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Multisystem inflammatory syndrome in children: a narrative review

Síndrome inflamatorio multisistémico en niños: una revisión narrativa

Maisa Flores Yumbato[1] ✉, Rut Pardave Ambicho[1], Eliana Alarcón Herrera[1], Alisson Gomez Orosco[1], Víctor Álvarez-Manrique[1]

[1]Escuela Profesional de Enfermería, Facultad de Ciencias de la Salud, Universidad Peruana Unión, Tarapoto, Perú

Corresponding author: Maisa Flores Yumbato ✉

ABSTRACT

Objective: to conduct a literature review on multisystem inflammatory syndrome in children, focusing on cardiac involvement, complications, and manifestations.
Method: literature review based on narrative synthesis. Data sources: Scopus, ScienceDirect, SciELO, PubMed, Web of Science. *Data selection*: Documents were selected and analyzed using a critical literature review, considering inclusion and exclusion criteria.
Results: a corpus of 22 articles was analyzed, of which 12 were retrospective, 6 prospective, 5 descriptive, 4 observational, and 2 cross-sectional. The study population included children under 8 years of age, adolescents, young adults, and adults, as well as general population registries in countries with diverse contexts. The studies were conducted in various countries, such as Mexico, the USA, Europe, India, Peru, Uruguay, Jordan, Spain, Argentina, Japan, Australia, China, and Brazil, each contributing a unique perspective to the research. The clinical condition of the participants in the studies seven articles analyzed the results—included fever, gastrointestinal symptoms, elevated troponin, cardiac involvement, respiratory distress and abdominal pain, hypoxia, shock, multi-organ dysfunction, coronary dilation, hypotension, elevated procalcitonin, tachycardia. Regarding socioeconomic status, some of the studies were conducted in low- and middle-income countries, reflecting improved access to and effectiveness in the diagnosis of multisystem inflammatory syndrome in children.
Conclusion: MIS-C represents a severe hyperinflammatory syndrome with multisystem involvement, especially cardiac and gastrointestinal, which can progress to shock and multi-organ failure. Its management requires early diagnosis, hemodynamic monitoring, and combined immunomodulatory therapy to improve prognosis and prevent long-term sequelae in the pediatric population.

Keywords: MIS-C; Pediatric Shock; Kawasaki Disease.

RESUMEN

Objetivo: realizar una revisión literatura sobre el síndrome inflamatorio multisistémico en niños, basándose en afectación cardiaca, complicaciones y manifestaciones.
Method: revisión de la literatura basado en una síntesis narrativa. *Fuentes de datos*: Scopus, Science direct, Scielo, Pubmed, Web of Science. *Selección de datos*: Los documentos fueron seleccionados y analizados bajo una revisión crítica de literatura tomando en cuenta los criterios

de inclusión y de exclusión.
Resultados: se analizó un corpus de 22 artículos de los cuales 12 son retrospectivo, 6 prospectivo, 5 descriptivos, 4 observacional y 2 transversal. La población estudiada incluye niños menores de 8 años, adolescentes, jóvenes y adultos, así como registros poblacionales generales en países de distintos contextos. Los estudios se desarrollaron en diversos países, tales como México, EE. UU, Europa, India, Perú, Uruguay, Jordania, España, Argentina, Japón, Australia, China y Brasil cada uno aportó una perspectiva única a la investigación. La condición clínica de los participantes de los mencionados estudios, 7 artículos analizaron los resultados fiebre, síntomas gastrointestinales, Troponina elevada, afectación cardíaca, dificultad respiratoria y dolor abdominal, hipoxia, shock, disfunción multiorgánica, dilación coronaria, hipotensión, procalcitonina elevada, taquicardia. Respecto al nivel socioeconómico, algunos de los estudios fueron realizados en países de ingresos bajos y medio recursos, reflejando una mejora al acceso y la eficacia en el diagnóstico del Síndrome inflamatorio multisistémico en niños.
Conclusión: el MIS-C representa un síndrome hiperinflamatorio grave con compromiso multisistémico, especialmente cardíaco y gastrointestinal, que puede evolucionar a shock y fallo multiorgánico. Su manejo requiere diagnóstico temprano, monitoreo hemodinámico y tratamiento inmunomodulador combinado para mejorar el pronóstico y prevenir secuelas a largo plazo en la población pediátrica.

Palabras clave: MIS-C; Shock Pediátrico; Kawasaki.

INTRODUCTION

Multisystem inflammatory syndrome in children (MIS-C) is associated with COVID-19 in pediatric and adolescent populations (Riphagen et al., 2020; Verdoni et al., 2020). An estimated 600 million people have contracted the virus, and 6,5 million have developed the disease, with a significant impact on adults (Chan et al., 2003). In Europe, 2 out of every 200 people under the age of 21 suffer from it, and the risk factors that determine why some children develop it, and others do not are not known with certainty.

