	48 (12-106)
Erythrocyte sedimentation rate (mm/h)[a]	67.5 (38-96)
Ferritin (pmol /L)[a]	454 (218 -1104)
Hemoglobin (g/L)[a]	10 (8.8 -10.9)
Lymphopenia	190 (73.93)
Anemia	137 (53.31)
Thrombocytopenia	118 (45.91)
Sodium (mmol/L)[a]	131 (128 -134)
Neutrophil:lymphocyte ratio[a]	3.84 (2.2-7.9)
Platelet at admission ($x10^9$/L)[a]	2.02 (1.2 -3.5)
Procalcitonin (ng/mL)[a]	9.11 (1.46 -42.36)
Prothrombin time (s)[a]	15.6 (13.95 -18.35)
White blood count ($x10^9$/L)[a]	11.4 (7.6 -16.5)
Interleukin 6 (pg/mL)[a]	61.6 (13.5 -313)
Triglycerides (mmol/L)[a]	224 (160-303)

Values in no. (%) or [a]median (IQR). aPTT: activated partial thromboplastin time.

MIS-C presented as an acute febrile illness with gastrointestinal symptoms and mucocutaneous features like red eye, red lips, red tongue and rashes. Among the 128

children with pain abdomen, 7 (5.5%) had undergone surgical management for intussusception and appendicitis prior to the diagnosis of MIS-C, out of which one child died. Neck swelling and submandibular lymphadenopathy at presentation was observed in 20 children (7.7%). Clinical and laboratory features of the study group are given in **Table I**. Fluid boluses at admission for shock, ranged from 10 mL/kg to 110 mL/kg with a mean of 18.5 mL/kg. Among the 118 (45.9%) children with shock, 100 (38.9%) children required inotropes with 55 children requiring one inotrope, 37 needing two inotropes and 8 children requiring 3 inotropes. Oxygen supplementation was required in 140 (54.5%) children out of whom 42 (16.4%) were mechanically ventilated;103 (39.6%) children required pediatric intensive care admission. Five children had discoloration and dermal gangrene which resolved over a few weeks without sequelae. Another five children had digital gangrene, out of whom two died. Six children had underlying immunocompromised conditions like leukemia, nephrotic syndrome and steroid treatment for immune thrombocytopenia, and they were IgG antibody negative despite a documented SARS-CoV-2 RT-PCR positivity in the previous 12 weeks. Other noted comorbid states were diabetic ketoacidosis, febrile seizures, reactive airway disease, autoimmune encephalitis, chronic idiopathic thrombocytopenia, congenital heart disease, developmental delay, achondroplasia, febrile seizures and seizure disorder.

Kawasaki disease (KD) phenotype was present in 114 (44.4%) children with a median age of 5.75 (2-9) years, and 118 (45.9%) had shock phenotype with a median age of 6 (2-9) years. 94 children (36.6%) had no specific phenotype, among whom 35 children had features of hemophagocytic lymphohistiocytosis (HLH). Sixty nine children (26.85%) had combination of more than one phenotype. 118 (45.9%) children had coronary abnor-malities in the form of dilatations, aneurysms, hyper-echogenic and non-tapering coronaries. LV dysfunction was observed in 78 (30.35%) and this normalized at the time of discharge in 70 children. Intracardiac thrombi was encountered in one child. The echocardiogarphic features such as mitral regurgitation (P=0.029), hyperechogenic coronaries (P=0.006), left ventricular dysfunction (P<0.001) and low ejection fraction (P=0.007) were significantly associated with shock.

Common hematological features were lymphopenia, anemia and thrombocytopenia (**Table I**). Hyponatremia and hypoalbuminemia were seen in 76% and 55%, respectively, while elevated AST and ALT enzymes were seen in 47% and 40% of children at admission. Two thirds of the study group had ferritin more than 500 pmol/L.

Along with supportive treatment, 155 (60%) children received IVIG, 191 (74.31%) children received methylprednisolone/prednisolone and 27 (10.5%) children received no therapy. All the 230 treated children were on aspirin. Tocilizumab was given to five children who were febrile without clinical improvement and with rising inflammatory markers despite IVIG and methylprednisolone. Children who fulfilled the MIS-C criteria but without the Kawasaki or HLH phenotype and who became afebrile during hospital stay with declining trend of inflammatory markers did not receive any treatment. The outcome among children who were treated and those who were not treated for MIS-C did not show statistically significant difference (P=0.36). Children with elevated liver enzymes received NAC infusion and among the 34 children with renal failure, three received peritoneal dialysis, six received hemo-

