International Journal of Contemporary Pediatrics
Jan M et al. Int J Contemp Pediatr. 2023 Jun;10(6):855-859
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20231489

Original Research Article

Clinical profile, cardiac involvement and outcome of children admitted with multisystem inflammatory syndrome in PICU at GB Pant children hospital Srinagar

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Received: 28 March 2023
Revised: 02 May 2023
Accepted: 04 May 2023

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ABSTRACT

Background: Multisystem inflammatory syndrome in children (MIS-C) is a severe hyper inflammatory post infectious complication of acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection, which typically occurs 2-6 weeks after exposure to SARS-CoV-2. Aim was to determine the clinical profile, cardiac involvement and outcome of children admitted with multisystem inflammatory syndrome in pediatric intensive care unit.
Methods: This prospective observational study was conducted in pediatric intensive care unit over period of two years. After informed consent from parents, all those patients meeting inclusion criteria were subjected to complete history, general and systemic physical examination. Routine baseline investigations included CBC, LFT, KFT, ABG, serum calcium and phosphorous, and other investigations like echocardiography, COVID-19 RAT and RTPCR and various inflammatory markers like serum ferritin, pro-calcitonin, CRP and ESR whenever required were done.
Results: In our study out of 77 MIS-C patients 40 were males and 37 were females with a male female ratio of 1.1:1. The mean average age was 7.4 years. Out of them 47 (61%) patients had a history of COVID-19 infection/contact with positive COVID-19 cases 3 to 4 weeks before presentation. In our study gastrointestinal, respiratory, and cardiac systems were mostly involved. Rash and conjunctival congestion was seen in 81% of MIS-C patients. On echocardiography out of 77 MIS-C patients, 15 (19.5%) had pericardial effusion, 25 (32.5%) had coronary artery dilatations and 32 patients (41.5%) had left ventricular systolic dysfunction with LVEF <55%.
Conclusions: Pediatric multisystem inflammatory syndrome is a serious and life-threatening illnesses having a significant impact on morbidity and mortality.

Keywords: Cardiac abnormalities, COVID-19, Multisystem inflammatory syndrome, Shock

INTRODUCTION

Multisystem inflammatory syndrome in children (MIS-C) is a severe hyper inflammatory post-infectious complication of acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection, which typically occurs 2-6 weeks after exposure to SARS-CoV-2.[1,2] Although the exact pathophysiology of MIS-C is uncertain, it is thought to be due to immune dysregulation occurring after recovery from acute infection. As per 2020 WHO definition, MSC-C is defined as children and adolescents 0-19 years of age with fever >3 days and two of the following five criteria: i) rash or bilateral non-purulent conjunctivitis or muco-cutaneous inflammation signs (oral, hands or feet); ii) hypotension or shock; iii) features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated troponin/NT-proBNP); iv) evidence of coagulopathy (by PT, PTT, elevated d-dimers); v) acute gastrointestinal problems (diarrhoea, vomiting, or abdominal pain).[3]

And elevated markers of inflammation such as ESR, C-reactive protein, or procalcitonin.

And no other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes.

And evidence of COVID-19 **(**RT-PCR, antigen test or serology positive), or likely contact with patients with COVID-19.

The aim of our study was to recognize clinical spectrum, cardiac involvement and immediate outcome of patients admitted with MIS-C.

METHODS

The study was prospective and observational conducted over a period of two years (December 2020-November 2022) in the pediatric intensive care unit of the GB Pant children hospital, postgraduate department of pediatrics GMC Srinagar, which is a tertiary care hospital for the children of Kashmir valley. Our study was approved by the ethical committee of Government Medical College Srinagar via communication number (Minutes-BOPGS) Acad/KU/22 02-02-2022 held on 29 and 30th September, 2021 under serial number 8. After informed consent from parents, all those patients meeting inclusion criteria were subjected to complete history, general and systemic physical examination. Routine baseline investigations included CBC, LFT, KFT, ABG, serum calcium and phosphorous, CRP, and ESR. Radiological investigation included USG, MRI, CT-scan whenever indicated. Other investigations like echocardiography, troponin-T, COVID-19 RAT and RTPCR, pro-calcitonin, serum ferritin, blood culture, routine urine exam and culture, CSF analysis and culture were done whenever indicated.