Despite the same exposure, symptoms appear weeks after COVID-19 infection and coincide with peaks in community transmission, reflecting an epidemiological pattern that is still poorly understood (Murray et al., 2020). However, in the acute phase, it presents cardiac complications and has been described as unlikely to occur in newborns, which marks a difference from other clinical series. During the acute period of 2 to 6 weeks, SARS-CoV-2 causes epithelial damage to the digestive and integumentary systems. Compared to adults, children show fewer symptomatic and severe cases (Lee et al., 2020), although they have higher rates of antibody seropositivity (Clarke et al., 2022). This syndrome is characterized by gastrointestinal and cardiac involvement, as well as erythema on the palms and soles, periorbital changes, swelling, and skin rashes (Sahn et al., 2021; Young et al., 2021).

Some studies report that MIS-C in children presents with mild manifestations, such as fever, that can progress to cardiac complications and, in severe cases, lead to mechanical ventilation (Ahmed et al., 2020). This hyperinflammatory disease has also been found to be comparable to Kawasaki disease, establishing clinical characteristics, diagnostic approaches, treatment strategies, and outcomes that involve immune system dysregulation and share clinical manifestations such as skin rash, gastrointestinal symptoms, and cardiovascular involvement, with treatments often focused on immunomodulatory therapies (Lupu et al., 2025). On the other hand, observational studies have determined that the clinical characteristics of MIS-C

in critically ill children vary according to socioeconomic context, with the highest mortality rate being found in high-income countries (Acevedo et al., 2021).In these critical cases, a wide spectrum of cardiac conditions has been described, with valvulitis being the most frequent.

At the same time, the worst prognosis is observed in patients with comorbidities and in infants (Ibrahim et al., 2024). In addition, NT-proBNP and troponin are reliable indicators of cardiac injury in MIS-C, while emerging biomarkers show diagnostic potential but still require further validation (Ciortea et al., 2025).

Research on multisystem inflammatory syndrome in children (MIS-C) associated with COVID-19 is of great importance because, although it is a rare complication, it can progress to severe and even fatal conditions in the pediatric population (Riphagen et al., 2020). (Verdoni et al., 2020). This syndrome is characterized by a hyperinflammatory response that occurs weeks after SARS-CoV-2 infection (Lee & Hsueh, 2023), leading to multisystem involvement primarily affecting the heart, gastrointestinal system, skin, and blood vessels.

For this reason, the present study aims to review the literature on multisystem inflammatory syndrome in children, focusing on cardiac involvement, complications, and manifestations.

METHOD

A comprehensive narrative review of multisystem inflammatory syndrome was conducted to explore the existing scientific literature, drawing on the following databases: Scopus, Web of Science, ScienceDirect, and PubMed. To refine the search, the following terms were used: (Multisystem Inflammatory Syndrome) (Children), "AND". In addition, the Boolean operator AND was used to refine and broaden the search scope.

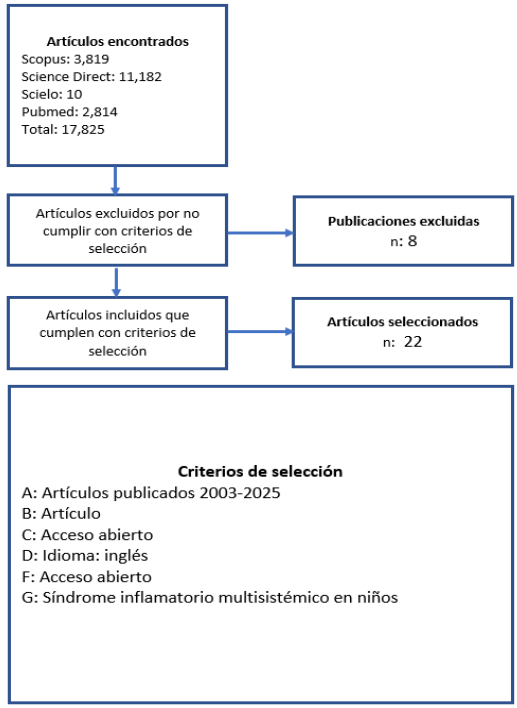

Figure 1. Flow diagram

The search period extended from August to November 2025, with articles published between 2003 and 2025 included in the review. This search covered texts written in any language, specifically excluding case reports, interviews, letters to the editor, theses, and books, as they are less empirical or have a specific focus. Within the aforementioned databases, a total of 17,907 articles were initially identified using the designed search thread. Of these, 3,819 corresponded to the Scopus database, 75 to Web of Science, 11,182 to Science, 10 to Scielo, and 2,814 to PubMed. Next, 0 duplicate articles were removed. Subsequently, 7 articles that did not align with the study objective and another 17,907 that did not meet the established inclusion criteria were excluded. As a result of this filtering and selection process, a final corpus of 22 articles relevant to the review was obtained.

