CLINICAL PROFILE AND OUTCOME OF MIS-C (MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN) IN A TERTIARY CARE CENTRE -A OBSERVATIONAL RETROSPECTIVE STUDY

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Abstract

Background: Children were thought to be spared from SARS Cov-2 initially but a month within this epidemic not only adults but also children were affected. Multisystem inflammatory syndrome (MIS) is a serious condition that occurs rarely but it affects children. The aim was to evaluate clinical profile and outcome of children with multisystem inflammation in children.

Methods: An observational retrospective study with children aged 2 months to 12 years at Tertiary care centre, MGM Medical College and Hospital, Aurangabad for a duration of 2 months from September, 2020 to November, 2020. Inclusion and exclusion criteria were set and ethical clearance was obtained. Demographic, disease characteristics, blood investigations, chest Xray, COVID rapid antigen test and RT-PCR and inflammatory marker details were noted at the time of admission and discharge. All the data was entered in Microsoft excel and analysed using SPSS version 24.

Results: The average age group of the patients was 7 years. Most of the patients were from low socioeconomic status. Patients with fever >7 days had increased heart rate and respiratory rate. Whereas, average saturation was 92% and average COVID antibodies (SARS-Cov-2 IgG) levels were 4.8. As per Kuppuswamy classification of socioeconomic status 8(80%) patients were from lower middle-class group. The average duration of hospital stay was 7.4 days and 2D ECHO changes were seen in 30% of patients who had large thrombus and dilated coronaries at the time of admission.

Conclusion: All the patients were given steroids, anticoagulants and or antiplatelet medications. None of them received IV Immunoglobulin. In our study 90% patients were cured with 10% mortality. Early supicion of immune mediated event following covid infection and early treatment with immunomodulator helped maximum children in recovery.

Keywords: SARS CoV-2; Tertiary care centres; Paediatric multisystem inflammatory disease; Steroids; Retrospective Studies.

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INTRODUCTION

In December 2019, a mysterious outbreak characterized by fever, dry cough, and weakness followed by gastrointestinal symptoms emerged in the Wuhan province of China.[1] At the beginning it was thought that adults are affected however, a month into epidemic, a novel multisystem inflammatory syndrome in children (MIS-C) or Paediatric inflammatory multisystem syndrome (PIMS) emerged. Multisystem inflammatory syndrome (MIS) is a serious condition that occurs rarelybut it affects children in various ways.[2] Some cases have reported hyper inflammatory shockwith receding severe acute respiratory syndrome corona virus 2 (SARSCoV-2). Initially, the syndrome was considered as an atypical form of Kawasaki disease (KD), an acute systemic vasculitis in young children, given the presence of fever, rash, conjunctivitis, mucocutaneous involvement, and cardiac complications.[3] However, it has become evident that shock, gastrointestinal symptoms, and coagulopathy, which are rarely seen in classic KD, are prominent features of this unique syndrome. Children with such presentation were very less after the first wave of SARSCoV-2. Diagnosis at that time was challenging and no proper treatment guidelines had been made for this newly emerging syndrome. In a study conducted by Jones, et al.[4]stated that KD and SARSCoV-2 have different clinical presentations. The study by Cheung, et al.[5] stated that KD and SARSCoV-2 have different cytokine expression and different pattern of interleukin-13 and tumour necrosis factor- α. Therefore, a new study was conducted to evaluate clinical profile and outcome of children in MIS after the first wave of SARSCoV-2. The objectives were to identify the clinical features and to observe the outcomes of PIMS patient in tertiary care centre.

MATERIALS AND METHODS

Study design –An observational retrospective study was carried out on children aged 2 months to 12 years at Tertiary care centre, MGM Medical College and Hospital, Aurangabad for a duration of 3 months from September, 2020 to November, 2020.

