

Kawasaki disease and multisystem inflammatory syndrome in children. Differences, and similarities in a pediatric center in Mexico.

Enfermedad de Kawasaki y síndrome inflamatorio multisistémico en niños. Diferencias y similitudes en un centro pediátrico de México

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Abstract

Objective: To evaluate the differences and similarities in clinical picture, laboratory findings and outcomes between children's with Kawasaki Disease (KD) *versus* multisystem inflammatory syndrome (MIS-C).

Methods: We conducted a retrospective, comparative study from children with Kawasaki Disease (KD) hospitalized in Sinaloa Pediatric Hospital from January 1, 2004, to March 31, 2020, and patients with multisystem inflammatory syndrome (MIS-C) according with World Health Organization (WHO) case definition criteria between May 1, 2020 and May 31, 2021. Demographic characteristics, epidemiological data, clinical features, laboratory findings, type of treatment and clinical outcomes were compared among both groups.

Results: Eighty-one patients were included (62 patients with KD and 19 with MIS-C). several clinical and laboratory differences were found among these two entities. Median age was lower in KD vs. MIS-C (25 vs 79 months). Those finding more frequent in KD were male gender (64.5 vs. 47.4%), Mucocutaneous features (93.5 vs. 63.2%); Oral changes (83.9 vs. 63.2%) and extremity changes (77.4 vs. 57.9%); complete form of KD was (75.8 vs. 47.4%), Coronary artery aneurysm (16.1 vs. 11.8%). Secondly, findings that were more frequent in MIS-C than KD were Gastrointestinal involvement (89.4 vs. 9.6%), shock (57.9 vs. 3.2%), neurological symptoms (63.1 vs. 11.2%), kidney involvement (52.6 vs. 16.1%), heart disease in general (52.9 vs 29%); Myocardial dysfunction (23.5 vs. 11.3%) and pericardial effusion (17.6 vs. 2.9%). Lymphocyte count (2.07 ± 2.03 vs. $4.28 \pm 3.01/\text{mm}^3$), platelet count (197.89 ± 187.51 vs. $420.37 \pm 200.08/\text{mm}^3$); serum albumin (2.29 ± 0.65 vs. $3.33 \pm 0.06/\text{g/dL}$), and CPR (21.4 ± 11.23 vs. $14.26 \pm 12.37 \text{ mg/dL}$). KD vs. MIS-C types of Treatment: IVIG (96.8 vs. 94.7%), systemic steroids (4.82 vs. 94.7%), IVIG resistance (19.4 vs. 15.8). Finally, mortality in KD was 0% and 5.3% in MIS-C.

Conclusion: Similarities were found in both groups such as fever, rash, and conjunctivitis. Nevertheless, significant differences such as severity of clinical presentation with multi-organ involvement and worst inflammatory response were found more frequently in MIS-C group than KD group, requiring more fluid replacement, use of inotropic agents and higher steroids dosages. Also, mortality rate was higher in patients with MIS-C than patients with KD. Similar results have been observed in other studies where both disorders were compared.

Key words: Multisystem inflammatory syndrome in children; Kawasaki disease; SARS-CoV-2; COVID-19.

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Resumen

Objetivo: Evaluar las diferencias y similitudes en el cuadro clínico, los hallazgos de laboratorio y desenlaces médicos de pacientes pediátricos con enfermedad de Kawasaki *versus* síndrome inflamatorio multisistémico.

Métodos: Estudio comparativo y retrospectivo, efectuado en niños con enfermedad de Kawasaki, atendidos en el Hospital Pediátrico de Sinaloa, entre el 1 de enero de 2004 al 31 de marzo de 2020, y pacientes con síndrome inflamatorio multisistémico (según los criterios de la Organización Mundial de la Salud), del 1 de mayo de 2020 al 31 de mayo de 2021. Se evaluaron las características demográficas, epidemiológicas y clínicas, además de los hallazgos de laboratorio, tipo de tratamiento y desenlaces clínicos en ambos grupos.

