Journal of Vessels and Circulation
Qom University of Medical Sciences
Autumn 2023. Volume 4. Number 4

Research Paper

Comparative Echocardiography and Cardiac Complications in Kawasaki vs. COVID-19-Associated Inflammatory Syndrome

Vida Saeidipoor[1, 2*], Reza Shiari[2, 3], Roxana Mansour Ghanaei[4], Mohammad Reza Khalilian[2, 5]

1. School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
2. Research Institute for Children Health, Mofid Children's Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
3. Department of Pediatric Rheumatology, Pediatric Infections Research Center, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
4. Department of Pediatric Infectious Disease, School of Medicine, Pediatric Infections Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
5. Department of Pediatrics, School of Medicine, Shahid Modarres Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Use your device to scan and read the article online

Please cite this article as Saeidipoor V, Shiari R, Mansour Ghanaei R, Khalilian MR. Comparative Echocardiography and Cardiac Complications in Kawasaki vs. COVID-19-Associated Inflammatory Syndrome. J Vessel Circ. 2023; 4(4):139-148. http://dx.doi.org/10.32598/JVC.4.4.31.36

http://dx.doi.org/10.32598/JVC.4.4.31.36

Article info:
Received: 24 Mar 2023
Accepted: 29 Jul 2023
Publish: 01 Oct 2023

Keywords:
Multisystem inflammatory syndrome (MIS), Kawasaki disease (KD), Children, COVID-19

ABSTRACT

Background and Aim: One of the observed phenomena during the COVID-19 pandemic is the occurrence of multisystem inflammatory syndrome in children (MIS-C). Patients with this disease have some overlapping symptoms and signs with Kawasaki disease (KD), which is associated with cardiac complications. This study was conducted to compare the echocardiography results and cardiac complications in patients with Kawasaki and Kawasaki-like inflammatory syndrome affected by COVID-19 who were referred to Mofid Hospital from 2020 to 2022.

Materials and Methods: This cross-sectional analytical study was conducted on children hospitalized at Mofid Hospital diagnosed with COVID-19 during 2020-2021. The clinical findings, echocardiographic results of patients, and cardiac complications were compared between the two groups of patients with Kawasaki and MIS-C.

Results: A total of 227 patients with a final diagnosis of MIS-C or KD were investigated in this study. Among the patients, 107 cases (50.5%) were girls and 105(49.5%) were boys. Of the patients, 180 cases had MIS-C (79.3%) and 47 cases had KD (20.7%). In terms of age, weight, and body mass index, a significant difference was observed between the two groups ($P<0.05$). However, no statistically significant difference was observed in the length of hospitalization between the two groups ($P>0.05$). In the laboratory investigations, significant differences were observed in the levels of erythrocyte sedimentation rate (ESR), uric acid, D-dimer, phosphorus (P), magnesium (Mg), white blood cell (WBC) count, platelet (PLT) count, mean corpuscular volume (MCV), blood urea nitrogen (BUN), albumin, and total protein between the MIS-C and KD groups ($P<0.05$). The clinical manifestations of gastrointestinal and pulmonary involvement were significantly higher in the MIS-C group compared to the KD group ($P<0.05$). No significant difference was observed in neurological, cardiac, and skin involvement between the two groups

*** Corresponding Author:**
Vida Saeidipoor, PhD.
Address: *Research Institute for Children Health, Mofid Children's Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran.*
Phone: *+98 (917) 7582356*
E-mail: *vida_saeidipoor@yahoo.com*

Journal of Vessels and Circulation
Qom University of Medical Sciences

(P>0.05). Also, no statistically significant difference was observed in the diagnostic indices between the two groups (P<0.05). In the results of the first echocardiography, pleural effusion and vascular involvement were significant, while in the second echocardiography, mild mitral regurgitation (MR) and pleural effusion showed significant differences between the two groups. Other echocardiography results were not significant on all three occasions (P>0.05).

Conclusion: MIS-C likely represents a new systemic inflammatory syndrome associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children, and MIS-C patients have cardiac complications. Further international studies are necessary to confirm these results and better understand the pathophysiology of MIS-C.