Inclusion and exclusion criteria – the inclusion criteria were

1. 1 month to 18 years age group.
2. Patient admitted in tertiary care centre.
3. Child fulfilling the diagnostic criteria of MIS-C according to WHO definition –

a) Age 0 to 19 years
b) Fever for >or= 3 days
c) Clinical signs of multisystem involvement (at least 2 of the following):
- rash, bilateral non-purulent conjunctivitis, or mucocutaneous inflammation signs (oral, hands, or feet)
- hypotension or shock
- cardiac dysfunction, pericarditis, valvulitis, or coronary abnormalities (including echocardiographic findings or elevated troponin/bnp)
- evidence of coagulopathy (prolonged pt or aptt; elevated d-dimer)
- acute gastrointestinal symptoms (diarrhoea, vomiting, or abdominal pain)

d) Elevated markers of inflammation (eg. ESR, CRP or procalcitonin)
e) No other obvious microbial cause of inflammation, including bacterial sepsis and staphylococcal/streptococcal toxic shock syndromes
f) Evidence of sars-cov-2 infection - any of the following:
- positive SARSCoV-2 RT-PCR
- positive serology
- positive antigen test
- contact with an individual with covid-19

Exclusion criteria- Children not fulfilling criteria of MIS-C as per WHO definition

Ethical clearance - Approval for the study was obtained from the Institutional Ethical Committee and Research Recognition Committee of MGM Medical College and Hospital, Aurangabad.

Data collection - Baseline characteristics of all patients like demography, disease characteristics, blood investigations and outcome were noted. Screenings of patients were done by taking chest X-ray, COVID 19 Rapid antigen test and RT-PCR. Patients with acute systemic vasculitis, given the presence of fever, rash, conjunctivitis, mucocutaneous involvement, cardiac complications and coagulopathies were taken into consideration. Data was collected from time of admission of patient and serial monitoring of inflammatory markers in blood like ferritin, D dimer and LDH. Coagulopathies in the form of thrombocytopenia and deranged prothrombin time and APPT were noted. Blood tests were noted on admission and serial monitoring done post start of treatment. All the patients were observed for outcome and prognosis.

Statistical analysis – All the data was entered in Microsoft excel and analysed using SPSS version

24. Standard deviation was calculated for quantitative variables and proportions for categorical variables.

RESULTS

A total of 10 patients with average age group of 7 years were included in this study. Out of 10 patients 6(60%) were females and 4(40%) were males. The socio-economic status was recorded using Kuppuswamy classification of socioeconomic status[6]. In our study 8(80%) patients were from lower middle class and 2(20%) belonged to upper middle class. None of the patients in the family had similar complaints. Only 1(10%) of patient had contact with COVID positive family member, rest all patients had no history of contact to COVID positive patient. The COVID RT-PCR and rapid antigen test was negative for all the patients. The clinical characteristics of children with PIMS-TS based on fever >7 and <7 days are presented in Table no 1.

Table no 1: Clinical characteristics of children with PIMS-TS based on fever >7 and <7 Days

Clinical Characteristics	**Fever > 7 Days (n=3) n(%)**	**Fever < 7 Days (n=7) n(%)**
Rash	-	2(20%)
Cough	1(10%)	2(20%)
Breathing difficulties	2(20%)	4(40%)
Pain In Abdomen	1(10%)	3(30%)
Generalized Oedema	1(10%)	1(10%)
Decrease In Urine Output	-	1(10%)
Bleeding Manifestation	1(10%)	2(20%)
Heart Rate (Median)	108	107.1
Respiratory rate (Mean)	39.3	33.4
Saturation (Mean)	92	96
COVID antibodies	4.8	10.9

PIMS-TS: Pediatric Inflammatory Multisystem Syndrome: Temporally Associated with SARS-CoV-2

None of the patients reported cold at the tertiary care centre. Chest radiography showed that 3(30%) had lobar consolidation. The duration of hospital stay on an average was for 7.4 days with maximum for 15 days and minimum for 4 days. The clinical outcomes at the time of admission and discharge based on fever >7 and <7 days are presented in Table no 2. The 2D ECHO changes were seen in 3(30%) patients as large thrombus and dilated coronaries at the time of admission.

