Review Paper

Clinical Characteristics of Multisystem Inflammatory Syndrome in Children and Young Adults With COVID-19: A Rapid Systematic Review

Manish Kumar[1], Swarnim Swarnim[2], Pallavi Pallavi[2*]

1. Department of Pediatrics, All India Institute of Medical Sciences, Gorakhpur, India.
2. Department of Pediatrics, Maulana Azad Medical College, New Delhi, India.

Use your device to scan and read the article online

Citation Kumar M, Swarnim M, Pallavi P. Clinical Characteristics of Multisystem Inflammatory Syndrome in Children and Young Adults With COVID-19: A Rapid Systematic Review. Journal of Pediatrics Review. 2022; 10(Special Issue):367-388. http://dx.doi.org/10.32598/jpr.10.SpecialIssue.1008.1

http://dx.doi.org/10.32598/jpr.10.SpecialIssue.1008.1

Article info:
Received: 02 Sep 2021
First Revision: 10 Sep 2021
Accepted: 27 Nov 2021
Published: 01 Jan 2022

Keywords:
COVID-19, Multisystem inflammatory syndrome in children, Hyperinflammatory state

ABSTRACT

Background: The associated multisystem inflammatory syndrome in children (MIS-C) with coronavirus disease (COVID-19) is a novel syndrome that has phenotypic similarity to Kawasaki disease (KD).

Objectives: This study systematically reviewed the demographic profile, clinical spectrum, treatment options, and outcomes of children and young adults under 21 years of age suffering from MIS-C.

Methods: PubMed and Embase databases were searched from inception to July 3, 2020. A total of 39 studies involving 799 participants were included in the review. Critical appraisal of included studies was done using Joanna Briggs Institute Critical Appraisal Checklist for studies reporting prevalence data. A narrative synthesis was performed through descriptive summaries of demographic variables, clinical features, investigations, treatment details, and clinical outcomes.

Results: The main complaints of the patients were fever (96.4%) followed by gastrointestinal symptoms. Serological evidence of preceding severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection was documented in 79.1% of the participants. Ventricular dysfunction (50.2%) was the most common echocardiographic finding. Intensive care was required for 77% of included participants, with 27.2% being mechanically ventilated. Also, 78.1% of the participants received intravenous immunoglobulins. The overall mortality rate was 1.5%.

Conclusions: MIS-C associated with COVID-19 clinically resembles a hyperinflammatory state. More extensive studies will help in better defining this entity and delineating its phenotypic subtypes.

** Corresponding Author:*
Pallavi Pallavi, PhD.
Address: *Department of Pediatrics, Maulana Azad Medical College, New Delhi, India.*
E-mail: *pallavi86.delhi@gmail.com*

1. Introduction

Several cases of a new kind of pneumonia were identified in Wuhan City, China, in 2019. This new disease is now a pandemic and a global health catastrophe. The World Health Organization (WHO) designated the disease as coronavirus disease (COVID-19), caused by a novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (1). In initial reports, the morbidity of this disease was relatively mild in children and adolescents compared to the adult population (2). However, since late April 2020, several cases have been reported of children presenting with circulatory shock and systemic inflammation, with phenotypic similarity to Kawasaki disease (KD) and toxic shock syndrome (TSS). The first cases were reported from the United Kingdom as a series of eight previously healthy children presenting with hyperinflammation and cardiovascular shock (3), followed by similar reports from other parts of Europe and the United States of America.

A case definition for this emerging hyperinflammatory disorder was formulated by The Royal College of Pediatrics and Child Health (RCPCH) in late April and was provisionally named pediatric inflammatory, multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS) (4). Later, in May 2020, following a health alert issued by the New York State Department of Health, the Centers for Disease Control and Prevention (CDC) issued a clinical case definition and designated this syndrome as the multisystem inflammatory syndrome in children (MIS-C) associated with COVID-19 (5). WHO has also developed a preliminary case definition and case report form for this multisystem inflammatory disorder in children and adolescents (6). Case definitions of this pediatric inflammatory disorder, given by RCPCH, CDC, and WHO, have been summarized in supplementary Table 1. There have been heterogeneous reports of MIS-C in the form of case reports or small case series. The lack of comprehensive clinical data describing the complete clinical spectrum, treatment options, and outcome of children and young adults under 21 years of age suffering from MIS-C has prompted this review.

2. Materials and Methods

This rapid review was initiated after registering the protocol in the International Prospective Register of Systematic Reviews (PROSPERO) database with registration No. CRD42020190751. This review was conducted following Cochrane guidance on Rapid Reviews (7) and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines (8) (Table 2).

Study objectives

The primary objective of this review was to systematically review the clinical characteristics, treatment options, and outcomes of MIS-C or KD-like hyperinflammatory states in children and young adults with COVID-19 infection.

Search strategy

Two authors independently searched PubMed and Embase databases from inception to July 3, 2020. The search was limited to publications in the English language. The search strategy consisted of CDC suggested COVID-19 search terms (9) along with a combination (using Boolean operator AND) of keywords and their corresponding Medical Subject Headings (MeSH).

Novel coronavirus

Multisystem inflammatory syndrome in children

Kawasaki disease

Details of the search strategy used for PubMed and Embase databases are presented in supplementary Table 3.

Eligibility criteria

Search results were uploaded to Rayyan web applicationand no single method fulfills the principal requirements of speed with accuracy. Automation of systematic reviews is driven by a necessity to expedite the availability of current best evidence for policy and clinical decision-making., We developed Rayyan (http://rayyan.qcri.org (10) for screening by two authors independently. We included all types of studies, including longitudinal studies, case series, case reports, or correspondences from all clinical settings reporting clinical-epidemiologic characteristics of MIS-C or KD-like illness in children and young adults up to the age of 21 years in the review. A third author screened all excluded records. Any disagreements regarding eligibility for inclusion were resolved by consensus.

Critical appraisal

Critical appraisal and assessment of the risk bias in included studies were done by all authors independently using Joanna Briggs Institute Critical Appraisal Checklist for studies reporting prevalence data (11).

Data extraction

Individual study data were extracted in a pre-designed format in Microsoft Excel by two authors independently. Study details included first author, location of study, study design, study period, demographic variables, clinical features, details of laboratory, radiological and other investigations, treatment details, and outcomes. Any disagreements related to collated data were resolved by consensus after discussion with the third author.

Data synthesis

Synthesis of included studies was performed through descriptive summaries (usually as a percentage) of demographic variables, clinical features, investigations performed, treatment details, and clinical outcomes.

3. Results

Search results and critical appraisal

A total of 408 records were identified using the search mentioned above strategy. After excluding duplicate records, the title and abstracts of 301 articles were screened. In the initial screening of title and abstracts, 94 full-text articles were assessed for eligibility, and 55 articles were excluded. Of these rejected studies, 41 were reviews, correspondences, or editorials with no individual patient data; 13 studies did not meet the inclusion criteria for this review, and one study was excluded because it was in the Swedish language. Then, 39 remaining articles (3, 12-50) were subjected to critical appraisal using Joanna Briggs Institute Checklists and were included for qualitative synthesis after confirming their methodological rigor.

Included studies

Twenty out of 39 included studies were from Europe, 7 studies from the UK and 7 from France, and 16 studies from the USA. Three case reports from India and 1 case report from Israel were also included. Of the 39 included studies, 16 were case reports, 9 case series, 10 retrospective observational studies, and 4 prospective observational studies or surveillance studies. The study period of most of the included studies ranged from March to April 2020, with Verdoni et al. (38) reporting data from as early as February 2020 (Table 1).

Demography

A total of 39 studies were included in this rapid review, constituting 799 participants with 446 males (55.8%). Feldstein et al. (44) and Belot et al. (26) studies were the largest studies in terms of participants, with 186 and 108 participants, respectively. The median age of participants in both studies was 8 years. Similar median age was reported by other included studies (3, 16, 23, 34). The youngest participant was a 4-month-old baby reported by Acharyya et al. (36), while in studies by Miller et al. (32) and Riollano-Cruz et al. (49), the maximum age of included participants was 20 years. Ancestry or racial characteristics were reported in 16 of 39 studies. Many studies from the USA and the UK documented an increased incidence of MIS-C in Black/Afro-American/Non-Hispanic races compared to other races or ethnicities (3, 13, 17, 24, 28, 34, 39, 44, 45).

Clinical features

Fever was a ubiquitous presenting feature in 96.4% (667/692) of patients. Respiratory symptoms were reported in 28 studies comprising 589 patients. Runny nose, sore throat, or cough was reported in 10% (59/589) of patients, while dyspnea was relatively more common and affected 33% of the patients (194/589). Gastrointestinal symptoms were the most common extra-pulmonary systemic feature of MIS-C. More than 50% of the participants in 25 of the 39 included studies presented with either abdominal pain, vomiting, or diarrhea. Neurocognitive features were present in 27.1 % of patients (162/597).

Amongst the symptoms characteristic of KD, rash and non-purulent conjunctivitis were most common, seen in 58.8% (374/635) and 59.9% (377/629), respectively. Other KD-like symptoms were lip/oral changes in 42.4% (242/570) of patients, extremity changes in 32.3% (135/417) of patients, and cervical lymphadenopathy in 17.95% (88/490) patients. More than half of the children in the hyperinflammatory state developed circulatory insufficiency, as 53% (358/668) of patients developed shock.

Comorbidities were reported in the participants of 12 of the 39 included studies. Obesity was the commonest comorbidity, seen in 113/581 (19.4%), asthma in 54/581 (9.2%), and various comorbidities in 49/581 (8.4%) patients.

