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ORIGINAL ARTICLE

Cardiac manifestations and echocardiographic findings associated with COVID-19 multisystem inflammatory syndrome in children: A single-center observational study during and after the pandemic

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Abstract

Introduction: In children hospitalized for multisystem inflammatory syndrome (MIS) due to COVID-19, cardiac manifestations may occur, the outcome of which may be fatal. This study analyzed the cardiac manifestations and echocardiographic findings associated with SIM in children with COVID-19.

Methods: The present observational study was conducted at the "Vicente Corral Moscoso" Hospital in Cuenca, Ecuador. The study period was from April 2020 to March 2022. Children with SIM and COVID-19 were included, and medical records and echocardiograms were examined.

Results: There were 19 patients; 31.6% of the affected children were between 1 and 4 years old, and 52.6% were girls. Notably, 63.2% were overweight. Obesity was the most common comorbidity, affecting 84.2% of the patients. The predominant symptoms were fever (68.4%), vomiting (47.4%), and abdominal pain (42.1%). The echocardiographic findings were pericardial effusion in 15.8% and right ventricular dysfunction in 5.3%. The most common cardiac complications were pericardial and valvular dysfunction, arrhythmias, and pericardial effusion, each occurring in 10.5% of patients. In addition, 26.3% mortality was recorded in the sample studied.

Conclusions: A clear relationship between inflammatory symptoms and cardiac complications after contracting COVID-19 infection was observed.

Keywords:

MeSH: Systemic Inflammatory Response Syndrome; SARS-CoV2; Signs and Symptoms; Heart; Mucocutaneous Lymph Node Syndrome; Children.

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Email: < jonathan.tipan@ucuenca.edu.ec > Jonathan Tipán-Barros/Address: 32Q4+HR4, Pje. of Paradise, Cuenca. Pediatric Intensive Care Department. Vicente Corral Moscoso Hospital, Cuenca, Ecuador. Telephone [593] 07 409 6000. Revista Ecuatoriana de Pediatría 2023;24(3):220-233 |

Introduction

The pandemic due to coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome type-2 virus (SARS-CoV-2), has had a significant global impact, with approximately 600 million cases and more than 6.4 million deaths [1]. However, upon contracting COVID-19, children tend to experience mild, predominantly upper respiratory symptoms, and the disease has shown wide variability in severity across all age groups, from asymptomatic cases to severe multiple organ failure dysfunction and death [2, 3]. In particular, children represent a smaller fraction of the total cases, with less than 2% of the pediatric population being affected. Most of these pediatric patients have been asymptomatic or had mild to moderate disease, with an expectation of recovery in one to two weeks, leading to the risk of severe disease being considered very low [4, 5].

With the global spread of SARS-CoV-2, reports emerged from Europe, North America, Asia, and Latin America of children and adolescents experiencing multisystem inflammatory conditions linked to COVID-19 [6]. However, the relationship between multisystem inflammatory syndrome in children (MIS-C) and COVID-19 remains unclear [7].

Multisystem inflammatory syndrome associated with COVID-19 has been identified as a significant medical problem in children and adolescents. This syndrome is characterized by severe symptoms such as acute heart failure, ventricular dysfunction, arrhythmias, and increased cardiac marker levels such as troponins and natriuretic peptides. Although the majority of the pediatric population with COVID-19 shows mild or no symptoms, those affected by MIS-C experience a systemic inflammatory response with potentially severe effects on the cardiovascular system [8].

Although SARS-CoV-2 has not been confirmed to be the direct cause of MIS-C, its temporal coincidence with COVID-19 outbreaks in Europe and the United States suggests a possible connection [9]. If the prevalence of MIS-C decreases as the pandemic is controlled, this will strengthen the theory of its association with the virus [10].

Among the severe effects of COVID-19, cardiovascular collapse is one of the most serious and potentially fatal. Furthermore, preexisting cardiovascular diseases increase the risk of mortality.

The most plausible mechanism for cardiovascular complications and cardiac damage in severe cases of COVID-19 appears to be prolonged endothelial dysfunction, which results from the interaction between inflammation and coagulation (Figure 1) [11, 12].

SARS-CoV-2 infection can cause cardiovascular problems during the acute phase of the disease, especially in patients with risk factors such as overweight, obesity, hypertension, or diabetes. However, severe cases of cardiovascular conditions have been reported in patients without a history of risk [13].

