Multisystem Inflammatory Syndrome in Children: An International Survey

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abstract

OBJECTIVES: To describe presentation, hospital course, and predictors of bad outcome in multisystem inflammatory syndrome in children (MIS-C).

METHODS: Retrospective data review of a case series of children meeting the published definition for MIS-C who were discharged or died between March 1, 2020, and June 15, 2020, from 33 participating European, Asian, and American hospitals. Data were collected through a Web-based survey and included clinical, laboratory, electrocardiographic, and echocardiographic findings and treatment management.

RESULTS: We included 183 patients with MIS-C: male sex, 109 (59.6%); mean age 7.0 ± 4.7 years; Black race, 56 (30.6%); obesity, 48 (26.2%). Overall, 114 of 183 (62.3%) had evidence of severe acute respiratory syndrome coronavirus 2 infection. All presented with fever, 117 of 183 (63.9%) with gastrointestinal symptoms, and 79 of 183 (43.2%) with shock, which was associated with Black race, higher inflammation, and imaging abnormalities. Twenty-seven patients (14.7%) fulfilled criteria for Kawasaki disease. These patients were younger and had no shock and fewer gastrointestinal, cardiorespiratory, and neurologic symptoms. The remaining 77 patients (49.3%) had mainly fever and inflammation. Inotropic support, mechanical ventilation, and extracorporeal membrane oxygenation were indicated in 72 (39.3%), 43 (23.5%), and 4 (2.2%) patients, respectively. A shorter duration of symptoms before admission was found to be associated with poor patient outcome and for extracorporeal membrane oxygenation and/or death, with 72.3% (95% confidence interval: 0.56–0.90; $P = .006$) increased risk per day reduction and 63.3% (95% confidence interval: 0.47–0.82; $P < .0001$) increased risk per day reduction respectively.

CONCLUSIONS: In this case series, children with MIS-C presented with a wide clinical spectrum, including Kawasaki disease–like, life-threatening shock and milder forms with mainly fever and inflammation. A shorter duration of symptoms before admission was associated with a worse outcome.

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WHAT'S KNOWN ON THIS SUBJECT: Clinical, laboratory, imaging, and treatment characteristics at presentation of children with multisystem inflammatory syndrome have been reported in specific cohorts from the United States, the United Kingdom, Italy, and France.

WHAT THIS STUDY ADDS: In this international case series, we report the wide clinical spectrum of this emerging disease associated with the severe acute respiratory syndrome coronavirus 2 pandemic.

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After the coronavirus 2019 pandemic hit Europe and America, several centers reported children presenting with an acute febrile illness accompanied by inflammation, gastrointestinal symptoms, and cardiac complications. This new condition has features similar to those of Kawasaki disease (KD) and toxic shock syndrome.[1–14] Whereas the clinical course of coronavirus 2019 is milder in children compared with adults, this pediatric inflammatory disease often leads to multiorgan failure and shock requiring admission to ICUs.[15,16] A case definition of pediatric inflammatory multisystem syndrome temporally associated with severe acute respiratory syndrome coronavirus 2 (PIMS-TS) was proposed by the Royal College of Pediatrics and Child Health in the United Kingdom.[17] The World Health Organization and the Centers for Disease Control and Prevention in Europe and the United States also issued their overlapping definitions and named the disorder multisystem inflammatory syndrome in children (MIS-C).[18–20] The etiopathogenesis of this syndrome and mechanisms of tissue damage are still unknown.[13,21,22]

Several initial studies have already been published on PIMS-TS and MIS-C. In multicenter studies, large cohorts of patients from US centers were described.[8–11] However, despite worldwide distribution of this new disease, an international study is lacking. Moreover, no predictors of adverse outcome have been so far identified.

Our aim in this study was to describe the presentation and hospital course of MIS-C from an international cohort and to identify clinical and biological markers that predicted severe disease.