Laboratory investigations

Table 3 summarizes the median values of laboratory investigations. Blood counts trends were non-specific. Out of 25 studies reporting median white cell counts, 14 showed trend towards leukocytosis (13, 14, 16-19, 21,

Table 1. Demographic variables

Lead Author	Country	Type of Study	Study Time	Total Participants	Age (y)	Male	Female	Race
Jones (12)	The USA	Case report	Not reported (NR)	1	0.5	1	0	NR
Chiotos (13)	The USA	Case series	NR	6	7.5 (5-14)	1	5	Black/not Hispanic or Latino-2; White/not Hispanic or Latino-2, Unknown -2
Labé (14)	France	Case report	NR	1	3	1	0	NR
Riphagen (3)	The UK	Case series	April 2020	8	8 (4-14)	5	3	Afro- Caribbean -6, Asian-1, Middle Eastern-1
Leon (15)	The USA	Case report	NR	1	6	0	1	NR
Balasuramanian (16)	India	Case report	NR	1	8	1	0	NR
Rivera-Figueroa (17)	The USA	Case report	NR	1	5	1	0	African-American
Belhadjer (18)	France	Retrospective observational study	March 22 to April 30, 2020	35	10	18	17	NR
Chiu (19)	The USA	Case report	NR	1	10	1	0	NR
Schnapp (20)	Israel	Case report	NR	1	16	1	0	NR
Greene (21)	The USA	Case report	NR	1	11	0	1	NR
Dolinger (22)	The USA	Case report	NR	1	14	1	0	NR
Cheung (23)	The USA	Retrospective observational study	April 18 to May 5, 2020	17	8 (1.8-16)	8	9	Ashkenazi Jewish:6; White, Non-Hispanic:2; White, Hispanic:4; Black:4; Asian:1
Whittaker (24)	England	Case series	March 23 to May 16, 2020	58	9 (0.25-17)	25	33	Black:22 Asian:18; White:12; Others:6
Blondiaux (25)	France	Case series	April 2020	4	9 (6-12)	1	3	NR
Belot (26)	France	Surveillance	March 1 to May 17, 2020	108	8 (IQR: 5-11)	53	55	NR
Pouletty (27)	France	Retrospective cohort	April 2020	16	10 (IQR:4.7-12.5)	8	8	NR
Ramcharan (28)	The UK	Retrospective observational study	April 10 to May 9, 2020	15	8.8 (IQR: 6.4–11.2)	11	4	African/Afro-Caribbean:6; South Asian:6; Mixed:2; Other:1
Waltuch (29)	The USA	Case series	May 2020	4	11 (5-13)	3	1	NR
Rauf (30)	India	Case report	Late April 2020	1	5	1	0	NR
Kaushik (31)	The USA	Retrospective observational study	April 23 to May 23, 2020	33	10 (IQR: 6-13)	20	13	Hispanic or Latino: 15; Black:13; White: 3; Asian:1; Other:1
Miller (32)	The USA	Retrospective observational study	April 18 to May 22, 2020	44	7.3 (0.58 - 20)	20	24	White, Non-Hispanic: 9; Black/African-American: 9; Hispanic: 15; Unknown/Declined: 11

Lead Author	Country	Type of Study	Study Time	Total Participants	Age (y)	Male	Female	Race
Yozgat (33)	Turkey	Case report	NR	1	3	0	1	NR
Toubiana (34)	France	Prospective observational study	April 27 to May 15, 2020	21	7.9 (3.7-16.6)	9	12	Ancestry: Sub-Saharan Africa/Caribbean: 12; Asia: 3
Grimaud (35)	France	Retrospective observational study	April 15 to April 27, 2020	20	10 (2.9-15)	10	10	NR
Acharyya (36)	India	Case report	NR	1	0.38	1	0	NR
Liccaiardi (37)	Italy	Case report	April 14 to April 18, 2020	2	9.5 (7-12)	2	0	NR
Verdoni (38)	Italy	Retrospective observational study	February 18 to April 20, 2020	10	# 7.5(SD: 3.5)	7	3	NR
Ng (39)	The UK	Case series	April – May 2020	3	16 (13-17)	2	1	Afro-American: 2; Asian Indian: 1
Capone (40)	The USA	Retrospective observational study	April 17 to May 13, 2020	33	8.6 (2.2-17)	20	13	White:3; Black:8; Asian:3; Others/Multiracial:15; Unknown/Declined: 12
Abdel-Mannan (41)	The UK	Case series	March 1 to May 8, 2020	4	12 (8-15)	2	2	South Asian: 2; Afro-American: 2
Bapst (42)	Switzerland	Case report	April 2020	1	13	1	0	NR
Rodriguez-Gonzalez (43)	Spain	Case report	NR	1	0.5	1	0	NR
Feldstein (44)	The USA	Prospective & retrospective surveillance study	March 15 to May 20, 2020	186	8.3 (3.3-12.5)	115	71	White, Non-Hispanic: 35; Black, Non-Hispanic: 46; Hispanic or Latino: 57; Other race, Non-Hispanic: 9; Unknown: 41
Dufort (45)	The USA	Surveillance	March 1 to May 10, 2020.	99		53	46	White: 29 (37%), Black: 31 (40%), Asian:4 (5%), Others:14 (18%)
Dasgupta (46)	South Dakota	Case report	April 2020	1	8	0	1	African American/ Caucasian
Perez-Toledo (47)	The UK	Case series	April 28 to May 8, 2020	8	9 (7-14)	5	3	NR
Hameed (48)	The UK	Case series	April 14 to May 9, 2020	35	11 (IQR 8)	27	8	NR
Riollano-Cruz (49)	The USA	Retrospective observational study	April 24 to June 19, 2020	15	12 (Mean) 3-20 years (Range)	11	4	Hispanic or Latino: 10

23, 24, 34, 36, 39, 43, 46). All 22 studies reporting median lymphocyte count had lymphopenia except 3 studies (15, 30, 46). In 6 case reports, children with features of MIS-C were anemic (1-17, 33, 36, 43) while median hemoglobin value was less than 11 g/dL in 3 other studies (24, 34, 46).

For documenting the underlying hyperinflammatory state, 35 studies reported median C-reactive protein (CRP) values raised in all except the French study by Leon et al. (15). The median value of other inflammatory markers was reported high in all reporting studies. These markers included procalcitonin (PCT) (19 studies), serum ferritin (28 studies), D-dimer (25 studies), and Interleukin (IL)- 6 (12 studies).

Underlying cardiac dysfunction associated with MIS-C was documented through measurement of cardiac markers like troponin (25 studies) and pro-BNP (pro-brain na-

Table 2. Clinical features

Authors	Total Participants	Fever	No.(%)					Neuro-cognitive	No.(%)					Shock	No.(%)		
			Respiratory Symptoms		Gastrointestinal Symptoms				Features of Kawasaki Disease						Co-morbidities		
			Cough/Sore throat/Runny Nose	Dyspnea	Diarrhea	Vomiting	Abdominal Pain		Rash	Lips or oral changes	Cervical lymph-adenopathy	Non-purulent conjunctivitis	Extremity changes		Obesity	Asthma	Others
Jones (12)	1	1(100	0	1(100	Not reported (NR)	NR	0	1(100%)	1(100)	1(100)	0	1(100)	1(100)	0	NR	NR	NR
Chiotos (13)	6	6(100)	NR	4(67)	4(67)	5(83)		2(33)	2(33)	3(50)	0	22(33)	22(33)	6(100)	NR	NR	0
Labé (14)	2	1(50)	0	0	0	0	0	NR	1(50)	1(50)	1(50)	1(50)	1(50)	0	NR	NR	NR
Riphagen (3)	8	8(100)	3(38)	7(88)	7(88)	4(50)	6(75)	NR	4(50)	NR	NR	5(63)	0	8(100)	0	0	2(25) (Autism 1; Hay-fever-1)-
Leon (15)	1	1(100)	1(100)	1(100)	0	0	0	1(100)	1(100)	0	0	1(100)	1(100)	1(100)	NR	NR	NR
Balasuramanian (16)	1	1(100)	1(100)	1(100)	0	0	0	NR	1(100)	1(100)	NR	1(100)	1(100)	1(100)	NR	NR	NR
Rivera-Figueroa (17)	1	1(100)	NR	1(100)	1(100)	NR	1(100)	NR	1(100)	1(100)	1(100)	1(100)	NR	1(100)	NR	NR	NR
Belhadjer (18)	35	35(100)	15 (43)	23(66)		29 (83)		11 (31)	20(57)	19(54)	21(60)	31(89)	NR	28(80)	6(17)	3(9)	Total comorbitity- 28% Lupus- 1 (3 %)
Chiu (19)	1	1(100)	1(100)	0	1(100)	NR	0	0	1(100)	1(100)	0	1(100)	NR	1(100)	NR	NR	NR
Schnapp (20)	1	1(100)	NR	NR	NR	NR	1(100)	NR	1(100)	NR	NR	NR	NR	1(100)	NR	NR	NR
Greene (21)	1	1(100)	1(100)	NR	NR	NR	1(100)	NR	1(100)	1(100)	0	NR	NR	1(100)	0	0	0