Table II Clinical and Laboratory Parameters of Children With MIS-C (N=257)

Parameters	*Died*	*Recovered*	*P value*
Clinical parameters			
Pain abdomen	12 (9.4)	116 (90.6)	0.26
Diarrhea	17 (12.4)	120 (87.5)	0.47
Bleeds	8 (53.3)	7 (46.6)	<0.001
Breathlessness	14 (22.9)	47 (77)	0.003
Altered sensorium	18 (21.1)	67 (78.8)	0.002
Red eye	15 (9.2)	148 (90.8)	0.045
Red lips	10 (10.2)	88 (89.8)	0.289
Seizures	8 (38.1)	13 (61.9)	<0.001
Vomiting	26 (13.3)	169 (86.7)	0.141
Rash	15 (11.8)	112 (88.2)	0.47
Skin necrosis	4 (26.7)	11 (73.3)	0.08
Edema	13 (11.4)	101 (88.6)	0.56
Shock	27 (22.9)	91 (77.1)	<0.001
Ascites	8 (21.1)	30 (78.9)	0.36
Gangrene	3 (60)	2 (40)	0.012
Hypotension	18 (29.5)	43 (70.5)	<0.001
Oliguria	10 (21.3)	37 (78.7)	0.043
Strawberry tongue	8 (9.1)	80 (90.9)	0.242
Skin peeling	3 (9.37)	29 (90.6)	0.49
Acute liver failure	21 (46.7)	24 (53.3)	<0.001
HLH	19 (54.3)	16 (45.7)	<0.001
Acute kidney injury	22 (64.7)	12 (35.3)	<0.001
MODS	18 (64.2)	10 (35.7)	<0.001
Mechanical ventilation	26 (61.9)	16 (38.1)	<0.001
ARDS	1 (50)	1 (50)	0.21
LV dysfunction	24 (30.8)	54 (69.2)	<0.001
Laboratory parameters			
Thrombocytopenia	25 (21.2)	93 (78.8)	<0.001
Hyponatremia	22 (11.3)	172 (88.7)	0.461
Thrombocytosis	4 (5.5)	68 (94.4)	0.039
Lymphopenia	17 (12.2)	122 (87.8)	0.38
Mitral regurgitation	17 (22.4)	59 (77.6)	<0.001
Coronary z score >2	17 (14.4)	101 (85.6)	0.287

All values in no. (%). HLH: hemophagocytic lymphohistiocytosis; MODS: multi organ dysfunction syndrome; ARDS: acute respiratory distress syndrome; LV: left ventricle.

WHAT THIS STUDY ADDS?

- Mortality in multisystem inflammatory system (MIS-C) is high.
- Acute kidney injury, hemophagolympho-histiocytosis (HLH), need for mechanical ventilation, and mitral regurgitation are associated with a poorer outcome.

dialysis and one child was on continuous renal replacement therapy (CRRT).

No statistically significant difference was observed in clinical presentation, complications and outcome among children referred from elsewhere and those who came directly. Comparison of laboratory parameters among the children who survived and died is summarized in **Tables II** and **Web Table I**. Urea, creatinine, AST, ALT, LDH, IL-6, ferritin, D-dimer, aPTT and INR were the laboratory parameters significantly higher in the children who died compared to the survivors; while platelet count, serum albumin and ejection fraction were significantly lower in those who died compared to the survivors. Pre-hospital illness duration and duration of hospital stay were significantly lower in the children who died when compared to the survivors (P=0.005 and P=0.004, respectively). The median (IQR) hospital stay was 9 (2-13) days. Multiple logistic regression revealed aOR (95% CI) for AKI [1709 (3.78-77.23); P<0.001], HLH [29.29 (4.43-102.27)], need for ventilatory support [25.45 (5.59-115.92)] and mitral regurgitation [7.16 (1.55-32.57)] as significant factors associated with mortality. Overall mortality (95% CI) was 11.67% (8.02-16.24).

DISCUSSION

In this prospective study, we report the clinical presentation, complications and outcome of MIS-C. Kawasaki-like illness and shock were the common phenotypes. Acute kidney injury, need for mechanical ventilation and HLH were poor prognostic factors. The median (IQR) age group of the study was 6 (2-9) years, which is similar to 7.2 years and 6 years as noted in studies from Mumbai [9] and Chennai [10], respectively. Shock was seen in majority of our children, as also reported in a study from Mumbai [11].

