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MIS-C A RETROSPECTIVE OBSERVATIONAL STUDY FROM TERTIARY CARE CENTERS OF PURVANCHAL AREA OF EASTERN U.P. AND ADJACENT SOUTH BIHAR.

Dr Sandesh Srivastava	JR II NMCH, Jamuhar, Sasaram;
Dr Rahul Kumar	JR II NMCH, Jamuhar, Sasaram;
Dr Sonam Karan	Assistant Professor. ACMS Delhi.
Dr Ritesh Kumar*	Associate Professor, HIMS ,Varanasi. *Corresponding Author
Dr (Maj) Udit Raghuvanshi	Medical Officer, Military Hospital, Varanasi.
Dr Roshni Bhattacharya	Consultant Pediatrician, Popular Supe rspeciality teaching Hospital, Varanasi.
Dr (Col) Om Prakash Singh	Professor Pediatrics, NMCH, Jamuhar, Sasaram.

ABSTRACT **Objective:** We are describing the temporal profile of 19 cases of **MIS-C** including demographic, clinical and laboratory findings along with the treatment and outcomes .We also studied the response to various available treatment modalities for MIS-C.

Method: This was a retrospective observational study carried out at a tertiary care center . Children satisfying WHO MIS-C criteria admitted from Apr 2021 to Aug 2021 to PICU were included. The clinical profile, treatment, laboratory parameters and outcomes in all 19 critically ill children diagnosed with MIS-C were analyzed from Apr 2021 to Aug 2021.

Results: The study population in this study included 19 patients with MIS-C . All 19 children had fever,15 of them had gastrointestinal features. Hypotension was observed in 12 cases. Eye changes in the form of conjunctival congestion, conjunctivitis,& conjunctival hemorrhage was observed in 14 children. Most of them were treated with steroids alone, Few of them required steroids as well as IVIg. There was no treatment failure observed in any of the cases. There was a gradual reduction of the CRP by day 3 in most of the cases.. Follow up studies have not revealed any abnormality on echocardiography

Conclusion: Steroids were found to be equally effective & were the first line of management in all the cases. IVIG was used in cases which were subjected to mechanical ventilation in children with SARS-CoV-2 related MIS-C. There was no mortality in this group.

KEYWORDS : SARS-CoV-2, COVID-19, MIS-C, IVIG, methyl Prednisolone, Kawasaki disease. Myocarditis,

INTRODUCTION

The multisystem inflammatory syndrome in children (MIS-C) is a post-viral immunological or hyper-inflammatory complication of severe acute respiratory syndrome corona virus-2 (SARS-CoV-2) . The infection is commonly seen in older children, who commonly present with fever, multi-systemic involvement including myocardial dysfunction and shock, and hyper-inflammation. The estimated incidence MIS-C in US population has been 2.1/100000 in persons younger than 19 yrs (0.2 - 6.3)[1]

This leads to significant morbidity, mortality and has affected healthcare delivery system throughout the world[1]. As compared with adults, children younger than 12 years of age are less affected by SARS-CoV-2, have milder disease severity and better outcome [2-4]. The MIS-C peeks follow 2-5 wks after covid.[1,2] Multisystem inflammatory syndrome in children (MIS-C) usually manifests with lethargy, headache, meningismus, conjunctivitis, rash, lymphadenopathy, stomatitis, swelling of extremities with erythema, skin peeling, nausea vomiting, pain abdomen, diarrhea, along with increased AST& ALT, There may be hypoxemia, chest pain and pulmonary infiltrates on X-ray chest. Involvement of heart may lead to myocarditis, hypotension, hypo perfusion ,tachycardia, myocarditis, coronary aneurysm, increased troponin & pro - BNP. There may be evidence of raised ESR, CRP,LDH, Pro-Calcitonin,IL-6, Fibrinogen, CPK,D-dimers. In the blood there may be evidence of thrombocytopenia, neutrophilia, and/or lymphopenia, Involvement of kidneys may lead to hyponatremia, and renal failure. Out of this the most common presentations of MIS-C are persistent fever, abdominal complaints, muco-cutaneous features, shock, myocardial dysfunction in older children 2–6 weeks after the exposure to SARS-CoV-2 infection [7]. CRP does not differentiate between MIS-C with alternate diagnosis among hospitalized children with fever.