Authors	Total Participants	Fever	No.(%)					Neuro-cognitive	No.(%)					Shock	No.(%)		
			Respiratory Symptoms		Gastrointestinal Symptoms				Features of Kawasaki Disease						Co-morbidities		
			Cough/Sore throat/Runny Nose	Dyspnea	Diarrhea	Vomiting	Abdominal Pain		Rash	Lips or oral changes	Cervical lymph-adenopathy	Non-purulent conjunctivitis	Extremity changes		Obesity	Asthma	Others
Dolinger (22)	1	1(100)	NR	NR	NR	NR	1(100)	NR	1(100)	NR	0	NR	NR	1(100)	NR	NR	Perianal Crohn's disease
Cheung (23)	17	17(100)	7(41)			15(88)		8(31)	12(71)	9(53)	6(35)	11(65)	3(18)	13(76)	0	3(18)	0
Whittaker (24)	58	58(100)	12(21)		30(52)	26(45)	31(53)	20(34)	30(52)	17(29)	9(16)	26(45)	9(16)	27(47)	0	3(5)	4(7)
Blondiaux (25)	4	4(100)	0	0	2	4	2	NR	4	2	1	2	NR	3	NR	NR	NR
Belot (26)	108	NR	NR	NR	NR	NR	NR	NR			66 (61)			NR	NR	NR	NR
Pouletty (27)	16	16(100)	2 (13)			13(81)		9(56)	13(81)	14(88)	6(38)	15(94)	11(69)	11(69)	0	2(13)	4(25)
Ramcharan (28)	15	15(100)	NR	NR		13(87)		NR			8(53)			NR	NR	NR	NR
Waltuch (29)	4	4(100)	2(50)	1(25)	3(75)	3(75)	3(75)	1(25)	2(50)	4(100)	1(25)	3(75)	2(50)	4(100)	0	1(25)	1(25) (Hypo-thyroidism)
Rauf (30)	1	1(100)	NR	NR	1(100)	NR	1(100)	1(100)	NR	NR	NR	1(100)	1(100)	1(100)	0	0	0
Kaushik (31)	33	31(100)	NR	11(33)	16(48)	23(33)	21(70)	4(12)	14(42)	7(21)	NR	12(36)	NR	21(64)	2 (6); 4 over-weight	0	0
Miller (32)	44	44(100)	NR	11(25)	18(41)	25(57)	33(75)	13(30)	31(70)	23(52)	NR	23(52)	NR	22(50)	16(37)	NR	NR
Yozgat (33)	1	1(100)	0	0	0	0	0	0	1(100)	1(100)	0	1(100)	1(100)	1(100)	NR	NR	NR
Toubiana (34)	21	11	NR	NR		21(100)		12(57)	16 (76)	16(76)	12(57)	17(81)	10(48)	12 (57)	NR	NR	NR
Grimaud (35)	20	20(100)	NR	NR	20(100)	20(100)	20(100)	5(25)	10(50)	5(25)	2 (10)	6 (30)	NR	20(100)	0	0	0

Authors	Total Participants	Fever	No.(%)					Neuro-cognitive	No.(%)					Shock	No.(%)		
			Respiratory Symptoms		Gastrointestinal Symptoms				Features of Kawasaki Disease						Co-morbidities		
			Cough/Sore throat/Runny Nose	Dyspnea	Diarrhea	Vomiting	Abdominal Pain		Rash	Lips or oral changes	Cervical lymph-adenopathy	Non-purulent conjunctivitis	Extremity changes		Obesity	Asthma	Others
Acharyya (36)	1	1(100)	NR	NR	NR	NR	NR	1(100)	1(100)	1(100)	1(100)	1(100)	1(100)	0	NR	NR	NR
Liccaiardi (37)	2	2(100)	2(100)		2(100)	2(100)	2(100)	NR	2(100)	2(100)	NR	2(100)	2(100)	1(50)	NR	NR	PFAPA: 1(50)
Verdoni (38)	10	10(100)	NR	NR	6(60)	NR	NR	4(40)	6(60)	6 (60)	1(10)	7(70)	5(50)	5(50)	NR	NR	NR
Ng (39)	3	3(100)	2(67)	2(67)	3(100)	3(100)	3(100)	2(67)	2(67)	1(33)	2(67)	3(100)	NR	3(100)	1(33)	NR	NR
Capone (40)	33	33(100)	17(52)			32(97)		19 (27)			21(64)			25(76)	13 (39); Over-weight: 2	5 (15)	2(6)
Abdel-Mannan (41)	4	4(100)	NR	2 (50)	NR	4(100)	1(25)	4(100)	4(100)	NR	NR	NR	NR	4(100)	1(25)	NR	NR
Bapst (42)	1	1(100)	NR	NR	NR	NR	1(100)	NR	1(100)	NR	NR	1(100)	1(100)	NR	NR	NR	NR
Rodriguez-Gonzalez (43)	1	1(100)	1(100)	1(100)	0	0	0	1(100)	0	0	0	0	0	1(100)	0	0	SBS:1(100)
Feldstein (44)	186	186(100)	NR	109(59)		171(92)		12 (6)	110(59)	78 (42)	18(10)	133(72)	69(37)	90(48)	45 (24)	33 (18)	18(10)
Dufort (45)	99	99(100)	31(31)	19(19)	49(49)	57(58)	60(60)	30(30)	59(60)	27(28)	6 (31)	55(56)	9 (9)	10(10)	29(29)	NR	14 (14)
Dasgupta (46)	1	1(100)	1(100)	NR	1(100)	1(100)	1(100)	1(100)	1(100)	1(100)	NR	1(100)	1(100)	1(100)	0	0	0
Perez-Toledo (47)	8	8(100)	NR			8(100)		NR			7(88)			NR	NR	NR	NR
Hameed (48)	35	33(95)	NR			30 (86)		NR	13 (37)	NR	NR	9 (26)	NR	21 (60)	NR	NR	NR
Riollano-Cruz (49)	15	15(100)	3(20)			13(87)		NR	7(47)	NR	NR	4 (27)	4 (27)	13(87)	0	4 (27)	1(7)

January 2022, Volume 10, Special Issue, Number 25

Journal of Pediatrics Review

Kumar M, et al. Multisystem Inflammatory Syndrome in Children and Young Adults with COVID-19. JPR. 2022; 10[Special Issue]:367-388

Table 3. Laboratory investigations

Lead Author	Hemoglobin(g/dL)	Total Leucocyte Count (×103/µL)	Lymphocytes (×103/µL)	Platelets (×103/µL)	Alanine Transaminase (IU/L)	Aspartate Transaminase (IU/L)	Sodium (mEq/L)	Albumin (g/L)	C- Reactive Protein (mg/L)	Procalcitonin (ng/ml)	Troponin-I/ Tropnin-T (ng/L)	Pro-Brain Natriuretic Peptide (pg/mL)	Ferritin (ng/ml)	IL-6 (pg/mL)	D-Dimer (ng/mL)	Nasopharyngeal SARS-CoV-2 RT PCR (Positive/ Tested)	Serological Test for SARS-CoV-2 (Positive/Tested)
Jones (12)	Not reported (NR)	NR	NR	NR	NR	NR	131	2.8	133	NR	NR	NR	186	NR	NR	1 (100%)	NR
Chiotos (13)	11.2 (9.6-12.5)	32.3 (11.7-50.1)	0. 3 (0.17-0.51)	155	66.8	NR	130 (125-134)	2.3(2.1-2.8)	22.8 (8.3-34.3)	49.4 (15.05->100)	300(50-1390)	NR	804(512.6-1267)	NR	11200	3/6 (50%)	5/5 (100%)
Labé (14)	NR	17.4	NR	104.5 (33-175)	64 (29 -108)	NR	NR	NR	195	NR	NR	NR	NR	NR	27700	1/2 (50%)	NR
Riphagen (3)	NR	NR	NR	105.15(61-296)	NR	NR	NR	22 (18-25)	303.7 (169-556)	75 (7.42-100)	252.5	13427	815.5	NR	4210	4/8 (50 %)	8/8 (100%)
Leon (15)	10.9	13.3	2	225	NR	NR	118	2.8	450	NR	114	NR	699.5	NR	4200	1/1 (100%)	NR
Balasuramanian (16)	8.9	23	NR	395	NR	NR	133	2.6	317	NR	NR	NR	1496	NR	NR	1/1 (100%)	NR
Rivera-Figueroa (17)	8	40	NR	104	55	NR	121	2	256	27	60	NR	1030	NR	NR	1/1 (100%)	NR
Belhadjer (18)	NR	16 (12-23)	NR	NR	NR	NR	NR	NR	241 (150-311)	36 (8-99)	408 (258-679)	41484 (35811-52475)	NR	135 (87-175)	5284 (4069-9095)	12/35 (34%)	30/35 (86%)
Chiu (19)	12.4	16.8	1.18	207	NR	NR	125	NR	280	28	84	9477	1089	NR	2727	1/1 (100%)	NR
Schnapp (20)	NR	NR	0.2	NR	NR	NR	NR	NR	335	NR	NR	NR	NR	NR	16100	0/1	2/2 (100 %)
Greene (21)	NR	14.18	NR	NR	NR	NR	NR	NR	>300	16.28	112	8718	1789	NR	1207	1/1 (100%)	NR
Dolinger (22)	NR	NR	NR	NR	98	145	NR	2.9	79.8	NR	NR	NR	920	73.6	2140	1/1 (100%)	NR