Introduction

In December 2019, a new coronavirus appeared in Wuhan City, China, and since then, it has rapidly spread to almost all countries worldwide, leading to an increase in both the number of patients and fatalities associated with the disease [1]. The clinical spectrum of COVID-19 in adults, children, and adolescents ranges from asymptomatic infection to severe pneumonia, acute respiratory failure, multiple organ dysfunction syndrome, and fatal disease [2]. However, epidemiological data from many countries show that children comprise only a small part of patients with COVID-19, which was initially reported as 1.7% in children younger than 18 years old [1]. While more than 90% of children with COVID-19 have been described as having asymptomatic, mild, or moderate disease, new concerns have arisen with reports of inflammatory states or Kawasaki-like diseases. The resulting phenotypes are a combination of typical and atypical Kawasaki disease (KD), Kawasaki shock syndrome, toxic shock syndrome, and macrophage activation/hemophagocytic lymphohistocytosis syndrome. Children with hyperinflammatory syndrome and multiple organ involvement were classified as having pediatric inflammatory multisystem syndrome (PIMS) or multisystem inflammatory syndrome in children (MIC-C) [2].

KD is a rare acute systemic vasculitis of medium-sized vessels, with coronary artery aneurysms as its main complication, primarily affecting children under 5 years old. Its cause is not clearly defined, but infectious stimuli have been suggested in the etiology of KD due to its specific epidemic and seasonal patterns [3, 4]. Various infectious agents, including bacteria and viruses, are involved in the pathogenesis of KD [2]. However, in April 2020, hyperinflammatory shock with clinical characteristics similar to KD was reported in children and adolescents in England [5]. Following the report of MIS-C cases from Europe in April 2020, many physicians noted similarities between the presentation of MIS-C and KD [6].

In KD, coronary artery aneurysm or pericardial dilatation and effusion are more common, whereas depressed ventricular function and significantly elevated brain natriuretic peptide (BNP) levels are more frequently observed in MIS-C. Some patients with MIS-C suffer from coronary artery dilatation and aneurysms, although most of these abnormalities are resolved upon follow-up. In contrast, KD is characterized by a subset of patients with persistent coronary artery abnormalities [7, 8]. Significant differences in laboratory results include an increased number of white blood cells, neutrophils, and thrombocytosis in KD compared to the normal number of white blood cells, lymphocytopenia, and thrombocytopenia in MIS-C [9]. Cardiac involvement occurs in 67% to 80% of children with MIS-C and is more common in MIS-C than in KD. The largest case series report on 539 children with MIS-C during the COVID-19 pandemic showed that cardiac manifestations included ventricular dysfunction, coronary aneurysms, conduction disturbances, and arrhythmias. Cardiac clinical manifestations of MIS-C can occur across a spectrum of disease severity. Many patients face cardiovascular disturbances and shock, which can be quite severe and sudden. Conversely, some patients may be referred without any cardiovascular involvement. If MIS-C is suspected, a complete cardiac evaluation, including measurements of troponin and BNP levels, an electrocardiogram (ECG), and a transthoracic echocardiogram, should be performed immediately. Additional cardiac tests, such as cardiac MRI (CMR) or computed tomography (CT) of the chest may also be warranted as indicated [10].

Early reports of MIS-C described a KD-like disease. There is a growing understanding that MIS-C is distinct from KD, but these disorders are common in some clinical features, including coronary artery dilatation. The prevalence of coronary artery aneurysms in the MIS-C is approximately 13-26%. The cause of coronary artery

disease is unclear. Coronary artery dilatation can be secondary to vasculitis or generalized hyperinflammation. The outcomes associated with coronary artery dilation and aneurysms in MIS-C are generally favorable, with many coronary artery abnormalities normalizing within 30 days [10]. In addition to echocardiography and cardiac magnetic resonance imaging, cardiac biomarkers, especially troponin I (TnI) and terminal proeB-type natriuretic peptide (NT-proBNP), have been used as biomarkers of cardiac involvement. For adults, both TnI and NT-proBNP are approved for the diagnosis and monitoring of ischemic heart damage and heart failure. Their role in the diagnosis and management of KD has been variable and is not recommended. However, abnormalities in NT-proBNP and TnI have been described in the context of MIS-C. Nonetheless, there is limited understanding of their role in the diagnosis, monitoring, and prognosis of MIS-C compared to KD. This study was conducted to examine the results of echocardiography and cardiac complications in patients with Kawasaki and Kawasaki-like inflammatory syndrome associated with COVID-19 who were referred to Mofid Hospital from 2020 to 2021. The aim is to better prepare healthcare providers to manage the influx of patients with severe KD, particularly in countries that have recently reached the peak of COVID-19.