METHODS

Patients and Data Collection

We conducted a retrospective data review of children aged ≤18 years who fulfilled the case definition of MIS-C[17] and had been discharged or died between March 1, 2020, and June 15, 2020, from 13 participating European, Asian, and American countries. Participating institutions obtained local institutional review board approval with a waiver of informed consent to collect and share deidentified data that did not include dates of birth, admission, discharge, or death.

Patient data and outcomes were collected through a standardized, secured, case study Web-based survey tool (SurveyMonkey, San Mateo, CA) between May 9, 2020, and June 16, 2020. Patients were included through 3 different types of presentation, which were mutually exclusive: (1) KD-like illness, patients with typical KD (presence of ≥4 of 5 principal features)[23,24]; (2) incomplete KD-like illness, patients not fulfilling typical KD criteria; and (3) shock, patients who required >20 mL/kg fluid boluses at admission. Because there are similarities between MIS-C and KD, we aimed to compare rates of coronary artery abnormalities (CAAs) in patients with MIS-C with classic 4 of 5 diagnostic features of KD, and in those without. We therefore did not use the presence of CAAs as part of the diagnosis of KD in children with incomplete KD-like presentation with <4 of 5 features. Instead, we explored the occurrence of CAAs in both groups.

Patients' data included age, sex, race, height, weight, and comorbidities. Main clinical symptoms at presentation, including fever, mucocutaneous involvement, presence of nonsuppurative laterocervical lymphadenopathy, conjunctivitis, and gastrointestinal, respiratory, cardiovascular and neurologic symptoms were also collected. The time between onset of symptoms and admission was included in the analysis.

Main laboratory findings including platelet count ($\times 10^9$ per liter), lactate (millimoles per liter), C-reactive protein (CRP) (milligrams per liter), ferritin (micrograms per liter), N-terminal pro–brain natriuretic peptide (NT-proBNP) and/or B-type natriuretic peptide (picograms per milliliter), and troponin I (nanograms per liter), and D-dimer (nanograms per liter) reported at patient's admission were also included in the survey. Electrocardiogram data at admission, including abnormal PR and QT intervals and ST- and T-wave changes, were recorded to describe arrhythmia and/or ischemic changes. Echocardiography findings within 24 hours of admission were reported, including assessment of the coronary arteries, ventricular function, valvulitis (nonphysiologic valve regurgitation) and pericardial effusion.[25,26]

Information about outcome measures, including admission to ICU, inotropic support, renal replacement therapy, extracorporeal membrane oxygenation (ECMO), and death at time of admission and during hospital course were also collected, as was information about medications used to treat the inflammatory syndrome or potential severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Some of the patients included in this study have been previously published in early reports.[6,7,14]

Confirmation of SARS-CoV-2 Infection

We surveyed test results from SARS-CoV-2 reverse-transcriptase polymerase chain reaction (PCR) on nasopharyngeal and/or oropharyngeal swab samples and detection of SARS-CoV-2 antibodies (immunoglobulin M and immunoglobulin G).

Statistical Analysis

Continuous variables were summarized as either means and SDs or medians with interquartile ranges,

when appropriate. Student's *t* test, the ×2 method, or Fisher's exact test, Mann-Whitney U, Wilcoxon tests, and Kruskal-Wallis were performed when appropriate. We used multiple logistic regression analysis to identify independent predictors of bad outcome for those who deteriorated after admission, as defined by the following: transfer to intensive care, mechanical ventilation, inotropic support, renal replacement therapy, ECMO, or death. The following criteria were analyzed: age, sex, race, clinical symptoms, and laboratory and echocardiographic findings. A *P* value of <.05 was considered significant. Data were analyzed with R (version 3.6; The R Foundation, Vienna, Austria).