Lead Author	Hemoglobin(g/dL)	Total Leucocyte Count (×103/µL)	Lymphocytes (×103/µL)	Platelets (×103/µL)	Alanine Transaminase (IU/L)	Aspartate Transaminase (IU/L)	Sodium (mEq/L)	Albumin (g/L)	C- Reactive Protein (mg/L)	Procalcitonin (ng/ml)	Troponin-I/ Tropnin-T (ng/L)	Pro-Brain Natriuretic Peptide (pg/mL)	Ferritin (ng/ml)	IL-6 (pg/mL)	D-Dimer (ng/mL)	Nasopharyngeal SARS-CoV-2 RT PCR (Positive/ Tested)	Serological Test for SARS-CoV-2 (Positive/Tested)
Cheung (23)	11.2 (7.9-12.9)	14 (4-35.9)	1.21(0.11-6.44)	237 (69-892)	49.6 (11-167)	51.5 (18-151)	133.1 (125-141)	NR	200 (17-300)	21.7 (0.8-127)	56.8 (6-278)	15833 (631-59291)	647.9 (83-1828)	226.3 (3.1--315)	? 4 (0.9-11) X 106	8/17 (47%)	9/17 (53%)
Whittaker (24)	9.2 (8.3-10.3)	17 (IQR:12-22)	0.8 (IQR: 0.5-1.5)	151 (IQR: 104-210)	42 (IQR: 26-95)	NR	NR	24 (IQR:21-27)	229 (IQR: 156-338)	NR	45 (IQR: 8-294)	788 (IQR: 174-10548)	610 (IQR: 359-1280)	NR	3578 (IQR: 2085-8235)	15/58 (25.8%)	40/46 (87%)
Blondiaux (25)	NR	NR	0.61 (0.4-0.78)	NR	NR	NR	129.5 (128-134)	NR	325 (131-456)	NR	442.5 (125-4607)	2722.5 (918-3214)	NR	NR	NR	0/4	4/4 (100%)
Belot (26)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	37/79 (46.8%)	51/79 (64.5%)
Pouletty (27)	NR	11.5 (IQR: 9-14.4)	1.15 (IQR: 0.8-1.7)	188 (IQR: 164-244)	NR	NR	130 (IQR: 127-134)	21 (19-23)	207 (IQR: 162-236)	NR	58 (36-165)	4319 (IQR: 2747-6493)	1067 (272-1709)	270 (IQR: 136-526)	NR	11/16 (68.7%)	7/8 (87.5%)
Ramcharan (28)	NR	NR	NR	NR	NR	NR	NR	NR	154 (129–231)	NR	396 (IQR: 100-1280)	24470 (IQR: 17212-26655)	558 (364-1325)	NR	2060 (IQR: 1160-2610)	2/15 (13.33%)	12/12 (100%)
Waltuch (29)	11.4 (11-13.1)	8.25 (5.1-17)	0.388 (0.245-0.61)	131.5 (111-205)	35.5 (23-93)	52.5 (28-95)	NR	NR	267.25 (202.2-363.8)	14.06 (2.35-25.49)	35 (10-320)	126.65 (72.44 – 3068.52)	1023.5 (288-2010)	330 (214-504)	3505 (2230-4460)	2/4 (50%)	4/4 (100%)
Rauf (30)	NR	11	1.76	300	60	85	124	21	120	NR	29	8000	600	NR	NR	Negative twice	Not done
Kaushik (31)	11.3 (IQR: 9.55-12.5)	11 (IQR: 8.45-14.4)	1.1 (IQR: 0.6-1.3)	176 (IQR: 130.5-282)	36 (IQR: 28-53)	48 (IQR: 27-69)	136 (IQR: 135-139)	35 (IQR: 26-39)	250 (IQR: 156-302)	6 (IQR: 2.7-16.5)	80 (IQR: 20-170)	15000 (IQR: 9329-15000)	568 (IQR: 340-954)	200 (IQR: 56.4-330)	3700 (2400-5100)	11/33 (33.33%)	27/33 (81.8%)
Miller (32)	9.3 (4.9-14.2)	9.68 (3.95-35.98)	NR	200 (69-892)	31 (8-4557)	33.5 (15-7000)	NR	37 (20-47)	146.5 (2.96-300)	NR	NR	NR	NR	219.2 (3.1-315)	NR	15/44 (34.1%)	31/32 (96.9%)

Kumar M, et al. Multisystem Inflammatory Syndrome in Children and Young Adults with COVID-19. JPR. 2022; 10[Special Issue]:367-388

Lead Author	Hemoglobin(g/dL)	Total Leucocyte Count (×103/µL)	Lymphocytes (×103/µL)	Platelets (×103/µL)	Alanine Transaminase (IU/L)	Aspartate Transaminase (IU/L)	Sodium (mEq/L)	Albumin (g/L)	C- Reactive Protein (mg/L)	Procalcitonin (ng/ml)	Troponin-I/ Tropnin-T (ng/L)	Pro-Brain Natriuretic Peptide (pg/mL)	Ferritin (ng/ml)	IL-6 (pg/mL)	D-Dimer (ng/mL)	Nasopharyngeal SARS-CoV-2 RT PCR (Positive/ Tested)	Serological Test for SARS-CoV-2 (Positive/Tested)
Yozgat (33)	11	NR	0.9	1	108	125	NR	32	NR	9.2	40000*	NR	520	NR	2818	0	0
Toubiana (34)	8.6 (5.3-12.2)	17.4 (5.4-42.8)	1.1 (0.4-5.6)	499 (78-838)	70 (6-257)	NR	130 (116-135)	21 (16-37)	253 (89-363)	22.5 (0.1-448)	282 (10-6900)	3354 (16-16017)	NR	170 (4-1366)	4025	8/21 (38%)	19/21 (90%)
Grimaud (35)	NR	10.95 (1.5-34.2)	1.15 (0.38-7.2)	210 (93-403)	27 (6-163)	NR	131 (122-139)	21 (17-26)	251 (94-458)	46 (1.6-448)	269000* (31000-4607000)	28855 (1516-161127)	NR	NR	NR	10/20 (50%)	15/15 (100%)
Acharyya (36)	9.9	14.47	NR	425	NR	NR	NR	30	178.2	NR	NR	NR	NR	NR	NR	1/1 (100%)	NR
Liccaiardi (37)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	738.5 (580-897)	NR	NR	0	2/2 (100%)
Verdoni (38) #	11 (SD: 1.2)	10.8 (SD: 6.1)	0.86 (SD: 0.4)	130 (SD: 32)	119 (SD: 217)	87 (SD: 70)	130 (SD: 3.8)	3.2 (SD: 0.3)	250 (SD: 153)	NR	1004 (SD: 1862)	1255 (SD: 929)	1176 (SD: 1032)	177.1 (SD: 137.4)	3798 (SD: 1318)	2/10 (20%)	8/10 (80%)
Ng (39)	NR	27.7 (23.1-38.1)	0.87 (0.45-1.15)	487 (111-636)	NR	NR	NR	21 (18-22)	399(328-403)	23.6 (4.3 - >75)	1766.5 (821.6-2035.1)	18620 (13222-22841)	1342 (540-5440)	NR	NR	1/3 (33%)	3/3 (100%)
Capone (40)	11.2 (IQR: 10.5-12)	9.14 (IQR: 7.19-12.33)	0.8 (IQR: 0.49-1.42)	154 (IQR: 104-205)	38 (IQR: 30-64)	54 (IQR: 36-76)	133 (IQR: 131-135)	34 (IQR: 30-37)	206 (IQR: 122-299)	12.05 (IQR: 2.87-24.96)	31 (IQR: 6-78)	3325 (IQR: 640-6676)	640 (IQR: 313-1192)	NR	1700 (IQR: 958-2410)	9/33 (27%)	30/33 (91%)
Abdel-Mannan (41)	NR	NR	NR	NR	NR	NR	NR	NR	320.5 (290-448)	NR	NR	NR	1316 (1192 – 1414)	NR	1364.2 (494.5 – 1625.4)	4/4 (100%)	2/4 (50%)
Bapst (42)	NR	NR	0.93	104	NR	NR	NR	NR	265	2.71	199000*	NR	NR	NR	NR	0	1 (100%)
Rodriguez-Gonzalez (43)	7	30.2	NR	98	NR	NR	NR	NR	86	3.46	90	26000	7634	198	4200	0	1 (100%)
Feldstein (44)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	1194.7 (IQR: 390.8 – 4833)	639 (IQR: 332.7 – 1178.2)	NR	4090 (2204 – 8404.5)	73	58

Lead Author	Hemoglobin(g/dL)	Total Leucocyte Count (×103/µL)	Lymphocytes (×103/µL)	Platelets (×103/µL)	Alanine Transaminase (IU/L)	Aspartate Transaminase (IU/L)	Sodium (mEq/L)	Albumin (g/L)	C- Reactive Protein (mg/L)	Procalcitonin (ng/ml)	Troponin-I/ Tropnin-T (ng/L)	Pro-Brain Natriuretic Peptide (pg/mL)	Ferritin (ng/ml)	IL-6 (pg/mL)	D-Dimer (ng/mL)	Nasopharyngeal SARS-CoV-2 RT PCR (Positive/ Tested)	Serological Test for SARS-CoV-2 (Positive/Tested)
Dufort (45)	NR	10.4 (6.7–14.5)	10.0 (5.0–16.0) in %	155 (105–233)	NR	NR	NR	31 (25–36)	219 (150–300)	6.2 (2.2–19.7)	NR Increased in 63 of 89 patients	NR Increased in 74 of 82 patients	522 (305–820)	116.3 (37.0–315.0)	2400(1200–3700)	50/98 (51%)	76/77 (98.7%)
Dasgupta (46)	8.95 (7.9-11.3)	24.5 (21.2-34.1)	8.5% (3%-255)	321.5 (272-616)	50.5 (36-81)	48 (31-76)	133 (125-136)	2.5 (2.5-3.4)	149.5 (116-250)	6 (4.0-42.77)	230 (one value)	585 (522-1399)	NR	NR	9070(one value)	0	0
Perez-Toledo (47)	NR	NR	NR	NR	NR	NR	NR	NR	188 (136-255)	NR	NR	NR	1325 (819-2121)	NR	NR	0	8/8 (100%)
Hameed (48)	NR	12.0 (10.5-17.2)	1.0 (0.8-1.3)	160 (135-224)	NR	NR	NR	NR	267(180-309)	NR	47 (39-185)	NR	631 (293 -1023)	NR	4900 (3300-10300)	0	27/30 (90%)
Riollano-Cruz (49)	NR	NR	NR	198(116.5-249.5)	NR	NR	NR	32 (24.5-37.5)	249 (191.5-295)	2.35 (0.48-8.47)	140 (60-980)	126 (72.4-1009.25)	628 (326-1397)	253 (149.95-298)	2615 (1782-4282)	9/15 (60%)	15/15 (100%)

Data for all studies are presented as median with range or interquartile range (IQR) in parenthesis except Verdoni et al. [38], where data are presented in mean with standard deviation (SD).