Resultados: Se incluyeron 81 pacientes: 62 con enfermedad de Kawasaki y 19 con síndrome inflamatorio multisistémico. Se encontraron varias diferencias clínicas y de laboratorio en ambas alteraciones. La mediana de edad fue menor en pacientes con enfermedad de Kawasaki *versus* síndrome inflamatorio multisistémico (25 *vs* 79 meses). La mayoría de los pacientes con enfermedad de Kawasaki fueron hombres (64.5 *vs* 47.4%), con características mucocutáneas (93.5 *vs* 63.2%); cambios orales (83.9 *vs* 63.2%) y cambios en las extremidades (77.4 *vs* 57.9%); la forma completa de enfermedad de Kawasaki fue 75.8 *vs* 47.4%, concomitante con aneurisma de la arteria coronaria (16.1 *vs* 11.8%). Los hallazgos más frecuentes en sujetos con síndrome inflamatorio multisistémico fueron: afectación gastrointestinal (89.4 *vs* 9.6%), choque (57.9 *vs* 3.2%), síntomas neurológicos (63.1 *vs* 11.2%), afectación renal (52.6 *vs* 16.1%) y cardiopatías en general (52.9 *vs* 29%): disfunción miocárdica (23.5 *vs* 11.3%) y derrame pericárdico (17.6 *vs* 2.9%). La concentración media de linfocitos fue: 2.07 + 2.03 *vs* 4.28 + 3.01/mm³, plaquetas (197.89 + 187.51 *vs* 420.37 + 200.08/mm³); albúmina sérica (2.29 + 0.65 *vs* 3.33 + 0.06 g/dL) y PCR (21.4 + 11.23 *vs* 14.26 + 12.37 mg/dL). Los tratamientos en enfermedad de Kawasaki *vs* síndrome inflamatorio multisistémico: IVIG (96.8 *vs* 94.7%), corticosteroides sistémicos (4.82 *vs* 94.7%), resistencia a IVIG (19.4 *vs* 15.8). La mortalidad fue de 0 *vs* 5.3%.

Conclusión: Se encontraron similitudes en cuanto a síntomas en ambos grupos (fiebre, exantema y conjuntivitis); no obstante, hubo diferencias significativas respecto de las manifestaciones clínicas, con afección multiorgánica y peor respuesta inflamatoria en pacientes con síndrome inflamatorio multisistémico, incluso mayor requerimiento de reposición de líquidos, administración de agentes inotrópicos, dosis más altas de corticosteroides, y elevada tasa de mortalidad. Estos resultados se han observado en otros estudios, donde se compararon ambos trastornos.

Palabras clave: Síndrome inflamatorio multisistémico en niños; enfermedad de Kawasaki; SARS-CoV-2; COVID-19.

INTRODUCTION

A new entity called MIS-C related to SARS-CoV-2 was reported at the end of April 2020 in Italy and the United Kingdom respectively.^{1,2} Subsequently, The Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO) issued criteria for case definitions for diagnosis of this new disease.^{3,4} Although it is true that KD already had case definition criteria established on September 6, 2016, by the American Heart Association (AHA), where fever and mucocutaneous were part of case definition. Several KD criteria are included in MIS-C, in addition to fever and mucocutaneous signs like the involvement of two or more systems, elevation of inflammatory markers,

past or current infection by SARS-CoV-2 and exclusion of other diseases.

Since then, similarities among both inflammatory disorders had become evident. Overall, MIS-C seems to overlap with KD, but both share the same trigger for an inflammatory febrile reaction, mucocutaneous signs, cardiovascular manifestation, and elevation of inflammatory markers in genetically susceptible children. Also, intravenous immunoglobulin (IVIG) forms part of treatment in both entities.⁵ The most outstanding differences between MIS-C and KD are *a)* older age of presentation; *b)* a deeper inflammatory response; *c)* more gastrointestinal involvement; *d)* other laboratory abnormalities including lymphopenia, thrombocyto-



penia; elevated levels of troponin, NT-pro-BNP, D-dimer, fibrinogen, and ferritin and 5) higher propensity to LV dysfunction and shock compared to KD patients.⁶

The Objective of this study is to compare the differences and similarities in clinical picture, laboratory findings and outcomes between these two entities admitted in a referral pediatric hospital located in north-western Mexico.

METHODS

A retrospective, observational, and comparative study was made, of children with Kawasaki disease hospitalized in a referral pediatric center in Northwestern Mexico, Hospital Pediátrico de Sinaloa “Dr. Rigoberto Aguilar Pico” from January 1, 2004, to March 31, 2020,⁷ and patients with MIS-C based on the WHO case definition criteria³ between May 1, 2020, and May 31, 2021 (**Table 1**). Demographic features, epidemiological data, laboratory tests, cardiologic findings, treatment, and clinical outcomes were compared in both groups.

Complete and incomplete KD were identified according to the American Heart Association (AHA) case definition.⁸ Probable cases of MIS-C were identified and evaluated to determine if they met the WHO case definition criteria³ (**Table 1**). Patients were excluded if they had another plausible explanation for the illness.