TABLE 1 Characteristics of the 183 Children With MIS-C

Characteristics	Results
Age in y, mean (± SD)	7.0 (± 4.7)
Male sex, *n* (%)	109 (59.6)
Race, *n* (%)	
Black	56 (30.6)
Asian	22 (12.0)
Other	105 (57.4)
Comorbidities, *n* (%)	
Obesity	48 (26.2)
Heart disease	4 (2.2)
Airway or lung disease	3 (1.6)
Immunosuppression	2 (1.1)
Ex-prematurity	2 (1.1)
SARS-CoV-2 PCR and/or serology, *n* (%)	114 (62.3)
Time of onset/admission, d, mean (± SD)	5.1 (± 3.0)
Duration of admission, d, mean (± SD)	8.6 (± 5.6)
Clinical features, *n* (%)	
Fever	124 (100)
Mucocutaneous involvement	120 (65.6)
Gastrointestinal symptoms	117 (63.9)
Conjunctivitis	73 (39.9)
Lymphadenopathy	72 (39.3)
Respiratory symptoms	71 (38.8)
Heart failure, excluding shock	65 (35.5)
Neurologic symptoms	22 (12.0)
Shock at admission	79 (43.2)

Onset/admission, from onset of symptoms to patient's admission.

RESULTS

Clinical Presentation

The survey included 183 pediatric patients with MIS-C at a mean age of 7.0 ± 4.7 years (range: 1.2 months–18 years old). Patients were from the United Kingdom (*n* = 56), France (*n* = 52), Spain (*n* = 32), the United States (*n* = 14), Italy (*n* = 8), Sweden (*n* = 6), Pakistan (*n* = 4), Belgium (*n* = 3), Peru (*n* = 2), Germany (*n* = 1), Russia (*n* = 1), Portugal (*n* = 1), Mexico (*n* = 1), and Chile (*n* = 1). Patient characteristics are summarized in Table 1. The distribution of patients' baseline variables according to their country of origin was not statistically different except for race. The percentage of Black patients was significantly higher in the United Kingdom (52.7%), France (63.4%), and the United States (33.3%) ($P < .001$). Those 3 countries also have higher rates of Black people in their population according to official government data (the United Kingdom: 14%, France: 15%, the United States: 20.6%). In our cohort, there was a predominance of male sex (59.6%) and Black race (30.6%). Obesity was the most frequent comorbidity (48 of 183; 26.9%). All patients presented with fever and most with gastrointestinal symptoms (63.9%). SARS-CoV-2 PCR results were positive in 43 of 114 (37.7%) tested patients, and SARS-CoV-2 serology test results were positive in 95 of 110 (86.3%) tested patients. In total, 114 of 183 (62.3%) patients had evidence of current or recent SARS-CoV-2 infection.

Patients presenting with shock (*n* = 78 of 183; 42.6%) were older (9.2 ± 4.0 vs 3.8 ± 3.6 years in patients with KD-like illness and 5.9 ± 4.6 years in patients with incomplete KD-like illness; $P < .001$). Patients presenting with shock were associated with Black race and had a significantly higher rate of gastrointestinal, cardiorespiratory, and neurologic symptoms. Such findings also apply to incomplete KD presentation, although with a lower percentage. Positive SARS-CoV-2 serology test results were significantly higher in patients who presented with shock (65.4% vs 14.8% in patients with KD-like illness and 51.3% in patients with incomplete KD-like illness; $P < .001$).

In Fig 1 and Table 2, the main clinical characteristics for the 3 types of presentation (KD-like, incomplete KD-like, and shock) are illustrated, and the close similarity between incomplete KD-like and shock presentation is demonstrated.

All patients had NT-proBNP, troponin, D-dimer, CRP, and ferritin levels higher than normal. However, patients who presented with shock had significantly lower platelet count and higher NT-proBNP, D-dimer, CRP, and ferritin levels. Electrocardiogram abnormalities were not different among groups. Ischemic changes, arrhythmia (mainly first degree atrioventricular block), and abnormal repolarization were the most common findings.