* Yozgat [33], Grimaud [35], and Bapst [42] reported total Troponin.

Table 4. Radiological investigations

Lead Author	Total Participants	Abnormal Chest X-ray	Abnormal computed Tomography Chest (%)	Abnormal Echo		
				Ventricular Dysfunction	Coronary Abnormalities	Others
Jones (12)	1	1 (100%)	NR	0	0	0
Chiotos (13)	6	5 (83.3%)	NR	3 (50%)	1 (16.7%)	0
Labé (14)	1	NR	1 (100%)	NR	NR	NR
Riphagen (3)	8	4 (50%)		7 (87.5%)	2 (25%)	AVVR-1 (12.5%)
Leon (15)	1	1 (100 %)	NR	1 (100%)	0	MR- 1 (100%)
Balasuramanian (16)	1	1 (100%)	NR	0	0	0
Rivera-Figueroa (17)	1	1 (100%)	NR	0	0	Pericardial effusion- 1 (100%)
Belhadjer (18)	35	NR	NR	35 (100%) Ejection fraction <30% (10/35), 30-50% (25/35)	6 (17%)	Takotsubo syndrome presentation -1(2.9%) Pericardial effusion-3 (8.6%)
Chiu (19)	1	NR	NR	1 (100%)	0	Pericardial effusion- 1 (100%)
Schnapp (20)	1	NR	NR	1 (100%)	0	0
Greene (21)	1	0	NR	1 (100%)	0	0
Dolinger (22)	1	0	0	NR	NR	NR
Cheung (23)	17	14 (82.3%)	NR	6/14 (35.3%)	0	Pericardial effusion-8/14 (47%)
Whittaker (24)	58	NR	NR	18/29 (62%)	8/55 (14.5%)	NR
Blondiaux (25)	4	NR	1 (25%)	4 (100%)	0	Pericarditis:3 (75%)
Belot (26)	108	NR	NR	NR	NR	NR
Pouletty (27)	16	5 (31.2 %)	2/8 (25%)	NR	3 (18.75%)	Myocarditis:7 (44%) Pericarditis:4 (25%)
Ramcharan (28)	15	7/14 (50%)	NR	12 (80%)	14 (93.3%)	Pericardial effusion: 8 (53.3%)
Waltuch (29)	4	1 (25%)	NR	1/3 (33.3%)	2/3 (66.6%)	MR & TR: 1/3 (33.3%) Pericardial effusion:1/3 (33.3%)
Rauf (30)	1	0	NR	1 (100%)	0	0
Kaushik (31)	33	Focal opacity:5 (15.15%) Bilateral opacities:6 (18.18%)	NR	21/32 (65.6%)	NR	Pericardial effusion: 15/32 (46.8%)
Miller (32)	44	NR	NR	NR	NR	NR
Yozgat (33)	1	0	0	0	1 (100%)	0
Toubiana (34)	21	8/18 (44%)	NR	NR	8/21 (38%)	NR

Lead Author	Total Participants	Abnormal Chest X-ray	Abnormal computed Tomography Chest (%)	Abnormal Echo		
				Ventricular Dysfunction	Coronary Abnormalities	Others
Grimaud (35)	20	NR	NR	20 (100%)	NR	NR
Acharyya (36)	1	0	NR	NR	1 (100%)	NR
Liccaiardi (37)	2	0	NR	2 (100%)	NR	1 (50%)
Verdoni (38)	10	5 (50%)	2/2 (100%)	5 (50%)	2 (20%)	Pericardial effusion 4 (40%); MR 4 (40%)
Ng (39)	3	3 (100%)	NR	1 (33%)	1 (33%)	2 (66%)
Capone (40)	33	NR	NR	19 (58%)	8 (24%)	NR
Abdel-Mannan (41)	4	NR	NR	1 (25%)	NR	MR: 1 (25%) ; Pericardial effusion:1 (25%)
Bapst (42)	1	1 (100%)	1 (100%)	0	0	0
Rodriguez-Gonzalez (43)	1	NR	1 (100%)	1 (100%)	NR	NR
Feldstein (44)	186	79 (42.4%)	NR	70 (37.6%)	15 (8%)	Pericardial effusion – 48 (25.8%)
Dufort (45)	99	35/90 (39%)		51/93 (52%)	9/93 (9%)	Pericardial effusion: 32/93 (32%)
Dasgupta (46)	1	1 (100%)	1 (100%)	1 (100%)	NR	Pericardial effusion: 1 (100%)
Perez-Toledo (47)	8	NR	NR	NR	NR	NR
Hameed (48)	35	19 (54%)	Basal consolidation with collapse: 13/33 (39%) Pleural effusion:10/33 (30%) Diffuse bilateral ground glass opacities: 3/33 (9%)	NR	6/30 (20%)	Total cardiac dysfunction: 18/35 (51%)
Riollano-Cruz (49)	15	12 (80%)	NR	7 (46.6%)	3 (20%)	NR

AVVR: atrioventricular valve regurgitation; MR: mitral regurgitation; TR: tricuspid regurgitation; NR: not reported. Journal of Pediatrics Review

triuretic peptide) (21 studies). Median values of these cardiac markers were raised in all the reporting studies.

Underlying SARS-CoV-2 infection was more often documented through serology. Of all patients included in this review, 212 of 560 (37.8%) had positive nasopharyngeal reverse transcription-polymerase chain reaction (RT-PCR), while 79.15% (410/518) had antibodies against SARS-CoV-2.

Radiological investigations

Chest x-ray abnormality was found in 161 of 369 (43.6%) patients. Very few studies reported imaging findings of chest computed tomography (CT). Hameed et al. (48) performed a chest CT scan on 33 of 35 patients. The main findings were basal consolidation with the collapse in 39% and pleural effusion in 30% of the patients. Three children had bilateral diffuse ground-glass opacities along with patchy dense consolidation. Dufort et al. reported either abnormal chest x-ray or abnormal chest CT in 35% of the patients (35) (Table 4).

In echocardiography, ventricular dysfunction was the major abnormality found in 50.2% (284/565) of the patients, while coronary dilatation was seen in only 15% (87/577) of the cases. Other findings like valvular in-

Table 5. Treatment and outcomes

Authors	Total Partici-pants	Non-invasive Oxygen Sup-port	Mechanical Ventilation	Inotrope	IVIG	Steroid	Immuno-mod-ulator	Aspirin	Anticoagulant	Duration of hospitalization (d)	Admitted in ICU	Duration of ICU Stay	Dis-charged	Expired	Admitted at time of publica-tion
Jones (12)	1	0	0	0	1 (100%)	0	0	1 (100%)	0	NR	NR	NR	1 (100%)	0	0
Chiotos (13)	6	2 (33.3%)	3 (50%)	5 (83.3%)	4 (66.6%)	6 (100%)	Anakinra: 1(16.6%)	2 (33.3%)	NR	11.8	1 (16.6%)	5.8	5 (83.3%)	0	1 (16.6%)
Labé (14)	1	NR	NR	NR	1 (100%)	NR	NR	NR	NR	NR	0	NR	1 (100%)	0	0
Riphagen (3)	8	3 (37.5%)	5 (62.5%)	8 (100%)	8 (100%)	5 (62.5%)	NR	6 (75%)	NR	NR	8 (100%)	4.6	7 (87.5%)	1 (12.5%)	0
Leon (15)	1	NR	1 (100%)	1(100%)	1 (100%)	NR	NR	1 (100%)	NR	NR	1 (100%)	NR	NR	0	NR
Balasurama-nian (16)	1	HFNC: 1 (100%)	NR	NR	1(100%)	NR	Tocilizumab:1	1 (100%)	NR	NR	1 (100%)	NR	NR	NR	NR
Rivera-Figueroa (17)	1	HFNC: 1 (100%)	0	NR	1 (100%)	1(100%)	NR	1 (100%)	NR	6	1(100%)	NR	1(100%)	0	NR
Belhadjer (18)	35	11 (31.4%)	22 (62.85)	28 (80%)	25 (71.4%)	12 (34.2%)	IL-1 receptor antagonist: 3 (8.5%)	NR	23 (65.7%)	10 (IQR 8-14)	35 (100%)	7 days (IQR 3.7-10 days)	34 (97.1%)	0	1 (2.8%)
Chiu (19)	1	NR	NR	1(100%)	NR	NR	NR	NR	NR	NR	1 (100%)	NR	0	0	1 (100%)
Schnapp (20)	1	NR	1 (100%)	1(100%)	NR	1(100%)	NR	NR	NR	NR	1 (100%)	NR	NR	0	NR
Greene (21)	1	NR	NR	1(100%)	1(100%)	1(100%)	Tocilizumab:1 (100%)	NR	1(100%)	NR	1(100%)	NR	1(100%)	0	0
Dolinger (22)	1	NR	NR	NR	0	0	Infliximab: 1 (100%)	0	1(100%)	NR	1(100%)	NR	1 (100%)	0	0
Cheung (23)	17	NR	0	10 (58.8%)	13 (76.4%)	14 (82.35)	Toclizum-ab:1(5.8%)	4 (23.5%)	11 (64.7%)	7.1 (3-18)	15 (88.2%)	6.4 (3-12)	17 (100%)	0	0
Whittaker (24)	58	NR	25 (43.1%); ECMO: 3 (5%)	27 (46.55)	41(70.6%)	37 (63.7%)	Anakinra: 3 (5%); Infliximab: 8 (13.7%)	NR	NR	NR	29 (50%)	NR	NR	1 (1.7%)	NR
Blondiaux (25)	4	HFNC: 3 (75%)	1 (25%)	3 (75%)	4 (100%)	3 (75%)	0	NR	NR	13 to 23 days	4 (100%)	NR	4 (100%)	0	0
Belot (26)	108	NR	31(28.7%)	52 (48%)	NR	NR	NR	NR	NR	NR	72 (66.6%)	NR	NR	1(0.9%)	NR