Recent research has revealed a notable incidence of cardiovascular disorders in children with multisystem inflammatory syndrome associated with COVID-19. These findings suggest a complex relationship between the systemic inflammatory response and the cardiovascular system in pediatric patients infected with SARS-CoV-2 [14].

Cardiac complications in children not only increase clinical severity but also require more intensive treatments. Patients with significant cardiac symptoms often require intensive care, inotropic medication, and other life-sustaining therapies [15]. This direct relationship between the severity of cardiac complications and the intensity of necessary treatment underlines the importance of careful and continuous evaluation for appropriate decision-making [16].

Early diagnosis improves the prognosis of the disease; however, this outlook is influenced by the results of serological tests. Obtaining a false positive or negative result for determining COVID-19 infection will depend on the time the sample takes during the disease phase. Upon hospital admission, if COVID-19 is suspected within the first five days of symptoms, the

primary study used the antigen test to detect SARS-CoV-2; if this test was positive, a diagnosis of COVID-19 was established [17].

In contrast, if symptoms are more than five days, a reverse transcriptase polymerase chain reaction (RT–PCR) test is used to diagnose the disease [18]. The RT–PCR test is considered the gold standard for diagnosing SARS-CoV-2 infection due to its high sensitivity and specificity, especially in more advanced stages of the disease. In these cases, antigen testing may be less effective due to decreased viral load [19]. The RT–PCR test can accurately detect the virus even at lower concentrations, which is crucial for identifying cases where the infection has passed the acute phase but could still contribute to developing complications such as MIS-C [20]. This differentiated diagnostic approach is vital for ensuring accurate detection of COVID-19 infection and, therefore, for appropriate management and early intervention in patients with MIS-C. Pediatrics [21].

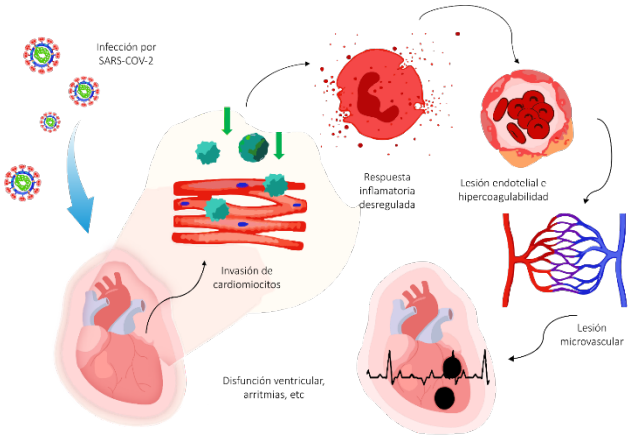
Additionally, in MIS-C, serological tests that detect IgM and IgG antibodies for COVID-19 are essential [22]. IgM antibodies indicate recent infection and usually appear in the first 4 to 10 days postexposure. IgG antibodies, which indicate past exposure, generally develop after two weeks and can persist for months, with an estimated average of 6 months [23, 24]. These tests are crucial for identifying acute or past infections and are beneficial for evaluating patients at risk of late complications, as described for MIS-C [21].

A positive antibody (IgG) test for SARS-CoV-2 is the most relevant laboratory test for diagnosing MIS-C associated with COVID-19 because it is more common for MIS-C to occur two months after COVID-19 infection [25]. However, positive IgG antibody testing is not an absolute criterion for diagnosing MIS-C, as MIS-C has been identified in patients with an acute infection confirmed by RT–PCR positive for COVID-19 [26]. This finding suggested that MIS-C can occur in both the early and late phases of SARS-CoV-2 infection [27]. Therefore, antibody tests and RT–PCR are essential when evaluating cases of MIS-C because MIS-C can occur at different times during COVID-19 infection, highlighting the complexity of its diagnosis and the need for a comprehensive diagnostic approach [28].

For this reason, three categories of patients were examined in our study: those with positive test results for antigen, RT–PCR, or IgG for COVID-19. This approach made it possible to identify and characterize MIS-C at different stages of COVID-19 infection, providing a comprehensive view of the syndrome and its connection with the SARS-CoV-2 virus. These data are crucial for improving the timely diagnosis and treatment of MIS-C in the pediatric population.