Materials and Methods

This study was conducted longitudinally, the research population included children admitted to Mofid Hospital with the diagnosis of COVID-19 who had Kawasaki and Kawasaki-like clinical manifestations. The sampling method was a census, meaning that all children referred to Mofid Hospital with a positive diagnosis from a COVID-19 polymerase chain reaction (PCR) test between 2020 and 2022, whose hospital records were complete, were included in the study.

In this study, the clinical diagnosis of MIS-C was performed based on the criteria of the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC) of the United States [11]. The diagnostic criteria for MIS-C included six requirements: Serious illness leading to hospitalization, being younger than 21 years, fever (body temperature >38.0 ˚C) or reported fever lasting at least 24 hours, laboratory evidence of inflammation, multisystemic involvement (i.e. involving at least two systems) and a positive PCR result for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) or positive immunology results.

According to the American Heart Association (AHA) criteria for the diagnosis of KD, any child with at least five days of fever and four or more of the following clinical —rash, cervical lymphadenopathy of at least 1.5 cm in diameter, conjunctivitis, mucosal changes in the oral cavity, and organ changes—were diagnosed with KD [12].

The exclusion criteria included underlying heart disease, signs and symptoms of acute respiratory distress syndrome, and patients with malignancy who had received chemotherapy. All patients were tested for SARS-CoV-2 virus via nasopharyngeal swab PCR and immunoglobulin G antibodies.

In the next step, by examining the patient records, the clinical and laboratory findings of the patients in the two groups were compared, and the echo results of the patients and heart complications between the two groups of KD and MISC patients were analyzed by a pediatric cardiologist. Data were analyzed using IBM SPSS software, version 25. Mean±SDs were used to describe quantitative variables, while frequencies and percentages were used to describe qualitative variables. Also, the t-test and chi-square test were used to measure the relationships.

Results

A total of 227 patients with a final diagnosis of MIS-C or KD were investigated in this study. Among the patients, 107 cases (50.5%) were girls and 105(49.5%) were boys. A total of 180 patients had MIS-C (79.3%) and 47 had KD (20.7%). Significant differences were observed in age, weight, and body mass index between the two groups, with all three variables being lower in the KD patients ($P<0.05$). However, no statistically significant difference was observed in the length of hospitalization between the two groups ($P>0.05$) (Table 1).

In the laboratory analysis, a significant difference was observed between the groups in the levels of erythrocyte sedimentation rate (ESR), uric acid, D-dimer, phosphorus (P), magnesium (Mg), white blood cell (WBC), platelet (PLT), mean corpuscular volume (MCV), blood urea nitrogen (BUN), albumin, and total protein ($P<0.05$). MIS-C patients showed lower levels of ESR, P, Mg, WBC, PLT, albumin, and total protein, while uric acid, d-dimer, MCV, and BUN were higher (Table 2).

No significant difference was observed in the incidence of fever between the MIS-C (78.3%) and KD (70.2%) groups ($P=0.24$) (Figure 1).

Table 1. Frequency of demographic and anthropometric variables in the MIS-C and KD groups

Variables		No. (%)/Mean±SD		P
		MIS-C	KD	
Gender	Girl	86(52.1)	21(44.7)	0.36*
	Boy	79(47.9)	26(55.3)	
Age (m)		45.5±41.3	14.4±6.4	0.001**
Hospitalization length (d)		4.1±2.5	4.6±2	0.37**
Weight (kg)		17.9±13.5	13.1±6.3	0.02**
Height (cm)		94.9±23.6	88.6±16.4	0.26 **
BMI (kg/m²)		0.32±0.1	0.27±0.06	0.04**

Journal of Vessels and Circulation
Qom University of Medical Sciences

Abbreviations: MIS-C: Multisystem inflammatory syndrome in children; KD: Kawasaki disease; BMI: Body mass index.

*Chi-square test, **T-test.

The clinical manifestations of gastrointestinal and pulmonary involvement were significantly higher in the MIS-C group compared to the KD group (P<0.05). No significant difference was observed in neurological, cardiac, and skin involvement between the two groups (P>0.05) (Table 3).

Also, no statistically significant difference was observed in the diagnostic indices between the two groups (P>0.05) (Table 4).