RESULTS AND DISCUSSION

A corpus of 22 articles was analyzed, comprising 12 retrospective, 6 prospective, 5 descriptive, 4 observational, and 2 cross-sectional studies. The population studied included children under 8 years of age, adolescents, young people, and adults, as well as general population registries in countries with different contexts. The studies were conducted in various countries, including Mexico, the US, Europe, India, Peru, Uruguay, Jordan, Spain, Argentina, Japan, Australia, China, and Brazil, providing perspectives from diverse social, economic, and cultural realities. Eight articles addressed cardiac factors, seven focused on manifestations, and seven dealt with complications. The clinical condition of the participants in the studies, 7 articles analyzed the results of fever, gastrointestinal symptoms, elevated troponin, cardiac involvement, respiratory distress and abdominal pain, hypoxia, shock, multiple organ dysfunction, coronary dilation, hypotension, elevated procalcitonin, tachycardia, and macrophage activation syndrome in terms of socioeconomic status. some of the studies were conducted in low- and middle-income countries, reflecting improved access and effectiveness in the diagnosis of multisystem inflammatory syndrome in children.

The findings have enabled the identification of cardiac involvement, complications, and manifestations of diabetes associated with multisystem inflammatory syndrome in children, and other sources will analyze these findings.

Cardiac involvement

Pediatric patients with multisystem inflammatory syndrome associated with COVID-19 (MIS-C) and cardiac involvement, presenting with cardiac shock requiring intensive care admission and electrocardiogram (ECG) abnormalities (Tangari et al., 2023), with hemodynamic compromise (failure to maintain perfusion: adequate blood flow to organs) (frequent).(Rodriguez et al., 2021) Due to rash with decreased troponin levels (proteins present in heart muscle cells that regulate muscle contraction (Penna et al., 2025). MIS-P is characterized by cardiac involvement and marked elevation of inflammatory and cardiac markers (Valverde et al., 2021).

However, some patients presented cardiac sequelae with favorable evolution in the medium term in the ICU (Tiwari et al., 2021). They required intensive immunomodulatory therapy (Cieza et al., 2021). These were less frequent and did not include coronary findings (Shalabi et al., 2025a).

Shock

Shock in children with MIS-C and cardiac involvement is a common cause of ICU admission and is associated with ECG abnormalities (Tangari et al., 2023).

Table 1. Results table

Study title	Methodology	Objective/Sample	Main results
Kawasaki disease and multisystem inflammatory syndrome in children. Differences and similarities in a pediatric center in Mexico (García et al., 2023)	Comparative and retrospective study	To evaluate the differences and similarities in the clinical picture, laboratory findings, and medical outcomes of pediatric patients with Kawasaki disease versus multisystem inflammatory syndrome. Sample: 81 patients were included: 62 with Kawasaki disease and 19 with multisystem inflammatory syndrome.	Symptoms: fever, rash, and conjunctivitis; multisystem inflammatory syndrome showed greater multiorgan involvement, a more severe inflammatory response, greater need for therapeutic support, and higher mortality.
Skin manifestations and clinical features related to multisystem inflammatory syndrome in children: a retrospective descriptive cohort study at Texas Children's Hospital (Penna et al., 2025)	Descriptive retrospective cohort study	We sought to describe the demographic background, key clinical characteristics, and clinical consequences of developing exanthematous manifestations (infectious diseases with skin manifestations) in patients with MISC at Texas Children's Hospital. Sample: 290 eligible patients hospitalized between May 2020 and April 2022.	Exanthematous manifestations in patients with MISC are associated with less cardiac involvement and decreased troponin levels.
Progression and management of pediatric multisystem inflammatory syndrome associated with SARS-CoV-2 infection in a pediatric ICU in Lima, Peru. (Cieza et al, 2021)	Observational, descriptive, and retrospective study.	To describe the clinical presentation, treatment, and evolution of MIS-C in patients at a referral pediatric intensive care unit (PICU). Sample: They identified 18 children with an average age of 8,76 years, 50 % male, all with positive serological tests.	Pediatric patients in the ICU (intensive care units) determine inflammatory indicators and myocardial depression, presenting with intermediate stays.
Cardiac involvement in post-SARS-CoV-2 multisystem inflammatory syndrome in children (Tangari et al., 2023)	Descriptive study	To describe the characteristics of eight pediatric patients who presented with multisystem inflammatory syndrome (MIS-C) associated with SARS-CoV-2 and cardiac involvement. Sample: eight patients aged between 1 and 13 years, diagnosed with MIS-C and cardiac involvement, treated at the CHPR	Pediatric patients presented with cardiac shock and ECG abnormalities requiring intensive care.
Multisystem inflammatory syndrome in children (MIS-C) associated with COVID-19, clinical characteristics: a multicenter observational study from Jordan (Shalabi et al., 2025a)	A retrospective study was conducted	The aim was to describe the clinical course of 74 patients diagnosed with this disease. Sample: During the study period, a total of 74 patients were diagnosed with MIS-C.	The study of MIS-C cases found that the severity of frequent abdominal pain in children who were only diagnosed with acute pain was consistent.

