

COVID-19 MIS-C at the Colonial War Memorial Hospital, Fiji: A Retrospective Descriptive Study

Amelita Lourdes P Mejia, MD, Laila MV Sauduadua, MBBS, Maryanne Kora'ai, MBBS, Joseph Tigarea MBBS, Oripa Fuatau, MBBS, Lagakali Tora Koyamaibole MBBS, Elizabeth Menon MBBS, Mikaele Lutumailagi MBBS, Ashnita D Prasad, MBBS, Laise-nia Baleilakeba MBBS and Valeria Natuman* MBBS

Pediatric Department, Colonial War Memorial Hospital, Suva, Fiji

Abstract

Background: The second wave of the Covid-19 pandemic in Fiji due to the delta variant started in April 2021. This has resulted in 672 deaths as of October 31, 2021. Though reports worldwide that looked at Covid-19 in children showed predominantly mild disease, a new condition emerged known as Multi-system Inflammatory Syndrome in Children and Adolescents (MIS-C). This study aims to describe the clinical features, investigations, treatment, outcomes, and complications of MIS-C in a country with limited resources.

Methods: This was a retrospective descriptive study that looked at all patients aged 0-<15 years admitted to the CWM Hospital between April 1, 2021, to October 31, 2021, who met the WHO and CDC criteria for MIS-C. The information analyzed included patient demographics, clinical data, investigations, treatment, complications, and outcomes.

Results: This study yielded 9 cases with the first case identified two months after community transmission. The indigenous I-Taukei infant (66.6%) was the most commonly affected with septic shock (55.5%) being the most common presentation. Cardiac and CNS symptoms were the chief symptoms in our cohort. All cases had RT PCR, of which 44.4% were positive, and 66.7% had parental exposure. Inflammatory markers included elevated CRP, LDH, troponin, and WCC. Echocardiogram and CXR were done. Management of these patients included IVIG, steroids, aspirin, and enoxaparin. Our case fatality rate was high at 55.5%, with 44% of patients discharged alive.

Conclusion: This study was able to effectively document the presentation, investigations, treatment plans, and outcomes of patients with MIS-C diagnosis in our hospital given our limited resources.

Keywords: MIS-C, Covid-19, Intravenous Immunoglobulin, Methylprednisolone.

Abbreviations: APTT: Activated Partial Thromboplastin Time; ASA: Aspirin; CDC: Centers for Disease Control and Prevention; CK: Creatine Kinase; CNS: Central Nervous System; CRP: C-reactive Protein; CSF: Cerebrospinal Fluid; CWMH: Colonial War Memorial Hospital; CXR: Chest Radiograph; DIC: Disseminated Intravascular Coagulation; ECG: Electrocardiogram; ECHO: Echocardiogram; EF: Ejection Fraction; ESR: Erythrocyte Sedimentation Rate; FBC: Full Blood Count; GCS: Glasgow Coma Scale; GI: Gastrointestinal; GIT: Gastrointestinal Tract; Hb: Hemoglobin; HHFNC: Humidified High-Flow Nasal Cannula; IVIG: Intravenous Immunoglobulin; LDH: Lactate Dehydrogenase; LV: Left Ventricle; MP: Methylprednisolone; MIS-C: Multisystem Inflammatory Syndrome in Children; PIMS-TS: Pediatric Multisystem Inflammatory Syndrome temporally associated with SARS-CoV-2; PT: Prothrombin Time; RAT: Rapid Antigen Test; RT-PCR: Real-Time; Polymerase Chain Reaction; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2; VLBW: Very Low Birth Weight; WCC: White Cell Count; WHO: World Health Organization

Introduction

Fiji is an archipelago of more than 300 islands in the South Pacific. The population is 884,887 (2017 census), with 260,514 (29%) under the age of 15 years. The Central/Eastern Division looks after 122,930 children less than 15 years old [1].

The initial Novel coronavirus was first identified in Wuhan, China in late 2019. Fiji recorded its first case of Covid-19 in March 2020. The Central division of Fiji became the epicenter of the second wave of the Covid-19 pandemic due to the Delta variant that started in April 2021. As of October 31, 2021, there were 52,110 cases of laboratory-confirmed infections with 71% of the cases from the Central Division, 28% from the Western Division, and 1% from the Eastern and Northern Divisions and with 672 deaths [2]. Globally and in Fiji, children typically had mild disease or were asymptomatic with lower rates of hospitalization and death compared to adults [3,4]. How-

ever, a hyperinflammatory condition known as Multisystem Inflammatory Syndrome in Children associated with COVID-19 (MIS-C), first reported in England in April 2020 as Paediatric Multisystem Inflammatory Syndrome temporally associated with SARS-CoV-2 (PIMS-TS) was observed with the peak of the pandemic [5,6].

