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**Original Research Article**

# Clinical characteristics of multi-inflammatory syndrome in children associated with COVID 19 at the time of first contact with a primary care physician: an observational study

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## ABSTRACT

**Background:** MIS-C is a new clinical syndrome with many similarities with well-known common childhood illness. This present study aims to describe the clinical profile at the time of first contact with the primary care provider and to delineate it from other common illness.
**Methods:** Retrospective observational study in a referral hospital, GMC Thrissur, Kerala. All 43 diagnosed cases during the study period were enrolled. Data was retrieved from the case sheets and reference letters. Data was analysed in Statistical package for social sciences (SPSS) 20 software.
**Results:** 43 patients were diagnosed with MIS-C with a mean age at diagnosis was 7.3 years with a male preponderance. Fever was the universal symptom, gastrointestinal symptoms in 27 (62.7%), rash in 24 (55.8%), shock in 2 (4.6%), lymphadenopathy in 2, seizures in 2, altered sensorium in 1, palatal palsy in 1etc were the presenting symptoms. 12 (27.9%) of patients had no history of COVID 19 infection. The mean latency for MIS-C was 21 days (range 6-60 days). 17 (39.5%) patients developed shock later.
**Conclusions:** The symptom triad of fever, rash and gastrointestinal symptoms was the common presenting symptom at the first contact. Fever was present in all children. One third of patients had no history of symptomatic covid 19. Shock was the presenting symptom only in 2 (4.6%), but subsequently 17 (39.5%) children developed shock within 5 days of onset of symptoms. High index of suspicion and vigilance should be maintained by the primary care provider for the timely diagnosis and referral to higher centre.

**Keywords:** Clinical presentation, Multisystem inflammatory syndrome in children, Primary care, COVID-19, Shock

## INTRODUCTION

COVID-19, a severe viral respiratory infection caused by SARS-CoV-2, affects all age groups, yet it is more severe in elderly and individuals with co-morbidities. Initial reports during the pandemic suggested children have milder illness during acute infection.[1] It is now recognised that SARS- COV- 2 related multi system inflammatory syndrome in children (MIS-C) is a dreaded delayed complication which is seen more often in children than in adults.[1-3] As many of these children may deteriorate quickly and initially present to non-tertiary care facilities, an high index of suspicion and timely referral to tertiary care centre is warranted.

There have been increasing reports from all over the world describing children and adolescents with COVID19 associated multisystem inflammatory conditions, which seem to develop after the infection rather than during the acute stage of COVID19. The clinical features of these

paediatric cases are both similar and distinct from other well described inflammatory syndromes in children, including Kawasaki disease, Kawasaki disease shock syndrome, and toxic shock syndrome.[2,3]

This new clinical entity presents a diagnostic challenge to the practicing paediatrician in early recognition and to institute appropriate management of MIS-C particularly in resource poor settings. The current guidelines suggest an extensive workup for suspected MIS-C patients, which are costly and are not easily available in the peripheral hospitals. The study aims to describe the clinical profile of MISC at the time of first presentation to the primary care provider there by streamlining the case management and also to prevent unnecessary referral and incurring hospital expenses.

### *Aims and objectives*

This present study aims to describe the clinical profile at the time of first contact with the primary care provider. To find the predictors and risk factors of myocardial involvement.

This retrospective observational study was conducted in a tertiary care referral centre, Government Medical College, Thrissur Kerala, India. The period of study was December 2020 to November 2021. All consecutive cases of MIS-C meeting the WHO criteria (Table 1) were enrolled for the study.4 Ethics committee approval was obtained before the start of the study. 43 patients was diagnosed as MIS-C during this period and was included in the study. Doubtful cases or cases that did not fulfil the WHO criteria was not included in the study.