Regarding the results of echocardiography, in the MISC group, 128 cases (60.37%) were normal, ten cases (4.71%) had vasodilatation, and 61 cases (28.7%) had mild pericardial effusion. Among these, two cases had aneurysms, five cases showed left ventricular (LV) dysfunction and diastolic dysfunction, three cases had moderate to severe mitral regurgitation (MR) and two cases had moderate tricuspid regurgitation (TR). In the one-month follow-up echocardiogram, 84 cases displayed abnormal findings. These 84 cases underwent a one-month follow-up, during which 21 cases had mild pericardial effusion, reflecting a decrease of approximately 66% compared to the previous echocardiogram, and this condition normalized. Additionally, one case of moderate to severe MR and one case of heart dysfunction were reported in the follow-up echocardiogram, while the remaining cases were normal. In the three-month follow-up echocardiogram, 23 cases that had abnormalities in the one-month echocardiogram were included in the study, and in this follow-up, the pericardial effusion was completely resolved, with only one case of moderate to severe MR and one case of heart dysfunction reported.

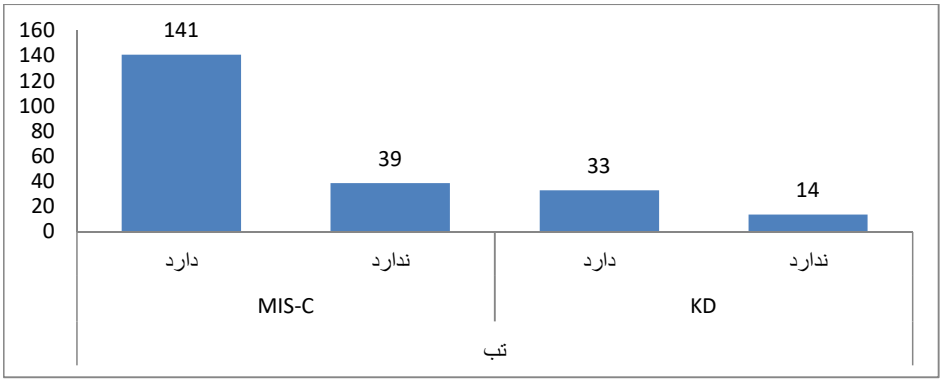

Figure 1. Comparison of fever in the MIS-C and KD groups

Journal of Vessels and Circulation
Qom University of Medical Sciences

Table 2. Laboratory data of the two groups

Variables*	Mean±SD		P
	MIS-C	KD	
ESR (mm/h)	40.4±26.9	60.1±27.9	0.001
CRP (mg/L)	27.8±17	29.5±14.9	0.58
Fibrinogen (mg/dL)	390.9±97.8	440.3±46.6	0.05
Ferritin (ng/mL)	162.7±177.9	96.4±80.1	0.1
LDH (U/L)	699.2±364.6	608.3±231.1	0.28
CPK (U/L)	131.5±159	78.4±65.4	0.26
Uric. acid (mg/dL)	4.8±2.3	3.01±0.95	0.03
D-Dimer (ng/mL)	807.1±650.2	452.2±331.3	0.04
PT (seconds)	12.6±2.4	12.6±1	0.96
PTT (seconds)	29.8±5	29.4±3	0.79
INR	1.09±0.42	1.06±0.12	0.78
Ca (mg/dL)	9.3±1.29	9.6±0.7	0.26
P (mg/dL)	4.1±0.99	4.77±0.81	0.002
Mg (mg/dL)	2.08±0.22	2.18±0.21	0.03
Na (mEq/L)	134.4±3.7	134.5±2.2	0.93
K (mEq/L)	4.16±0.5	4.33±0.52	0.08
WBC (cells/µL)	9.72±6.49	14.4±6.35	0.001
WBC.lymp (cells/µL)	33.1±19.3	34.39±16.11	0.73
HB (g/dL)	10.83±1.48	10.99±1.24	0.57
PLT (cells/µL)	287.4±157.4	451.12±150.58	0.001
HCT (%)	32.82±3.77	32.71±2.93	0.87
RBC (cells/µL)	4.1±0.52	4.19±0.4	0.45
MCV (fL)	80.13±4.96	77.46±5.41	0.01
MCH (pg)	26.23±2.67	26.4±3.26	0.76
BUN (mg/dL)	12.81±7.66	9.07±3.95	0.007
Cr (mg/dL)	9.07±3.95	0.59±0.1	0.27
AST (U/L)	54.79±42.12	40.94±28.07	0.07
ALT (U/L)	46.04±61.14	50.38±62.62	0.71
Alkp (U/L)	493.1±364.73	588.87±247.13	0.16
Albumin (g/dL)	3.99±0.75	4.61±0.46	0.001
Total protein (g/dL)	6.17±1.16	6.99±0.94	0.01

Journal of Vessels and Circulation
Qom University of Medical Sciences

Abbreviations: ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; LDH: Lactate dehydrogenase; CPK: Creatine phosphokinase; PT: Prothrombin time; PTT: Partial thromboplastin time; INR: International normalized ratio; Ca: Calcium; P: Phosphorus; Mg: Magnesium; Na: Sodium; K: Potassium; WBC: White blood cell; HB: Hemoglobin; PLT: Platelet; HCT: hematocrit; RBC: Red blood cell; MCV: Mean corpuscular volume; MCH: Mean corpuscular hemoglobin; BUN: Blood urea nitrogen; Cr: Creatinine; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; Alkp: Alkaline phosphatase; MIS-C: Multisystem inflammatory syndrome in children; KD: Kawasaki disease; fL: Femtoliters; pg: Picograms.