Severe manifestations of SARS-CoV-2 in children and adolescents: from COVID-19 pneumonia to multisystem inflammatory syndrome: a multicenter study in pediatric intensive care units in Spain. (García et al., 2020)	Prospective study	To describe the characteristics of children admitted to pediatric intensive care units (PICUs) with MIS-C compared to those admitted with SARS-CoV-2 infection with other characteristics such as COVID-19 pneumonia. Sample: Seventy-four children were recruited.	MIS-C was the most common form in severely ill children with COVID-19. These children were older and generally healthy, with more digestive symptoms and shock. They also received more treatments for inflammation but required less mechanical ventilation than those without MIS-C.
Multisystem inflammatory syndrome in pediatrics: importance of initial evaluation of laboratory parameters. (Kibrik et al., 2022)	An analytical and retrospective study	Describe and analyze the characteristics of patients with SIM-C and their relationship to laboratory findings. Sample: Thirty-two patients were studied, 17 female (53,13 %) and 15 male (46,87 %).	Although mortality due to MIS-C is low, cardiovascular involvement and hemodynamic compromise in patients with this syndrome can be common.
National survey on multisystem inflammatory syndrome in children associated with coronavirus disease 2019 in Japan (Matsubara et al., 2025)	Prospective and retrospective study	To determine the epidemiological and clinical characteristics of MIS-C in Japan. Samples: Included 2,080 centers throughout Japan.	The clinical characteristics showed a phenotype more similar to Kawasaki disease in clinical manifestations.
Recovery from pediatric multisystem inflammatory syndrome ( ) temporarily associated with SARS-CoV-2: Follow-up of a nationwide German cohort (Lohrmann et al., 2025)	In a multicenter study	Investigating the medium-term health impacts of pediatric multisystem inflammatory syndrome temporarily associated with SARS-CoV-2 (PIMS-TS). Sample: Follow-up data were collected from 127 patients at 6 pediatric centers	Patients with PIMS-TS generally have a good medium-term prognosis, but prolonged sequelae, particularly cardiovascular, were observed in older children and those admitted to the ICU , so close follow-up and multidisciplinary management are recommended.
COVID-19-related multisystem inflammatory syndrome in children (MIS-C): a prospective cohort study based on a hospital in Kerala, India (Tiwari et al., 2021)	Prospective cohort study	To study the epidemiological factors, clinical profile, and outcomes of multisystem inflammatory syndrome associated with COVID-19 in children (MIS-C), the clinical profile across all age groups, medium-term outcomes, and parameters associated with disease severity. Sample: Forty-one patients with MIS-C were reported, with a mean age of 6,2 (4,0) years, and 33 (80 %) were previously healthy.	In our cohort, patients with MIS-C showed symptoms ranging from mild forms to severe multiorgan dysfunction. The outcome was generally favorable, although some patients presented with cardiac sequelae that tended to resolve. Hyperferritinemia was associated with a greater need for mechanical ventilation.

Treatment of multisystem inflammatory syndrome in children: understanding differences in outcomes from comparative efficacy studies (Melgar et al., 2022)	Enrollment and inclusion	We sought to determine whether the application of different definitions of MISC and different disease severity among cohorts underlie the discrepant results. Sample: Of 349 patients with OC19, 9,5 % did not meet the WHO definition. Of 350 patients with BATS, 10,3 % did not meet the CDC definition.	The greater cardiovascular involvement in OC19 in the initial treatment of MIS-C requires intensive immunomodulatory therapy.
Multisystem inflammatory syndrome in children from 16 Latin American countries (García et al., 2024)	A multicenter observational, retrospective, and prospective study	To describe the epidemiology and outcomes of multisystem inflammatory syndrome in children (MISC) in Latin America. Sample: of the 1,239 children reported with MIS-C, 84,18 % were previously healthy.	Untreated MIS-C patients have the greatest need for awareness and diagnosis.
Cardiovascular system changes in children with pediatric multisystem inflammatory syndrome temporarily associated with COVID-19 – A single-center experience (Stasiak et al., 2022a)	A single-center retrospective study	To evaluate changes in the cardiovascular system of patients with PIMS-TS, particularly changes in the electrocardiogram (ECG) and echocardiography. Sample: 51 patients with PIMS-TS were hospitalized at our center	In PIMS-TS, there is diverse cardiovascular involvement, and most patients require cardiac monitoring.
Multisystem inflammatory syndrome in children in New York State (Dufort et al., 2020a)	Descriptive study	To describe patients hospitalized with the syndrome. Sample: Of 95 patients with confirmed MIS-C	The syndrome coincided with COVID with dermatological, mucocutaneous, and gastrointestinal manifestations associated with cardiac involvement.
Acute cardiovascular manifestations in 286 children with multisystem inflammatory disease syndrome associated with COVID-19 infection in Europe (Valverde et al., 2021a)	We conducted a rapid, real-time audit	To document cardiovascular clinical findings, cardiac imaging, and laboratory markers in children presenting with the new multisystem inflammatory syndrome associated with coronavirus disease 2019 (COVID-19) infection. Sample: A total of 286 children from 55 centers in 17 European countries were included.	MIS-C is characterized by cardiac involvement, marked elevation of inflammatory and cardiac markers, and low mortality compared to adults.