The common presentation of acute febrile illness of MIS-C is also seen in sepsis and common tropical infections like dengue, scrub typhus and leptospirosis. MIS-C mimicking acute appendicitis and MIS-C co-existing with acute appendicitis has been reported in literature [12].

While coronary measurements more than 2.5 z score are 98% specific for KD [13], literature reveals that non-KD conditions are rarely associated with coronary dilatation and aneurysm [14]. Coronary involvement varies across different studies from 9-25% and studies have also reported giant aneurysms [15]. In the present study, in majority of cases, left ventricular dysfunction normalized before discharge and is similar to the existing published literature on MIS-C [16].

Mortality of MIS-C in the current study was 11.67%. Being a tertiary care referral center, the proportion of sick cases was much higher in this study group. Mortality up to 10.9% and as high as 18% from pediatric intensive care units have been reported [17,18]. Reported risk factors for mortality are need for ventilation, renal replacement therapy, higher ferritin and cardiovascular complications [17]. No mortality was encountered among children without Kawasaki or shock phenotype. This could be because the untreated children were the mild cases who were recovering at the time of hospitalization. Multicentric studies done elsewhere have shown no significant difference in death among children treated with different modes of immunotherapy However, the influence of immunotherapy and its outcome needs to be assessed by well-planned RCTs.

Limitation of this study is that cardiac enzymes were not done in all children. Severity of the illness might vary with the different strains, and this was not analyzed in this study. The proportion of children presenting with MIS-C following COVID-19 may depend on many factors, which needs to be addressed in future research.

We conclude that Kawasaki-like and shock phenotype were the common presentations in MIS-C, and a high proportion of children present with coronary abnormalities (45.9%). Majority of left ventricular dysfunction resolved before discharge. Acute kidney injury, HLH, mitral regurgitation and need for ventilation are indicators of poor outcome in MIS-C.

Acknowledgements: Dr Aiswarya Venkataraman, ICMR-NIRT, Chennai help and support for COVID antibody tests.
Ethics clearance: Institutional ethics committee, Madras Medical College, Chennai; No. 44042020, dated April 8, 2020.
Prior publication: Part from this dataset, pertaining to the period July-October, 2020, was published previously [12].
Contributors: PV: conceptualized and designed the study, data collection and analyzed data and participated in manuscript writing critical review of the intellectual content of the article; ES: designing the study, statistical analysis and interpretation of data, Critical revision of manuscript for intellectual content; RS: designing of the study, Statistical analysis, manuscript writing and drafting

of manuscript; SS: data acquisition, analysis and interpretation of data, drafting of manuscript; RS: data collection and analysis, manuscript writing, contributed to the critical revision of manuscript for intellectual content; NR: designed the study, data acquisition, data analysis, manuscript writing, revision of manuscript; GS: designing of the study, statistical analysis, manuscript writing and drafting of manuscript. All authors approve the final version of manuscript, and are accountable for all aspects related to the study.

Funding: None; *Competing interests*: None stated.

Note: Additional material related to this study is available with the online version at *www.indianpediatrics.net*