*T-test.

Table 3. Comparison of the involvement of different body systems between the MIS-C and KD groups

Clinical Manifestations	No. (%)		P
	MIS-C	KD	
Digestive involvement	94(52.2)	8.5(4)	0.001*
Pulmonary involvement	36(20)	2(4.3)	0.01*
Neurological involvement	13(7.2)	0(0)	0.512*
Cardiac involvement	48(26.7)	10(21.3)	0.45*

*Chi-square test.

Journal of Vessels and Circulation
Qom University of Medical Sciences

Regarding KD patients, among the 47 patients, five cases had coronary artery dilatation, five cases had aneurysm, and 14 cases had pericardial effusion in the first echocardiogram upon hospital admission, while 23 cases exhibited normal echocardiograms during hospitalization. In the one-month follow-up echocardiogram, 24 KD patients who had abnormal echocardiograms during hospitalization underwent follow-up. Of these, 1 case (with an 80% reduction) exhibited vasodilatation, 4 cases had pericardial effusion, and 2 cases had aneurysms (with a 60% reduction), while 17 cases were reported as normal. In the three-month follow-up echocardiogram, seven cases from the one-month follow-up echocardiogram were re-evaluated. Following treatment, one case had an aneurysm and one case had coronary artery dilatation, while the remaining cases were reported to be normal (Table 5).

Discussion

An outbreak of a severe pediatric inflammatory disease, with some features of KD, has been described since late March in areas with high SARS-CoV-2 prevalence [5, 13, 14]. Whether this is a particularly aggressive form of KD caused by SARS-CoV-2 or a completely different entity is still debated.

This study was conducted to examine cases of patients with MIS-C and KD who had many overlapping features in terms of systemic inflammation and organ dysfunction. However, several fundamental differences exist between MIS-C and KD, which we discuss below.

The results of the study revealed a significant difference between the two groups in terms of age, length of hospitalization, weight, and body mass index, with these values being higher in MIS-C patients. One feature that distinguishes MIS-C as a unique disease process compared to KD is that the mean age of MIS-C cases in the largest reported series, was 9–10 years, while KD primarily occurs in children aged five years or younger, with its peak incidence around ten months of age [15]. Similarly, in the study conducted by Cattalini et al., MIS-C children were significantly older (seven years vs

Table 4. Diagnostic indices in the MIS-C and KD groups

Variables	Mean±SD		P
	MIS-C	KD	
IgM (mg/dL)	218.4±202.7	124.6±19.1	0.46*
IgE (mg/dL)	481.2±813.7	145.3±105.6	0.51*
IgG (mg/dL)	1042.6±562.5	1003.6±453.3	0.92*
IgA (mg/dL)	102.2±58.7	80.3±46.3	0.6*
CIgM (mg/dL)	0.22±0.12	0.57±0.95	0.19*
CIgG (mg/dL)	0.94±1.61	1.7±2.5	0.3*

Ig: Immunoglobulin.

*T-test.

Journal of Vessels and Circulation
Qom University of Medical Sciences

Table 5. Comparison of echocardiography results before hospitalization and at one- and three-month follow-ups between the MIS-C and KD groups