In addition, this study aimed to detail and analyze the cardiac manifestations and echocardiographic findings after infection with the multisystem inflammatory syndrome linked to COVID-19, focusing on evaluating the incidence and characteristics of MIS-C during the acute phase and the post-phase. -infection in children. The investigation focused on pediatric patients treated at the "Vicente Corral Moscoso" Hospital in Cuenca, from the first cases reported in April 2020 to March 2022.

Figure 1. Possible cause of heart disease in patients with multisystem inflammatory syndrome associated



with COVID-19.

Source: the authors. Based on [12].

Materials and methods

Type of study

The study was observational and descriptive. The source was retrospective. The observation is transversal.

Scenery

The study was conducted in the pediatric hospitalization area of the "Vicente Corral Moscoso" Hospital in Cuenca, Ecuador. The study period was from April 1, 2020, to March 31, 2022.

Participants

Pediatric patients under 16 years of age who were hospitalized with an established diagnosis of multisystem inflammatory syndrome with a possible association with COVID-19 according to a positive PCR test, positive antigen test, or positive antibody test were included in the study. The diagnosis of multisystem inflammatory syndrome was established with the involvement of ≥ 2 systems. Patients who fully or partially met the Kawasaki disease (KD) criteria were included. All incomplete records were excluded from the analysis. Patients diagnosed with staphylococcal or streptococcal shock, bacterial sepsis, or infections associated with myocarditis were excluded. Patients whose family members and representatives did not agree to provide informed consent were also excluded.

Variables

The variables analyzed in this study included the following:

Independent variables:

* Sociodemographic: age, sex, and nutritional status.
* Respiratory, immunological, cardiac, hematological, endocrine, and neurological comorbidities.
* Hospitalization time (days).
* Signs: Fever, abdominal pain, vomiting, diarrhea, skin rash, conjunctivitis.

Dependent variables:

* Multisystem cardiac manifestations: shock, cardiac arrhythmias, myocardial dysfunction, pericardial dysfunction, valvular dysfunction, coronary abnormalities, pericardial effusion, and dilation of the coronary arteries.
* Echocardiographic findings: LVEF <50%, right ventricular dysfunction, and pericardial effusion or segmental contractility abnormalities.

Data sources/measurements

The observational method and survey technique were used through a form designed for data collection, facilitating the capture of information directly from the medical records. To ensure the quality of the data, a review and comparison were carried out with the original medical records. The procedure used in the study is described below.

Obtaining Authorization: Permission was obtained from the authorities of the "Vicente Corral Moscoso" Hospital in Cuenaca-Ecuador to access the data required for the research.

Academic supervision: This study was developed under the supervision of a treating pediatrician from the Children's Intensive Care Unit in collaboration with a pediatric cardiologist from the Pediatric Cardiology Service who treated the children at the "Vicente Corral Moscoso" Hospital since the beginning of the pandemic.

Study Procedure

* With permission from the "Vicente Corral Moscoso" Hospital in Cuenca, access to the medical records was requested.
* Permission was obtained from the pediatric patients' parents or guardians for the data's academic use.
* The necessary data were extracted from the medical records and compiled in files.
* The echocardiograms of the patients included in the sample were analyzed.
* The information from the questionnaires was transcribed and statistically analyzed to obtain aggregate results.

* The confidentiality and protection of the data collected in the questionnaire were maintained.

Control of sources of bias

To minimize interviewer, information, and memory biases, the researchers rigorously followed a guide and records established in the research protocol. The strict application of participant selection criteria reduced observation and selection biases. All clinical and paraclinical variables recorded during the study period were documented. Two researchers examined each record independently and in parallel, ensuring consistency before inclusion in the database.

Universe and Sample

The universe comprised all the patients registered in the institution. The sample size was nonprobabilistic and discretionary since all incident cases in the study period were included.

Quantitative variables

Inferential statistics were used. Categorical results are expressed as frequencies and percentages.

Statistical analysis

The collected data were entered into a database developed in Microsoft Excel 2019, which allowed them to be organized according to specific variables. Subsequently, the data were analyzed with SPSS version 26 software. The descriptive results are shown as absolute frequencies and percentages. For numerical variables, means and standard deviations were calculated and are presented in tables. These findings were interpreted and discussed compared to the academic literature and similar studies published in peer-reviewed scientific journals. The SPSS 26.0 statistical package was used for the analysis (IBM Corp. Released 2018. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp.).