Echocardiography at admission was often abnormal (121 of 183; 66.1%)

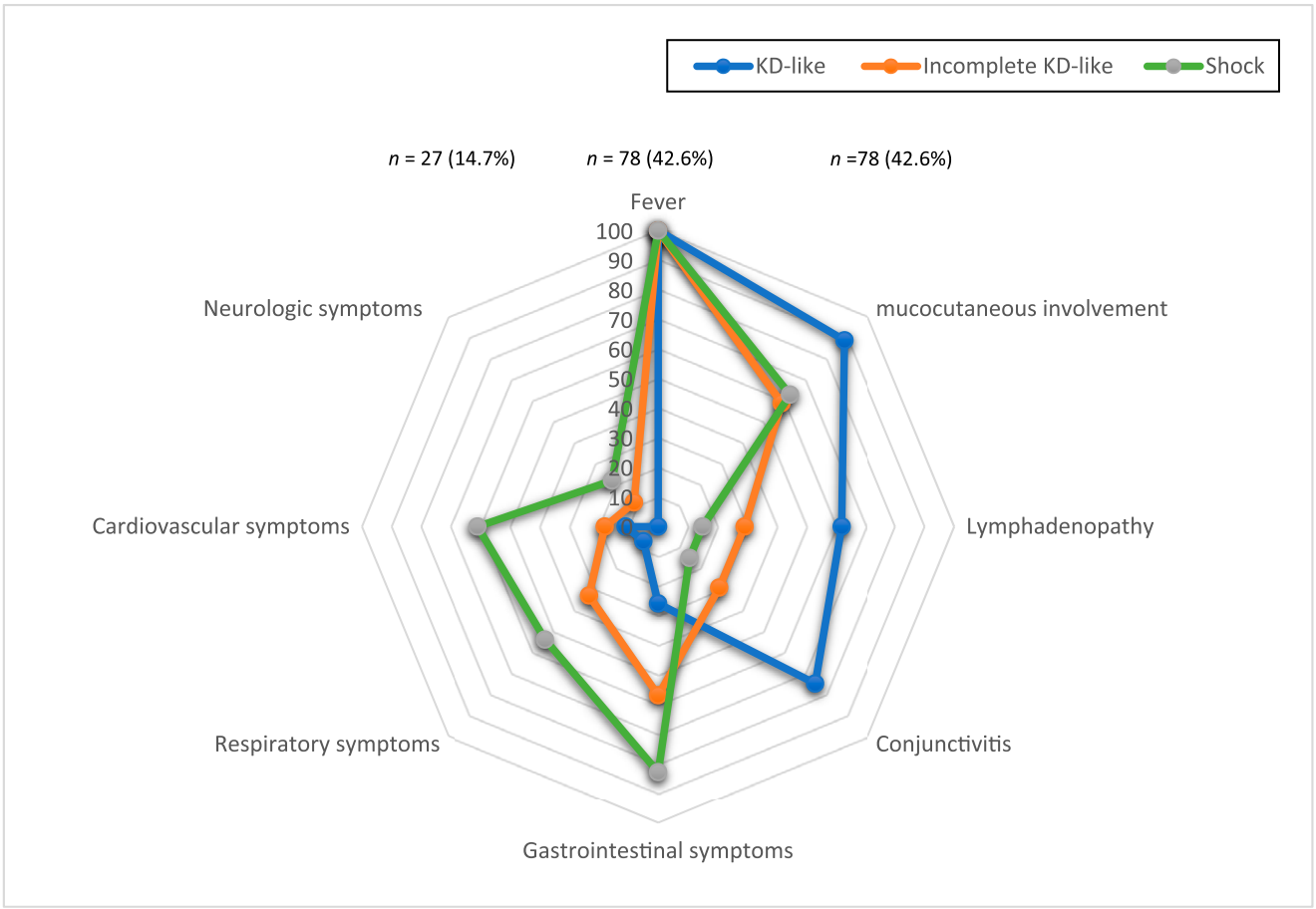

FIGURE 1

Clinical profiles at presentation for patients MIS-C with KD-like, incomplete KD-like, and shock presentations represented in a radar chart. The radar chart represents the symptoms for each clinical profile. Each spoke represents one of the variables, and its length is proportional to the magnitude of the percentage of the variable at presentation. A line is drawn connecting the data values for each spoke related to the same type of clinical profile.

with dilated coronaries, pericardial effusion, and valvulitis across all types of presentation. Dilated coronaries at admission were seen in 25.9% of patients with KD-like illness, 27.3% of incomplete KD-like, and 12.8% of those presenting with shock (P = .06). Shock was associated with a significantly higher rate of pericardial effusion, valvulitis, and left ventricular dysfunction on echocardiography.

