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Multisystem Inflammatory Syndrome In Children: A Hospital Based Retrospective Study From Eastern India

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Abstract

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Introduction

Multisystem inflammatory syndrome in children (MIS-C), a novel clinical syndrome, is a potentially serious and life-threatening disease in children. It appears to be a delayed complication of severe acute respiratory syndrome Coronavirus 2 (SARS- CoV2) infection. [1][2].

MIS-C is characterized by persistent fever (>3 days), abdominal pain, vomiting, diarrhoea, as well as mucocutaneous, cardiovascular, hematological, musculoskeletal, and neurological manifestations, among others [3][4]. Similar condition has been termed as pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 virus (PIMS-TS) by Royal College of Paediatrics and Child Health [5].

During the course of the COVID-19 pandemic, in May 2020 , several European countries reported cases of new multisystem inflammatory syndrome in children with clinical features of shock and atypical Kawasaki disease (KD)and the possibility of its link with SARS-CoV-2 was considered [6][7].Thereafter Centers for Disease Control and Prevention (CDC) and WHO defined these cases as multisystem inflammatory syndrome in children (MIS-C) temporarily related with Corona virus disease19 (COVID-19) [3][4].

MIS-C appears to share the features of pediatric hyperinflammatory state such as Kawasaki disease (KD), macrophage activation syndrome and Toxic shock syndrome (TSS) [8]. Though little is known about the epidemiology, cases of MIS-C seem to appear few weeks after the COVID-19 infection. SARS-CoV-2 related MIS-C is a dreaded complication that is seen more often in children than in adults [7].

There is paucity of data on MISC from the Northern part of West Bengal. Our Institute, serves as the 1st referral unit of its surrounding districts. The various clinical spectrum, aetiologies and short term outcome were evaluated thoroughly on MIS-C.

Materials And Methods

This was a hospital based retrospective study, conducted in the department of Pediatric Medicine of a medical college, in a district of West Bengal, India, over a period of three months, 1st June 2021 to 31st August 2021.

Ethical approval: The study was approved by the Institutional Ethics Committee.

Study definition – we used WHO case criteria to define a case of MIS-C. Patients with age ranged from 1 month to 12 years were included in this study, as per the age criteria for admitting the patients in pediatric ward.

Exclusion criteria: Patients with tropical infections or sepsis lacking features of hyper-immune state and negative serology for Immununoglobulin G for SARS-CoV-2 were excluded.

Primary Outcome: to evaluate the detailed clinical characteristics and short term outcome of the patients. Secondary Outcome: This study may provide in-depth understanding of the epidemiological, clinical aspects of SARS-Cov2 infection and MIS-C in this region of West Bengal, for developing effective public health prevention and intervention programs.

Statistical Methods Categorical variables are expressed as Number of patients and percentage of patients and compared across the groups using Pearson's Chi Square test for Independence of Attributes/ Fisher's Exact Test as appropriate.

The statistical software: SPSS version 22 has been used for the analysis.

Results

Base line characteristics

A total of 105 patients who were diagnosed with MIS-C were included in the study.

The male to female ratio in this cohort was 1.33:1.

Median age was 36 Months. Thirty two patients (31%) were under 1 year age and 50 patients (48%) belonged to age group 1-5 years. (Figure 1).

Coexisting comorbidities were present in 12 (11%) patients. These were -congenital heart disease, Down syndrome, diabetic ketoacidosis, obesity, Vitamin D deficiency.(Table 1).

Clinical characteristics

Fever was present in all the patients. Median duration of fever was 7 days. Mucocutaneous involvement were present in the majority of patients. (Figure 2). Most common involvement was non-exudative and non-purulent conjunctivitis, seen in 65(62%) patients. Oropharyngeal changes included red lips, red tongue, cheilitis, glossitis, were present in 59(56%) patients. Different types of skin rashes were present in 48 (46%) patients. These were macular, maculopapular, itchy and purpuric.

Lower respiratory symptoms were present in 56 (53%), including cough, shortness of breath,

Gastrointestinal involvement were pain abdomen, nausea, vomiting, hematemesis, malena,were present in 37(35%) of patients.

Cardiovascular involvement was present in 21 (20%) of patients, who presented with shock, heart failure, arrhythmia.

Central nervous system involvement was seen in 18(17%) patients. They presented with febrile seizures, encephalopathy, and acute encephalitic syndrome (AES) like presentation.

Bleeding manifestations from different sites were seen in 8 (8%) patients- including hematemesis and/or malena, hematuria.

Concomitant infections were associated in 17 (16%) patients. These were Scrub, Japanese encephalitis, urinary tract infection, meningitis, dengue, brain abscess. (Table 2).

Laboratory investigations

Inflammatory markers were raised in most of them on admission. ESR was raised in 77(73%) patients, and CRP was raised in 81 (77%) patients. Neutrophilia was present in 95 (90%) patients. Prothrombin time (P time) was elevated in 51 (49%) and patients. D-dimer level was elevated in 69(66%) patients. Low serum albumin was present in 25 (24%) patients. Echocardiographic changes were noted in 43 (41%) of patients.