Table 2: Clinical outcomes at the time of admission and discharge based on fever >7 and <7 Days

Outcomes	**Fever >7 Days**		**Fever < 7 Days**	
	Admission	**Discharge**	**Admission**	**Discharge**
Hemoglobin	10.87	11.17	11.3	9.47
TLC	8125.7	15538.5	7146.6	8150
Platelets	180142.9	471285.7	176333.3	399666.6
CRP(Q)	58.08	8.8	88.36	6.9
PT	13.42	12	15.37	13.5
APTT	37.48	23.8	29.35	26.2
INR	1.12	0.96	1.28	0.9
D Dimer (ng/mL FEU) (Median)	7.3	1.9	7.4	1.2
Ferritin	388.5	62.3	1886.3	66
LDH	311	254.5	420	-

TLC: Total Leucocyte Count; CRP: C-reactive protein; PT: Prothrombin time; APTT: Activated partial thromboplastin time; INR: International normalized ratio; LDH: Lactate Dehydrogenase.

The line of treatment of the patients was Dexamethasone, Methylprednisolone (MPS), Low molecular weight Heparin (LMWH), and or oral aspirin. The IV MPS (10mg/kg) was administrated

in 2 (20%) and MPS (2mg/kg/day) was given to 7 (70%) patients for a duration of 4-7 days. Dexamethasone (0.15mg/kg/dose) was given to 1 (10%). 80% patients received subcutaneous injection of LMWH (0.5mg/kg/day) for 3-7 days and then were shifted to Aspirin. 20% were directly started with Aspirin. Oral steroids and aspirin were given to patients for 10 and 14 days respectively. The percentage of patients that were cured, ventilated and expired are shown in Figure no 1.

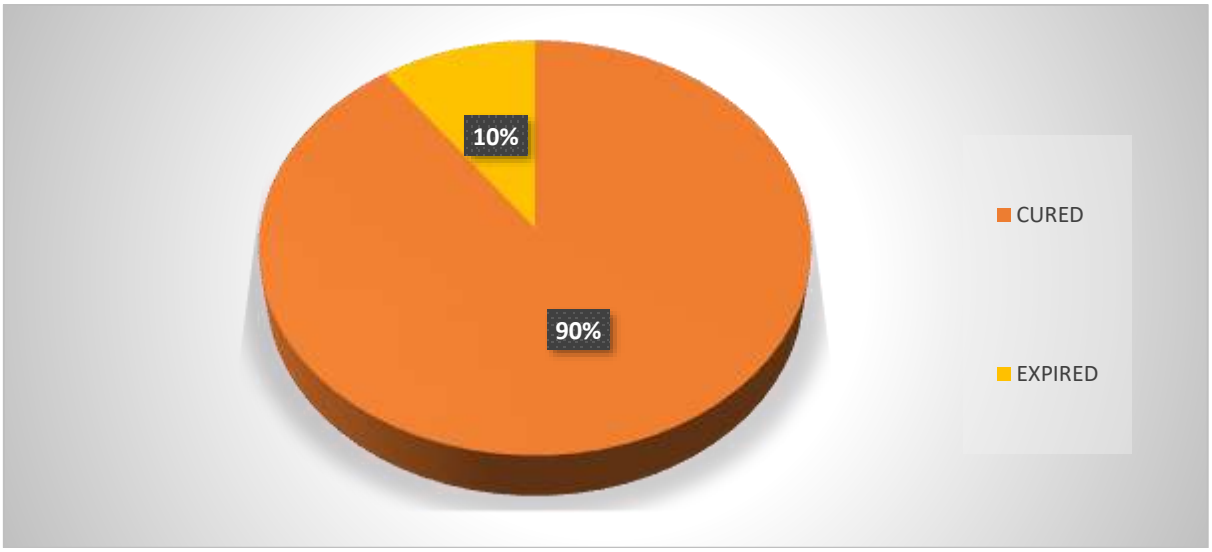

Figure 1: Outcome of patients post treatment for MIS-C.