Results

Study participants

Nineteen patients were included in the study.

Patient characteristics

The pediatric patients studied ranged in age from one month and 25 days to 15 years and 11 months, with a mean age of 6.2 years and a standard deviation of 5.3 years. A total of 31.6% of these children were between 1 and 4 years old. Among them, 52.6% were girls, and 63.2% were overweight (Table 1).

Table 1. Frequency and percentages of pediatric patients with Multisystem Inflammatory Syndrome associated with COVID-19 according to the variables age, gender, and nutritional status. "Vicente Corral Moscoso" Hospital, Cuenca, April 2020–March 2022.

Characteristics	Frequency	%
Age		
Under one year old (0 years old)	4	21.1
From 1 to 4 years	6	31.6
From 5 to 9 years	4	21.1
From 10 to 15 years	5	26.3
Minimum = One (1) month with 25 days		
Maximum = 15 years and 11 months		
Mean = 6.2 years Std . Its T . = 5.3 years		
Sex		
Male	9	47.4
Female	10	52.6
Nutritional condition		
Underweight	1	5.3
Normal	2	10.5
Overweight	12	63.2
Obesity	4	21.1

COVID-19 diagnosis

Among the 19 pediatric patients with multisystem inflammatory syndrome associated with COVID-19, 73.7% underwent PCR, and 42.9% had positive results. A total of 57.9% of patients received antigen tests, 27.3% of whom were positive. Additionally, 84.2% of the patients were tested for antibodies, and 93.8% were positive for COVID-19 IgG (Table 2).

Table 2. Frequency and percentages of pediatric patients with Multisystem Inflammatory Syndrome associated with COVID-19 according to PCR, Antigen and Antibody tests. "Vicente Corral Moscoso" Hospital, Cuenca, April 2020–March 2022.

Proof	Frequency	%
RT–PCR		
Made	14	73.7
Positive	6	42.9
Negatives	8	57.1
Antigens		
Made	11	57.9
Positive	3	27.3
Negatives	8	72.7
Antibodies		
Made	16	84.2
IgG Positives	15	93.8
Negative IgG	1	6.3

Ultrasound studies

In echocardiographic studies of pediatric patients with MIS-C, pericardial effusion was observed in 3 patients (15.8%), and right ventricular dysfunction was observed in 1 patient (5.3%). The most common cardiac manifestations in the sample studied included pericardial dysfunction, valvular dysfunction, cardiac arrhythmias, and pericardial effusion, each present in 10.5% of the patients (Table 3).

Regarding the clinical signs of MIS-C presented by pediatric patients, 68.4% had fever at the time of admission to the health facility, 47.4% had vomiting, 42.1% had abdominal pain, 31.6% had diarrhea, 31.6% had skin rash, and only 15.8% had conjunctivitis (Table 4).

Table 3. Frequency and percentages of pediatric patients with Multisystem Inflammatory Syndrome associated with COVID-19 according to cardiac manifestations. "Vicente Corral Moscoso" Hospital, Cuenca, April 2020–March 2022.

MIS-C	Frequency	%
Pericardial dysfunction	2	10.5
Valve dysfunction	2	10.5
Cardiac arrhythmias	2	10.5
Pericardial effusion	2	10.5
myocardial dysfunction	1	5.3
coronary abnormalities	1	5.3
Dilation of the coronary arteries	1	5.3

Figure 2. Echocardiogram showing the coronary arteries.