Determination of sample size

Using GPOWER software (version 3.0.10), it was estimated that the least number of patients required with 90% power, 5% significance level and an effect size of 0.32 was 77. Therefore, we included a total of 77 patients in our study.

Inclusion criteria

Age >1 year and <18 years admitted in PICU with a diagnosis of MIS-C by clinical and/or laboratory parameters as defined by 2020 WHO definition.[3]

Exclusion criteria

Patients with proven infective cases like bacterial sepsis, dengue and leptospirosis were excluded by appropriate investigations. COVID-19 RTPCR was done in all patients.

Statistical analysis

Data was entered in a Microsoft Excel spreadsheet and analyzed using SPSS version 22 software. Categorical variables were summarized as frequency and percentage. Continuous variables were summarized as mean and SD.

RESULTS

In our study 77 cases with a diagnosis of pediatric inflammatory multisystem syndrome (MIS-C) were included in the study. It included 40 males and 37 females with an average age of 7.4 years and a male female ratio of 1.1:1. The most Common symptoms was fever in 76 (98.7%) patients followed by vomiting in 46 (59.7%) patients, rash in 37 (48%) patients, loose stools in 28 (36.3%) patients, red eyes in 25 (32.4%) patients, pain abdomen in 17 (22%) patients, oral rash in 15 (19.5%) patients and respiratory symptoms including cough and fast breathing in 13 (17%) patients as depicted in Table 2. Out of them 47 (61%) patients had a history of COVID-19 infection/contact with positive COVID-19 cases 3 to 4 weeks before presentation.

Table 1: Gender distribution of study population.

Gender	Frequency	Percentage
Male	40	52
Female	37	48
Total	77	100

Table 2: Various symptoms in MIS-C patients.

Symptoms	No. of patients (n=77)	Percentage
Fever	76	94.3
Vomiting	46	59.7
Rash	37	48
Loose stools	28	36.3
Red eyes	25	32.4
Pain abdomen	17	22
Oral rash	15	19.5
Cough and fast breathing	13	17
Drowsiness/lethargy	6	7.8
Headache	4	5.2
Swelling over limb	3	3.9
Blood with stools	2	2.6
Decreased urine output	1	1.3

In our study the most common signs in MIS-C patients were fever in 76 patients (98.7%) with average temperature of 102.1°F and tachycardia in 75 (97.4%) patients. It was followed by hypotension in 69 (89.6%) patients, tachypnea in 61 (79.2%) patients, rash in 37 (48%) and conjunctivitis in 26 (33.7%) patients. Other common signs are listed in Table 3.

In our study on CBC, leukocytosis was seen in 40 (52%) patients and leukocytopenia was seen in 7 (9.1%), whereas 2 (2.6%) patients in our study had normal total leucocyte count. Neutrophilia with leukocytosis was seen

in 27 (35%) patients, leukocytopenia with neutropenia was seen in 1 (1.3%) patient, 23 (29.9%) patients had lymphopenia and 45 (58.4%) patients had thrombocytopenia. Platelet count was normal in 32 (41.5%) patients and 3 (2.2%) patients had thrombocytosis. Hemoglobin was low in 42 (54.5%) patients and normal in 35 (45.5%) patients. In biochemistry on admission 10 (13%) MIS-C patients had raised creatinine (AKI) and 67 (87%) patients had normal KFT, 13 patients (16.9%) had raised bilirubin and significantly elevated liver enzymes (2×times upper limit) and 15 patients (19.5%) had low albumin levels whereas 64 (83.1%) patients had normal liver function tests. Serum calcium levels were decreased in 11 patients (14.3%) and coagulogram was deranged in 7 (9.1%) patients. Among inflammatory markers CRP was raised in all 77 (100%) patients, ESR was raised in 70 (91%) patients and was normal in 7 (9%) patients, LDH was raised in 35 (45.5%) patients and normal in 42 (54.5%) patients, ferritin was raised in 52 (67.5%) patients and normal in 25 (32.5%) patients, fibrinogen (done in 36 MIS-C patients) was raised in 28 (77.8%) patients and normal in 8 (22.2%) patients, D-DIMER (done in 53 patients) was raised in 49 (92.4%) patients and normal in 4 (7.6%) patients, IL-6 (done in 30 patients) was raised in 28 patients (93.3%) and normal in 2 patients (6.7%) and procalcitonin (done in 13 patients) was raised in 10 patients (77%) and normal in 3 patients (23%). Blood culture and baseline septic profile was negative in all MIS-C patients except that 2 (2.6%) patients had UTI. COVID-19 IgG antibodies were positive in all patients and COVID-19 RTPCR and RAT were negative in all patients. Chest x-ray in 10 (13%) patients showed bilateral chest infiltrates and USG abdomen was suggestive of hydronephrosis in 1 (1.3%) patient and hepatosplenomegaly in one (1.3%) patient.