The aim and the objective of this study was to describe the temporal profile of MIS-C cases presented to us during this period.

MATERIAL AND METHODS

This was a retrospective observational study at tertiary pediatric care centers of Narayan Medical College and Hospital, Jamuhar, dist-Rohtas, Bihar, Heritage Institute of Medical Sciences. Varanasi, Popular super speciality Hospital Varanasi & Military Hospital Varanasi. This study was carried out during the period Apr 2021 to Aug 2021. This was an observational retrospective study.

The Inclusion criteria included confirmed cases of children with MIS-C as per WHO guidelines. All children up to the age of 15 years admitted with above symptoms were included , during Apr2021 to Aug, 2021. RT-PCR (Reverse transcriptase polymerase chain reaction) test was done in all patients along with SARS-CoV-2 antibody testing. The exclusion criteria included confirmed sepsis, scrub typhus, leptospirosis, and dengue fever diagnosed by appropriate investigations.2D-Echo was done in all cases presenting with myocarditis and shock. Children were labeled to be having shock if CRT was prolonged > 3 seconds, cold peripheries & requirement of more than 20 ml/kg of intravenous (IV) fluids or an inotropic support to maintain blood pressure above the 5th centile.

The particulars of the patients with clinical variables were recorded on a Performa including the demographic characteristics, symptoms and clinical signs, laboratory parameters, type of immunomodulator used, need for inotropic support, duration of shock, duration and type of respiratory support, Echo findings and 2 weeks follow up and mortality.

The dosage of dexamethasone used was 0.15 mg/kg & dosage of methyl Prednisolone was 30 mg/kg once daily for three days followed by oral Prednisolone at 2 mg/kg for 1 week or till CRP normalized, whichever was later. The dosage of IVIG was 2 g/kg as a continuous infusion over 8-12 hours. CRP and D-dimer were repeated on the third and seventh day after the start of IVIG or methylprednisolone.

Children with treatment failure with pulse steroids were treated with IVIg additionally. Time to fever defervescence was recorded at 12-hourly intervals. Treatment failure was defined as persistence of fever or worsening of clinical condition beyond 36 hours from the start of first-line therapy . All patients were followed for two weeks after discharge. All patients with shock were started on low dose aspirin.. Children receiving steroids also received prophylactic IV pantoprazole.