This study looks at MIS-C in children below 15 years admitted to the Colonial War Memorial Hospital (CWMH), Suva, Fiji. This hospital serves as the national referral center for COVID-19 confirmed cases in the Central/Eastern Division including those with MIS-C. This is a retrospective descriptive study of the clinical presentations, investigation parameters, the treatment offered, the outcome (dead or alive), and the associated complications seen in MIS-C cases in a country with limited resources. It also aims to create awareness of MIS-C in Fiji and the other Pacific Island Countries.

***Corresponding Author:** *Valeria Natuman, Paediatric Registrar/ Masters Student in Paediatric, Paediatrics Department, Colonial War Memorial Hospital, Fiji National University, Suva, Fiji.

Citation: V Natuman*, COVID-19 MIS-C at the Colonial War Memorial Hospital, Fiji: A Retrospective Descriptive Study. Jour of Clin & Med Case Rep, Imag 2026; 5(2): 1161.

Methodology

This study was approved by the Fiji National Health Research and Ethics Committee. It includes all cases of MIS-C diagnosed between April 1st 2021 to October 31st 2021 that met the WHO and US CDC MIS-C criteria. These two criterias were used because of the variability in presentation seen in children and the evolving evidence on MIS-C. The patients were identified using the ward patient registers. They were then coded to de-identify and protect patient confidentiality and their clinical and laboratory characteristics were entered into a questionnaire. The data was summarized and analyzed in an excel spreadsheet.

Results

A total of 9 cases of MIS-C were identified and admitted during the study period. Tables 1, 2 and 3 details the clinical characteristics, laboratory results, management, and outcomes of these patients. There was one case in May, three in July, three in September, and two in October. Admission days ranged from 0 to 5 days to more than 30 days. Four of the nine children were admitted between 0 to 5 days with 100% mortality, three were for 6 to 30 days with one death, and the two who were admitted beyond 30 days, both survived. Therefore, percentage death was 55.5% which is also defined as the Case Fatality Rate.

During the study period, there were six I-Taukei Fijians (66.6%) and three Fijians of Indian descent (33.3%) who had MIS-C. This cohort's age ranges were 11.1% neonates, 66.6% infants, 11.1% >1 year to < 5 years, and 11.1% less than 15 years. There were seven males and two females. Their nutritional status was also analyzed. There were four who were malnourished, four who were well-nourished, and one who was overweight. Five patients did not have any pre-existing illness, while four had comorbidities. Those with preceding illness included two born preterm with VLBW and two with Downs Syndrome. Of the two with Downs Syndrome, one had chronic malnutrition with global developmental delay, and the other had severe acute malnutrition with hypothyroidism.

RT-PCR and RAT were used to identify Covid-19 infection. Because RT-PCR was widely available in Fiji during the study period, it was used as the marker of Covid-19 infection. All nine members of the cohort were tested with RT PCR. 44.4% were positive while 55.6% were negative. RAT was not available in the country with this cohort of cases. Only 55.6% of our cases had Covid antibody testing because it was not available initially. In terms of Covid-19 exposure, 66.7% had at least one infected parent, while 33.3% had unknown exposure.

The latency of Covid-19 infection and the onset of symptoms varied widely from one week and up to ten weeks. One patient developed symptoms 7 days after a known Covid-19 exposure, another after 15 days, and two others after 6 and 10 weeks respectively. We could not define the timeline of exposure to the onset of symptoms in 5 patients.

The initial presentation was also evaluated. Suspected diagnosis of Sepsis was seen in 22.2% of patients; one had Sepsis alone, and the other had Sepsis and Meningitis. There were 55.5% of cases that had Septic Shock as their presentation, making it the most common presentation in children with MIS-C. One of these children also had DIC.