Multisystem inflammatory syndrome in children (MIS-C) during the SARS-CoV-2 pandemic in Brazil: a multicenter prospective cohort study. (Lima et al., 2021)	Prospective, multicenter cohort study	To describe the clinical, laboratory, and radiological characteristics, as well as the evolution of children with MIS-C. Sample: Fifty-six patients with the following conditions were included: Kawasaki-like disease (n = 26), incomplete Kawasaki disease (n = 16), acute cardiac dysfunction (n = 10), toxic shock syndrome (n = 3), and macrophage activation syndrome (n = 1).	Pediatric patients share clinical findings with other cohorts, but long-term follow-up is required to rule out sequelae such as chronic heart dam .
Multisystem inflammatory syndrome in children (MIS-C) and "near MIS-C": a continuum? (Khafaja et al., 2023)	A retrospective review was conducted	Review these cases and describe their characteristics in comparison to cases that met the CDC criteria for MIS-C and those that had an alternative diagnosis. Sample: A total of 29 subjects were included in our cohort.	MIS-C is difficult to diagnose due to its symptoms, clinical presentation, and ongoing diagnostic criteria that require review.
Imaging findings in pediatric multisystem inflammatory syndrome (MIS-C) associated with coronavirus disease (COVID-19) (Blumfield et al., 2021a)	To evaluate the imaging findings of MIS-C associated with COVID-19. Retrospective	To evaluate the imaging findings of MIS-C associated with COVID-19. Sample: Sixteen patients (10 males and six females; age range: 20 months to 20 years) were included in this study.	MIS-C associated with COVID-19 predominantly cardiovascular, as well as ascites, from the multisystem inflammatory process.
Severe clinical spectrum with high mortality in inflammatory syndrome (Pereira et al., 2020)	Cross-sectional study	To evaluate the outcomes of pediatric patients with laboratory-confirmed coronavirus disease (COVID-19) with or without multisystem inflammatory syndrome in children (MIS-C). Sample: 371 patients (age ≥ 18 years)	Children with gastrointestinal involvement and hypoxemia have a high mortality rate.
Pediatric multisystem evaluation pattern PMIS inflammatory syndrome in children during the COVID-19 pandemic: experience in the emergency department of a tertiary care center in a lower-middle-income country (Akhtar et al., 2024a)	This prospective observational study	To determine the frequency, clinical presentation patterns, and laboratory parameters of children with PMIS who visited the emergency department during the COVID-19 pandemic. Secondary objectives included evaluating factors associated with hospital mortality. Sample: Among 56 patients with primary immunodeficiency syndrome (PID).	Stevens Johnson syndrome (SMI) affects all individuals with respiratory symptoms and elevated levels (LDH, ferritin, D-dimer, ProBNP).

Multisystem inflammatory syndrome in children (MISC) associated with COVID-19 – Single-center experience (Varadarajan et al., 2023b)	Prospective study	Describe the clinical presentation, phenotype, and evolution of multisystem inflammatory syndrome (MISC) in children associated with coronavirus disease 2019 (COVID-19) at a tertiary care center in southern India Sample: Among 312 children with acute febrile illness and The duration of illness (RIC) was 5 (37) days.	Children with MIS-C may experience complications such as acute kidney injury, HLH, mitral regurgitation, and the need for mechanical ventilation. These indicate a more severe condition and a less favorable prognosis.
Alteration of inflammatory markers in children and adolescents with multisystem inflammatory syndrome during infectious disease caused by the novel coronavirus 2019: a systematic review and meta-analysis (Biswas et al., 2021)	A retrospective study	Compare MIS and non-MIS cases in relation to elevated inflammatory marker in children and adolescents due to COVID-19. Sample: 186 children and adolescents from the US	During COVID-19, the markers studied (CRP, PC, F, and ESR) increased in young people.

This syndrome is characterized by shock with marked inflammation that mimics toxic shock syndrome (Nogueira et al., 2021), typically presenting with fever, gastrointestinal symptoms, and shock requiring management with immunomodulators (Shobhavat et al., 2020). Physiopathologically, the shock combines vasodilation and myocardial dysfunction (Kantimas Sitthikoo, 2024) and can progress to cardiogenic shock due to myocarditis (Vecchia et al., 2025), where MIS-C predominantly reduces left ventricular function (Jain et al., 2025). To identify these severe cases, elevated initial procalcitonin levels are a key risk factor (Wu et al., 2024).

Hemodynamic compromise and troponin levels

In these patients, cardiac involvement is evidenced by hemodynamic compromise, manifested by difficulty in maintaining adequate blood perfusion to the organs (Rodriguez et al., 2021), while markers of severity inclu r low hemoglobin, platelet, albumin, and potassium levels, along with elevated levels of leukocytes, neutrophils, troponin, and brain natriuretic peptide (Kaidar et al., 2023). This hemodynamic compromise, accompanied by multiorgan dysfunction, is associated with hypertrophic cardiomyopathy that can lead to shock and death (Taweevisit et al., 2022), as well as elevated troponins, ProBNP, and ferritin, thrombocytopenia, and coronary abnormalities observed by echocardiogram (Luis Calvo M, 2022). It is common in hospitalized children, with nonspecific and transient symptoms, notably elevated troponin, high ferritin, and thrombocytopenia (Diaz et al., 2022), and patients with MIS-C have also been observed to have increased BNP levels even in the absence of coronary abnormalities (Zhao et al., 2021a).