Hospital Course

Treatment

Intravenous immunoglobulin was used in 26 of 7 (96.2%) patients with KD-like illness and in 137 of 156 (87.8%) of the remaining patients; 15 of 27 (55.6%) patients with KD-like illness and 90 of 156 (57.7%) of the remaining patients received steroids. Azithromycin was prescribed in 3 of 27 (11.1%) patients with KD-like illness and in 11 of 156 (7.0%) of the remaining patients with MIS-C. Anakinra, infliximab, and hydroxychloroquine were administered in 8, 10, and 5 patients of the total cohort, respectively, especially in patients with incomplete KD-like and shock presentations. Aspirin was used in 20 of 27 (74.1%) patients with KD-like illness and in 104 of 156 (66.7%) of the other patients with MIS-C. Anticoagulation with heparin was used in 9 of 27 (33.3%) patients with KD-like illness and in 69 of 156 (44.2%) of the patients with non-KD MIS-C.

Outcome of The Patients

Overall, 72 of 183 (39.3%) patients required intravenous inotropic support, 43 of 183 (23.5%) required mechanical ventilation, and 4 of 183 (2.2%) required ECMO (Table 3). Three patients died: 1 8-month-old boy with typical KD was admitted after 4 days of symptoms. Echocardiography revealed preserved left ventricular function and normal coronary arteries. He was treated with 2 doses of intravenous immunoglobulin and aspirin but continued to be febrile and was started on steroids and infliximab. On

TABLE 2 Demographics, Clinical Presentation, Electrocardiographic, and Echocardiographic Comparison Between KD-Like, Incomplete KD-Like, and Shock Presentation at Admission