DISCUSSION

The present study describes the clinical characteristics and outcomes in children with MIS after the first wave of SARSCoV-2. This observational retrospective study was conducted in children aged 2 months to 12 years at Tertiary care centre, MGM Medical College and Hospital, Aurangabad for a duration of 3 months from September, 2020 to November, 2020. MIS-C is a rare disorder that affect children below 21 years with SARS CoV-2.[7] Among 10 patients 3(30%) and 7(70%) had fever > 7 days and <7 days respectively. The duration of fever has role in having different clinical characteristics and outcomes. It the present study it's clear that patients with fever >7 days had increased heart rate, respiratory rate, lower saturation rate, and lesser COVID antibodies than patients having fever < 7 days. The symptoms like rash, pain in abdomen and breathing difficulties was reported in the present study. Dufort, et al[7] reported similar finding in 0 to 12 children, it was also seen that MIS-C with SAR CoV-2 occurred in all racial and ethnic backgrounds.

The inflammatory markers were higher than normal at the time of admission and continued to be slightly high at the time of discharge. Similar findings were observed by Whitaker, et al[3]and Wu H, et al[13]who proposed clinical patterns of PIMS with elevated levels of inflammatory markers and also mentioned that such changes don't happen in KD. The 2D ECHO showed that 3 (30%) had coronary changes a similar pattern of observation was directed in previous studies. It stated that all patient with MIS-C should have ECHO monitoring even if the initial readings appear to be normal.[3,9] In regards to SARS CoV-2 in children more severe symptoms like coagulation dysfunction, renal disorders, respiratory failure, gastrointestinal infections and coronary involvement are newly added. Monitoring and echocardiography are highly recommended at 1 to 2 weeks and 4 to 6 weeks post treatment.

At present in India, steroids are most commonly used for the treatment of SAR CoV-2. Steroids and aspirin were given to patients throughout the stay at hospital and also post discharge. In US and UK glucocorticoids (49%) and corticosteroids (64%) respectively were used in most of the patients. Corticosteroids still remain the first line of treatment in children. It has also shown that IV MPS and oral MPS are useful aides to IV Immunoglobulins.[15] Studies have also reported the use of IVIG along with steroids in UK and US.[7,8] The use of IVIG was not the common due to increased cost of cost and therefore couldn't be choice of treatment in India.[10]Also, in India the socio-economic status of people in availing treatment plays an important role. Although there has been no proper treatment line of methods in children but a recent reviewsuggests similar methods of treatment that was followed in the present study.[14]

In the present study 9(90%) of the patients were cured and 1(10%) expired. 3(30%) out of 10required ventilations. Most of the patients recovered well and had better values of coagulation factors, inflammatory markers, ferritin, and LDH post discharge. This maybe because the patients were young children and has good recovery without much complications. The patient which expired was 2 months old and had increased heart rate, CRP, D Dimer, Ferritin, TLC, 2D ECHO showed large thrombus, low Haemoglobin and platelet count at admission.

The limitation of the study was smaller number of patients and a short duration of study. Often children are less frequently test because of the notion that SAR CoV-2 affects adults more. A study with long term data and different ethnic groups will give better and clear confirmation of the sequelae of MIS-C.

CONCLUSION

Since MIS-C is a newly emerging syndrome, it is important to know its presenting factors in order to differentiate it from other systemic diseases like Kawasaki disease, Septic shock, Viral haemorrhagic fever. This study shows that an early diagnosis and prompt treatment with the steroids, anticoagulantsand or antiplatelet medications is life saving for the patients and leads to a positive outcome. In this study although there was a small sample size, we can note that maximum patients were females, in the age group of >10 years. As per Kuppuswamy classification of socioeconomic status 8(80%) patients were from lower middle-class group. Also, we see that all the 10 cases received steroids and none received IVIG since cases showed improvement on steroids.

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