Data were collected retrospectively from all patients who met the criteria for KD and MIS-C, including demographic data, clinical manifestations, laboratory findings, medical treatment, and outcome. For laboratory findings, the worst value within the first three days upon admission was chosen for analysis.

All patients admitted for MIS-C underwent RT-PCR for SARS-CoV-2 from nasal swabs, as well as serum IgM and IgG. Cardiac involvements were recorded as positive in the presence of any of the following echocardiogram findings: Myocardial depression (left ventricular ejection fraction, LVEF < 55%), pericarditis, valvular dysfunction/valvulitis, coronary aneurysm (coronary artery diameter z-score ≥ 2.5), or coronary dilation (z-score > 2 - < 2.5). The different therapeutic modalities used were also compared, such as: Use of IVIG, systemic steroids, therapy with immunomodulators, inotropes and vasopressors, anticoagulant therapy, admission to the intensive care unit and invasive mechanical ventilation. Patients were defined as resistant to IVIG if they had persistent or recurrent fever at least 36 h after completing the first dose of IVIG. Those markers that were not recorded in more than 20% of the medical records were not analyzed.

Statistical analysis

Categorical variables were compared with the Chi-square test to identify differences among both group

Table 1. Case definition of MIS-C, World Health Organization (WHO)

Terminology	Multisystem inflammatory disorder in children and adolescents
Age	0 – 19 years
Clinical case definition	Fever > 3 days and 2 of the following: (i) Rash or bilateral non-purulent conjunctivitis or mucocutaneous signs (oral, hands or feet) (ii) Hypotension or shock (iii) Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including echocardiography findings or elevated Troponin/NT-pro-BNP) (iv) Evidence of coagulopathy (by PT, APTT, elevated D-dimers) (v) Acute gastrointestinal problems (diarrhea, vomiting, or abdominal pain)
Laboratory criteria of inflammation	Elevated ESR, CRP, or procalcitonin
Evidence of SARS-CoV-2 infection	Evidence of COVID-19 infection (RT-PCR, antigen test or serology positive), or likely contact with patients with COVID-19
Exclusion of other microbial cause	No other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes

CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; RT-PCR: reverse transcription-polymerase chain reaction; APTT: Activated partial thromboplastin time; PT: prothrombin time.

of patients with MIS-C and KD. To compare continuous variables, Analysis of Variance Test (ANOVA) was used to find the mean values and the differences between the groups. For all analyses, a 2-sided probability <0.05 was considered statistically significant. All analyzes were performed with SPSS version 25.0 software. The study was approved by the ethics committee of the “Hospital Pediátrico de Sinaloa”.

RESULTS

Eighty-one patients were included in this study (62 patients with KD and 19 with MIS-C). **Table 2**

SARS-CoV-2 infection associated with MIS-C patients were confirmed in 89.4% including: confirmed/suspected contact within four weeks. Nasopharyngeal RT-PCR for SARS-CoV-2 was positive in 21%, serology test with IgM negative and IgG was positive in 84.5%. Prior to arrival at the emergency room, 70% had more than 2 medical evaluations, 74% received treatment with 1 - 2 antibiotics and/or antivirals.

Median age was lower in KD vs MIS-C (25 vs. 79 months, $p < 0.001$), male sex was more frequent in KD vs MIS-C (64.5 vs 47.4%), fever was present in 100% of patients in both groups. The median for duration of fever in KD was 8.44 ± 8.06 days and in MIS-C was 6.63 ± 4.56 days ($p = 0.356$). We do not know days of stay for KD patients but for MIS-C patients the mean of days was 10.2 (3-39 days). Four patients were obese, and one patient had Down syndrome.

Mucocutaneous features were higher in KD vs MIS-C as rash (93.8 vs 63.2%); conjunctivitis (85.5 vs 78.9%); oral changes (82.3 vs 63.2%); and extremity changes (77.4 vs 57.9%). The complete form of KD was observed 75.8 vs 47.4% in MIS-C.

Other manifestations were higher in MIS-C over KD as gastrointestinal involvement (89.4 vs. 9.6%, $p < 0.001$), acute abdomen in 68.4% (four patients required surgery), shock (57.9 vs 3.2%); neurological symptoms (63.1 vs 11.2%) and kidney involvement (52.6 vs 16.1%).