In terms of symptoms, all cases had cardiac symptoms, with 77.8% having tachycardia and 22.2% having bradycardia. One of the patients with bradycardia also had AV dissociation. All of the cases had CNS symptoms such as irritability 44.4%, low GCS 22.2%, seizures 22.2% and status epilepticus 11.1%. This makes cardiac and CNS symptoms

the most common in this MIS-C cohort. Fever was present in 88.9% of the patients in the study. The only patient who did not have a fever was a 2-month-old (corrected age 42 weeks) VLBW baby born prematurely. There were 88.9% who reported respiratory symptoms. GIT symptoms were also prevalent, with 88.9% of cases exhibiting diarrhea, vomiting, or both. As a result, fever, respiratory symptoms, and GI symptoms were the second most commonly reported symptoms in this study.

In the analysis of shock, one patient developed shock during the course of admission, in addition to the five patients who had shock at the time of admission. During the admission, only 22.2% of patients had a rash and 11.1% had oliguria. Other symptoms to mention include poor feeding in 22.2% of cases of which one had hyperglycemia, reduced appetite in 22.2% of cases, strawberry mucositis in 11.1% of cases, and 44.4% did not have any additional symptoms.

In terms of laboratory results, all cases had FBC, with 77.8% showing elevated WCC, 22.2% were normal, and 77.8% of cases were anemic with Hb range from 6.4 g/dl to 10.9 g/dl. Platelets were normal in 55.6% of the cases, low in 22.2%, and high in 22.2%. For inflammatory markers, CRP was tested in 7 patients and was found to be elevated in all the cases tested. Two patients were not tested as the test was not available at the time of their admission. ESR was measured in eight of the nine patients, with 37.5% having elevated levels and 62.5% having normal levels. One patient did not have an ESR as the test was not available during the admission.

Seven of the nine patients had their coagulation profiles checked. The findings revealed that 71.4% of the participants had normal PT and 28.6% had prolonged PT and APTT. Six children were not tested because D-dimer was initially unavailable locally. However, 66.7% of the three tested were positive. LDH was found to be elevated in all six cases tested. Unfortunately, three patients' LDH tests were either not performed or the results were unknown because they could not be retrieved. Lactate was measured in one patient and found to be elevated. In 44.4% of cases, CK was not performed or was unknown, while 55.6% were tested. The results revealed that 60% were normal, 20% were low, and 20% had a very high CK of 3339 u/L. Troponin was tested in eight of the cases. The result was elevated in 87.5% and normal in 12.5%.

LDH was found to be elevated in all six cases tested. Unfortunately, three patients' LDH tests were either not performed or the results were unknown because they could not be retrieved. Lactate was measured in one patient and found to be elevated. In 44.4% of cases, CK was not performed or was unknown, while 55.6% were tested. The results revealed that 60% were normal, 20% were low, and 20% had a very high CK of 3339 u/L. Troponin was tested in eight of the cases. The result was elevated in 87.5% and normal in 12.5%.

Electrolytes were tested in 100% of the cases. Sodium levels were low in 44.4%, normal in 44.4%, mild hyponatremia of 152 in 11.1%, and severe hyponatremia of 101 in 11.1%. The severe hyponatremia of 101 was likely a spurious result, as repeat sodium levels were normal. Potassium was elevated in 77.8% of cases and normal in 22.2%. Blood cultures showed no significant growth in 100% of the cases although one was contaminated with coagulase negative staphylococcus. Urine culture had no growth in 100% of cases that were tested. CSF culture also showed no growth in all nine cases in this study. nECHO and CXR imaging studies were also performed. An echocardiogram was done in seven of the nine cases, and 85.7% had no abnormal findings related to MIS-C, while one had severe cardiomyopathy with a poor ejection fraction of 18-27%. An echocardiogram

performed during his previous admission revealed no prior cardiac abnormalities. He died after 18 days due to persistent left ventricular dysfunction. Two patients were unable to have ECHOs. In 66.6% of cases, CXR was not performed or the results were unknown. Positive findings on CXR included patchy and homogenous opacities, pleural effusion and pneumothorax.

During the admission of these children with MIS-C, 77.8% required oxygen support. Of these, 28.6% had HHFNC, 14.2% required free flow oxygen, and 57% needed mechanical ventilation. All patients were started on antibiotics for suspected sepsis. In terms of inotropic support, approximately 66.7% were critically ill and were given inotropes. Immunomodulatory treatment in the form of IVIG and steroids was initiated when other infections were ruled out as part of the MIS-C criteria. IVIG was administered in 55.6% of cases, and 66.6% received methylprednisone. Three of the cases (33.3%) were initially kept on low dose steroid and then escalated to methylprednisone pulse doses as a step-up treatment. Three cases were critically ill and died before treatment could be started. Only one patient with severe left ventricular dysfunction received enoxaparin, while ASA was given to 55.6% of patients. Due to the small sample size, the results were only expressed in numbers and percentages.