	KD-Like Presentation, *n* = 27 (14.8%)	Incomplete KD-Like Presentation, *n* = 78 (42.6%)	Shock Presentation, *n* = 78 (42.6%)	*P*
Age in y, mean (± SD)	3.8 (± 3.6)	5.9 (± 4.6)	9.2 (± 4.0)	<.001
Male sex, *n* (%)	19 (70.4)	45 (57.7)	45 (57.7)	.46
Weight, kg, mean (± SD)	19.8 (± 28.0)	26.1 (± 16.6)	36.9 (± 20.8)	<.001
Obesity, *n* (%)	3 (15.8)	13 (27.7)	14 (23.7)	.59
Black race, *n* (%)	3 (11.1)	19 (24.7)	34 (43.6)	.004
Time of onset/admission, d, mean (±SD)	5.5 (± 3.6)	5.0 (± 2.9)	5.0 (± 3.0)	.898
SARS-CoV-2 PCR results positive, *n* (%)	4 (14.8)	16 (20.5)	23 (29.5)	.36
SARS-CoV-2 serology test results positive, *n* (%)	4 (14.8)	40 (51.3)	51 (65.4)	<.001
Gastrointestinal symptoms, *n* (%)	7 (25.9)	45 (57.7)	65 (83.3)	<.001
Mucocutaneous involvement, *n* (%)	24 (88.9)	47 (60.3)	49 (62.8)	.02
Respiratory symptoms, *n* (%)	2 (7.4)	28 (35.9)	41 (52.6)	<.001
Heart failure (excluding shock) , *n* (%)	3 (11.1)	15 (19.2)	47 (60.3)	<.001
Neurologic symptoms, *n* (%)	0	3 (3.8)	19 (24.3)	<.001
Laboratory findings, mean (± SD)				
Platelet count, $\times 10^9$/L	300 (± 185)	293 (± 201)	207 (± 106)	.02
Lactate, mmol/L	1.8 (± 0.9)	2.1 (± 1.6)	3.0 (± 2.7)	.14
NT-proBNP, pg/mL	2148 (± 2593)	7443 (± 15 975)	17 678 (± 39 609)	<.001
Troponin, ng/mL	0.4 (± 0.5)	1.0 (± 2.0)	1.0 (± 1.7)	.52
D-dimer, ng/mL	2699 (± 1465)	2334 (± 2055)	4594 (± 4597)	.003
CRP, mg/L	125.5 (± 116.0)	150.4 (± 111.4)	217.7 (± 226.1)	.004
Ferritin, μg/L	384.5 (± 532.8)	394.0 (± 364.3)	1131.2 (± 1627.1)	<.001
Electrocardiogram abnormalities at admission, *n* (%)				
Ischemia	5 (18.5)	9 (11.7)	14 (17.9)	.49
Arrythmia	1 (3.7)	4 (5.2)	9 (11.5)	.23
QTc >500 ms	0	1 (1.3)	3 (3.8)	.39
Abnormal repolarization	1 (3.7)	5 (6.5)	6 (7.7)	.77
Echocardiography at admission				
Dilated coronaries, *n* (%)	7 (25.9)	21 (27.3)	10 (12.8)	.06
Valvulitis, *n* (%)	1 (3.7)	13 (16.9)	25 (32.0)	.004
Pericardial effusion, *n* (%)	4 (14.8)	11 (14.3)	23 (29.5)	.04
LV dysfunction, *n* (%)	4 (14.8)	19 (24.7)	58 (74.4)	<.001
RV dysfunction, *n* (%)	0	1 (1.3)	2 (2.6)	.63
LVEF, mean (± SD), %	59.6 (± 11.6)	58.3 (± 10.1)	44.7 (± 12.4)	<.001

Normal range values are as follows: platelet count, >150 and <400 × 10^9/L; lactate, <2 mmol/L; NT-proBNP, 0–300 pg/mL; troponin, 0–0.4 ng/mL; D-dimer, <250 ng/mL; CRP, <10 mg/L; and ferritin, 40–400 μg/L. BNP, B-type natriuretic peptide; LV, left ventricle; LVEF, left ventricular ejection fraction; RV, right ventricle.

day 11, echocardiography revealed dilated right and left coronaries. Clopidogrel and heparin were added to the treatment. He abruptly deteriorated 2 weeks after admission. He developed giant coronary aneurysms in all 3 vessels and experienced fatal cardiac arrest because of massive myocardial infarction. Another 2-year-old boy presented with <24 hours of fever, respiratory distress, and shock. Echocardiography revealed severe left ventricular dysfunction with normal coronary arteries, moderate mitral regurgitation, and pericardial effusion. He experienced hemodynamically significant ventricular arrhythmia. He was put on ECMO and subsequently died after cerebral injury while on ECMO. The last patient who died was a 14-month-old girl with a history of tetralogy of Fallot status post–complete repair and invasive ventilation through tracheostomy. She developed fever, rash, gastrointestinal symptoms, shock, and severe left ventricular dysfunction without CAAs. She died after multiple cardiac arrests after 7 days of admission.

Patients with KD-like illness had shorter lengths of stay than those with other presentations (7.3 ± 6.4 vs 8.1 ± 6.3 days in incomplete KD-like illness and 9.5 ± 4.3 days; $P <$ .001) and required overall less intensive care support when compared with the remaining patients with MIS-C. Data are summarized in Table 3.