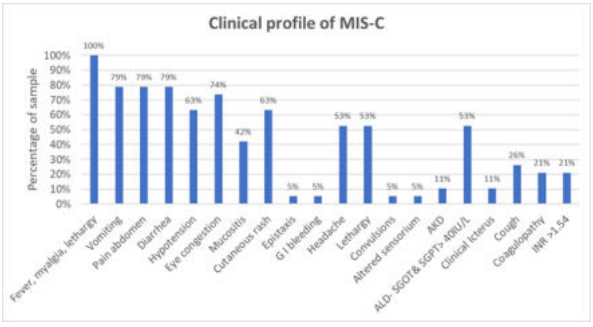

Chart 1- Clinical profile of MIS-C -Total No.-19

Chart-2-Age & gender profile of MIS-C -Total No.-19

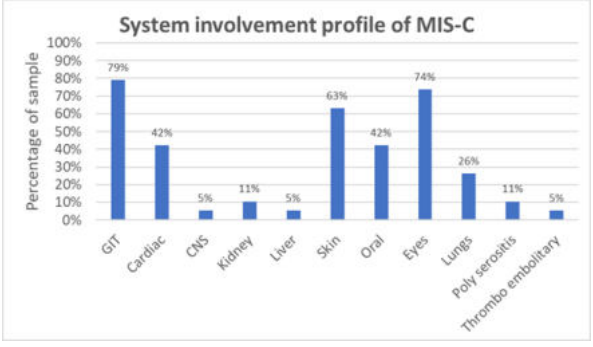

Chart-3-System involvement profile of MIS-C -Total No.-19

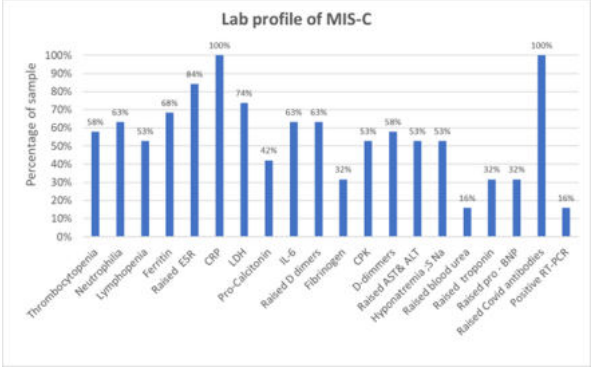

Chart-4,Lab profile of MIS-C -Total No.-19

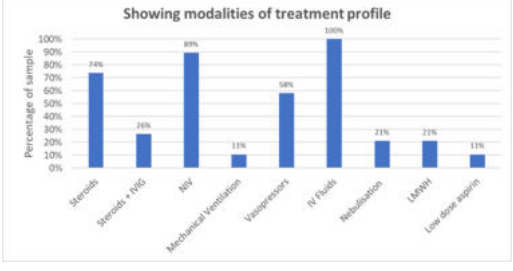

Chart- 5- Showing modalities of treatment ; Total no -19

RESULTS

Chart -2 reveals the age & gender profile of the case. Out of 19 children with MIS-C , all of them had constitutional symptoms in the form of Fever, myalgia, lethargy. Chart-1 reveals that 15 Patients (65.38%) had gastrointestinal symptoms in the form of nausea ,vomiting, diarrhea, pain abdomen, 8 (36.46%) had cardiac symptoms including Chest pain, Palpitation ,tachycardia, hypotension, arrhythmias, 14 children (57.69%) had eye changes including conjunctivitis,& conjunctival congestion, 08 (23.07%) had oral mucosal changes, 05 (19.23%) (table 1,chart 1) patients had lung involvement including cough, chest pain, breathlessness & Patchy lung infiltrates , most of which were bilateral. Skin rash was present in 12 out of 19 patients & it comprised of areas of erythema with vesicles or pustules, urticarial, maculo-pappular. Kidney involvement was present in 02 cases(10%) the presenting symptoms included Pain abdomen, icterus, hepatomegally. Kidney involvement in the form of oliguria & AKI was present in only one case. Neurological involvement was present in only one case and the symptoms included encephalopathy -headache, altered sensorium. seizures .Three children had polyserositis in the form of plural effusion ascites and pericardial effusion. The commonest system involved were GIT, Skin, CVS, respiratory, renal, liver, CNS in that order. 09(47%) children had involvement of more than five Systems.06 (32%) children had four systems & 04(21%) had involvement of three systems.

Chart -4 reveals that CRP was raised in all the19 cases. All 19 children(100%) had raised anti Covid antibodies.LDH was raised in15 children(79%),ESR in16 (84%),thrombocytopenia in11(58%).neutrophilia in12(63%), lymphopenia in10 (53%),ferritin raised in13(68%) ,pro -calcitonin in 8 (42%), IL in 6(32%),raised D-dimers were found in 12 (63%),fibrinogen levels were raised in 6 (32%),raised CPK in10 (53%),raised AST & ALT in 10 (53%),hyponatremia in 10 (53%), raised blood urea in 3 (16%), and raised troponin in 6 (32%) of the cases.