Echocardiography Results	Variables	No. (%)		P
		MIS-C	KD	
1st-time echo results	Mild MR	33(78.6)	9(21.4)	0.14*
	Mild AR	1(100)	0(0)	0.46*
	Mild to severe MR	3(100)	0(0)	0.46*
	Moderate TR	2(100)	0(0)	0.46*
	Minimal PE	61(81.3)	14(18.7)	<0.001*
	Mild PH	7(100)	0(0)	0.46*
	NL	99(85.3)	17(14.7)	0.04*
	Coronary artery involvement	10(83.3)	2(16.7)	<0.001*
	Aneurysm	2(28.6)	5(71.4)	0.32*
	Arrhythmia	1(100)	0(0)	0.46*
2nd-time echo results	Mild MR	17(70.8)	7(29.2)	0.024*
	Mild AR	0(0)	0(0)	-
	Mild to severe MR	1(100)	0(0)	0.46*
	Moderate TR	0(0)	0(0)	-
	Minimal P.E	21(80.8)	5(19.2)	0.007*
	Mild PH	0(0)	0(0)	-
	Coronary artery involvement	0(0)	0(0)	-
	Aneurysm	0(0)	3(100)	0.46*
	Arrhythmia	0(0)	0(0)	-
	NL	48(68.6)	22(31.4)	0.12*
3rd-time echo results	Mild MR	2(33.3)	4(66.7)	0.21*
	Mild AR	0(0)	0(0)	-
	Mild to severe MR	0(0)	0(0)	-
	Moderate TR	0(0)	0(0)	-
	Minimal P.E	2(100)	0(0)	0.46*
	Mild PH	0(0)	0(0)	
	Coronary artery involvement	0(0)	0(0)	
	Aneurysm	0(0)	2(100)	0.46*
	Arrhythmia	0(0)	0(0)	
	NL	64(76.2)	20(2.8)	0.73*

Journal of Vessels and Circulation
Qom University of Medical Sciences

Abbreviations: AR: Aortic regurgitation; MR: Mitral regurgitation; NL: Normal; TR: Tricuspid Regurgitation; P.E: pericardial effusion.

*Chi-square test.

Journal of Vessels and Circulation
Qom University of Medical Sciences

two years), and had a longer length of hospital stay (12 days vs ten days) [16]. In the study by Pouletty et al., the Kawa-COVID-19 group was older (10 vs 2 years) compared to the KD group [17]. In the study conducted by Verdon et al., Kawasaki-like patients were older than KD patients [6]. In a study conducted in Brazil, all PIMS patients were hospitalized and the average length of hospitalization was ten days (range: Five to 15) [18]. In the study conducted by Fridman et al., the KD group was younger than the MIS-C group, and had a lower body mass index, while MIS-C patients also experienced a longer mean stay in the intensive care unit (ICU) and total hospitalization duration [19].

In this study, gastrointestinal and pulmonary involvement was significantly higher in the MIS-C group compared to the KD group. Similarly, a study conducted in Italy showed that gastrointestinal and respiratory involvement was more associated with MIS-C, while skin and mucosal involvement was significantly more in KD [16]. In the study conducted by Pouletty et al., gastrointestinal involvement was higher in the Kawa-COVID-19 group compared to the KD group [17]. A study in Bergamo (Italy) showed that Kawasaki-like patients had more respiratory and digestive involvement than KD patients [6]. A study in the United Kingdom on patients with MIS-C reported gastrointestinal involvement in 171 patients (92%) [20]. In a Russian study, gastrointestinal symptoms were more common among MISC patients [21]. A systematic review also showed that most MIS-C patients have gastrointestinal symptoms [22].

The MIS-C group showed lower levels of ESR, P, Mg, WBC, PLT, albumin, and total protein, while uric acid, d-dimer, MCV, and BUN levels were higher. One study found that the MIS-C group exhibited lower counts of leukocytes, lymphocytes, monocytes, and platelets compared to KD, while C-reactive protein (CRP) was higher in MIS-C, as well as troponin, troponin-T, ferritin, and D-dimer [16]. In a study conducted in France, platelet counts were lower in the Kawa-COVID-19 group compared to the KD group [17]. It seems that most patients with MIS-C experience a hyperinflammatory state, characterized by neutrophilic leukocytosis, increased ESR, hyponatremia, hypertriglyceridemia, and elevated levels of CRP, procalcitonin, D-dimer, and serum ferritin. Patients with MIS-C typically have lower platelet counts and higher ferritin levels compared to patients with KD. While lymphopenia has been observed in patients with MIS-C, neutrophilic leukocytosis is considered normal in KD [23].

Cardiovascular complications are the most obvious manifestations in patients with MIS-C. Hence, the results of our study showed that cardiac involvement was higher in MIS-C patients than in KD patients. However, no statistically significant difference was observed. For example, in a study conducted in Italy, cardiac involvement was more common in MIS-C patients with 60.4% of patients presenting with myocarditis, while coronary artery anomalies (CAA) were more prevalent in KD [16]. In our study, regarding coronary artery involvement, a significant difference was observed in the results of the initial echocardiogram, but no significant difference was found in vascular involvement between the two groups in the follow-up echocardiogram results.

