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Original Research Article

Clinical profile of multisystem inflammatory syndrome in children associated with COVID-19 in a rural medical college

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ABSTRACT

Background: Multisystem inflammatory syndrome in children (MIS-C) is a newly recognised syndrome temporally associated with SARS CoV-2 infections.
Methods: This was an observational both retrospective and prospective study in a rural medical college in eastern India. MIS-C was diagnosed as per the criteria given by the WHO.
Results: First case of MIS-C of the institute was found in November 2020, maximum cases were seen during the second wave. There were 66 cases. Mortality was 6%. All presented with fever. There was swelling of joints in 56.6% cases, gastrointestinal symptoms in 65%, respiratory distress in (43.9%) and shock was present in 12.1% of cases in this study. Co-morbidities were present only in four cases (6%).
Conclusions: All cases of MIS-C had evidence of past infection with SARS CoV-2. There were relatively more cases of joint involvement and relatively less cases of shock in this study. The treatment using IVIG and methyl prednisolone was satisfactory. The 50% of the mortality was due to co-morbidities.

Keywords: PIMS-TS, SARS CoV-2, Mortality, Arthritis

INTRODUCTION

As early as May 2020, during the first wave of COVID-19, a series of hyper-inflammatory shock syndromes were reported from UK.[1,2] Soon similar cases were reported from USA, Italy, France and Spain.[3,7] India reported first such case series in November 2020.[8]

This novel syndrome was termed 'pediatric inflammatory multisystem syndrome-temporally associated with SARS CoV-2' (PIMS-TS) by royal college of paediatrics and child health, UK.[9] The term MIS-C put forward by WHO defines the disorder more objectively and preferred terminology currently.[10,11]

MIS-C can be a life-threatening illness, which develops 4-6 weeks after SARS CoV-2 infection. Though many patients may be RTPCR negative by this time, they usually test positive for antibody to SARS CoV-2. MIS-C shares many features of Kawasaki disease (KD) and toxic shock syndrome (TSS). However, the typical age for presentation is >5 years in MIS-C as opposed to <5 years in KD. MIS-C cases usually occur in previously healthy children, while symptomatic COVID-19 cases manifest mostly in children with underlying co-morbidities.[11,12]

The objective of the study was to find out the clinical profile of MIS-C in the children admitted to the institution.

METHODS

This study was undertaken in the pediatrics department of Midnapore medical college and hospital, a rural medical college in the eastern India after ethical committee approval (Memo no. MMC/IEC-2021/46 dated 05/03/2021). Though largely this was a prospective study, from April 2021 to March 2022, cases from the previous year (April 2020 to March 2021) were also included, after retrospective analysis of the case records if they met the diagnostic criteria. All the cases of MIS-C admitted to the study institute up to March 2021 were included in this study.

MIS-C was diagnosed as per the criteria given by WHO.[10]

Inclusion criteria were, any child with fever >3 days and any two of the following, (i) skin rashes or bilateral conjunctivitis or other signs of muco-cutaneous inflammation; (ii) hypotension or shock; (iii) evidence for cardiac involvement in form of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (detected by echocardiography findings) or elevated Troponin/NT-proBNP); (iv) coagulopathy (PT, PTT and elevated d-dimers) (v); and gastrointestinal symptom (diarrhea, vomiting, or abdominal pain).

Exclusion criteria were absence of markers of inflammation such as normal erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), or procalcitonin or presence of infective causes of inflammation, including bacterial sepsis and *Staphylococcal* or *Streptococcal* shock syndromes.

Evidence of COVID-19 infection in past was ascertained with RTPCR, positive antibodies for SARS CoV-2. Where these two were negative history of COVID-19 in the family was taken as an evidence of past SARS CoV2 infection.

The data were entered in the Microsoft excel spreadsheet. IBM SPSS Statistics for windows version 20.0 Armonk, NY: IBM Corp was used for statistical analysis. Continuous variables were expressed as means and standard deviations, and categorical variables were expressed as percentages.

RESULTS

First case of MIS-C of the institute was found in November 2020 from the retrospective analysis of the case records. Six cases of MIS-C were in the first wave (April 2020 to March 2021). Most (58 out of 66 or 87.9%) of the cases occurred during the second wave (between April 2021 and December 2021) and there were only 2 cases after January 2022 till the end of the study period.

Demographic characteristics are summarized in Table 1.

Table 1: Demographic characteristics, (n=66).

Characteristics	N (%)
Age (Years)	
1-4	2 (3)
5-9	48 (72.7)
10-14	16 (24.2)
Sex ratio (Male: female)	41:15
Mean and median age (Years)	7.2 and 8
Rural urban ratio	28:38
Discharged	60 (90.9)
Death	4 (6)
LAMA	2 (3)
H/o COVID-19 in family	57 (86.4)

Fever was presenting complain of all the cases. This was followed by swelling of joints (56.6%), particularly ankle and knees. Gastrointestinal symptoms were common. Respiratory distress was common (43.9%) and required oxygen therapy. Shock was present only in 12.1% of cases in this study. Co-morbidities were present only in four cases (6%) and two of them died. Two cases, which did not have any severe symptoms left against medical advice (LAMA). Conjunctivitis and skin rashes were also present in a good number of cases (Table 2).

Table 2: Clinical features, (n=66).