Discussion

Multisystem inflammatory syndrome associated with Covid-19 (MIS-C) is a severe hyperinflammatory disease that affects multiple organ systems. Riphagen Dhar et al. described it as Pediatric Multisystem Inflammatory Syndrome temporally associated with SARS-CoV-2 (PIMS-TS) in April 2020 [6,7]. As more cases were reported in other European countries and the United States [8-11], the WHO and CDC developed clinical and epidemiologic criteria to identify these cases and named it Multisystem Inflammatory Syndrome in Children and Adolescents (MIS-C) [11,12]. The definitions of WHO and CDC are similar and include children ≤ 21 years old, with fever, clinically severe illness involving at least two organ systems (respiratory, cardiac, GIT, renal, neurologic, mucocutaneous, hematologic), elevated inflammatory markers, no other obvious cause of inflammation, and evidence of SARS-CoV-2 infection by RT-PCR, serology, or antigen test or has had exposure to a suspected or confirmed COVID-19 case prior to the onset of symptoms [11,12]. Our first case, like the majority of studies demonstrating a geographic and temporal association of MIS-C with current or within 2 to 8 weeks of recent illness or exposure to Covid-19 [8,13,14], was diagnosed two months after the start of community transmission of the Covid-19 delta variant in April 2021. The patient developed symptoms two weeks after exposure to her Covid positive mother. The highest number of MIS-C cases (6 out of 9) also coincides with the pandemic's peak in Fiji in July-August 2021. The latency of Covid infection/exposure to onset of symptoms ranged from 7 days to 10 weeks but in 55% of our cases, it was unknown.

As of January 2022, the CDC had reported 6,851 MIS-C cases, with male children (60%) aged 5 to 11 years old being the most frequently affected [15]. It remains uncommon compared to SARS-CoV-2 infection. In their study, Payne et al. estimated a MIS-C incidence of 316 persons per million SARS-CoV-2 infections in persons younger than 21 years. Estimates for population-based incidence and incidence among persons with infection were higher among people who were Black, Hispanic or Latino, or Asian or Pacific Islander [16]. Our study identified only 9 cases out of the 4,308 Covid-19 confirmed cases in children under the age of 15 in Fiji's Central/Eastern Division as of October 31, 2021. The majority of our cases (78%) were less than one year old, with a median age of 10 weeks, and more males (78%) and I-Taukei Fijian (66%). There are no studies in MIS-C that clearly define the relationship between race, ethnicity, and age group.

MIS-C cases often occurred with no known preceding illness. Nonetheless, Bowen et al. in their study of 2,818 MIS-C cases found 38.5% had preexisting medical condition most commonly obesity. They also note that having one or more underlying comorbid conditions, particularly neurologic disorders (cerebral palsy, developmental disabilities, autism and other neurologic conditions) or noncardiac congenital abnormalities were associated with death [17]. Five (55.5%) of our cases had known comorbidities including prematurity with VLBW (22.2%), Down's syndrome, hypothyroidism, malnutrition, and global developmental delay (22.2%) and overweight (11%). Four of these five cases (80%) resulted in death.

Dhar et al. found that SARS-CoV-2 antibodies had a much higher positivity rate (66.1%) than RT-PCR (36.5%) in a systematic review of 833 patients with MIS-C from 18 publications (18).

Our cases were Covid-19 serology positive only (44%), RT-PCR positive only (33%), positive for both serology and RT-PCR (11%) and one case negative for both serology and RT-PCR (11%) but with confirmed Covid-19 exposure. Covid serology was not available initially and this posed difficulty in meeting diagnostic criteria at times. Similar to other reports, we found a febrile hyperinflammatory syndrome with multiorgan involvement, notably cardiac, CNS, respiratory and GIT symptoms. The symptoms included fever, shock, respiratory symptoms, tachycardia, bradycardia, arrhythmia, vomiting, diarrhea, skin rash and mucocutaneous involvement similar to Kawasaki disease, irritability, seizures, low GCS, poor feeding, hyperglycemia, and oliguria. All of our cases had ≥ 4 organ systems affected with cardiac and CNS being the most common.