Infective causes like dengue, leptospirosis, scrub and bacterial sepsis were excluded by appropriate investigations. COVID-19 RT PCR was done in all patients. COVID 19 antibody testing was done using Vitros CoV2T kit.[5]

Study variables collected using pre designed proforma included patient demographic characteristics, symptoms, laboratory parameters, duration of hospital stay, need for inotropic support and ICU care etc. were collected. A detailed history of illness regarding onset, progression and duration of symptoms were recorded from the case sheets and from the referral letters from the primary physician. Telephonic clarifications was also done. The temperature were recorded at admission for all patients. A temperature of more than 100.4 deg F is defined as fever. Children were examined for skin rashes and dermatology consultation were sought when necessary. Appropriate investigations to support the diagnosis of MISC as recommended by WHO were done at admission and the patients were managed according to the existing hospital protocol.[4,5]

Bedside echocardiography was done in all patients with MIS-C at admission. All patients were subsequently seen by cardiologist to look for cardiac dysfunction.[6]

Shock was defined when a patient required more than 20 mL/kg of IV fluid resuscitation or inotropic support to maintain blood pressure above the 5th centile. Myocardial dysfunction was defined as Left Ventricular ejection fraction less than the age-appropriate cut-offs.[6]

### *Statistical analysis*

Data was entered in MS Excel and analyzed using Statistical package for social sciences (SPSS) 20. The results were expressed as mean (SD) for parametric data and median (IQR) for non-parameteric data.

## RESULTS

A total of 43 children were enrolled for the study. They were 30 (69.76%) males 13 (30.23%) females. This series showed a preponderance for males with an average age of presentation was 7.3 years. The youngest age at presentation was 7 months and oldest was 12 years. The median age at presentation was 9 years (Figure 1).

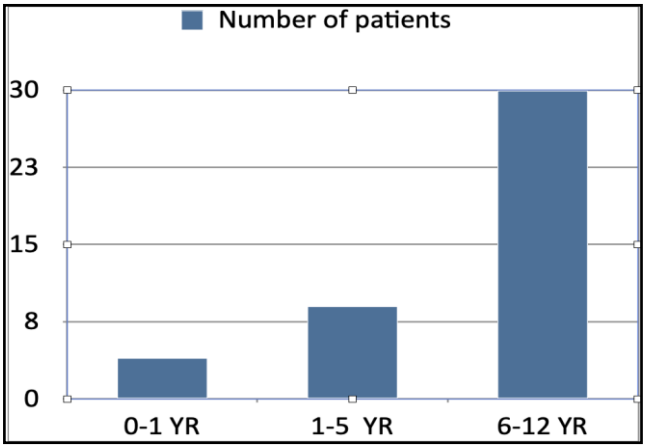


**Figure 1: Age distribution of MIS-C patients.**

All 43 patients were COVID antibody positive, 5 patients were both PCR and antibody positive. The rapid antigen test were negative in all patients.

History of symptoms of covid or contact with SARS covid 19 was not obtained in 12 (27.7%) patients and mean duration of COVID 19 and onset of MISC was 21 days with range of 6 days to 60 days.

The universal symptom that was present in all patients was fever at the time of first contact. 27 patients had gastrointestinal symptoms, it included abdominal pain, diarrhoea and vomiting. Some patients were treated in surgical wards before the diagnosis was made (Figure 2).

CNS symptoms were prominent in 3 patients, which included 2 episodes of seizures and altered sensorium. One patient presented with palatal palsy.

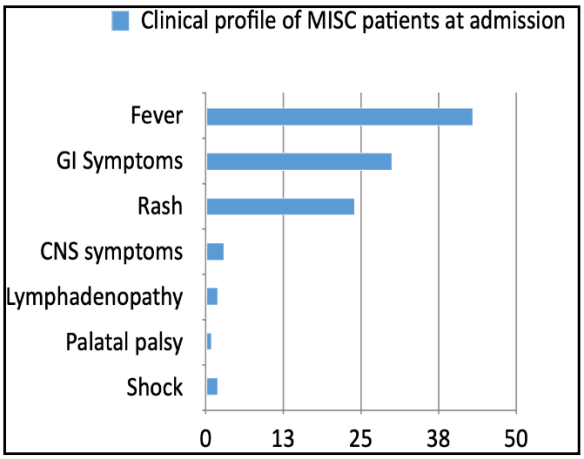


**Figure 2: Symptom profile of study participants.**

**Table 1: WHO case definition of MIS-C.**

Children and adolescents 0–19 years of age with fever ≥ 3 days

AND two of the following:

1. Rash or bilateral non-purulent conjunctivitis or muco-cutaneous inflammation signs (oral, hands or feet).
2. Hypotension or shock.
3. Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated Troponin/NT-proBNP),
4. Evidence of coagulopathy (by PT, PTT, elevated d-Dimers).
5. Acute gastrointestinal problems (diarrhoea, vomiting, or abdominal pain).