Inflammatory markers

Cardiac involvement is characterized by elevated inflammatory and cardiac markers (Valverde et al., 2021). In the case of SIM-P in the PICU, it is characterized by fever, respiratory distress, abdominal pain, and myocardial depression, requiring corticosteroids, immunoglobulin, and ventilatory support (Cieza et al., 2021), allowing identification of the risk of myocardial dysfunction (Lohrmann et al., 2025). Associations with appendicitis were also observed based on leukocyte, neutrophil, and lymphocyte-monocyte ratio (LMR) levels (Guevara Castro, 2025), and primary immunodeficiency syndrome (PID), ferritin, D-dimer, and pro-BNP, which are associated with higher mortality (Akhtar et al., 2024b). In other words, it is a severe hyperinflammatory condition that requires early identification and management. (Fernandez B, 2025) that due to the higher levels, it is comparable to Kawasaki disease. (Rodríguez-Alcocer et al., 2022).

Cardiac sequelae

Cardiac involvement in patients with MIS-C may have sequelae, although with a favorable outcome (Tiwari et al., 2021). It should be monitored and treated according to established protocols, including repeated biological tests and echocardiography (Grabot et al., 2023). Alterations in the coronary vessels, including dilations and aneurysms, were also observed, along with myocardial hypokinesia (Stasiak et al., 2022b). Similarly, abnormalities such as coronary artery dilation, pericardial effusion, and mitral valve insufficiency were reported (Wolf et al., 2023). Finally, MIS-C presents frequent cardiac abnormalities, including valve insufficiency and pericardial effusion. However, the use of steroids significantly reduced the likelihood of ventricular dysfunction and valvular insufficiency (Ghodsi et al., 2023).

Intensive immunomodulation

Immunomodulatory treatment in children with multisystem inflammatory syndrome (MIS-C) aims to control hyperinflammation and stabilize the patient, preventing long-term sequelae (Toledo et al., 2023). Several studies agree that early intervention significantly improves prognosis (Solanki et al., 2022). During the pandemic, intravenous immunoglobulin (IVIG),

traditionally used in Kawasaki disease, was adopted as a main therapy for MIS-C. Although it was initially used alone, evidence eventually showed that its use in combination with corticosteroids was more effective (Jain et al., 2025). Likewise, in cases with cardiac involvement, such as myocarditis, treatment includes supportive therapy, immunoglobulin, steroids, and other immunomodulatory drugs (Mangalamoorthy et al., 2025), which, in some situations, may require intensive immunomodulatory therapy to achieve adequate recovery (Cieza et al., 2021).

Coronary findings

These were less frequent and did not include coronary findings (Shalabi et al., 2025). However, patients with MIS-C showed a higher prevalence of shock and cardiac dysfunction (García et al., 2020), as well as cardiovascular involvement (arterial hypotension, heart failure, pericardial effusion, myocardial dysfunction, pericarditis without effusion, myocarditis (Mileva et al., 2023), as well as acute myocardial injury, myocardial edema, troponin increases, ventricular dysfunction, cardiogenic shock, and coronary alterations (dilatation or aneurysms) (Kurz & Gombala, 2021), as well as cardiac function in pediatric patients with MIS-C that are not detected by echocardiography. These abnormalities are associated with increased use of intensive therapies (Basu et al., 2022). Finally, the presence of coronary atheromatous disease, characterized by CT coronary angiography (CTA) showing coronary artery stenosis, was analyzed (Grazia et al., 2014).

Complications

MIS-C associated with COVID-19 is characterized by cardiovascular involvement and ascites (Blumfield et al., 2021). In children, it usually presents with gastrointestinal involvement and hypoxemia (Pereira et al., 2020), with sequelae such as chronic cardiac impairment (Lima et al., 2021) being detected, compared to Stevens-Johnson Syndrome (SJS), which manifests with respiratory symptoms and elevated inflammatory markers (Akhtar et al., 2024a).

Cardiovascular involvement

MIS-C associated with COVID-19 is characterized by predominant cardiovascular involvement and the presence of ascites (Blumfield et al., 2021b). This involvement includes myocardial lesions (Aeschlimann et al., 2021), which can cause lasting heart damage, necessitating long-term medical follow-up (Stasiak et al., 2022a). The most serious complication of this syndrome is acute heart failure, which can progress to cardiogenic shock (Ludwikowska et al., 2023). In many cases, MIS-C can trigger multiple organ failure with significant cardiac damage (Cantarutti et al., 2022). In contrast, Kawasaki disease presents a different spectrum of cardiovascular complications, mainly including coronary lesions, myocarditis, pericarditis, and arrhythmias (Maggio et al., 2024).