Unlike KD, MIS-C required more complex management as admission to the intensive care unit 63.2 vs 0%; mechanical ventilation 15.7 vs 0% ($p = 0.014$);

Table 2. Comparison between patients with KD and MIS-C

Variables	KD (n = 62)	MIS-C (n = 19)	p
Demographic characteristics			
Median age, months (min-max)	25 (3- 96)	79 (4-192)	0.001
Sex	64.5	47.4	0.125
male (%)	22.6	15.8	0.389
< 12 months (%)			
Clinical characteristics			
SARS-CoV-2 association (%)	NA	89.4	
Epidemiological contact (confirmed)	-	23.6	--
Epidemiological contact (suspected)	-	47.3	--
Positive RT-PCR %	-	21	--
Positive serology IgM	-	0	--
Positive serology IgG	-	84.2	--
COVID-19 infection	-	21	--
Kawasaki disease features			
KD complete (%)	75.8	47.4	0.021
KD incomplete (%)	24.2	21.1	0.523
Conjunctivitis (%)	85.5	78.9	0.359
Cervical adenopathy (%)	58.1	52.6	0.437
Oral changes (%)	83.9	63.2	0.057
Rash (%)	93.5	63.2	0.003
Extremity changes (%)	77.4	57.9	0.086
Clinical symptoms			
Days of fever (Main) $\pm$ SD	8.44 ± 8.06	6.63 ± 4.56	0.356
Fever (%)	100	100	-
Gastrointestinal (%)	9.6	89.4	0.001
Vomiting / diarrhea	3.2	84.2	0.001
Abdominal pain	8.1	68.4	0.001
Cardiovascular (%)	29	52.9 (n = 17)	0.062
Myocardial dysfunction	11.3	23.5 (n = 17)	0.182
Pericardial effusion	3.2	17.6 (n = 17)	0.064
CAA	29	17.6 (n = 17)	0.270
Aneurism	19.4	11.8 (n = 17)	0.373
Kidney (%)	16.1	52.6	0.001
Neurologic (%)	11.2	63.1	0.002
Respiratory	NA	21.1	-
BCG reaction (%)	4.8	21.1	0.049
Treatment and Outcome (%)			
IVIG, 2gkg	96.8	94.7	0.557
Second dose IVIG	19.4	15.8	0.511
Steroids (%)	4.82	94.7	0.001
High dose (%)	1.6	44.4	0.001
IV pulse (%)	3.22	52.6	0.001
Second pulse steroids	0	15.8	0.011
Biologic therapy	0	10.5	0.053
Anticoagulation therapy	1.6	36.8	0.001
Low blood pressure	3.2	57.9	0.001
Mechanical ventilation	0	15.8	0.014
Fluid resuscitation	3.2	68.4	0.001
Inotropic therapy	1.6	52.6	0.001
Albumin therapy	4.8	52.6	0.001
Death	0	5.3	0.235

KD: Kawasaki disease; MIS-C: multisystem inflammatory syndrome in children; RT-PCR: Reverse transcription polymerase chain reaction; CAA: Coronary artery abnormalities; BCG: Calmette-Guerin Bacilli; IVIG: Intravenous immunoglobulin.

fluid resuscitation 68.4 vs 3.2% ($p < 0.001$); inotropic therapy 52.6 vs 1.6% ($p < 0.001$) and biological therapy 10.5 vs 0% ($p = 0.053$). Overall cardiac involvement also was observed more in MIS-C 52.9 vs 29% in KD ($p = 0.062$), myocardial dysfunction (23.5 vs 11.8%, $p = 0.182$) and pericardial effusion (21.1 vs 2.9%, $p = 0.064$) were higher in MIS-C than in KD. Pneumonia was documented in 10.5% of MIS-C cases. Only Coronary artery aneurysm was more common in KD 19.4% vs 11.8% ($p = 0.373$) in MIS-C.

Laboratory findings in MIS-C (**Table 3**) were lower in total lymphocyte count (2.07 ± 2.03 vs $4.28 \pm 3.01/\text{mm}^3$, $p = 0.004$), platelet count (197.89 ± 187.51 vs $420.37 \pm 200.08/\text{mm}^3$, $p < 0.001$); albumin serum (2.29 ± 0.65 vs $3.33 \pm 0.06\text{g/dL}$) than KD. The other hand, inflammatory markers were higher in MIS-C than KD; CPR (21.4 ± 11.23 vs $14.26 \pm 12.37\text{ mg/dL}$, $p = 0.034$). In MIS-C, chest ray and TC showed abnormalities in 52.6%, sonography and TC abdominal were abnormal in 31.5% of cases.

Treatment with intravenous immunoglobulin (IVIG) was 96.7 vs, 94.7%, in KD vs. MIS-C, IVIG resistance 19.3 vs 15 respectively. Systemic steroids were the opposite, 4.82 vs 94.7% ($p < 0.001$). Patients with MIS-C required other interventions such as supplemental oxy-

gen (53%), antibiotic therapy (cefotaxime, vancomycin, meropenem, metronidazole), albumin serum (47.4%), and antiviral therapy in 21.4%. In KD, two patients with shock syndrome were documented (3.2%), in MIS-C two cases (10.5%) developed Macrophage activation syndrome. Mortality in KD was 0 vs 5.3% in MIS-C.