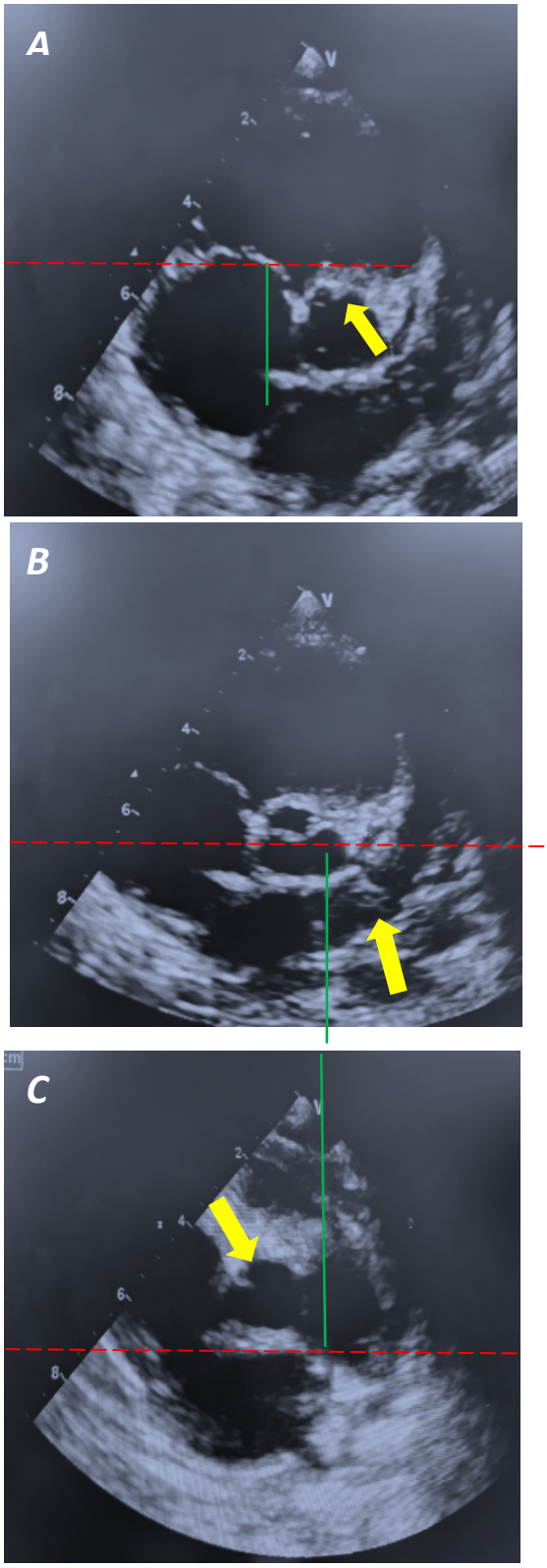


Figure 2. Image A. Origin of the dilated left coronary artery. ***Image B.*** Left coronary artery with bifurcations: circumflex and dilated anterior descending artery. ***Image C.*** Right coronary artery of average caliber. **Source:** Lourdes Valeria López Izquierdo, Pediatric Cardiologist of the Pediatric Cardiology Service of the "Vicente Corral Moscoso" Hospital. Cuenca - Azuay, 2023.

Table 4. Frequency and percentages of pediatric patients with Multisystem Inflammatory Syndrome associated with COVID-19 according to signs. "Vicente Corral Moscoso" Hospital, Cuenca, April 2020–March 2022.

Signs	Frequency	%
Fever	13	68.4
Vomiting	9	47.4
Abdominal pain	8	42.1
Diarrhea	6	31.6
Acne	6	31.6
Conjunctivitis	3	15.8
Total	**19**	**100**

Discussion

The MIS-C in children has gained importance in medicine due to its association with COVID-19. The results of this study at the "Vicente Corral Moscoso" Hospital between April 2020 and March 2022 contributed to the understanding of MIS-C pathology in children in Cuenca, Ecuador.

The sample showed a diverse range of ages, from slightly over a month to almost 16 years, with the highest frequency occurring in young children (31.6% between 1 and 4 years). This finding suggested that MIS-C can affect children of all ages but has a higher incidence in early childhood, given the average age of 6.2 years. This age distribution differs from what is reported in the Anglo-Saxon literature, which indicates a greater frequency of pregnancy in adolescents and an almost zero incidence in young children. However, studies such as those of Payne et al. [29] and Smith et al. [30] have also shown a greater incidence of MIS-C in younger children, which supports our findings and suggests geographic or demographic variations in the presentation of this condition. These differences highlight the need for a personalized approach to diagnosing and treating MIS-C, considering the diversity of disease manifestations depending on age and geographic context.

In contrast, according to Graciano-Machuca et al. [31], although COVID-19 illnesses are typically milder in children than adults, MIS-C shows clinically significant symptoms in this age group.