Several studies have noted that cardiovascular involvement is prevalent in 80-85% of MIS-C cases [14,19,20]. Reports have characterized cardiovascular involvement in MIS-C during the inpatient phase as left ventricular dysfunction, coronary artery abnormalities and elevated troponin levels [21-23]. Conventional echocardiography revealed that approximately 50% of children with MIS-C had decreased LV systolic function during the acute illness, which rapidly improved before discharge [14,20]. The reported incidence of coronary artery abnormalities varies widely from 4% to 24% (19,20), and includes cases of progressive coronary artery aneurysms after discharge [24]. There was only one case with severe dilated cardiomyopathy with LV ejection fraction range of 18% to 27% in this study.

The American College of Rheumatology recommends a tiered approach for laboratory testing in suspected cases of MIS-C that do not have life-threatening manifestations [13]. Tier one tests available in Fiji included FBC, electrolytes, renal and liver function tests, albumin, inflammatory markers - ESR and CRP, and SARS-CoV-2 RT-PCR and/or serology. Blood, urine and CSF cultures were obtained to rule out other infections. All of the cases had severe MIS-C, and tier 2 bloods were drawn upon presentation with a high index of suspicion. Available tier 2 tests included troponin, D-dimer, PT, PTT, LDH, triglycerides, ECG, and echocardiogram. Similar to the majority of reported cases of MIS-C, our cases had elevated CRP (100%), elevated ESR (37%), elevated WCC (78%), anemia (78%), thrombocytopenia (22%) or thrombocytosis (33%), elevated LDH (100%), low sodium (45%), elevated troponin (88%), positive D-dimer (67%), and deranged coagulation in (28%). However, not all tests were available at all times, and in this case series, a combination of different markers was used to identify MIS-C.

The management of MIS-C evolved over the course of the pandemic.

Table 1: Clinical characteristics of patients with MISC in Children in CWMH, Fiji, April - October 2021.

Case Number	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	
Age	28 days: CA 37 weeks	5 weeks	11 months	2 months: CA 40 weeks	10 months	14 years	8 weeks	10 weeks	3 years	
Gender	Female	Female	Male	Male	Male	Male	Male	Male	Male	
Race	Fijian of Indian descent	Fijian of Indian descent	I-Taukei	I-Taukei	Fijian of Indian descent	I-Taukei	I-Taukei	I-Taukei	I-Taukei	
Comorbidities	Preterm 33/40, VLBW	None	None	Preterm 31/40, VLBW	None	None	None	Down's Syndrome, Hypothyroidism	Down's Syndrome, Chronic malnutrition, Global Developmental Delay	
Evidence of Covid infection	RT-PCR	Positive	Positive	Positive	Negative	Positive	Negative	Negative	Negative	
	Rapid antigen test	Not done	Not done	Not done	Not done	Not done	Not done	Not done	Not done	
	Covid Antibody	Not done	Not done	Not done	Not done	IgG positive	IgM and IgG positive	IgM and IgG positive	IgG positive	
	Documented Covid Exposure	Mother Covid positive	Father Covid positive	Mother Covid positive	Mother Covid positive	Unknown	Unknown	Mother Covid positive	Mother Covid positive	
Latency Covid 19 infection/exposure - onset of symptoms	15 days	7 days	unknown	6 weeks	Unknown	Unknown	Unknown	10 weeks	Unknown	
Nutritional Status	Under nourished < -2SD	Undernourished. Between -2SD & -3SD	Well-nourished, Weight 50 th centile	Undernourished < -2SD	Well-nourished. Weight 50 th centile	Overweight - BMI 25	Well -nourished	Undernourished < -2SD	Well nourished, weight 50 th centile	
Suspected diagnosis on admission	Sepsis	Septic Shock	Sepsis, Meningitis, Pneumonia with Effusion	Septic shock	Acute Gastroenteritis, Meningitis	Pneumonia with Effusion	Acute Gastroenteritis, Severe Dehydration, Shock	Severe Pneumonia, Septic Shock	Septic Shock, Disseminated Intravascular Coagulation	
Clinical Presentation	Fever	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	
	Shock	No	Yes	No	Yes	No	Yes	Yes	Yes	
	Respiratory Symptoms	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	
	Cardiac symptoms	tachycardia	bradycardia, low BP, arrhythmia	tachycardia	tachycardia	tachycardia	tachycardic, low BP	tachycardia	tachycardia	bradycardia
	GIT	vomiting, diarrhea	diarrhea	diarrhea	diarrhea	vomiting, diarrhea	vomiting, diarrhea, abdominal pain	vomiting, diarrhea	No	vomiting
	Skin Rash	Yes	No	No	No	Yes	No	No	No	No
	Renal symptoms	No	No	No	No	No	Oliguria	No	No	No
	Neurological	irritability	low Glasgow Coma Scale	Status epilepticus	irritability	irritability	Low GCS	irritability	seizure	blank stares, floppy
	Others symptoms	No	poor feeding, hyperglycemia	No	No	mucositis-strawberry tongue, injected lips, bilateral bulbar conjunctivitis, cervical lymphadenopathy	decreased appetite	poor feeding	No	reduced appetite