DISCUSSION

MIS-C has been published in different pediatric centers worldwide, allowing to know the epidemiological, clinical data, treatment, and results in the short and medium term, characterizing the spectrum of severity.

Due to post-infectious nature of MIS-C, triggered by a viral infection and characterized by an hyperinflammatory and/or autoimmune state, where the clinical manifestations and severity of the immune response depends on genetically predisposed host⁹⁻¹¹ compared to typical proinflammatory signature in KD due to an increase in levels of IL-1, 8, 6, 17A and INF γ may explain the clinical features differences among these two entities. Patients with MIS-C are characterized for increased and greater intensity with predominance of lymphopenia of CD4⁺,¹² marked increased acute inflammatory reactants such as CRP, procalcitonin, ferritin, fibrinogen, D-dimer, BNP and, troponin.^{13,14}

Table 3. Laboratory features in patients with KD and MIS-C

Laboratory test $\pm$ SD	KD (n = 62)	MIS-C (n = 19)	p
Hemoglobin (g/dL)	10.89 $\pm$ 1.36 (n=61)	10.32 $\pm$ 2.62	0.217
WBC (x 103/mL)	17.93 $\pm$ 7.41 (n=61)	14.49 $\pm$ 3.58	0.055
Neutrophil count (x 103/mL)	12.23 $\pm$ 6.25 (n=59)	11.11 $\pm$ 4.31	0.470
PMN (%)	66.57 $\pm$ 15.2 (n=59)	75.01 $\pm$ 21.15	0.470
Lymphocyte count (x 103/mL)	4.28 $\pm$ 3.01 (n=59)	2.07 $\pm$ 2.03	0.004
Platelet count (x 103/mL)	420.37 $\pm$ 200.08 (n=61)	197.89 $\pm$ 187.51	0.001
ESR (mm/hr)	46.75 $\pm$ 13.69 (n=41)	50.66 $\pm$ 11.96 (n = 15)	0.333
CRP (mg/dL)	14.26 $\pm$ 12.37 (n=53)	21.4 $\pm$ 11.23 (n = 18)	0.034
Procalcitonin (ng/mL)	ND	11.75 $\pm$ 12.59 (n = 17)	--
Ferritin (ng/mL)	ND	946.81 $\pm$ 975.35 (n = 12)	--
Fibrinogen (mg/dL)	ND	406.66 $\pm$ 126.9 (n = 12)	--
NT-pro-BNP (pg/mL)	ND	2709.25 $\pm$ 3185.77 (n = 11)	--
Troponin (ng/L)	ND	19.16 $\pm$ 32.04 (n = 15)	--
D-dimer (ng/mL)	ND	2.52 $\pm$ 1.73 (n = 15)	--
Albumin (g/L)	3.33 $\pm$ 0.06 (n = 25)	2.29 $\pm$ 0.65	0.307
Na (mEq/L)	136.38 $\pm$ 2.63 (n = 39)	135.62 $\pm$ 4.81	0.446
LDH (U/L)	455.47 $\pm$ 261.33 (n = 36)	336.44 $\pm$ 170.21 (n = 18)	0.086
ALT (IU/L)	71.98 $\pm$ 77.07 (n = 51)	70.27 $\pm$ 97.01 (n = 18)	0.940

KD: Kawasaki disease; MIS-C: multisystem inflammatory syndrome in children; WBC: White blood cells; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; AST: Aspartate aminotransferase; ALT: alanine aminotransferase; LDH: Lactate dehydrogenase; N/D: Not disponible; NT-pro-BNP: N-terminal pro hormone B-type natriuretic peptide.

Our report provides information on the differences and similarities between these two entities that are consistent with the findings described by several other authors.¹⁵⁻²⁰ **Table 4**

Forty seven percent of patients with MIS-C met the KD, and 21.1% incompletely KD, Feldstein et al. reports 20.4% and 19.3% respectively (n = 186), while McArdle et al., 36.6% and 30.2%, respectively (n = 614).^{21,22} In addition to fever, the most common mucocutaneous signs were conjunctivitis 78.9%, oral changes, and rash 63.2%, McArdle et al., reported 59.4%, 65.5%, and 53.3%, respectively.²² In our KD patients, the most common mucocutaneous sign was rash 93.8%, conjunctivitis (85.5%) and oral changes 82.3%.