Clinical course, treatment and immediate outcome

In view of the fact that MIS-C must be identified and treated early, we started their treatment as per management guideline of Indian Academy of Pediatrics (IAP) and also management guideline from Ministry of Health and Family Welfare, Government of India.

Symptomatic management given to them as they needed, including respiratory support, blood component therapy, insulin infusion, vasoactive medicines. Management with corticosteroids and/or immunoglobulin was given to all. Intravenous antibiotics, doxycycline /oral azithromycin was given to them when infection suspected and when serology came positive to scrub typhus. Patients with elevated D-dimer and/or echocardiographic changes received low dose aspirin and molecular weight heparin therapy as indicated.

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Management in Pediatric Intensive Care Unit (PICU) was required in 29 (28%) patients. These were the patients presented with shock, AES, respiratory distress, diabetic ketoacidosis, pancypopenia, bleeding manifestations, anasarca.

Immediate outcome was excellent, all the patients survived. Median duration of hospital stay was 7 days while minimum duration of staying was 3 days, and maximum duration was 17 days (standard deviation 3.29). Duration of staying in hospital was significantly affected with duration of fever at admission (p value 0.023), involvement of gastro-intestinal system (p value 0.004), presence of shock (p value 0.011), patients with raised CRP (p value 0.035), and in patients with raised P time (p value 0.002).(Table 3) (Table 4).

Discussion

MIS-C /PIMS-TS is an emerging disease in post-COVID patients. It is a serious and life-threatening illness in previously healthy children. Children presenting with MIS-C would have varied and wide spectrum of disease symptoms depending on the organ system involvement, ranging from fever, rash, mild respiratory illness, gastrointestinal symptoms to severe disease like inflammatory vasculopathy and coagulopathy.[9].

In our study, under 5 year patients comprised 78% of cohort. Gupta S et al reported 60% of children presented with MISC were <5 years of age in their studies.[10]. Median age was 7.2 years studies done by Jain S et al and Dufort et al reported that 80% of children were aged between 6 to 12 years.[11][12].

Most common presentation in our study was fever and non-purulent conjunctivitis, which is similar with the study conducted by Dufort et al.[12]. Respiratory symptoms were more common (53%) than gastrointestinal (GI) involvement (35%) patients in our study. GI involvement was reported in 90% by Tiwari et al , in 80% by Dufort et al and in 42% of patients by Dhanalakshmi K et al in their studies .[6][12][13] . Jain S reported abdominal pain in 78% of patients in their study.[11].

Predominantly CNS was involved in the study done by Gupta S, in 80% patients, and CNS involvement was seen in 17% of patients in our study.[10]

Limitation

The limitations in this study are it was a retrospective study, and, a single -center study as well. Being a single center study, all the patients were diagnosed and treated in the same manner. Due to non-availability of bedside echocardiography, it was done when the patients were clinically stable rather than at admission .Also, we could not assess pro BNP, IL 6, in our study due to non-availability at the present time in our institute.

Conclusion

With the emergence of MIS-C and increased reporting of such cases, physicians should be aware of the different phenotypes of hyper-inflammatory features associated with COVID-19 and MIS-C. In the Indian context, several tropical infections may mimic MIS-C or may coexist with MIS-C. Several co-morbidities also may co-exist with MIS-C as well. Concomitant infections and co-morbidity may play an important role in determining the prognosis MIS-C and hence maintaining a high index of clinical suspicion is necessary.

Prompt recognition, diagnosis, and timely management will improve the prognosis, reduce mortality and morbidity, will facilitate their intact survival and would have long term effect in the child's prognosis. Early and appropriate intervention will also aid in reduction of the irrational use of antibiotics, to establish the necessary antibiotic stewardship.