After admission, 26 of 183 patients experienced worse outcomes with escalation of care from ward to PICU and/or need for major treatment (inotropic support, mechanical ventilation, renal replacement therapy, and/or ECMO) and/or death. Univariate analysis revealed that a shorter duration of symptoms before admission was found to be associated with poor patient outcome as measured by requiring inotropes, mechanical ventilation, or ECMO and/or death (bad outcome). There was an increase of 72.3% risk of worse outcome per everyday reduction (95% confidence interval: 0.56–0.90; P = .006). Similarly, this shorter duration of symptoms before admission was a risk factor for ECMO and/or death in the total patient population, with a 63.3% increased risk per day reduction (95% confidence interval: 0.47–0.82; $P <$ .0001).

TABLE 3 Comparison of Outcomes Among Patients With KD-Like Illness Versus Incomplete KD-Like Illness and Shock

Patients	KD-Like Illness, *n* = 27	Incomplete KD-Like Illness, *n* = 78	Shock, *n* = 78	*P*
Length of stay, d, mean (±SD)	7.3 (± 6.4)	8.1 (± 6.3)	9.5 (± 4.3)	<.001
Intensive care admission, *n* (%)	4 (14.8)	20 (25.6)	66 (84.6)	<.001
Inotropic support, *n* (%)	1 (3.7)	5 (6.4)	66 (84.6)	<.001
Mechanical ventilation, *n* (%)	0	9 (11.5)	34 (43.6)	<.001
Renal replacement therapy, *n* (%)	1 (3.7)	0	4 (5.1)	.3
ECMO, *n* (%)	0	1 (1.3)	3 (3.8)	.32
Death, *n* (%)	1 (3.7)	0	2 (2.6)	.41

DISCUSSION

We report the largest international series of children with MIS-C after their full hospital course has been completed. More than 40% of patients with MIS-C presented with shock. They had higher levels of NT-proBNP, D-dimer, CRP, and ferritin and developed more cardiac complications other than CAAs, especially pericardial effusion, valvulitis, and left ventricular dysfunction. Not surprisingly, their hospital stay was longer and required more inotropic support and mechanical ventilation. A minority (nearly 15%) of the patients with MIS-C fulfilled criteria for KD. These patients were usually stable at admission, with fewer symptoms and less inflammation than other patients with MIS-C. They did not experience shock and only had a few cardiac complications other than CAAs. Their hospital stays were shorter, with less PICU management, inotropic support, and mechanical ventilation, although one of them experienced sudden death in the setting of multiple giant aneurysms. The remaining patients with MIS-C who did not experience shock predominantly had fever and inflammation. These patients had a higher rate of CAAs but less valvulitis, pericardial effusion, and ventricular dysfunction. They generally had a better outcome.

In other studies, researchers have reported clinical characteristics of PIMS-TS and MIS-C cases. Belhadjer et al[6] described the hospital course and early outcomes of 35 critically sick children with acute heart failure in cases in which ECMO was needed in 28% with a favorable outcome in all cases. Davies et al[10] reported a larger cohort of 78 patients with PIMS-TS managed in a UK PICU, revealing that the indication for ECMO was much less than in the French study. In that cohort, male patients and those from ethnic minority backgrounds were overrepresented. CAAs were present in 36% of the patients.

Dufort et al[8] described the results of active surveillance for MIS-C in New York State, with 191 cases reported to the state health department, of which only 99 met the case definition. Up to 80% of them required treatment in the ICU. This percentage differs from our study cohort, in which 11% of patients with KD-like illness and 55% of patients with non–KD-like illness required intensive care admission. It is likely that inclusion criteria in the study conducted by Dufort et al[8] favored the inclusion of the sickest patients, whereas our study included a wider spectrum of presentations. Feldstein et al[9] reported 186 MIS-C cases identified by targeted surveillance in 26 US states over a 2-month period. In this group, multiorgan-involvement was similar to our cohort. Coronary artery aneurysms were documented in 8% of children and KD-like features in 40%. Not all patients had been discharged at the time of publication, and therefore, it is difficult to comment on the outcome. All these findings are confirmed in our international survey. Additionally, our study is the first to reveal that a shorter period of symptoms before admission is a risk factor for worse outcome and for ECMO and/or death.