Gastrointestinal involvement

In cases of MIS-C with gastrointestinal involvement, pancreatitis has been associated with a more severe clinical course, underscoring the need to evaluate it in patients with digestive symptoms (Aylin Yucel & Ozge Akcan, 2023). Likewise, this condition may resemble acute abdomen, highlighting the importance of careful evaluation and timely diagnosis to avoid unnecessary surgery (Turer et al., 2022). In some cases, this syndrome can be confused with appendicitis, although computed tomography angiography (CTA) is useful in differentiating between the two (Kurtmen et al., 2023). In addition, most children present with abdominal pain and other gastrointestinal symptoms, which could serve as clinical indicators in patients with a history of or recent contact with COVID-19 (Lazova et al., 2023). However, the condition tends to worsen with age and is associated with milder symptoms, less respiratory compromise,

and a lower need for intensive care. (Garcia et al., 2024b)

Cardiac impairment

MIS-C is associated with significant cardiac complications that require constant monitoring to prevent sequelae such as chronic cardiac impairment (Lima et al., 2021). Elevated BNP levels indicate cardiac overload with a risk of ventricular dysfunction or heart failure (Zhao et al., 2021b). This condition is more severe than in cases of acute COVID-19 and can cause myocardial inflammation, coronary abnormalities, and persistent ventricular dysfunction (Hensley et al., 2023). Some patients develop acute cardiac decompensation and prolonged left ventricular myocardial dysfunction (Sanil et al., 2021). In the most severe cases, shock and significant myocardial damage requiring intensive care are observed (Fridman et al., 2023). However, with appropriate treatment, most patients recover cardiac function without serious sequelae (Mannarino et al., 2022), even after clinical recovery, indicating the impact.

Multiple organ involvement

MIS-C is characterized by intense multi-organ involvement, a strong inflammatory response, and an increased need for therapeutic support, which increases its severity and mortality (García et al., 2024). It compromises not only the heart, but also the nervous, digestive, and respiratory systems, requiring prolonged medical follow-up (Sezer et al., 2022). In the most recent phases of the pandemic, virus variants caused more severe symptoms, and increased NT-proBNP was highlighted as a key marker of severity (Renson et al., 2023). This syndrome causes severe inflammation in several organs and can range from mild forms to cases with multiple organ failure and shock, especially in older children with comorbidities (Encinosa et al., 2023).

Respiratory symptoms

Stevens-Johnson syndrome (SJS) presents with respiratory symptoms and elevated inflammatory markers (Akhtar et al., 2024a). At the same time, pediatric patients with MIS-C show post-infection IgG (immunoglobulin G) antibodies and few respiratory symptoms, requiring early treatment and further research (Shhada et al., 2024). They are also often present radiographic pulmonary abnormalities that warrant prolonged medical follow-up (Ibrahim et al., 2022). COVID-19 in children can cause respiratory and digestive symptoms, and elevated inflammatory markers indicate greater severity and a higher risk of complications (Akhtar et al., 2024a), mainly affecting the lungs, although it can also cause seizures. However, in Thailand, there is a lack of studies on its impact (Praphaphanthasak & Saengow, 2025). Finally, pediatric cases of COVID-19 range from mild to severe with multi-organ dysfunction (Alshehri et al., 2024).

Manifestations

The study of MIS-C cases, a syndrome linked to COVID-19, showed a diverse clinical presentation that includes abdominal pain (Shalabi et al., 2025a) and dermatological, mucocutaneous, gastrointestinal, and cardiac manifestations (Dondi et al., 2022). Although in our cohort the outcome was mostly favorable with mild to moderate symptoms (Tiwari et al., 2021), serious complications such as acute kidney injury, HLH, and mitral regurgitation were observed (Varadarajan et al., 2023b). This syndrome, whose characteristics resemble Kawasaki disease (Matsubara et al., 2025), showed a marked inflammatory profile with elevated CRP (C-reactive protein), ferritin, and ESR (erythrocyte sedimentation rate) (Penna et al., 2025), which consolidated MIS-C as the most common form of severe COVID-19 in the pediatric population, requiring intensive anti-inflammatory treatment.

Dermatological manifestations

Pediatric multisystem inflammatory syndrome (MIS-C) associated with COVID-19 is characterized by dermatological, mucocutaneous, gastrointestinal, and cardiac manifestations. Patients presenting with rash or conjunctival hyperemia upon admission are more likely to require pediatric intensive care (Martinez et al., 2021). Skin lesions such as urticaria, maculopapular or vesicular rashes can occur at any age, while chilblains, erythema multiforme (Dufort et al., 2020b), and lobular-type lesions are common in children after coronavirus infection (Ivanchikov et al., 2022). However, exanthematous manifestations are usually associated with less cardiac involvement and reduced troponin levels (Penna et al., 2025).

Acute kidney injury

It has been reported that patients with pediatric multisystem inflammatory syndrome (MIS-C) may present with serious complications such as acute kidney injury (AKI), hemophagocytic syndrome, and mitral insufficiency (Varadarajan et al., 2023b), with ARI being one of the most frequent and associated with a poor prognosis in critically ill children (Tripathi et al., 2023), observed most frequently in patients admitted to the PICU, where it was associated with hyperferritinemia, longer hospital stays, and the need for mechanical ventilation. Its origin is attributed to combined prerenal and inflammatory damage with tubular involvement, providing new insights into its clinical management (Meneghel et al., 2023). causes proposed include cardiac dysfunction, hyperinflammatory state, and exposure to nephrotoxic drugs used in the treatment of COVID-19, in addition to the possible influence of inflammation and dehydration (Basalely et al., 2021).