Authors	Total Partici-pants	Non-invasive Oxygen Sup-port	Mechanical Ventilation	Inotrope	IVIG	Steroid	Immuno-mod-ulator	Aspirin	Anticoagulant	Duration of hospitalization (d)	Admitted in ICU	Duration of ICU Stay	Dis-charged	Expired	Admitted at time of publica-tion
Pouletty (27)	16	Oxygen: 4 (25%); NIV: 3 (18.7%)	2 (12.5%)	6 (37.5%)	15 (93.7%)	4 (25%)	Anti-IL-1: 1(6.2%); Anti IL-6: 1 (6.2%)	15 (93.7%)	NR	NR	7 (43.7%)	NR	16 (100%)	0	0
Ramcharan (28)	15	HFNC: 4 (26.66%)	4 (26.6%)	10(66.6%)	10 (66.6%)	5 (33.3%)	0	11(73.3%)	NR	12 (IQR: 9-13)	10 (66.6%)	4 (IQR:3-5)	15 (100%)	0	0
Waltuch (29)	4	BiPAP:1 (25%)	1(25%)	3 (75%)	4 (100%)	NR	Anakinra: 1 (25%); Tocilizumab: 4 (100%)	NR	2 (50%)	NR	4 (100%)	NR	NR	0	NR
Rauf (30)	1	HFNC: 1(100%)	0	1(100%)	1(100%)	1 (100%)	0	1 (100%)	NR	6	1 (100%)	6	1 (100%)	0	0
Kaushik (31)	33	NIV: 12 (36.3%)	5 (15.15%); ECMO: 1 (3%)	17 (51.5%)	18 (54.5%)	17 (51.5%)	Anakinra: 4 (12.1%); Tocilizumab: 12 (36.3%)	NR	33 (100%)	7.8 (IQR: 6-10.1)	33 (100%)	4.7 (IQR: 4-8)	32 (97%)	1 (3%)	0
Miller (32)	44	11(25%)	0	22 (50%)	36 (81.8%)	42 (95.4%)	Anakinra: 8 (18.2%)	NR	40 (90.9%)	NR	NR	NR	43 (97.7%)	0	1 (2.2%)
Yozgat (33)	1	NR	NR	NR	1 (100%)	NR	NR	1(100%)	NR	NR	NR	NR	1 (100%)	0	0
Toubiana (34)	21	NR	11 (52.3%)	15 (71.4%)	21 (100%)	10 (47.6%)	NR	21(100%)	NR	8 (5-17)	17 (81%)	5 (3-15)	21 (100%)	0	0
Grimaud (35)	20	NIV: 11 (55%); HFNC: 1(5%)	8 (40%)	19 (95%)	20 (100%)	2 (10%)	IL-1 antago-nist: 1(5%); IL-6 receptor antibody: 1(5%)	NR	NR	NR	20 (100%)	4 (1-8)	15 (75%)	0	5 (25%)
Acharyya (36)	1	NR	0	0	1(100%)	0	0	1(100%)	NR	NR	0	NA	0	0	1(100%)
Liccaiardi (37)	2	1 (50%)	0	1(50%)	1 (50%)	2 (100%)	0	1(50%)	NR	NR	NR	NR	NR	NR	NR
Verdoni (38)	10	NR	NR	2 (20%)	10 (100%)	8 (80%)	NR	10 (100%)	NR	NR	NR	NR	10 (100%)	0	0
Ng (39)	3	2 (66.6%)	1 (33.3%)	2 (66.6%)	2 (66.6%)	2 (66.6%)	NR	2 (66.6%)	NR	13 (13-16)	3 (100%)	4 (3-10)	3 (100%)	0	0
Capone (40)	33	17 (51.5%)	6 (18.1%)	25 (75.7%)	33 (100%)	23 (69.6%)	Anakinra: 4 (12%); Tocili-zumab: 3 (9%); Infliximab: 1(3%)	NR	14 (42.4%)	4 (IQR: 4-8)	26 (78.7%)	NR	33 (100%)	0	0

Authors	Total Partici-pants	Non-invasive Oxygen Sup-port	Mechanical Ventilation	Inotrope	IVIG	Steroid	Immuno-mod-ulator	Aspirin	Anticoagulant	Duration of hospitalization (d)	Admitted in ICU	Duration of ICU Stay	Dis-charged	Expired	Admitted at time of publica-tion
Abdel-Mannan (41)	4	NR	4 (100%)	NR	2 (50%)	2 (50%)	Anakinra: 1 (25%); Ritux-imab: 1 (25%)	NR	NR	18 (11-32)	4 (100%)	6.5 (2-14)	2 (50%)	0	2 (50%)
Bapst (42)	1	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Rodriguez-Gonzalez (43)	1	NR	1(100%)	1(100%)	NR	1 (100%)	Tocilizumab: 1(100%)	NR	1 (100%)	21	1 (100%)	7	1(100%)	0	0
Feldstein (44)	186	HFNC: 49 (26.3%) CPAP: 32 (17.2%)	37 (19.9%); ECMO: 8 (4.3%)	90 (48.3%)	144 (77.4%)	91 (48.9%)	IL-6 inhibitor: 14 (7.5%); IL-1Ra inhibi-tor: 24 (13%)	NR	87 (46.7%)	7 (IQR: 4-10)	148 (79.5%)	NR	130 (69.8%)	4 (2.1%)	52 (27.9%)
Dufort (45)	99	BiPAP/ CPAP: 7 (7%) HFNC:16 (16.2%)	10 (10.1%)	61 (61.^%)	69 (69.6%)	63 (63.6%)	NR	NR	NR	6.0 (4.0–9.0)	79 (79.7%)	NR	76 (76.7%)	2 (2%)	21 (21.2%)
Dasgupta (46)	1	NR	NR	1(100%)	1(100%)	1(100%)	NR	1(100%)	NR	8	1(100%)	NR	1(100%)	0	0
Perez-Toledo (47)	8	NR	NR	6 (75%)	8(100%)	NR	NR	NR	6 (75%)	NR	8 (100%)	0	0	0	0
Hameed (48)	35	NR	7 (20%)	20 (57.1%)	NR	NR	NR	NR	NR	NR	24 (68.5%)	NR	34 997%)	1 (2.8%)	0
Riollano-Cruz (49)	15	5 (33.3%)	3 (20%)	9 (60%)	12 (80%)	3 (20%)	Tocilizumab: 12 (80%) Anakinra:2 (13.3%)	NR	15 (100%)	8 (6-13)	14 (93.3%)	NR	14 (93.3%)	1 (6.6%)	0

NR: not reported; BiPAP/CPA, bilevel positive airway pressure/continuous positive airway; HFNC, high-flow nasal cannula; CPAP, Continuous Positive Airway Pressure; ECMO, extracorporeal membrane oxygenation; IL, interleukin; NIV, non-invasive ventilation; IVIG, intravenous Immunoglobulin; ICU, intensive care unit.

volvement and pericardial effusion were documented in around 33% (148/446) of the cases.

Treatment and outcomes

About 77% (571/741) of patients in this review required admission to the intensive care unit (ICU). Mechanical ventilation was required in 211 of 773 (27.2%) patients, while 56.35% (448/795) required inotropic support to maintain hemodynamic stability (Table 5).

Amongst treatment modalities used to manage MIS-C, intravenous immunoglobulins (IVIG) was the most common modality, which was used in 510 of 653 patients (78.1%), followed by steroids which were administered to 357 of 639 (55.8%) patients. In refractory cases, immunomodulators were used. Anti-IL-1 (anakinra and others) use was reported in 10.8% (54/500), anti-IL-6 (tocilizumab and others) in 10.2% (51/500), and infliximab in 2% (10/500) of patients. Very few studies reported the use of aspirin and anticoagulants. Aspirin was given in 80 of 108 (74%), while anticoagulants were used in 234 of 380 (61.5%) patients. The mortality rate of MIS-C documented in this review was 1.5%, with only 12 out of 797 participants succumbing to it. Median duration of hospital admission was 7-8 days in many studies (23, 31, 34, 41, 46, 49).

4. Discussion

There is significant scope and need for studies defining the clinical characteristics of MIS-C in children and young adults because most of the 39 studies in this review were either case reports or case series with small sample sizes. However, their results provide a sneak peek into this previously unrecognized clinical syndrome associated with COVID-19 with KD-like presentation.

Although initial reports of MIS-C reported a phenotypic resemblance to KD, our review emphasizes specific important demographic differences. The median age of MIS-C presentation appears to be higher than that for KD. There is an increased incidence of this clinical entity in Black/Afro-American races than KD, which is more common in Asian ethnicities. Barring 3 case reports from India, none of the studies in this review hailed from Asia despite the COVID-19 pandemic having its origin in China. This racial predilection may emanate from genetic differences, mutations in the virus, or undetermined factors.

Certain manifestations of MIS-C are worth mentioning. As documented in this review, unlike KD, gastrointestinal symptoms are predominant in MIS-C. Similarly, circulatory insufficiency and myocardial dysfunction are distinctly more common than KD, affecting more than half of patients with MIS-C, as evident from clinical manifestations and increased cardiac markers reported by studies included in this review.

The hyperinflammatory state of MIS-C is well established through laboratory evidence synthesized in this review. This hyperinflammation is similar to cytokine storm syndrome associated with acute COVID-19 infection in adults, albeit delayed. Delay in interferon response and slow viral clearing has been putatively implicated in the pathogenesis of MIS-C (51).