Table 2: Laboratory and imaging results for MISC in CWMH, Fiji, April-October 2021.

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9
WCC	17,900	12,600	11,000	26,200	29,800	10,500	17,800	24,600	26,000
Hgb (g/dl)	13.2	10.3	10.9	6.6	8.9	15.3	8.9	6.4	9.3
Platelet	493,000	269,000	269,000	126,000	733,000	289,000	640,000	266,000	90,000
ESR	5	5	7	45	87	6	21	2	NA
CRP (mg/L)	100	90	not done	1160	227	510	60	53	NA
Coagulation Profile									
PT (seconds)	12	Not done	Not done	12	14	normal	14	23	prolonged
APTT (seconds)	44	Not done	Not done	38	36	normal	34	64	>120
d-Dimer	not done	Not done	Not done	positive	positive	Not done	Negative	Not done	Not done
CK	99	Not done	Not done	unknown	3	88	237	3339	Not done
LDH (U/L)	793	Not done	586	unknown	572	1054	509	2950	Not done
Lactate	Not done	Not done	Not done	unknown	Not done	Not done	2.6	Note done	7.4
Troponin (ng/L)	101	34	25.64	38	3.54	138	39	512	unknown
Sodium	101	152	137	130	134	129	139	141	140
Potassium	8.8	4.9	4.5	6.7	5.7	4.9	5.2	3.6	5.4
Blood culture	Hemolyzed	CNS	No growth	No growth	No growth	No growth	No growth	No growth	No growth
Urine culture	No growth	No growth	Not done	No growth	No growth	No growth	No growth	No growth	No growth
CSF culture	No growth	No growth	No growth	No growth	No growth	No growth	No growth	No growth	No growth
CXR	not done	not done	not done	Pneumothorax	unknown	patchy opacities with bilateral pleural effusion	unknown	unknown	unknown
Echocardiogram	Normal study	Normal study	not done	Normal study	Normal study	Severe dilated cardiomyopathy with Ejection Fraction of 18-27%	Normal study	not done	not done

WCC, white cell count; Hgb, hemoglobin; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; PT, prothrombin time; APTT, activated prothrombin time; CK, creatine kinase; LDH, lactate dehydrogenase; CSF cerebrospinal fluid; CXR, chest x-ray; CNS, coagulase negative staphylococcus

Table 3: Management and Outcome of MIS-C in CWMH, Fiji, April - October 2021.

Case No.	O ₂ support	Medications	Length of stay	Outcome
Case 1	none	IVIG, MP, ASA	>30 days	Alive
Case 2	Mechanical ventilation	Inotropes, IVIG, MP ⁺ , ASA	>30 days	Alive
Case 3	Mask O ₂	none	≤5 days	Died
Case 4	Mechanical ventilation	Inotropes, MP ⁺	≤5 days	Died
Case 5	none	IVIG, MP ⁺ , ASA	21-30 days	Alive
Case 6	HHFNC	Inotropes, IVIG, MP ⁺ , ASA, enoxaparin	11-20 days	Died
Case 7	HHFNC	Inotropes, IVIG, MP, ASA	6-10 days	Alive
Case 8	Mechanical ventilation	Inotropes	≤5 days	Died
Case 9	Mechanical ventilation	Inotropes	≤5 days	Died

HHFNC, humidified high flow nasal cannula; IVIG, intravenous immunoglobulin; MP, methylprednisone; MP⁺, methylprednisone pulse dose; ASA, aspirin.