Table 3: Various signs in MIS-C patients.

Sign	No. of patients (n=77)	Percentage
Fever	76	98.7
Tachycardia	75	97.4
Hypotension	69	89.6
Tachypnea	61	79.2
Rash	37	48
Conjunctivitis	26	33.7
Signs of dehydration	25	32.4
Lethargy/drowsiness	15	19.5
Oro-mucosal rash	15	19.5
Irritable/agitated behavior	11	14.3
Respiratory distress	7	9.1
Abdominal tenderness	6	7.8
Pallor	5	6.5
Encephalopathy	5	6.5
Swelling over limb	3	3.9
Lymphadenopathy	2	2.6
Convulsions	2	2.6

Table 4: Pericardial effusion in MIS-C patients.

Pericardial effusion	No. of patients (n=77)	Percentage
Mild	11	14.3
Moderate	3	3.9
Severe	1	1.3
Total	15	19.5

Table 5: Coronary lesions in MIS-C patients.

Finding	No. of patients (n=77)	Percentage
RCA ectasia	1	1.3
LCA ectasia	4	5.2
LAD ectasia	7	9.1
RCA+LCA ectasia	7	9.1
LCA+LAD ectasia	1	1.3
RCA aneurysm	2	2.6
LAD aneurysm	2	2.6
LCA aneurysm	1	1.3
Total	25	32.5

On echocardiography out of 77 MIS-C patients, 15 (19.5%) had pericardial effusion ranging from mild to massive, 25 (32.5%) had coronary artery dilatations as depicted in tables 4 and 5 and 32 patients (41.5%) had left ventricular systolic dysfunction with LVEF <55%. 12 (15.5%) patients had mild LV dysfunction (EF=41-55%), 16 (20.8%) patients had moderate LV dysfunction (EF=31-40) and 4 (5.2%) patients had severe LV dysfunction (EF≤30). Coronary arteries were normal in 52 (67.5%) patients and LVEF function was normal in 45 (58.5%) patients.

DISCUSSION

This study comprised of 40 males and 37 females with a male female ratio of 1.1:1 (52% males) and mean age on presentation was 7.4 years. In a recent Indian study by Angurana et al involving 122 MIS-C patients, mean age was 7 years and 67% of cases were males.[4] Most common symptom in MIS-C cases in our study was fever in 98.7% patients followed by skin rash in 48% patients and respiratory system involvement in 35% cases which were similar to results by Whittaker et al who reported fever in 96% cases followed by skin rash in 52% and followed by respiratory involvement in 31% patients.[6] In our study 96.1% MIS-C cases had gastrointestinal symptoms mainly vomiting, loose stools and pain abdomen. Similar results were observed by Jain et al, Feldstein et al and Godfred-Cato et al showing GIT symptoms in 95%, 92% and 90.9% cases respectively.[10-12] In this study oromucosal changes were seen in 19.5% MIS-C patients and similar results were reported by Jain et al with oromucosal changes in 21.7% patients.[10] Cardiovascular system involvement was seen in 89.6% MIS-C patients on admission mainly in the form of shock which was comparable to results shown by Davies et al

who reported 87% patients having cardiovascular system involvement on admission.[7] Neurological system involvement was seen in 42.8% MIS-C patients our study mainly in the form of lethargy, agitated behavior, irritability and encephalopathy. In literature similar observations were made by Leora et al reporting neurological manifestations in 40% patients.[14]