Feldstein et al. have documented a temporal association between MIS-C and preceding SARS-CoV-2 infection (44). Also, based on the results of this review, the serological evidence of a preceding SARS-CoV-2 infection is more common than positive nasopharyngeal RT-PCR for viral nucleic acid, which probably suggests that these hyperinflammatory states are post-infectious phenomena brought about by a dysregulated immune response. However, given the lack of definitive data regarding causality other than the temporal association, an evolving body of evidence describing this clinical syndrome, and a myriad of clinical mimickers of its presentation, it is pertinent that the scientific community adopts a meticulous as well as the cautious approach in attributing these hyperinflammatory states to COVID-19.

The collated echocardiographic findings in this review show that ventricular dysfunction was more common than coronary changes in MIS-C. This pattern is distinct from KD, where coronary artery abnormalities are reported in about one-fourth of cases (52). Also, given the lack of follow-up data, the long-term cardiac sequel of MIS-C is still unknown.

Intravenous immunoglobulin (IVIG) was used as the primary treatment modality in 78.1% of participants included in this review. The indirect evidence for the use of IVIG in MIS-C stems from its use in other conditions with phenotypic similarities, such as KD or toxic shock syndrome (TSS). Adjunctive therapy has been used in the form of steroids and, in some studies, immunomodulators of IL-1 and IL-6. Their use, with a mostly favorable response, lends credence to the putative theory of MIS-C being a diffusely hyperinflammatory state of the dysregulated immune response.

Another important finding of this review is that 77% of children required intensive care with a need for mechanical ventilation in about a quarter of included participants. Hence, early recognition and treatment in an appropriate setting are necessary to decrease mortality which in this review was 1.5%.

5. Conclusion

MIS-C is a clinical mimic of hyperinflammatory states such as KD and TSS. However, evidence collated in this review show notable clinical and epidemiological differences compared to KD, like an increased median age of presentation, a higher incidence in Afro-Americans, the preponderance of gastrointestinal manifestations, and ventricular dysfunction. More extensive epidemiological studies will help in better defining this entity and delineating its phenotypic subtypes

There are inherent limitations of our rapid review. Our search strategy had a selection bias as only articles in English were included. Despite the systematic search of two major databases of PubMed and Embase, the data from studies indexed in the Chinese database of China National Knowledge Infrastructure (CNKI) has not been included. In the absence of a consensus clinical definition, this review includes all studies which have reported a hyperinflammatory state resembling KD, which brings heterogeneity and inadequate generalizability to its findings. This rapid review lacks follow-up data to characterize squeal and reflect the evolving nature of both the pandemic and our understanding of it.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this research.

Funding

This research did not receive any grant from funding agencies in the public, commercial, or non-profit sectors.

Authors' contributions

Conceptualized and Methodology: Manish Kumar; Data collection: Swarnim Swarnim and Pallavi Pallavi; Investigation: Manish Kumar; Writing – original draft, and Writing – review & editing: All authors.

Conflicts of interest

The authors declared no conflict of interest.

References

1. World Health Organization (WHO). Coronavirus disease (COVID-19) pandemic [Internet]. 2020 [Updated 2022]. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019

2. Liguoro I, Pilotto Ch, Bonanni M, Ferrari ME, Pusiol A, Nocerino A, et al. SARS-COV-2 infection in children and newborns: A systematic review. European Journal of Pediatrics. 2020; 179(7):1029-46. [DOI:10.1007/s00431-020-03684-7] [PMID] [PMCID]

3. Riphagen Sh, Gomez X, Gonzalez-Martinez C, Wilkinson N, Theocharis P. Hyperinflammatory shock in children during COVID-19 pandemic. The Lancet. 2020; 395(10237):1607-8. [DOI:10.1016/S0140-6736(20)31094-1]

4. Royal College of Paediatrics and Child Health. Guidance: Paediatric multisystem inflammatory syndrome temporally associated with COVID-19 [Internet]. 2020 [Updated 2020]. Available from: https://www.rcpch.ac.uk/sites/default/files/2020-05/COVID-19-Paediatric-multisystem-%20.pdf

5. Health Alert Network (HAN). HAN00432: Multisystem Inflammatory Syndrome in Children (MIS-C) associated with coronavirus disease 2019 (COVID-19) [Internet]. 2020 [Updated 2020 May 14]. Available from: https://emergency.cdc.gov/han/2020/han00432.asp

6. World Health Organization. Multisystem inflammatory syndrome in children and adolescents temporally related to COVID-19: Scientific brief [Internet]. 2020 [Updated 2020 May 15]. Available from: https://www.who.int/news-room/commentaries/detail/multisystem-inflammatory-syndrome-in-children-and-adolescents-with-COVID-19

7. Garritty C, Gartlehner G, Kamel C, King VJ, Nussbaumer-Streit B, Stevens A, et al. Cochrane rapid reviews. Interim guidance from the cochrane rapid reviews methods group [Internet]. 2020 [Updated 2020 March]. Available from: https://methods.cochrane.org/rapidreviews/sites/methods.cochrane./cochrane_rr_-_guidance-23mar2020.pdf

8. Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. PLoS Medicine. 2009; 6(7):e1000097. [DOI:10.1371/journal.pmed.1000097] [PMID] [PMCID]

9. Centers for Disease Control and Prevention. COVID-19 PubMed search alert [Internet]. 2020 [Updated 2020 October 9]. Available from: https://www.cdc.gov/library/researchguides/2019novelcoronavirus/pubmedsearchalert.html

10. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan - a web and mobile app for systematic reviews. Systematic Reviews. 2016; 5:210. [DOI:10.1186/s13643-016-0384-4] [PMID] [PMCID]

11. Munn Z, Moola S, Lisy K, Riitano D, Tufanaru C. Chapter 5: Systematic reviews of prevalence and incidence. In: Aromataris E, Munn Z, editors. JBI Manual for Evidence Syn-

thesis. Adelaide: JBI; 2020. https://jbi-global-wiki.refined.site/space/MANUAL/3283910689

12. Jones VG, Mills M, Suarez D, Hogan CA, Yeh D, Segal JB, et al. COVID-19 and Kawasaki disease: Novel virus and novel case. Hospital Pediatrics. 2020; 10(6):537-40. [DOI:10.1542/hpeds.2020-0123] [PMID]

13. Chiotos K, Bassiri H, Behrens EM, Blatz AM, Chang J, Diorio C, et al. Multisystem inflammatory syndrome in children during the coronavirus 2019 pandemic: A case series. Journal of the Pediatric Infectious Diseases Society. 2020; 9(3):393-8. [DOI:10.1093/jpids/piaa069] [PMID] [PMCID]

14. Labé P, Ly A, Sin C, Nasser M, Chapelon-Fromont E, Ben Saïd P, et al. Erythema multiforme and Kawasaki disease associated with COVID-19 infection in children. Journal of the European Academy of Dermatology and Venereology. 2020; 34(10):e539-41. [DOI:10.1111/jdv.16666] [PMID] [PMCID]

15. Deza Leon MP, Redzepi A, McGrath E, Abdel-Haq N, Shawaqfeh A, Sethuraman U, et al. COVID-19-associated pediatric multisystem inflammatory syndrome. Journal of the Pediatric Infectious Diseases Society. 2020; 9(3):407-8. [DOI:10.1093/jpids/piaa061] [PMID] [PMCID]

16. Balasubramanian S, Nagendran TM, Ramachandran B, Ramanan AV. Hyper-inflammatory syndrome in a child with COVID-19 treated successfully with intravenous immunoglobulin and tocilizumab. Indian Pediatrics. 2020; 57(7):681-3. [DOI:10.1007/s13312-020-1901-z] [PMID] [PMCID]

17. Rivera-Figueroa EI, Santos R, Simpson S, Garg P. Incomplete Kawasaki disease in a child with COVID-19. Indian Pediatrics. 2020; 57(7):680-1. [DOI:10.1007/s13312-020-1900-0] [PMID] [PMCID]

18. Belhadjer Z, Méot M, Bajolle F, Khraiche D, Legendre A, Abakka S, et al. Acute heart failure in multisystem inflammatory syndrome in children in the context of global SARS-CoV-2 pandemic. Circulation. 2020; 142(5):429-36. [DOI:10.1161/CIRCULATIONAHA.120.048360] [PMID]

19. Chiu JS, Lahoud-Rahme M, Schaffer D, Cohen A, Samuels-Kalow M. Kawasaki disease features and myocarditis in a patient with COVID-19. Pediatric Cardiology. 2020; 41(7):1526-8. [DOI:10.1007/s00246-020-02393-0] [PMID] [PMCID]

20. Schnapp A, Abulhija H, Maly A, Armoni-Weiss G, Levin Y, Faitatziadou SM, et al. Introductory histopathological findings may shed light on COVID-19 paediatric hyperinflammatory shock syndrome. Journal of the European Academy of Dermatology and Venereology. 2020; 34(11):e665-7. [DOI:10.1111/jdv.16749] [PMID] [PMCID]

21. Greene AG, Saleh M, Roseman E, Sinert R. Toxic shock-like syndrome and COVID-19: Multisystem Inflammatory Syndrome in Children (MIS-C). The American Journal of Emergency Medicine. 2020; 38(11):2492.e5-6. [DOI:10.1016/j.ajem.2020.05.117] [PMID] [PMCID]

22. Dolinger MT, Person H, Smith R, Jarchin L, Pittman N, Dubinsky MC, et al. Pediatric crohn disease and Multisystem Inflammatory Syndrome in Children (MIS-C) and COVID-19 treated with infliximab. Journal of Pediatric Gastroenterology and Nutrition. 2020; 71(2):153-5. [DOI:10.1097/MPG.0000000000002809] [PMID] [PMCID]

23. Cheung EW, Zachariah Ph, Gorelik M, Boneparth A, Kernie SG, Orange JS, et al. Multisystem inflammatory syndrome related to COVID-19 in previously healthy children and adolescents in New York City. JAMA. 2020; 324(3):294-6. [DOI:10.1001/jama.2020.10374] [PMID] [PMCID]