REFERENCES

1. World Health Organization. Multisystem inflammatory syndrome in children and adolescents with COVID-19: scientific brief. 2020. Accessed February 6, 2022. Available from: *https://www.who.int/publications-detail/multisystem-inflammatory-syndrome-in-children-and-adolescents-with-covid-19*
2. Jayashree M, Kulgod V, Sharma AK. Recognition of a sick child: A structured approach. *In*: Jayashree M, Kulgod V, Sharma AK, editors. IAP ALS Handbook. 2nd ed. Deepak Printographics; 2020. p.10-28.
3. World Health Organization. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. Vitamin and Mineral Nutrition Information System (WHO/NMH/NHD/MNM/11.1). Accessed June 12, 2022. Available from: *http://www.who.int/vmnis/indicators/haemo globin.pdf*
4. 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.
5. Alonso EM, Horslen SP, Behrens EM, Doo E. Pediatric acute liver failure of undetermined cause: A research workshop. Hepatology. 2017;65:1026-37.
6. Filipovich AH. Hemophagocytic lymphohistiocytosis (HLH) and related disorders. Hematology Am Soc Hematol Educ Program. 2009;127-31.
7. Pediatric Acute Lung Injury Consensus Conference Group. Pediatric Acute Respiratory Distress Syndrome: Consensus Recommendations from the Pediatric Acute Lung Injury Consensus Conference. Pediatr Crit Care Med. 2015;16:428-39.
8. McCrindle BW, Rowley AH, Newburger JW, et al. Diagnosis, treatment, and long-term management of Kawasaki disease: a scientific statement for health professionals from the American Heart Association. Circulation. 2017;135:e927-99.
9. Dhanalakshmi K, Venkataraman A, Balasubramanian S, et al. Epidemiological and clinical profile of pediatric inflammatory multisystem syndrome–temporally associated with SARS-CoV-2 (PIMS-TS) in Indian children. Indian Pediatr. 2020;57:1010-4.
10. Elilarasi S, Poovazhagi V, Kumaravel G, et al. Pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2. Indian J Pediatr. 2022;89: 879-84.
11. Jain S, Sen S, Lakshmi Venkateshiah S, et al. Multisystem inflammatory syndrome in children with COVID-19 in Mumbai, India. Indian Pediatr. 2020;57:1015-9.
12. Anderson JE, Campbell JA, Durowoju L, et al. COVID-19-associated multisystem inflammatory syndrome in children (MIS-C) presenting as appendicitis with shock. J Pediatr Surg Case Rep. 2021;71:101913.
13. Muniz JC, Dummer K, Gauvreau K, et al. Coronary artery dimensions in febrile children without Kawasaki disease. Circ Cardiovasc Imaging. 2013;6:239-44.
14. Reyna J, Reyes LM, Reyes L, et al. Coronary artery dilation in children with febrile exanthematous illness without criteria for Kawasaki disease. Arq Bras Cardiol. 2019;113:1114-8.
15. Friedman KG, Harrild DM, Newburger JW. Cardiac dysfunction in multisystem inflammatory syndrome in children: A call to action. J Am Coll Cardiol. 2020;76:1962-4.
16. Belhadjer Z, Méot M, Bajolle F, et al. Acute heart failure in multisystem inflammatory syndrome in children in the context of global SARS-CoV-2 pandemic. Circulation. 2020;142:429-36..
17. Acevedo L, Piñeres-Olave BE, Niño-Serna LF, et al. Mortality and clinical characteristics of multisystem inflammatory syndrome in children (MIS-C) associated with Covid-19 in critically ill patients: An observational multicenter study (MISCO study). BMC Pediatr. 2021;21:516.
18. Chandran J, James EJ, Verghese VP, Kumar TS, Sundaravalli EKR, Vyasam S. Clinical spectrum of children with multisystem inflammatory syndrome associated with SARS-CoV-2 infection. Indian Pediatr. 2021;58:955-8.

Web Table I Comparison of Study Parameters Among the Study Group (*N*=257)

Parameter	*Died*	*Recovered*	*P value*
Prothrombin time (s)	19.9 (15-24.5)	34.2 (27-39)	<0.001
International normalized ratio	1.59 (1.18-2.07)	1.16 (1.04-1.33)	<0.001
Creatinine (µ mol/L)	0.65 (0.4-1.4)	0.4 (0.3-0.5)	0.001
Urea (mmol/L)	35.5 (22-65)	22 (16-32)	<0.001
C-reactive protein (mg/L)	34 (6-96)	48 (12-107)	0.219
Leukocyte coun ($\times 10^9$/L)	19.2 (13.2-34)	14.45 (9.7-19.6)	0.004
Lowest platelet count ($\times 10^9$/L)	0.59 (0.35-1.06)	1.58 (0.95-2.69)	<0.001
Neutrophil-lymphocyte ratio	6.5 (3-11.49)	3.5 (2.2.-7.4)	0.289
D-dimer (ng/mL)	5.3 (3.8-7.6)	2.2 (1.1-4.2)	<0.001
Interleukin-6 (pg/mL)	319 (24.1-1131)	59 (12.5-200)	0.078
Ferritin (pmol/L)	1577 (284-2701)	446 (288-891)	0.002
Fluid bolus (mL/kg)[b]	15 (10-20)	10 (10-30)	0.502
Triglycerides (mmol/L)	260 (119-397)	222 (162-297)	<0.001
Lactate dehydrogenase (U/L)	1194 (597-1878)	386 (298-546)	<0.001
Alanine aminotransferase (U/L)	63 (31-151)	28 (16-52)	<0.001
Aspartate aminotransferase (U/L)	96 (38-330)	36 (25-66)	<0.001
Erythrocyte sedimentation rate (mm/h)[a]	35 (25.5)	56 (35.21)	<0.001
Albumin (g/L)[a]	2.7 (0.69)	3.07 (0.57)	0.009
Ejection fraction (%)[a]	44.29 (12.73)	53.45 (10.72)	<0.001

All values as median (IQR) or [a]mean (SD). [b]Fluid bolus in the emergency room.