Leucocytosis was seen in 87% MIS-C patients whereas one previous Indian study showed leucocytosis in 71% patients.[15] Liver enzymes were raised (>2 times upper limit normal) in 16.9% and leucopenia in 10.4% MIS-C patients in our study which were similar to results as reported by Nayak et al showing elevated liver enzymes in 21.3% patients and leucopenia in 4.47% patients respectively.[5] Neutrophilia was seen in 35% MIS-C patients in our study which was comparatively less than that seen by Dhanalakshami et al, Balagurunathan et al and Nayak et al with neutrophilia in 68.4%,76.2% and 77.6% patients respectively.[5,7,13] Lymphopenia was seen in 30% MIS-C patients which is almost similar to results reported by Dhanalakshami et al and Godfred-Cato et al with lymphopenia in 36.8% and 35.4% patients respectively.[12,13] Thrombocytopenia was seen in 58.4% patients followed by anemia in 54.5% MIS-C patients which were similar to results as reported by Feldstein et al showing thrombocytopenia in 56% patients and anemia in 47% patients respectively.[11] Acute kidney injury was seen in 12.9% MIS-C patients in our study and same results were observed by Bagri et al showing AKI in 12.9% patients.[18] In our study19.4% MIS-C patients had low serum albumin and in a US study by Leora et al 32% patients had hypoalbuminemia.[14] In our study multiple inflammatory markers were raised in MIS-C patients. CRP was raised in all 77 (100%) patients, LDH in 45.5% patients, fibrinogen in 77.8% D-dimer in 92.4% patients. Similar results with CRP positive in 100% patients, LDH in 53.8% patients, fibrinogen in 77.7% patients, d-dimer in 92.8% patients were observed by Dhanalakshami et al.[13] ESR was raised in 91% MIS-C patients which resembled results from an Indian study showing raised ESR in 85% patients.[17] Ferritin was raised in 67.5% MIS-C patients in our study similarly it was raised in 61% patients as reported by Feldstein et al.[11] Procalcitonin was raised in 77% MIS-C patients similarly it was raised in 80.3% patients as reported by Angurana et al.[4]

In our study a total of 19.5% MIS-C patients had mild to massive pericardial effusion which was similar to Godfred-Cato et al who reported 23.9% patients had pericardial effusion.[12] In our study 32 (41.5%) MIS-C patients developed left ventricular dysfunction with ejection fraction <55%. Same observation was made by Feldstein et al with LV dysfunction in 41.7% patients and Godfred-Cato et al found LV dysfunction in 40.6% MIS-C patients.[11,12] In our study 25 (32.5%) had coronary artery dilatations. Same results were observed by Sen et al with coronary artery dilatation in 32% patients.[15] In our study troponin-t was positive in 35.1% MIS-C patients. Balagurunathan et al also reported similar results with troponin-t positive in 30.8% MIS-C patients.[17] In our study 89.6% MIS-C patients were managed as MIS-C with shock, 71.4% patients received IVIG, 84.4% patients received steroids, 19.5% received aspirin, 9.1% patients received LMWH, 9.1% patients were on mechanical ventilation and 7 (9.1%) patients expired during hospitalization, which was comparable to results seen by Nayak et al with mortality of 11.2%.[5]

The main limitation of this study was that all inflammatory markers in MIS-C patients could not be studied well because of unavailability of facilities for such tests and another limitation was that follow up of patients was not done so to throw light on chronic complications of MIS-C in children.

CONCLUSION

In our study, fever, lethargy, poor feeding, vomiting, abdominal pain, loose stools and cough are the common symptoms of MIS-C syndrome in children and common signs include, rash, conjunctival congestion, hypotension, tachycardia, tachypnea, and hypoxemia. The majority of MIS-C patients had cardiovascular and gastrointestinal involvement leading to significant morbidity and mortality.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee Government Medical College Srinagar via communication number (Minutes-BOPGS) Acad/KU/22 02-02-2022 held on 29 and 30th September, 2021 under serial number 8