Chart - 5 reveals that steroids were used in all 19 (100%) children, steroids and IVIG in 5 (26%) cases ,Vasopressors were required in 11 (58%),NIV was required by 17 (89%) of cases and mechanical ventilation by 2 (11%) children. All 19 children required intravenous fluids. Nebulization was needed in 4 (21%) cases.

DISCUSSION

The present study reveals very good outcomes with steroids in MIS-C cases. Cardiac involvement is the most frequently reported organ dysfunction in MIS-C as also seen in the present study.[1,6,10] We did not find any coronary dilatation or coronary aneurism in our patients on two weeks follow up.

Many of the studies have found that all children had fever with a higher proportion of GI symptoms, while cough was found to be rare. [12,14] Similar results were seen in the present study also. Many children in our study had eye changes in the form of conjunctivitis, conjunctival congestion,& hemorrhage. Some of them also had oral mucosal changes. [12,13]

A higher seropositivity rate with or without SARS CoV-2 RT-PCR positivity is reported in patients with MIS-C with shock and multiorgan involvement.[14] Presence of positive COVID-19 antibody in patients with positive SARS-CoV-2 PCR at admission probably indicates a greater role of immune-mediated inflammatory response than acute SARS-CoV-2 viremia in the pathogenesis of MIS-C.

In an study by Dufort et all 15 the number of PICU admissions were to the tune of 80%,chidren requiring NIV was 23%.IMV requirement was 10%,vasopressures 62%,steroids 64%,IV Ig 70%, IV Ig plus steroids 48%.In another study Feldstein et all 16.reported PICU admissions in -80%,NIV-17 %,IMV-32%,Vaspressures-49%,steroids-49%,IV Ig77%,biologicals20%.[16,18]

French covid-19 pediatric inflammation consortium had concluded that combined treatment with steroids & IV Ig was associated with better course in MIS-C.[22]

In another study the CDC -overcoming Covid 19 surveillance registry, concluded that initial treatment with IV Ig plus steroids is associated with lower risk of new or persistence of cardiovascular dysfunction.

The BATS Consortium found no substantial difference in the two

primary outcome measures among the three treatment arms ,Sub groups who met WHO criteria for MIS-C , found modest evidence of benefit from steroids alone compared to IV Ig alone.

In an Indian study by Shreeja Sugunan et al [20] steroids were used as first line treatment in children with MISC& this was associated with favorable immediate& short come term follow up outcomes.

It is reasonable to consider treating children with steroid as first line especially in setting where IV IG is expensive and difficult to access.[19]

We found very good response with steroids alone, however in 5 children we have used both. Treatment with IVIG in resource limited settings is a challenge. In this study outcome measures showed a very good response to steroids in the treatment of MIS-C. Another recent study [14]also found a more favorable outcome in those treated with IVIG and steroids than those treated with IVIG alone. Small sample size, observational nature and absence of matched cohorts are the main limitations of this study.

No mortality was noticed in this study, follow up study of the children with coronary dilatation at two weeks did not reveal in abnormality on echo.

CONCLUSIONS

MIS-C is a immune mediated process & is still evolving, as it has not been reported from most parts of the country. It is an uncommon complication of SARS CoV-2 infection in children characterized by fever, multisystem involvement, shock, hyperinflammation. In Indian settings, we should always try to rule out tropical infection & bacterial sepsis before labeling as MIS-C. Stratifying children based on severity at presentation should be done. The disease is a dynamic process and phenotypes may evolve. Immunomodulation aggression keeps pace with disease aggression, More and more evidence is emerging towards steroids use. Short term outcomes are favorable and longer follow up is the need of the hour. Treatment includes supportive intensive care including hemodynamic and respiratory support, immunomodulatory therapies and antiplatelets & anticoagulants. The response to treatment is generally good and most patients recover. The long-term complications especially cardiac morbidity of MIS-C is uncertain, and require further long-term follow-up of children with MIS-C.

This study is just tip of the ice berg as many more cases must have occurred which went unreported.

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Conflict of interest - none
Ethical approval obtained

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