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.

**Table 2: Cardiovascular system involvement in study participants.**

| Myocardial dysfunction /shock | Number of patients | % |
|---|---|---|
| **Yes** | 17 | 39.5 |
| **No** | 26 | 60.5 |
| **Total** | 43 | 100.0 |

Lymphadenopathy was prominent in 2 patients with prominent cervical adenopathy which were painful and severe enough to cause torticollis and trismus.

Shock requiring resuscitative fluids was the presenting symptoms for 2 patients. 15 patients after getting admission to the hospital developed cariogenic shock later. A total of 17 (39.5%) of patients developed shock , that developed after 5 days of onset of symptoms with a range of 1-7 days. Day one onset of shock was associated with bad outcome.

2 MISC children died of refractory shock were females. Mortality rate of 4.65% was recorded in this study. Both children died with in 48 hours of admission and were characterised by rapid progression of refractory shock.

## DISCUSSION

The clinical profile of the patients described in this series are similar to that reported from other parts of the world. The lowest age was 7 months and highest was 12 years.[8] The maximum age mentioned in this study is affected by the admission policy of the hospital to the paediatric ward which is capped at 12 years. So many adolescents with MISC and their profile was not included in the study.

The mean age at presentation was 7.9 years. There are reports that the symptoms of MIS-C and Kawasaki disease were overlapping and cause confusion. But this study shows that MIS-C is more common above 5 yrs while KD is more common less than 5 years.[9,10]

There is an overwhelming proportion of males are affected in this study. There were similar observations in other studies as well.[11] The mortality rate of this study was 4.65% and both children were females. The sample size was not adequate to comment that females sex is a risk factor for mortality in MIS-C.

The mortality rate of children that were hospitalised with COVID-19 was 0.18%.6 and for MISC was 1.8 to 9%.[7,11]

Fever was present in all patients with MISC at presentation. The next common symptom was GI symptoms which included abdominal pain, vomiting and diarrhoea. Majority of the children had abdominal pain.[11]

Maculopapular rash a common presentation in 24 patients.[12,13] Lymphadenopathy was significant in 2 patients which was cervical in both patients. Lymphnodes were very tender in both cases producing torticollis and trismus in them. 2 patients had convulsions and had prolonged drowsiness after the seizures in both cases. Palatal palsy was seen in one patient.

Cardiac manifestation was the leading cause of morbidity and mortality in MIS -C patients. 17 (39.5%) developed myocardial dysfunction but shock was present only in 2 (4.6%) at first contact.[6,12] Coagulopathy and shock is two important WHO diagnostic criteria, but clinically significant bleeding and shock at presentation was rare in this series. Shock developed within 5 days of onset of symptoms in 88% of the patients (1-7 days range). So the primary care provider should maintain strict vigilance and follow up of these cases even it appears mild at presentation. 16 (37.2%) children had coagulopathy on investigations but were clinically silent.[12,13]

Even though the diagnostic criteria was strictly laid by WHO and other authorities still there are certain lacunae in diagnosis. Newer symptoms are added everyday with

varied severity of presentations with in the diagnostic criteria. There is a need of multi-centric studies to address the fast changing demography and clinical characteristics of COVID 19 and MIS-C.

The major limitation of this study is that the data is from a single referral centre. Another limitation is that the hospital policy restricts admission of children above 12 years to paediatric ward so the data of adolescents are missing in this study.

## CONCLUSION

Fever more than 100.40 F is a universal symptom of MIS-C and workup should start after documenting it. Children more than 5 years, male sex, presence of symptom complex of fever, maculopapular rash and gastrointestinal involvement is more suggestive of MIS-C. Absence of clinical bleeding will not exclude MIS-C and testing for coagulation parameters are warranted in all suspected cases. Myocardial dysfunction at presentation was in only 2 patients, but subsequently 17 (39.5%) of them developed shock within 5 days of onset of symptoms. High index of suspicion and vigilance should be maintained by the primary care provider for the timely diagnosis and referral to higher centre even it appears mild at the onset.

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