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FIGURE 1: Age Distribution

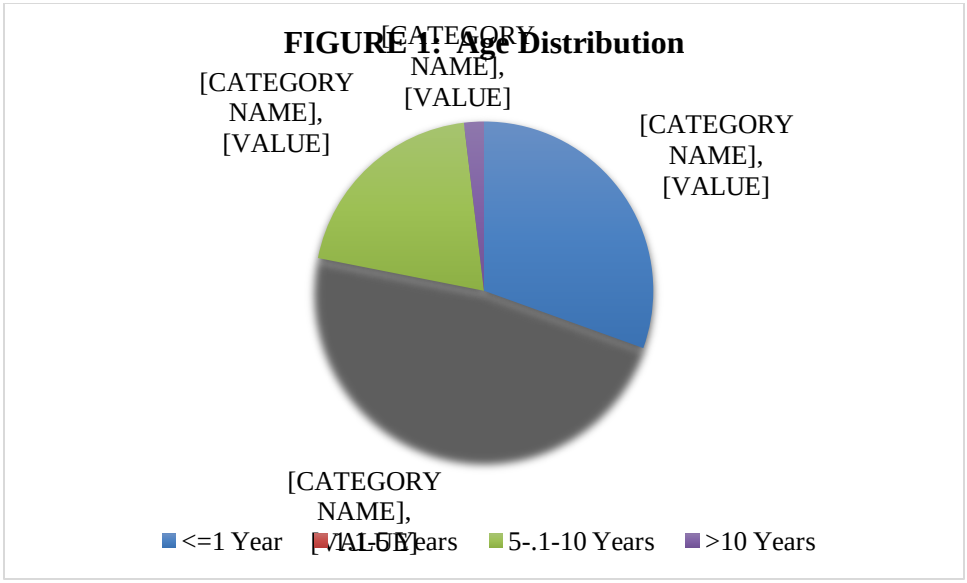

FIGURE 2: System Involvement

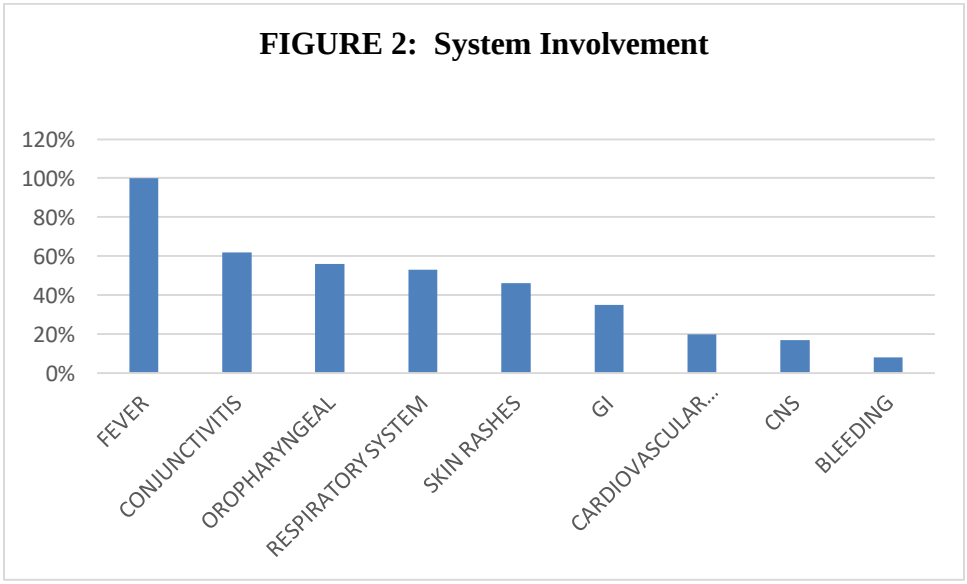

TABLE 1: Co- morbidities associated with MIS-C

Co-morbidity	Frequency (%)
Obesity	1
Vitamin Deficiency	1

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Nephrotic syndrome (relapse)	2
Congenital heart disease	4
Diabetic ketoacidosis(New onset)	2
Down syndrome	2
Total	12(11%)

TABLE 2: Concomitant infections associated with MIS-C

Concomitant infection	Frequency (%)
Scrub	10
Urinary Tract Infection	2
Meningitis	1
Japanese Encephalitis	1
Dengue	2
Brain Abscess	1
Total	17(16%)

TABLE 3 : Duration of staying in hospital in relation with duration of fever and shock at admission, and involvement of gastro-intestinal system

	Fever duration			Total		
	Upto 5 days	5-10 days	>10 days		p Value	Significance

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Hospital Stay Days	<=7 Days	29(65.91)	19(40.43)	11(78.57)	59(56.19)	0.023	Significant
	8-14 Days	12(27.27)	25(53.19)	2(14.29)	39(37.14)		
	>14 Days	3(6.82)	3(6.38)	1(7.14)	7(6.67)		
Total		44(100)	47(100)	14(100)	105(100)		

		GIT		Total		
		PRESENT	ABSENT		p Value	Significance
Hospital Stay Days	<=7 Days	13(35.14)	46(67.65)	59(56.19)	0.004	Significant
	8-14 Days	20(54.05)	19(27.94)	39(37.14)		
	>14 Days	4(10.81)	3(4.41)	7(6.67)		
Total		37(100)	68(100)	105(100)		

		Shock		Total		
		PRESENT	ABSENT		p Value	Significance
Hospital Stay Days	<=7 Days	6(28.57)	53(63.1)	59(56.19)	0.011	Significant
	8-14 Days	12(57.14)	27(32.14)	39(37.14)		
	>14 Days	3(14.29)	4(4.76)	7(6.67)		
Total		21(100)	84(100)	105(100)		

TABLE 4: Duration of staying in hospital in relation to raised CRP and raised P time

		CRP		Total		
		Normal	Raised		p Value	Significance
Hospital Stay Days	<=7 Days	19(79.17)	40(49.38)	59(56.19)	0.035	Significant
	8-14 Days	5(20.83)	34(41.98)	39(37.14)		
	>14 Days	0(0)	7(8.64)	7(6.67)		
Total		24(100)	81(100)	105(100)		

		P time		Total		
		Normal	Raised		p Value	Significance
Hospital Stay	<=7 Days	39(72.22)	20(39.22)	59(56.19)	0.002	Significant

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Days	8-14 Days	12(22.22)	27(52.94)	39(37.14)		
	>14 Days	3(5.56)	4(7.84)	7(6.67)		
Total		54(100)	51(100)	105(100)		

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