CAA has been reported in 9% to 24% of patients with MIS-C. CAAs are dilated or small aneurysms in most patients. Pericarditis, pericardial effusion, and valvular insufficiency have also been reported [23]. However, the results of other studies also show that cardiac involvement occurs in 67%-80% of children with MIS-C, which is more common in MIS-C than in KD [10, 24, 25], supporting the findings of our study. It can also be said that the clinical manifestations of MIS-C can occur across a spectrum of disease severity [26-28].

However, it is recommended that in patients without cardiovascular involvement, a complete cardiac evaluation, including troponin and BNP levels, ECG, and echocardiography, should be performed if MIS-C is suspected, as ventricular dysfunction is a common finding in MIS-C, affecting 33% to 50% of patients [10, 29, 30].

Conclusion

The present study showed that an autoinflammatory disease similar to KD is associated with SARS-CoV-2 infection. However, this disease differs from classic KD because it occurs at older ages and is associated with a higher frequency of cardiac involvement. Also, MIS-C children often exhibit gastrointestinal and respiratory involvement compared to those with KD, while KD patients exhibit more skin involvement. Further prospective studies of MIS-C, including the evaluation of host immunological and genetic factors, are necessary to better understand this new disease.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Ethics Committee of Qom University of Medical Sciences (Code: IR.SBMU.MSP.REC.1401.475).

Funding

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

Authors' contributions

All authors equally contributed to preparing this article.

Conflict of interest

The authors declared no conflict of interest.

Acknowledgments

The authors would like to thank the Vice-Chancellor for Research and Technology of Shahid Beheshti University of Medical Sciences, the Vice-Chancellor for Research at the School of Medicine, and the Clinical Research Development Unit of Mofid Hospital in Qom City.

References

[1] CDC. COVID-19 Response Team. Coronavirus Disease 2019 in children - United States, February 12-April 2, 2020. MMWR Morb Mortal Wkly Rep. 2020; 69(14):422-426. [PMID]

[2] Akca UK, Kesici S, Ozsurekci Y, Aykan HH, Batu ED, Atalay E, et al. Kawasaki-like disease in children with COVID-19. Rheumatol Int. 2020; 40(12):2105-15. [DOI:10.1007/s00296-020-04701-6] [PMID]

[3] Chang LY, Lu CY, Shao PL, Lee PI, Lin MT, Fan TY, et al. Viral infections associated with Kawasaki disease. J Formos Med Assoc. 2014; 113(3):148-54. [DOI:10.1016/j.jfma.2013.12.008] [PMID]

[4] Razavi SMR, Azadegan M, Rezvan S, Noori E. A case report of Kawasaki Disease with manifestations of acute renal. J Vessel Circ. 2020; 1(2):17-20. [DOI:10.29252/jvesselcirc.1.2.17]

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

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

[7] Bar-Meir M, Guri A, Godfrey ME, Shack AR, Hashkes PJ, Goldzweig O, 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] [PMID]

[8] Rowley AH, Shulman ST, Arditi M. Immune pathogenesis of COVID-19-related multisystem inflammatory syndrome in children. J Clin Invest. 2020; 130(11):5619-21. [DOI:10.1172/JCI143840] [PMID]

[9] Molloy EJ, Nakra N, Gale C, Dimitriades VR, Lakshminrusimha S. Multisystem inflammatory syndrome in children (MIS-C) and neonates (MIS-N) associated with COVID-19: Optimizing definition and management. Pediatr Res. 2023; 93(6):1499-508. [DOI:10.1038/s41390-022-02263-w] [PMID]

[10] Feldstein LR, Tenforde MW, Friedman KG, Newhams M, Rose EB, Dapul H, et al. Characteristics and outcomes of US children and adolescents with multisystem inflammatory syndrome in children (MIS-C) compared with severe acute COVID-19. JAMA. 2021; 325(11):1074-87. [PMID]

[11] Go E, El Tal T, Tsoukas P, Kraus R, Gamulka BD, Mizzi T, et al. Comparing apples to apples in post-COVID-associated multisystem inflammatory syndrome in children (MIS-C). 2021. [DOI:10.2139/ssrn.3894907]

[12] McCrindle BW, Rowley AH, Newburger JW, Burns JC, Bolger AF, Gewitz M, 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-e99. [DOI:10.1161/CIR.0000000000000484] [PMID]

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

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

[15] Matucci-Cerinic C, Caorsi R, Consolaro A, Rosina S, Civino A, Ravelli A. 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] [PMID]