REFERENCES

1. 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.
2. Angurana SK, Awasthi P, Thakur A, Randhawa MS, Nallasamy K, Kumar et al. Intensive care needs and short-term outcome of multisystem inflammatory syndrome in children (MIS-C): Experience from North India. J Trop Pediatr. 2021;67(3):fmab055.
3. World Health Organization. Multisystem inflammatory syndrome in children and adolescents temporally related to COVID-19. 2020 May 15, 2020; Available from: https://www.who.int/news-room/commentaries/detail/multisyste inflammatory syndrome-in-children-and-adolescents-with-covid-19. Accessed on 1 December 2022.
4. Angurana SK, Kumar V, Nallasamy K, Kumar MR, Naganur S, Kumar M, et al. Clinico-laboratory profile, intensive care needs and short-term outcome

of multisystem inflammatory syndrome in children (MISC): experience during first and second waves from north India. J Trop Pediatr. 2022;68(5):fmac068.
5. Nayak S, Panda PC, Biswal B, Agarwalla SK, Satapathy AK. Eastern India Collaboration on Multisystem Inflammatory Syndrome in Children (EICOMISC): a multicenter observational study of 134 cases. Front Pediatr. 2022;10:834039.
6. Whittaker E, Bamford A, Kenny J, Kaforou M, Jones CE, Shah P, et al. Clinical characteristics of 58 children with a pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2. Jama. 2020;324(3):259-69.
7. Davies P, Evans C, Kanthimathinathan HK, Lillie J, Brierley J, Waters G, et al. Intensive care admissions of children with paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS) in the UK: a multicentre observational study. Lancet Child Adolesc Health. 2020;4(9):669-77.
8. Lee PY, Day-Lewis M, Henderson LA, Friedman KG, Lo J, Roberts JE, et al. Distinct clinical and immunological features of SARS–CoV-2–induced multisystem inflammatory syndrome in children. J Clin Investig. 2020;130(11):5942-50.
9. 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.
10. Jain S, Sen S, Lakshmivenkateshiah S, Bobhate P, Venkatesh S, Udani S, et al. Multisystem inflammatory syndrome in children with COVID-19 in Mumbai, India. Indian Pediatr. 2020;57:1015-9.
11. Feldstein LR, Rose EB, Horwitz SM. CDC COVID-19 Response Team. Multisystem inflammatory syndrome in US children and adolescents. N Engl J Med. 2020;383(4):334-46.
12. Godfred-Cato S, Bryant B, Leung J, Oster ME, Conklin L, Abrams J, et al. COVID-19–associated multisystem inflammatory syndrome in children-United States, March–July 2020. Morb Mortal Week Rep. 2020;69(32):1074.
13. Dhanalakshmi K, Venkataraman A, Balasubramanian S, Madhusudan M, Amperayani S, Putilibai S, et al. Epidemiological and clinical profile of pediatric inflammatory multisystem syndrome- temporally associated with SARS-CoV-2 (PIMS-TS) in Indian children. Indian Pediatr. 2020;57:1010-4.
14. 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.
15. Sen B, Sarkar M, Raychaudhuri D, Pal P, Roychowdhoury S, Chattopadhyay A, et al. Clinical profile and outcome of pediatric inflammatory multisystem syndrome temporally associated with severe acute respiratory syndrome coronavirus 2 series in Eastern India. Med J DY Patil Vidyapeeth. 2022;5:S 210-4.
16. Lima-Setta F, Magalhães-Barbosa MC, Rodrigues-Santos G, Figueiredo EA, Jacques ML, Zeitel RS. Brazilian Research Network in Pediatric Intensive Care (BRnet-PIC). Multisystem inflammatory syndrome in children (MIS-C) during SARS-CoV-2 pandemic in Brazil: a multicenter, prospective cohort study. J Pediatr (Rio J). 2021;97(03):354-61.
17. Balagurunathan M, Natarajan T, Karthikeyan J, Palanisamy V. Clinical spectrum and short-term outcomes of multisystem inflammatory syndrome in children in a south Indian hospital 20212;63:531-7.
18. Bagri NK, Deepak RK, Meena S, Gupta SK, Prakash S, Setlur K, et al. Outcomes of multisystem inflammatory syndrome in children temporally related to COVID-19: a longitudinal study. Rheumatol Int. 2022;42(3):477-84.

Cite this article as: Jan M, Kasana SA, Khan YR, Bashir A. Clinical profile, cardiac involvement and outcome of children admitted with multisystem inflammatory syndrome in PICU at GB Pant children hospital Srinagar. Int J Contemp Pediatr 2023;10:855-9.