The latest published literature has now favored administration of both IVIG and glucocorticoids to all hospitalized children with MIS-C, as well as the early initiation of immunomodulatory treatment in patients with life-threatening conditions, even before a full evaluation [25,26]. In this cohort, our patients received immunomodulatory treatment in the form of IVIG and steroids. Our patients were either given IVIG plus methylprednisolone (55%), or just methylprednisolone (11%). Due to supply issues, IVIG and methylprednisolone were not usually started at the same time. Steroids were given first, followed by IVIG as soon as it was available. Three out of nine patients (33%) died before receiving immunomodulatory treatment due to rapid clinical deterioration.

Guidelines also recommend giving thromboprophylaxis to all patients unless there are contraindications [25-27]. Antithrombotic treatment with low dose aspirin was given to 55.6% of the cases in this series and was continued for a total of 4 weeks. A single patient with severe left ventricular dysfunction received therapeutic anticoagulation with enoxaparin.

The overall mortality for MIS-C is 1-2% [27]. Our case series shows a high case fatality rate of 55.5%. Forty-four percent were discharged alive. On initial and follow-up echocardiograms (done ≈2 weeks - 3 months after the 1st echo in three of our patients), cardiac function and coronary arteries were normal, and no arrhythmias were noted. The long-term cardiac sequelae for MIS-C patients have yet to be determined, and chronic follow-up for our cases is planned.

Addition to the literature

This is the first report to describe a MIS-C case series in Oceania. It aims to create MIS-C awareness in Fiji and other Pacific Island Countries. MIS-C can affect infants, including neonates. This series reports multiorgan involvement, with cardiac and CNS symptoms being the most common. Our patients also demonstrate that, although rare, MIS-C is a life-threatening disease with a high mortality rate when patients present late. Our deceased patients did not have any concomitant infections. The patients who were discharged alive were well without any apparent sequelae.

Limitations

Our study only includes cases that were admitted to CWMH with a relatively small number of patients. Patients with mild disease may not have sought hospital care. Cases may have been missed due to a lack of recognition and a low index of suspicion for MIS-C, resulting in no testing for inflammatory markers. Earlier in the pandemic, Covid serology tests were not available in Fiji, increasing the number

of potential missed cases, including those who presented with Kawasaki-like illness. Nasal swabs for other viruses were not available and therefore not ruled out. There was no standard surveillance for MIS-C cases in Fiji. As a result, this report likely underestimates the number of cases of MIS-C during the study period.

Conclusion

We described nine cases of MIS-C in Fiji that occurred during the delta variant community transmission. These children presented with moderate to severe symptoms, with CNS and cardiac symptoms as the most common. Treatment offered included IVIG, steroids, aspirin and enoxaparin. Patients who were in refractory shock at the time of presentation died, resulting in a high case fatality rate of 55.5 % in this series. There were no complications observed for the patients who were discharged alive. Clinicians are advised to remain vigilant for signs of MIS-C in future waves and variants of Covid-19, as well as the long-term effects of MIS-C. A national MIS-C surveillance is important to provide more analyzable data for the other SARS-CoV-2 variants.