The present study revealed that overweight and obesity were common comorbidities observed together in 84.2% of patients, followed by a neurological condition represented by 21.1%. In contrast, respiratory, cardiac, hematological, and immunological diseases or allergic comorbidities became less common, accounting for 5.3% of the comorbidities. Both overweight and obesity suggest a possible relationship between chronic inflammation, which is typical of obesity, and the acute inflammatory response in MIS-C patients. Acevedo et al. reported that this comorbidity was found in 37.0% of patients, emphasizing that being overweight and obese increases the risk of cardiovascular and metabolic problems, in addition to generating a proinflammatory state [32]. In addition, adipose tissue, especially visceral tissue, produces proinflammatory cytokines such as TNF-**α** and IL-6. Its chronic elevation in overweight or obese people could be exacerbated in situations of intense inflammatory response [33].

In our study, 68.4% of the pediatric patients developed fever upon admission to the hospital, while 47.4% experienced vomiting, which is common in several pediatric conditions; this could complicate the early diagnosis of MIS-C. Additionally, 42.1% had abdominal pain, 31.6% had diarrhea and rash, and only 15.8% had conjunctivitis, which is a less common symptom and could indicate a generalized inflammatory response similar to Kawasaki disease. Naranjo et al. noted that this symptomatic similarity represents a challenge for early diagnosis and may cause delays in identifying and treating more severe conditions, such as MIS-C [34].

Despite the association between MIS-C and COVID-19, in the present study, 57.1% of patients tested negative according to the SARS-CoV-2 RT–PCR test.

According to the antigen test, only 27.3% of the patients were positive. However, 93.8% of the patients tested positive for the IgG antibody, indicating that most had been exposed to the virus and developed an immune response. This variation in positivity rates between tests highlights the challenges in detecting and diagnosing the virus and its link to the syndrome. The low positivity for antigen and PCR, in contrast to the high positivity for antibodies, maybe because many children have already passed the acute phase of SARS-CoV-2 infection and developed symptoms of MIS-C, such as a subsequent immune response.

Similar to Sözeri et al.'s findings, most children with MIS-C also had negative PCR results for SARS-CoV-2 but positive results in antibody tests [35]. The time lag between acute COVID-19 infection and subsequent development of MIS-C could explain this difference. The virus may have already been cleared from the body when MIS-C manifests, resulting in a negative PCR [27].

In the available literature, several studies have addressed the relationship between MIS-C and tests for COVID-19, including both PCR and antigen tests. Notably, nasopharyngeal PCR tests for COVID-19 patients harm many MIS-C patients. Still, for serum anti-SARS-CoV-2 antibodies, this finding suggests that MIS-C is a postviral inflammatory disease rather than a persistent COVID-19 infection [36]. These findings support the complexity of diagnosing MIS-C and its relationship with SARS-CoV-2 infection.

It is essential to correctly detect and diagnose MIS-C in children with COVID-19 for effective treatment and timely clinical care. Antibody testing has become a crucial tool for confirming MIS-C in pediatric patients, as it establishes a clear connection with previous SARS-CoV-2 infection, which is essential for confirmation of the syndrome. Its importance aligns with other studies highlighting the diagnosis of MIS-C by antibody testing [37]. Although PCR is the gold standard for the acute diagnosis of COVID-19, it is not always used in patients with MIS-C [2]. Instead, antigen testing is preferred in the first five days of illness, especially in patients suspected of having severe COVID-19 [17].

The detection of COVID-19 and MIS-C requires different diagnostic strategies. The antigen test is used in MIS-C patients, while PCR is used when there is uncertainty between severe COVID-19 and MIS-C or if the antigen test is negative after five days of symptoms. A COVID-19 diagnosis was considered to be confirmed by positive results on both tests or even just one test. This diagnostic flexibility underscores the need for a multifaceted approach to such a complex virus and syndrome.

From a cardiological point of view, our study's echocardiographic results and cardiac manifestations show how MIS-C affects the cardiovascular system of children. Although in smaller proportions, pericardial effusion and right ventricular dysfunction highlight the importance of rigorous cardiac follow-up in these patients. Mannarino et al. also observed that ventricular dysfunction, pericardial effusion, and valvulitis are common diagnoses in MIS-C patients, which supports the findings of this investigation [38].