Clinical presentation	N (%)
Fever	66 (100)
Conjunctivitis	23 (34.8)
Loose motions	28 (42.4)
Pain abdomen	43 (65.2)
Vomiting	19 (28.8)
Dehydration	23 (34.8)
Congestive cardiac failure/ shock	8 (12.1)
Respiratory distress	29 (43.9)
Seizure	2 (3)
Altered sensorium	5 (7.5)
Swelling of joints	38 (56.6)
Skin rashes	12 (18.2)
Co-morbidities (Asthma)	2 (3)
Co-morbidity (Nephrotic syndrome)	1(1.5)
Co-morbidity (Cerebral palsy)	1 (1.5)

CRP and ESR were raised in all cases. Echocardiography could be done in 46 cases only and more than half of them showed abnormalities. The abnormalities included reduced left ventricular function (LVF), pericarditis and cornorary artery dilatations/aneurysm.

Most (86.4%) cases had someone in the family who was SARS CoV-2 positive in the 3-month period. Only 18.2% cases were RTPCR positive but most (95.4%) of them were positive for SARS CoV-2 antibody. Three cases were both RTPCR negative and Antibody negative, but there was strong history of contact in form of a close family member (Table 3).

Table 3: Laboratory investigations, (n=66).

Laboratory markers	N (%)
TLC > 11000	56 (84.8)
Lymphopenia	45 (68.2)
CRP raised	66 (100)
ESR raised	66 (100)
Raised D-dimer	23 (34.8)
RTPCR positive	12 (18.2)
Antibody	63 (95.4)
Echo abnormality	25 (54.3), n=46

The 20 cases were relatively mild and did not require any treatment other than observation. Steroids, IVIG and oxygen were used in most cases along with IV fluids and other supportive treatment (Table 4).

Table 4: Treatment, (n=66).

Treatment modalities	N (%)
IVIG only	4 (6)
Steroids only	25 (37.8)
IVIG + Steroids	21 (31.8)
Oxygen	35 (53.1)
NIV	10 (15.1)
Intubation	2 (3)
Inotropes	9 (13.6)

DISCUSSION

Age of presentation is of particular interest. The mean and median ages of the children in the present study were 7.2 and 8 years respectively, with majority (72.7%) of them between 5-9-year age group. This observation was similar to other studies. The landmark papers from UK and USA had reported the median ages of 9 and 8.3 years respectively.[2,3] Hoste et al performed a systematic review of 953 cases and reported the median age to be 8 years.[11] A multi-centric study from Odisha reported the mean age to be 9.09 years.[13] Two Indian studies from northern and eastern India showed the median age to be 6 years and 7 years respectively.[14,15] One study from Kerala found the mean age to be 6.2 years. We may infer from the above that MIS-C is a disorder of children aged more than five years, in contrast to the KD where children of age less than 5 years are mostly affected.

In this study boys far outnumbered the girls (41:15). Most of the studies have reported male preponderance and. Only few studies found girls to be affected more.[2,3,8,13-17]

Most of the cases recovered. Only 4 (6%) patients died in this study. This mortality was higher than that reported in the western literature (around 2%).[2,3,11] However Indian studies have reported mortality rate ranging from 0 to 27.5%.[13-16,18-20] Mortality was higher in children with associated co-morbidities. Two out of four children (50%) died who had co-morbidities. There were higher numbers of children with co-morbidities in the eastern India collaboration study which also reported higher mortality of 11.2%.[15]

Fever was a symptom in 100% of cases, followed by arthritis, gastrointestinal symptoms and respiratory distress. Shock was presenting features of relatively few cases. Rarest manifestations were neurological involvement. The systemic review of 68 studies involving 953 cases of MIS-C (mostly from US and UK) found most common symptoms to be fever (99.4%), gastrointestinal (85.6%), cardiovascular (79.3%) and respiratory (50.3%).[11] However the eastern India collaboration study reported the common symptoms in following order fever (100%), conjuctivitis (71%), gastrointestinal (50.7%), skin rash (40%), respiratory (39.6%), shock (35%) and joint involvement.[15] There were relatively more cases of joint involvement and relatively less cases of shock in this study. This may be due to relatively more awareness about MIS-C during and after second wave. Echocardiography though not done in all cases showed abnormality in more than 50% of cases, but only 12% were symptomatic. The relatively higher shock like presentation in western studies might also be because the studies were mostly from intensive care set ups, whereas this study was done in an institution, which catered to general pediatric population. Neurological involvement has been reported in other studies including studies from eastern India.

In the presence study 84.8% children had total leukocyte count more than 11000 and 68.2% had lymphopenia. This finding was similar to other studies from eastern India.[13,15] We observed rise inflammatory markers CRP and ESR in all cases and d-dimer in 34.8%. This finding was similar to other studies.[13,15,20]

The various treatment modalities were successful in management of the majority of the children and fatality was relatively low. IVIG (2 g/kg in infusion over 12 hours) was used along with steroids in most cases with severe manifestations. Pulse methyl prednisolone therapy was used in the dose of 30 mg per kg for day, which was followed by oral prednisolone after improvement of clinical conditions. Reports of successful treatment with these modalities have been reported by other studies.[8,21]

There were many limitations to our study, this being an observational study. Some cases during the first wave might have been missed because of unfamiliarity of the pediatricians with the presentations of MIS-C at that time. We could not present some data because of non-uniformity due to inclusion of some cases retrospectively. Echocardiography could not be performed in all cases because of multiple factors.

CONCLUSION

All cases of MIS-C had evidence of past infection with SARS CoV-2. There were relatively more cases of joint involvement and relatively less cases of shock in this

study. The treatment modality using IVIG and methyl prednisolone was satisfactory and the mortality was only 6%. The 50% of the mortality was due to presence of co-morbidities.

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