Kawasaki disease

This syndrome, which resembles Kawasaki disease (Matsubara et al., 2025), shares multiple clinical manifestations with it. However, they differ in the available evidence and therapeutic approach, as Kawasaki disease has robust studies, whereas the management of MIS-C is mainly based on expert recommendations (Díaz, 2025). However, although both can present with shock, patients with Kawasaki disease show more severe coronary involvement, while those with the syndrome have a lower left ventricular ejection fraction (Jain et al., 2025). In addition, inflammatory cytokine and chemokine levels are significantly elevated in both (Deepthi et al., 2025), and machine learning algorithms have been shown to predict ICU admission in pediatric patients effectively (Woo et al., 2025).

This research has certain limitations, as it was not possible to cover all the existing literature on the subject. Therefore, only some associated and clinical factors were addressed. In addition, the studies mentioned in the discussion have a particular focus depending on the population and methodology used, while this study conducted a more general analysis. For this reason, it is recommended that the review of sources be expanded to develop a systematic review in the future. Similarly, many articles did not report relevant sociodemographic variables such as socioeconomic status or access to health services, which limits the analysis of possible inequalities or prognostic factors associated with the social context. This lack of standardization and the dispersion of approaches reduces the possibility of generating more robust and generalizable inferences. Therefore, future research should consider the inclusion of comparative methodologies, the reporting of socioeconomic characteristics, and the harmonization of clinical criteria to strengthen the validity and applicability of the evidence.

CONCLUSION

Shock in children with MIS-C and cardiac involvement is characterized by fever, gastrointestinal

symptoms requiring immunomodulators, physiologically combined with vasodilation and myocardial dysfunction, reducing left ventricular function with elevated procalcitonin levels. Cardiac involvement, as indicated by inflammatory markers such as fever, respiratory distress, abdominal pain, and myocardial depression, requires corticosteroids, immunoglobulin, and ventilatory support. When associated with appendicitis, there is a risk of mortality compared to Kawasaki disease. Hemodynamic compromise is evidenced by low troponin levels, low hemoglobin, platelet, albumin, potassium, and leukocyte values, and high neutrophil and brain natriuretic peptide levels, resulting in multiple organ dysfunction. Immunomodulatory treatment seeks to control hyperinflammation and prevent long-term sequelae.

Evidence shows that early combination therapy with intravenous immunoglobulin and corticosteroids improves prognosis, especially in cases with cardiac involvement, where intensive care may be required to achieve adequate recovery. These were less frequent and did not include coronary findings; however, patients had a higher prevalence of shock, cardiac dysfunction, and various cardiovascular disorders, such as myocarditis, ventricular dysfunction, and coronary aneurysms. In addition, cardiac abnormalities not detectable by echocardiography were observed, associated with a greater need for intensive care, and cases with coronary stenosis were evidenced by CT angiography (computed tomography angiography).

MIS-C associated with COVID-19 is characterized by predominant cardiovascular involvement with ascites and myocardial lesions causing lasting cardiac damage, with acute heart failure and cardiogenic shock being its most serious complications. Gastrointestinal involvement may include pancreatitis and mimic acute abdomen or appendicitis, requiring careful evaluation. It usually presents with abdominal pain and digestive symptoms and is more common in older children.

Cardiac complications, such as myocardial inflammation and ventricular dysfunction, are common; however, elevated levels of BNP (B-type natriuretic peptide) indicate overload and risk of heart failure or shock in severe cases. This syndrome indicates severe multi-organ involvement (heart, nervous, digestive, respiratory) and a strong inflammatory response, which increases its severity and mortality and can lead to multi-organ failure and shock. An increase in NT-ProBNP (N-terminal brain natriuretic peptide) is a serious marker that requires prolonged medical follow-up. Stevens-Johnson Syndrome presents with respiratory symptoms and inflammation, while MIS-C is distinguished by IgG antibodies and few respiratory complaints, but with pulmonary abnormalities that require prolonged monitoring.

MIS-C manifests with dermatological, mucocutaneous, gastrointestinal, and cardiac involvement. Patients with rash or conjunctival hyperemia on admission are more likely to require intensive care. However, skin lesions vary, and exanthematous manifestations are usually associated with less cardiac involvement and lower troponin levels. Serious complications such as acute kidney injury (AKI), hemophagocytic syndrome, and mitral regurgitation are common. They are associated with poor outcomes in critically ill children, often requiring admission to the PICU, longer hospitalization, and mechanical ventilation. Their origin is attributed to prerenal damage, inflammation (hyperferritinemia), and possibly cardiac dysfunction or nephrotoxic drugs used in treatment. This syndrome resembles Kawasaki disease in many clinical manifestations and in the high presence of inflammatory cytokines, and both can progress to shock; however, they differ in that MIS-C is associated with a lower left ventricular fraction, while Kawasaki disease presents with more severe coronary involvement.

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