Previous multicenter reviews from US centers provided a comprehensive description of MIS-C and clarified its differences from KD, KD shock syndrome, and toxic shock syndrome.[10,11] In our study, patients classified as KD-like also had additional uncommon clinical features for KD, such as a higher rate of gastrointestinal symptoms and frequent association with Black race.[4,6–11] Moreover, this group of patients showed more heterogeneous cardiac involvement at presentation than in KD, such as ischemic changes on electrocardiogram, left ventricular dysfunction, pericardial effusion, and valvulitis on echocardiography. Finally, this cardiac phenotype was often present within the first days of the disease, as opposed to KD, in which cardiac features usually occur after 2 or 3 weeks.[23–29] Hence, despite clinical similarities with KD, our results support the concept that these patients with MIS-C belong to a different entity.

Almost one-half of the patients fulfilling MIS-C criteria in our series presented with shock. These patients presented as having a fulminant disease with rapidly progressing symptoms requiring immediate intensive care management, and they were associated with ECMO and/or death, especially when the time interval between the onset of symptoms and admission was short. This type of presentation is rare in KD. Kawasaki shock syndrome has been typically described in younger

patients, after a long period of symptoms before admission, and with a higher rate of CAAs.[30–32]

Finally, there were numerous patients who presented with incomplete KD features who did not experience shock and had little cardiac involvement. The main characteristics of these patients were fever and inflammation. Their outcome was generally favorable.

By means of a survey, we were able to collect the largest available MIS-C data set rapidly and worldwide. The symptoms categorized under gastrointestinal, respiratory, cardiovascular, and neurologic were not detailed in the data collection. Data collection was kept to a minimum to maximize responses, and this was a drawback to gather management variables such as doses of drugs. This limited our ability to develop a detailed risk stratification for this cohort of patients.

Our study is based on the broader UK definition of PIMS-TS and therefore includes patients who are critically ill, patients meeting diagnostic criteria for KD, and some patients with unexplained fever and inflammation. Evidence of SARS-CoV-2 infection or exposure is not mandatory on the basis of such a definition, whereas the Centers for Disease Control and Prevention and the World Health Organization definitions require evidence of such. This requirement might be problematic because asymptomatic infections are common and antibody testing is neither universally available nor reliable.

CONCLUSIONS

MIS-C has emerged with a wide clinical spectrum at presentation, including KD-like, life-threatening shock and milder forms with mainly fever and inflammation. The risk for worse outcome (ECMO and/or death) is associated with a short time interval between the onset of symptoms and admission. More studies encompassing larger numbers of patients are needed to better describe this new disease, its optimal treatment, and long-term monitoring.

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ABBREVIATIONS

CAA: coronary artery abnormality
CRP: C-reactive protein
ECMO: extracorporeal membrane oxygenation
KD: Kawasaki disease
MIS-C: multisystem inflammatory syndrome in children
NT-proBNP: N-terminal pro–brain natriuretic peptide
PCR: polymerase chain reaction
PIMS-TS: pediatric inflammatory multisystem syndrome temporally associated with severe acute respiratory syndrome coronavirus 2
SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

Drs Bautista-Rodriguez, Sanchez-de-Toledo, Levin, Bonnet, and Fraisse conceptualized and designed the study, coordinated and supervised data collection, conducted the initial analyses, performed interpretation of data, drafted the initial manuscript, and critically reviewed and revised the manuscript; Dr Foldvari conceptualized and designed the study, conducted the initial analyses, and performed interpretation of data; Dr Singh conceptualized and designed the study, coordinated and supervised data collection, and performed interpretation of data; Dr Clark coordinated and supervised data collection and critically reviewed and revised the manuscript; Drs Bajolle, Randanne, Salas-Mera, and Bianco coordinated and supervised data collection; Dr Herberg conducted the initial analyses, performed interpretation of data, and critically reviewed and revised the manuscript; Drs Chowdhury and Munoz critically reviewed and revised the manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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