Gastrointestinal involvement in the MIS-C group was 89.4 vs 9.6% (p < 0.001) in KD group; CNS 63.1 vs. 11.2% (p = 0.002); cardiovascular 52.9 vs. 29% (p = 0.062); and kidney 52.6 vs 16.1% (p < 0.001) respectively. Data like those reported by other authors comparing MIS-C vs KD, Gastrointestinal involvement 60-100% vs 15-33%; cardiovascular 50 -87 vs 29%, and CNS 22-37% vs 8.5-40.6%, respectively.¹⁵⁻²⁰

Coronary artery abnormalities in the MIS-C group were 17.6 vs 29% in the KD group (p = 0.270), while the presence of coronary aneurysms in MIS-C was 11.7 vs 19.3% (p = 3.73) in KD.¹⁵⁻²⁰

Relevant hematologic findings were a lymphocyte count in the MIS-C group of 2.07 ± 2.03 vs 4.28 ± 3.01 ($\times 10^9/\mu\text{L}$) in the KD group (p = 0.004), the platelet count was 197.89 ± 187.51 vs 420.37 ± 200.08 ($\times 10^9/\mu\text{L}$) (p = 0.001); CRP levels 21.4 ± 11.23 vs 14.26 ± 12.37 (mg/dL) (p = 0.034); respectively, similar to that reported by other authors.^{15-20,23-25}

Other relevant hematological findings seen in MIS-C group but not in KD group, because they were not performed as routine studies for KD, were elevated levels of ferritin, fibrinogen, D-dimer, and NT-pro-BNP. Low levels of serum albumin are consistent data as reported in other studies.^{15-20,23-25}

IVIG treatment in the MIS-C group was 88.9 vs 96.7% in KD, systemic steroids 97 vs 4.82% (p < 0.001) IVIG resistance 15.7 vs 19.3% (p = 0.511); steroid second dose 16.7 vs 0% (p = 0.011); fluid resuscitation 68.4 vs 3.2% (p < 0.001); inotropic therapy 52.6 vs 1.6% (p < 0.001); anticoagulation therapy 36.8 vs 1.6% (p < 0.001), and biological therapy 20 vs 0%, respectively (p = 0.002).

Worldwide IVIG treatment in MIS-C was administrated in 50% to 100% of patients and systemic steroid between 10 to 80% of patients, meanwhile in KD IVIG treatment was 80 to 100% and systemic steroid <15%.^{15-20,23-25}

In our study mortality was 5.3% for MIS-C patients and 0% for KD group (p = 0.235). Overall, the mortality rate in MIS-C varies from 2.1% to 18% comparative greater than mortality in KD (<1%).^{15-20,23-25}

CONCLUSION

Both entities share overlapping clinical and inflammatory similarities, with a profile characterized by increased inflammation, multisystem involvement, complications, severity, and mortality. Both may require treatment with IVIG, systemic steroids, intensive care, inotropic therapy, mechanical ventilation, ECMO, and biological therapy, being more frequent in patients with MIS-C. Like all KD centers, we see an increase in the number of MIS-C cases, particularly in covid-19 waves of infection.