Regarding the discussion about MIS-C and its associated cardiological conditions, a systematic study and meta-analysis carried out by Ferreira et al. [39] revealed that among children hospitalized with MIS-C, the combined incidence of myocarditis or pericarditis was 34.3% and that of echocardiogram abnormalities reached 40.8%. In this study, Kawasaki disease was also present in 14.8% of the patients, and coronary dilation was observed in 15.2%. The rate of electrocardiogram abnormalities was 5.3%, and the mortality rate was 0.5%. In addition, 186 children had persistent complications upon discharge, with a combined long-term prevalence of these manifestations of 9.3%.

The study's results confirm that MIS-C considerably affects the cardiovascular system in children, highlighting the need for careful cardiac follow-up. In addition, they point out the importance of future research to determine whether these patients will face an elevated cardiovascular risk, including an increased risk of heart

attack, arrhythmias, or thrombosis, a crucial aspect of planning medical care.

Finally, the 26.3% mortality rate in the present study underscores the seriousness of MIS-C and the critical need for early and effective clinical intervention. Although children are considered to be at low risk for COVID-19, the severity of MIS-C requires rethinking treatment strategies in this population. A similar percentage was observed in the study by Gupta et al., who reported a mortality rate of 18.6% in children with MIS-C post-COVID-19 [40].

Limitations

The present investigation reported a patient with coronary involvement (Figure 2) utterly compatible with Kawasaki disease (KD). Despite its limited visualization, echocardiography was used as a diagnostic imaging modality (Figure 2). Studies affirm that patients with KD who present coronary alterations proven by echocardiogram require complementary images obtained using more complex imaging methods, such as coronary angiography (CAG), the gold standard, or coronary computed tomography angiography (CCA) [41]. According to van Stijin et al. [42], cCTA detects up to twice as many additional coronary lesions in KD patients previously evaluated by echocardiography. The institution where the study was conducted does not have additional diagnostic imaging modalities. This has become a limiting factor in confirming a diagnosis and establishing long-term treatment.

Conclusions

It is evident that MIS-C associated with COVID-19 mainly affects young children and is strongly correlated with overweight and obesity. Common clinical manifestations, such as fever, vomiting, and abdominal pain, reinforce the importance of considering MIS-C in pediatric diagnoses. Although many patients tested negative by PCR, significant cardiac conditions were observed, including pericardial effusion and ventricular and valvular dysfunctions. This highlights the relevance of the MIS-C as a serious cardiovascular risk factor in children, regardless of the result of the COVID-19 test. The high mortality rate of 26.3% underscores the severity of MIS-C and the need for timely diagnosis and treatment. This study, conducted at the "Vicente Corral Moscoso" Hospital in Cuenca, highlights the need to raise awareness about MIS-C and its connection with COVID-19. This finding emphasizes the importance of adequate clinical management and continuing research.

Abbreviations

COVID-19: Coronavirus 2019.
SARS-CoV-2: severe acute respiratory syndrome type 2 virus.
MIS-C: Multisystem Inflammatory Syndrome in Children
KD: Kawasaki disease.
CAG: Coronary angiography.
cCTA: coronary computed tomography angiography.

Supplementary information

No supplementary materials are declared.

Acknowledgments

Not declared.

Author contributions

María de los Ángeles Zhingri Angamarca: Conceptualization, data curation, formal analysis, funding acquisition, research, writing - original draft.
Mónica Valeria Peñafiel Sampedro: data curation, formal analysis, acquisition of funds, research.
María Isabel Ruilova Castillo: conceptualization, methodology, project administration, resources, software, supervision, validation, visualization, writing - review and editing.
Jonathan Tipán-Barros: Methodology, project administration, resources, Software, supervision, validation, visualization, writing - review and editing.
All the authors read and approved the final version of the manuscript.

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Availability of data and materials

The data were collected from medical archives and are not publicly available due to patient confidentiality but are available through the corresponding author upon reasonable academic request.

Statements

Ethics committee approval and consent to participate

The study obtained approval from the Human Research Ethics Committee of the University of Cuenca and the board of directors of the "Vicente Corral Moscoso" Hospital in Cuenca, Ecuador. The guardians, fathers, mothers, or representatives of the participants signed the consent for participation.

Publication consent

The authors have consented to the publication of the ultrasound images from the guardians of the study patients. Informed consent for the use of images will be provided if needed.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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