[16] Cattalini M, Della Paolera S, Zunica F, Bracaglia C, Giangreco M, Verdoni L, et al. 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, multicenter survey. Pediatr Rheumatol Online J. 2021; 19(1):29. [DOI:10.1186/s12969-021-00511-7] [PMID]

[17] Pouletty M, Borocco C, Ouldali N, Caseris M, Basmaci R, Lachaume N, et al. Paediatric multisystem inflammatory syndrome temporally associated with SARS-CoV-2 mimicking Kawasaki disease (Kawa-COVID-19): A multicentre cohort. Ann Rheum Dis. 2020; 79(8):999-1006. [DOI:10.1136/annrheumdis-2020-217960] [PMID]

Journal of Vessels and Circulation
Qom University of Medical Sciences

[18] Cavalcanti A, Islabão A, Magalhães C, Veloso S, Lopes M, do Prado R, et al. Paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS): A Brazilian cohort. Adv Rheumatol. 2022; 62(1):6. [DOI:10.1186/s42358-022-00237-4] [PMID]

[19] Fridman MD, Tsoukas P, Jeewa A, Yeung RSM, Gamulka BD, McCrindle BW. Differentiation of COVID-19-associated multisystem inflammatory syndrome from kawasaki disease with the use of cardiac biomarkers. Can J Cardiol. 2023; 39(6):815-23. [DOI:10.1016/j.cjca.2022.11.012] [PMID]

[20] Feldstein LR, Rose EB, Horwitz SM, Collins JP, Newhams MM, Son MBF, et al. Multisystem inflammatory syndrome in US children and adolescents. N Engl J Med. 2020; 383(4):334-46. [PMID]

[21] Kostik MM, Bregel LV, Avrusin IS, Dondurei EA, Matyunova AE, Efremova OS, Iet al. Distinguishing between multisystem inflammatory syndrome, associated with COVID-19 in children and the Kawasaki disease: Development of preliminary criteria based on the data of the retrospective multicenter cohort study. Front Pediatr. 2021; 9:787353. [DOI:10.3389/fped.2021.787353] [PMID]

[22] Hoste L, Van Paemel R, Haerynck F. Multisystem inflammatory syndrome in children related to COVID-19: A systematic review. Eur J Pediatr. 2021; 180(7):2019-34. [DOI:10.1007/s00431-021-03993-5] [PMID]

[23] Kabeerdoss J, Pilania RK, Karkhele R, Kumar TS, Danda D, Singh S. 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] [PMID]

[24] Zhang QY, Xu BW, Du JB. Similarities and differences between multiple inflammatory syndrome in children associated with COVID-19 and Kawasaki disease: Clinical presentations, diagnosis, and treatment. World J Pediatr. 2021; 17(4):335-40. [DOI:10.1007/s12519-021-00435-y] [PMID]

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

[26] Islam N, Ebrahimzadeh S, Salameh JP, Kazi S, Fabiano N, Treanor L, et al. Thoracic imaging tests for the diagnosis of COVID-19. Cochrane Database Syst Rev. 2021; 3(3):CD013639. [PMID]

[27] Valverde I, Singh Y, Sanchez-de-Toledo J, Theocharis P, Chikermane A, Di Filippo S, et al. Acute cardiovascular manifestations in 286 children with multisystem inflammatory syndrome associated with COVID-19 infection in Europe. Circulation. 2021; 143(1):21-32. [PMID]

[28] Ahmed M, Advani S, Moreira A, Zoretic S, Martinez J, Chorath K, et al. Multisystem inflammatory syndrome in children: A systematic review.EClinicalMedicine. 2020; 26:100527. [DOI:10.1016/j.eclinm.2020.100527] [PMID]

[29] Bermejo IA, Bautista-Rodriguez C, Fraisse A, Voges I, Gatehouse P, Kang H, et al. Short-term sequelae of multisystem inflammatory syndrome in children assessed by CMR. JACC Cardiovasc Imaging. 2021; 14(8):1666-7. [DOI:10.1016/j.jcmg.2021.01.035] [PMID]

[30] Penner J, Abdel-Mannan O, Grant K, Maillard S, Kucera F, Hassell J, et al. 6-month multidisciplinary follow-up and outcomes of patients with paediatric inflammatory multisystem syndrome (PIMS-TS) at a UK tertiary paediatric hospital: A retrospective cohort study. Lancet Child Adolesc Health. 2021; 5(7):473-82. [DOI:10.1016/S2352-4642(21)00138-3] [PMID]