**Table 4.** Main differences and similarities of KD and MIS-C

Variables	Bar-Meir, et al		GO Yener, et al		QY Zhang, et al		Sahoo, et al		Cattalini, et al		Sole, et al	
	KD (n = 13)	KD/MIS-C (n = 5)	MIS-C (n = 10)	KD (n = 59)	MIS-C (n = 154)	KD (n = 154)	KD (n = 154)	MIS-C (n = 154)	KD (n = 96)	MIS-C (n = 53)	KD (n = 14)	MIS-C (n = 14)
Age (months)	18 (5-36)	36 (24-193)	136 (60-204)	36 (6-174)	98.4 (12-240)	<60 (75%)	72-120	2 (1.5 - 3.6)	24 (12-48)	84 (54-132)	24 (6-72)	34-56 (3-168)
Male sex (%)	54	20	60	35.5	34.4	Male	M:F 1.5:1	70	60	4	57	50
Duration of fever (days)	5.8 + 2	4.4 + 2	3.7 + 1	8	5			6	4		5.5	6
Shock (%)	0	60	60			2-7%	33-87	1	37.8	21.4	21.4	21.4
Cardiac involvement (%)				17.1	50.6	rare	18-87					
Gastrointestinal involvement (%)	15	40	90	25.4	72.7	rare	60-100		33.3	96.2	42.9	85.7
Neurological involvement (%)				8.5	22.1			40.6	37.7	0	35.7	
Renal involvement (%)				3.4	8.4							
Lymphocytes ($\times 103/\mu\text{L} \pm \text{SD}$)	5.6 + 4	1.5 + 1	0.7 + 0.5	1.7	0.95	rare	37-81% (< 1500)	2750	0.939	0.94	5.55	1.95
Platelets ($\times 103/\mu\text{L} \pm \text{SD}$)	518 + 365	260 + 109	136 + 81	355	173	Increased	Decreased	346.5	177	186	440	232.5
Na (mEq/L)	135 + 1.8	134 + 3	134 + 4.5								136	136.5
Albumin (g/dL)	3.6 + 0.4	3.0 + 0.5	3.1 + 0.6	3.3	3.1			4.3	2.9		3.55	3.5
ALT	62 + 71	80 + 119	52 + 46	28	19			29	27		18	26.5
ESR, mm/hr				57	40			61.5	44		34.5	18.5
CPR (mg/dL)	13 + 7	16 + 4	18 + 8	6.4	15.1			6	21		11.69	15.62
Procalcitonin (ng/mL)				3	2.6						0.6	2.28
D-dimer (mcg/mL)	1.638 + 0.108	1.455 + 2.511	2.372 + 2.22	1.7	2.7	Significantly increase	Normal	ND	1.94	2.514	NA	4.32
Fibrinogen (mg/dL)	952	699 + 187	688 + 212	644	482				570.5	643		
BNP, pg/mL (nL < 100)			799 + 37	55	1108	Mild increased	Marked increased	ND	33		1445	3102
CAA (%)	30.7	40	0		17.5	4	14-36	50	28.1	13.2	7.1	21.4

KD: Kawasaki disease; MIS-C: multisystem inflammatory syndrome in children.

1. Riphagen S, Gomez X, Gonzalez-Martinez C, Wilkinson N, et al. Hyperinflammatory shock in children during COVID-19 pandemic. *Lancet* 2020; 395 (10237): 1607-1608. DOI: 10.1016/S0140-6736(20)31094-1
2. Verdoni L, Mazza A, Gervasoni A, Martelli L, 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. DOI: 10.1016/s0140-6736(20)31103-x
3. World Health Organization. Multisystem inflammatory syndrome in children and adolescents temporally related to COVID-19. Available from: <https://www.who.int/news-room/commentaries/detail/multisystem-inflammatory-syndrome-in-children-and-adolescents-with-covid-19>.
4. US Centers for Disease Control and Prevention. Multisystem inflammatory syndrome in children (MIS-C) associated with coronavirus disease 2019 (COVID-19) [Internet]. 2020. <https://emergency.cdc.gov/han/2020/han00432.asp>.
5. Whittaker E, Bamford A, Kenny J, et al. Clinical Characteristics of 58 Children With a Pediatric Inflammatory Multisystem Syndrome Temporally Associated With SARS-CoV-2. *JAMA* 2020. DOI: 10.1001/jama.2020.10369
6. Loke YH, Berul CI, Harahsheh AS. Multisystem inflammatory syndrome in children: Is there a linkage to Kawasaki disease? *Trends Cardiovasc Med* 2020; 30 (7): 389-396. doi: 10.1016/j.tcm.2020.07.004.
7. García-Domínguez M, Quíbrera J, Canizales-Muñoz S, et al. Enfermedad de Kawasaki, casos diagnosticados en dos hospitales pediátricos en México de enero de 2004 a marzo de 2020. *Alerg Asma Inmunol Pediatr* 2021; 30 (2): 37-42. doi: 10.35366/101640.
8. McCrindle BW, Rowley AH, Newburger JW, Burns JC, 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 (17): e927-e999. doi: 10.1161/cir.0000000000000484
9. Matucci-Cerinic C, Caorsi R, Consolaro A, Rosina S et al. Multisystem Inflammatory Syndrome in Children: Unique Disease or Part of the Kawasaki Disease Spectrum? *Front Pediatr* 2021; 9: 680813. doi: 10.3389/fped.2021.680813.
10. Ravelli A, Martini A. Kawasaki disease or Kawasaki syndrome? *Ann Rheum Dis* 2020; 79 (8): 993-995. doi: 10.1136/annrheumdis-2020-218110
11. Lee PY, Day-Lewis M, Henderson LA, Friedman KG, et al. Distinct clinical and immunological features of SARS-CoV-2-induced multisystem inflammatory syndrome in children. *J Clin Invest* 2020; 130 (11): 5942-5950. doi: 10.1172/JCI141113