24. Whittaker E, Bamford A, Kenny J, Kaforou M, Jones CE, Shah P, et al. Clinical characteristics of 58 children with a pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2. JAMA. 2020; 324(3):259-69. [DOI:10.1001/jama.2020.10369] [PMID] [PMCID]

25. Blondiaux E, Parisot P, Redheuil A, Tzaroukian L, Levy Y, Sileo Ch, et al. Cardiac MRI in children with multisystem inflammatory syndrome associated with COVID-19. Radiology. 2020; 297(3):E283-8. [DOI:10.1148/radiol.2020202288] [PMID] [PMCID]

26. Belot A, Antona D, Renolleau S, Javouhey E, Hentgen V, Angoulvant F, et al. SARS-CoV-2-related paediatric inflammatory multisystem syndrome, an epidemiological study, France, 1 March to 17 May 2020. Eurosurveillance. 2020; 25(22):pii=2001010. [DOI:10.2807/1560-7917.ES.2020.25.22.2001010] [PMID] [PMCID]

27. Pouletty M, Borocco Ch, Ouldali N, Caseris M, Basmaci R, Lachaume N, et al. Paediatric multisystem inflammatory syndrome temporally associated with SARS-CoV-2 mimicking Kawasaki disease (Kawa-COVID-19): A multicentre cohort. Annals of the Rheumatic Diseases. 2020; 79(8):999-1006. [DOI:10.1136/annrheumdis-2020-217960] [PMID] [PMCID]

28. Ramcharan T, Nolan O, Lai CY, Prabhu N, Krishnamurthy R, Richter AG, et al. Paediatric Inflammatory Multisystem Syndrome: Temporally associated with SARS-CoV-2 (PIMS-TS): Cardiac features, management and short-term outcomes at a UK tertiary paediatric hospital. Pediatric Cardiology. 2020; 41(7):1391-401. [DOI:10.1007/s00246-020-02391-2] [PMID] [PMCID]

29. Waltuch T, Gill P, Zinns LE, Whitney R, Tokarski J, Tsung JW, et al. Features of COVID-19 post-infectious cytokine release syndrome in children presenting to the emergency department. The American Journal of Emergency Medicine. 2020; 38(10):2246.e3-6. [DOI:10.1016/j.ajem.2020.05.058] [PMID] [PMCID]

30. Rauf A, Vijayan A, John ST, Krishnan R, Latheef A. Multisystem inflammatory syndrome with features of atypical Kawasaki disease during COVID-19 pandemic. The Indian Journal of Pediatrics. 2020; 87(9):745-7. [DOI:10.1007/s12098-020-03357-1]

31. Kaushik Sh, Aydin SI, Derespina KR, Bansal PB, Kowalsky Sh, Trachtman R, et al. Multisystem Inflammatory Syn-

drome in Children associated with severe acute respiratory syndrome coronavirus 2 infection (MIS-C): A multi-institutional study from New York City. The Journal of Pediatrics. 2020; 224:24-9. [DOI:10.1016/j.jpeds.2020.06.045] [PMID] [PMCID]

32. Miller J, Cantor A, Zachariah Ph, Ahn D, Martinez M, Margolis KG. Gastrointestinal symptoms as a major presentation component of a novel multisystem inflammatory syndrome in children that is related to coronavirus disease 2019: A single center experience of 44 cases. Gastroenterology. 2020; 159(4):1571-4.E2. [DOI:10.1053/j.gastro.2020.05.079] [PMID] [PMCID]

33. Yozgat CY, Uzuner S, Bursal Duramaz B, Yozgat Y, Erenberk U, Iscan A, et al. Dermatological manifestation of pediatrics multisystem inflammatory syndrome associated with COVID-19 in a 3-year-old girl. Dermatologic Therapy. 2020; 33(4):e13770. [DOI:10.1111/dth.13770] [PMCID]

34. Toubiana J, Poirault C, Corsia A, Bajolle F, Fourgeaud J, Angoulvant F, et al. Kawasaki-like multisystem inflammatory syndrome in children during the COVID-19 pandemic in Paris, France: Prospective observational study. BMJ. 2020; 369:m2094. [DOI:10.1136/bmj.m2094] [PMID] [PMCID]

35. Grimaud M, Starck J, Levy M, Marais C, Chareyre J, Khraiche D, et al. Acute myocarditis and multisystem inflammatory emerging disease following SARS-CoV-2 infection in critically ill children. Annals of Intensive Care. 2020; 10:69. [DOI:10.1186/s13613-020-00690-8] [PMID] [PMCID]

36. Acharyya BC, Acharyya S, Das D. Novel coronavirus mimicking Kawasaki disease in an infant. Indian Pediatrics. 2020; 57(8):753-4. [DOI:10.1007/s13312-020-1924-5] [PMID] [PMCID]

37. Licciardi F, Pruccoli G, Denina M, Parodi E, Taglietto M, Rosati S, et al. SARS-CoV-2-induced Kawasaki-like hyperinflammatory syndrome: A novel COVID phenotype in children. Pediatrics. 2020; 146(2):e20201711. [DOI:10.1542/peds.2020-1711] [PMID]

38. Verdoni L, Mazza A, Gervasoni A, Martelli L, Ruggeri M, Ciuffreda M, et al. An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: An observational cohort study. The Lancet. 2020; 395(10239):1771-8. [DOI:10.1016/S0140-6736(20)31103-X]

39. Ng KF, Kothari T, Bandi S, Bird PW, Goyal K, Zoha M, et al. COVID-19 multisystem inflammatory syndrome in three teenagers with confirmed SARS-CoV-2 infection. Journal of Medical Virology. 2020; 92(11):2880-6. [DOI:10.1002/jmv.26206] [PMID] [PMCID]

40. Capone CA, Subramony A, Sweberg T, Schneider J, Shah S, Rubin L, et al. Characteristics, cardiac involvement, and outcomes of multisystem inflammatory syndrome of childhood associated with severe acute respiratory syndrome coronavirus 2 infection. The Journal of Pediatrics. 2020; 224:141-5. [DOI:10.1016/j.jpeds.2020.06.044] [PMID] [PMCID]

41. Abdel-Mannan O, Eyre M, Löbel U, Bamford A, Eltze Ch, Hameed B, et al. Neurologic and radiographic findings associated with COVID-19 Infection in children. JAMA Neurology. 2020; 77(11):1440-5. [DOI:10.1001/jamaneurol.2020.2687] [PMID] [PMCID]

42. Bapst T, Romano F, Müller M, Rohr M. Special dermatological presentation of paediatric multisystem inflammatory syndrome related to COVID-19: Erythema multiforme. BMJ Case Reports CP. 2020; 13(6):e236986. [DOI:10.1136/bcr-2020-236986] [PMID] [PMCID]

43. Rodriguez-Gonzalez M, Rodríguez-Campoy P, Sánchez-Códez M, Gutiérrez-Rosa I, Castellano-Martinez A, Rodríguez-Benítez A. New onset severe right ventricular failure associated with COVID-19 in a young infant without previous heart disease. Cardiology in the Young. 2020; 30(9):1346-9. [DOI:10.1017/S1047951120001857] [PMID] [PMCID]

44. Feldstein LR, Rose EB, Horwitz SM, Collins JP, Newhams MM, Son MBF, et al. Multisystem inflammatory syndrome in U.S. children and adolescents. The New England Journal of Medicine. 2020; 383(4):334-46. [DOI:10.1056/NEJMoa2021680]

45. Dufort EM, Koumans EH, Chow EJ, Rosenthal EM, Muse A, Rowlands J, et al. Multisystem inflammatory syndrome in children in New York State. The New England Journal of Medicine. 2020; 383(4):347-58. [DOI:10.1056/NEJMoa2021756] [PMID] [PMCID]

46. Dasgupta K, Finch SE. A case of pediatric multisystem inflammatory syndrome temporally associated with COVID-19 in South Dakota. South Dakota Medicine. 2020; 73(6):246-51. [PMID]

47. Perez-Toledo M, Faustini SE, Jossi SE, Shields AM, Kanthimathinathan HK, Allen JD, et al. Serology confirms SARS-CoV-2 infection in PCR-negative children presenting with paediatric inflammatory multi-system syndrome. medRxiv. 2020; June. [DOI:10.1101/2020.06.05.20123117]

48. Hameed Sh, Elbaaly H, Reid CEL, Santos RMF, Shivamurthy V, Wong J, et al. Spectrum of imaging findings at chest radiography, US, CT, and MRI in multisystem inflammatory syndrome in children associated with COVID-19. Radiology. 2020; 298(1):E1-10. [DOI:10.1148/radiol.2020202543] [PMID] [PMCID]

49. Riollano-Cruz M, Akkoyun E, Briceno-Brito E, Kowalsky Sh, Reed J, Posada R, et al. Multisystem inflammatory syndrome in children related to COVID-19: A New York City experience. Journal of Medical Virology. 2021; 93(1):424-33. [DOI:10.1002/jmv.26224] [PMID] [PMCID]

50. Horne A, Nordenhäll L. Hyperinflammation hos barn kan ha samband med COVID-19. [Severe inflammation in children: Cause for awareness during the current pandemic (Swedish)]. Lakartidningen. 2020; 117:20094. [PMID]

51. Rowley AH. Understanding SARS-CoV-2-related multisystem inflammatory syndrome in children. Nature Reviews Immunology. 2020; 20(8):453-4. [DOI:10.1038/s41577-020-0367-5] [PMID] [PMCID]

52. Dominguez SR, Anderson MS, El-Adawy M, Glodé MP. Preventing coronary artery abnormalities: A need for earlier diagnosis and treatment of Kawasaki disease. The Pediatric Infectious Disease Journal. 2012; 31(12):1217-20. [DOI:10.1097/INF.0b013e318266bcf9] [PMID]

This Page Intentionally Left Blank