References

1. Fiji Bureau of Statistics (2018) Release No. 63. Suva: Fiji Bureau of Statistics; 2018 Sep 21.
2. Fiji MOHMS Covid-19 Update 1/11/21. <https://www.health.gov.fj/01-11-20213>
3. Lu X, Zhang L, Du H, Zhang J, Li YY, Qu J, et al. (2020) SARS-CoV-2 infection in children. *N Engl J Med* 382(17):1663-1665.
4. Dong Y, Mo X, Hu Y, Qi X, Jiang F, Jiang Z, Tong S (2020) Epidemiology of COVID-19 among children in China. *Pediatrics* 145(6): e20200702.
5. Riphagen S, Gomez X, Gonzalez-Martinez C, Wilkinson N, Theocharis P. (2020) Hyperinflammatory shock in children during COVID-19 pandemic. *Lancet* 395(10237): 1607-1608.
6. Royal College of Paediatrics and Child Health. Guidance: paediatric multisystem inflammatory syndrome temporally associated with COVID-19. London: RCPCH; 2020.
7. Whittaker E, Bamford A, Kenny J, Kaforou M, Jones CE, Shah P, et al. (2020) Clinical characteristics of 58 children with a paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2. *JAMA* 324(3): 259-269.
8. Verdoni L, Mazza A, Gervasoni A, Martelli L, Ruggeri M, Ciffreda M, et al. (2020) An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study. *Lancet* 395(10239): 1771-1778.
9. Koskela U, Helve O, Sarvikivi E, Helminen M, Nieminen T, Peltola V, et al. (2021) Multisystem inflammatory syndrome and Kawasaki disease in children during the COVID-19 pandemic. *Acta Paediatr* 110(11): 3063-3068.
10. Viner RM, Whittaker E (2020) Kawasaki-like disease: emerging complication during the COVID-19 pandemic. *Lancet* 395(10239): 1741-1743.
11. World Health Organization. Multisystem inflammatory syndrome in children and adolescents with COVID-19: scientific brief. Geneva: WHO; 2020 May.
12. Centers for Disease Control and Prevention. Emergency preparedness and response: multisystem inflammatory syndrome in children (MIS-C) associated with COVID-19. Atlanta: CDC; 2020.
13. Henderson LA, Canna SW, Friedman KG, Gorelik M, Lapidus SK, Bassiri H, et al. (2020) American College of Rheumatology clinical guidance for multisystem inflammatory syndrome in children associated with SARS-CoV-2. *Arthritis Rheumatol* 72(11):1791-1805.
14. Dufort EM, Koumans EH, Chow EJ, Rosenthal EM, Muse A, Rowlands J, et al. (2020) Multisystem inflammatory syndrome in children in New York State. *N Engl J Med* 383(4): 347-358.
15. Campbell A, Godfred-Cato S, Yousaf A. CDC COVID-19 updates: what clinicians need to know about MIS-C. CDC Clinical Outreach and Communication Activity Call; 2022.
16. Payne AB, Gilani Z, Godfred-Cato S, Belay ED, Feldstein LR, Patel MM, et al. (2021) Incidence of multisystem inflammatory syndrome in children among U.S. persons infected with SARS-CoV-2. *JAMA Netw Open* 4(6): e2116420.
17. Bowen A, Miller AD, Zambrano LD, et al. (2021) Demographic and clinical factors associated with death among persons <21 years with MIS-C. *Open Forum Infect Dis* 8(8): ofab388.
18. Dhar D, Dey T, Samim MM, Padmanabha H, Chatterjee A, Naznin P, et al. (2021) Systemic inflammatory syndrome in COVID-19 (SISCoV): systematic review and meta-analysis. *Pediatr Res.*
19. Godfred-Cato S, Bryant B, Leung J, Oster ME, Conklin L, Abrams J (2020) COVID-19-associated multisystem inflammatory syndrome in children-United States, March-July 2020. *MMWR Morb Mortal Wkly Rep* 69: 1074-1080.
20. Valverde I, Singh Y, Theocharis P, Chikermane A, Di Filippo S, Kucinska B, et al. (2021) Acute cardiovascular manifestations in 286 children with MIS-C in Europe. *Circulation* 143: 21-32.
21. Alsaied T, Tremoulet AH, Burns JC, Saidi A, Dionne A, Lang SM (2021) Review of cardiac involvement in MIS-C. *Circulation* 143: 78-88.
22. Kelly MS, Valle CW, Fernandes ND, Cummings BM, Lahoud-Rahme M, Chiu JS. (2020) Cardiac biomarker profiles and echocardiographic findings in MIS-C. *J Am Soc Echocardiogr* 33:1288-1290.
23. Feldstein LR, Tenforde MW, Friedman KG, Newhams M, Rose EB, Dapul H, et al. (2021) Characteristics and outcomes of U.S. children with MIS-C compared with severe COVID-19. *JAMA* 325: 1074-1087.
24. Matsubara D, Kauffman HL, Wang Y, Calderon-Anyosa R, Nadaraj S, Elias MD, et al. (2020) Echocardiographic findings in pediatric MIS-C in the United States. *J Am Coll Cardiol* 76: 1947-1961.
25. COVID-19 Treatment Guidelines Panel. Coronavirus disease 2019 (COVID-19) treatment guidelines. Bethesda (MD): National Institutes of Health.
26. Henderson LA, Canna SW, Friedman KG, Gorelik M, Lapidus SK, Bassiri H, et al. (2022) American College of Rheumatology guidance for MIS-C: Version 3. *Arthritis Rheumatol* 74(4): e1-e20.
27. Son MBF, Friedman KG (2023) COVID-19: multisystem inflammatory syndrome in children-management and outcome. In: Fulton D, et al., editors. UpToDate. Waltham (MA): UpToDate Inc.