12. Sharma C, Ganigara M, Galeotti C, Burns J, et al. Multisystem inflammatory syndrome in children and Kawasaki disease: a critical comparison. *Nat Rev Rheumatol* 2021; 17 (12): 731-748. doi: 10.1038/s41584-021-00709-9
13. Sancho-Shimizu V, Brodin P, Cobat A, Biggs CM, et al. SARS-CoV-2-related MIS-C: A key to the viral and genetic causes of Kawasaki disease? *J Exp Med* 2021; 218 (6): e20210446. doi: 10.1084/jem.20210446.
14. Kabeerdoss J, Pilania RK, Karkhele R, Kumar TS, et al. Severe COVID-19, multisystem inflammatory syndrome in children, and Kawasaki disease: immunological mechanisms, clinical manifestations and management. *Rheumatol Int.* 2021; 41 (1): 19-32. doi: 10.1007/s00296-020-04749-4
15. Bar-Meir M, Guri A, Godfrey ME, Shack AR, et al. Characterizing the differences between multisystem inflammatory syndrome in children and Kawasaki disease. *Sci Rep* 2021; 11 (1): 13840. doi: 10.1038/s41598-021-93389-0.
16. Otari Yener G, Paç Kisaarslan A, Ulu K, Atalay E, et al Differences and similarities of multisystem inflammatory syndrome in children, Kawasaki disease and macrophage activating syndrome due to systemic juvenile idiopathic arthritis: a comparative study. *Rheumatol Int* 2022; 42 (5): 879-889. doi: 10.1007/s00296-021-04980-7.
17. Zhang QY, Xu BW, Du JB. Similarities and differences between multiple inflammatory syndromes in children associated with COVID-19 and Kawasaki disease: clinical presentations, diagnosis, and treatment. *World J Pediatr* 2021; 17 (4): 335-340. doi: 10.1007/s12519-021-00435-y.
18. Sahoo D, Katkar GD, Shimizu C, Kim J, et al. Pediatric Emergency Medicine Kawasaki Disease Research Group, Bocchini J, Das S, Burns JC, Ghosh P. An AI-guided signature reveals the nature of the shared proximal pathways of host immune response in MIS-C and Kawasaki disease. *bioRxiv [Preprint]*. 2021. doi: 10.1101/2021.04.11.439347
19. Cattalini M, Della Paolera S, Zunica F, Bracaglia C, et al; Rheumatology Study Group of the Italian Pediatric Society. Defining Kawasaki disease and pediatric inflammatory multisystem syndrome-temporally associated to SARS-CoV-2 infection during SARS-CoV-2 epidemic in Italy: results from a national, multi-center survey. *Pediatr Rheumatol Online J.* 2021; 19 (1): 29. doi: 10.1186/s12969-021-00511-7
20. Esteve-Sole A, Anton J, Pino-Ramirez RM, Sanchez-Manubens J, et al. Similarities and differences between the immunopathogenesis of COVID-19-related pediatric multisystem inflammatory syndrome and Kawasaki disease. *J Clin Invest* 2021; 131 (6): e144554. doi: 10.1172/JCI144554
21. Feldstein LR, Rose EB, Horwitz SM, Collins JP, et al; Overcoming COVID-19 Investigators; CDC COVID-19 Response Team. Multisystem Inflammatory Syndrome in U.S. Children and Adolescents. *N Engl J Med* 2020; 383 (4): 334-346. doi: 10.1056/NEJMoa2021680
22. McArdle AJ, Vito O, Patel H, Seaby EG, et al; BATS Consortium. Treatment of Multisystem Inflammatory Syndrome in Children. *N Engl J Med* 2021; 385 (1): 11-22. doi: 10.1056/NEJMoa2102968.
23. Chen MR, Kuo HC, Lee YJ, Chi H, et al. Phenotype, Susceptibility, Autoimmunity, and Immunotherapy Between Kawasaki Disease and Coronavirus Disease-19 Associated Multisystem Inflammatory Syndrome in Children. *Front Immunol* 2021; 12: 632890. doi: 10.3389/fimmu.2021.632890.
24. Loke YH, Berul CI, Harahsheh AS. Multisystem inflammatory syndrome in children: Is there a linkage to Kawasaki disease? *Trends Cardiovasc Med* 2020; 30 (7): 389-396. doi: 10.1016/j.tcm.2020.07.004.
25. Lee MS, Liu YC, Tsai CC, Hsu JH, et al. Similarities and Differences Between COVID-19-Related Multisystem Inflammatory Syndrome in Children and Kawasaki Disease. *Front Pediatr* 2021; 9: 640118. doi: 10.3389/fped.2021.640118.



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