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CLINICAL PROFILE OF CHILDREN WITH MIS-C IN NORTH EAST INDIA : A TERTIARY CARE EXPERIENCE

Paediatrics

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ABSTRACT

Background Recent publications have reviewed the clinical profile of MIS-C in children temporally associated with SARS-Cov2. The aim of this study is to determine the clinical profile in North East Indian children and compare with the findings of recent publications. **Method** Clinical, biochemical and radiological parameters have been compared in all the paediatric patients with a suspected multi-inflammatory syndrome with a recent or antecedent COVID infection and their findings have been reviewed. **Conclusion** A recent or a past COVID infection can trigger a multi-inflammatory response with a wide clinical and biochemical spectrum, which is more common in children as compared to adults.

KEYWORDS

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARSCoV-2), causing Coronavirus disease 2019 (COVID-19), led to a pandemic health crisis within a few months time. [1-3]. Since the outbreak, COVID-19 was generally described as asymptomatic or mild in children, causing few paediatric hospitalisations and minimal mortality [4-7]. Since April 2020, several countries from Europe and North America have reported young patients with a severe multi-system inflammatory syndrome associated with SARS-CoV-2. The initial descriptions exposed important clinical heterogeneity, partially overlapping with features of Kawasaki disease (KD) or toxic shock syndrome (TSS), but nevertheless distinct from these known inflammatory conditions. [8,9]. In contrast with (acute) COVID-19 respiratory disease, a significant proportion of children were reported with severe or fatal disease [10-14]. Since its description, this novel disease is mostly referred to as paediatric inflammatory multi-system syndrome temporally associated with SARS-CoV-2 infection (PIMSTS) [15,16] or multi-system inflammatory syndrome in children (MIS(-C)). Till date, dispersed reviews and case reporting have been published without concrete guidelines. A wide spectrum of clinical findings and a broad range of differentials have made it cumbersome in evidence-based medicine in the recent era. The purpose of this study is to give further in-sight into the clinical and biochemical pattern of this disease in children and the course of the illness. Further, paucity of research on children belonging to North East India mandates a research on this clinical syndrome to aid in future guidelines.

METHOD

A retrospective observational study was done in Gauhati Medical College and Hospital involving 25 children, within the time frame of June 2021 to June 2022, after obtaining informed parental consent and ethical committee clearance. Children fulfilling the WHO case definition of MIS-C were included.

Data was imbibed from the patients' records. Data included clinical profile on admission and during hospital stay, biochemical parameters throughout the course of the disease process with universal screening of all the children for current or past COVID infection; with either a positive serology or a positive RT-PCR or RAT antigen test. Tests to rule out alternative diagnosis based on clinical profile were also done on individual case basis, mostly cultures based on suspected foci.

RESULTS

Patient Particulars	
Mean Age (years)	6
Sex	
Male	17 (68%)
Female	8 (32%)
Requiring ICU care	25 (100%)
Outcome	
Discharged	24 (96%)
Death	1 (4%)

Clinical Spectrum	
Fever	25 (100%)
Mucocutaneous Involvement	12 (48%)
Musculoskeletal (myalgia)	3 (12%)
Respiratory involvement	17 68%)
Cough	14
Sore throat	3
Rhinorrhea	10
Respiratory distress	8
Gastrointestinal involvement	8 (32%)
Diarrhoea	4
Pain abdomen	3
Nausea and vomiting	1
Jaundice	1
Ascites	1
Comorbidities	2 (8%)
VSD with PAH	1
MR	1
Hemodynamic instability (hypotension/shock)	8 (32%)
Myocardial involvement (myocarditis, decreased LVEF, coronary artery dilatation)	13 (52%)
Coagulopathy	11 (44%)

Laboratory Parameters	
Elevated ESR	24 (96%)
Elevated CRP	24 (96%)
Abnormal 2D ECHO	
LVEF (<40%)	2 (8%)
Minimal Pericardial Effusion	3 (12%)
Coronary Dilatation	1 (4%)
Myocarditis with MR	2 (8%)
Elevated D-Dimer	11 (44%)
Elevated Procalcitonin	12 (48%)
Leukocytosis	15 (60%)
Evidence of COVID-19 infection	

Positive RAT	1 (4%)
Positive RT PCR	2 (8%)
Positive serology	22 (88%)
Deranged PT/APTT	2 (8%)
Elevated NT Pro BNP	5 (20%)
Deranged platelet count	10 (40%)
Treatment details	
Antibiotics	25 (100%)
Methylprednisolone alone	10 (40%)
IVIG and Methylprednisolone	15 (60%)
Vasopressors	8 (32%)
Mechanical Ventilation	1 (4%)
Oxygen support	16 (64%)
LMWH	13 (52%)
Aspirin	5 (20%)
MISC Phenotype	
MIS-C with shock	8 (32%)
Kawasaki phenotype	11(44%)
MIS-C without shock	6 (24%)

Out of the 25 patients included in our study, 17 were males (68%) and 8 were females (32%), pointing towards a possible genetic predilection for males. Fever was common to all the patients, with 5 of them having concurrent COVID-19 infection (20%), and 22 of them with positive serology titres (88%), highlighting a good seroconversion rate and a possible immunological phenomenon. Systemic involvement included respiratory symptoms (68%) such as cough, rhinorrhea, sore throat, which were mutually inclusive and relatively common; along with respiratory difficulty in the form of tachypnea, seen in 6 patients (24%). Gastro-intestinal symptoms (32%) included diarrhoea, nausea and vomiting, abdominal pain, jaundice, ascites, with one patient having a clinical overlap with appendicitis. Two patients were known to have cardiovascular co-morbidities, one of which expired (VSD with PAH). Renal function was fairly normal in all the patients. Myocardial involvement was seen in 13 patients (52%), in the form of coronary dilatations, myocarditis, abnormal ventricular function, effusions and/or biochemical evidence of deranged NT Pro BNP. Haemodynamic instability was seen in 8 patients (32%), requiring vasopressor support. None of the patients presented with neurological symptoms in our study.

Laboratory parameters revealed a uniform elevation in general inflammatory markers; ESR and CRP (96%). Elevated D-dimer (60%) and Procalcitonin (48%) correlated with disease severity. Deranged PT/APTT (8%) mandated Vitamin K administration. Antibiotics were prescribed empirically to 100% of patients to provide coverage for any missed foci of infection and to prevent secondary nosocomial infections. 15 patients received both methylprednisolone and IVIG, while the rest 10 received methylprednisolone alone. Patients with coronary dilatations, cardiomyopathy and thrombocytosis were treated with LMWH (52%). 64% of patients received oxygen therapy, in view of haemodynamic instability and/or respiratory compromise. Further, patients with coronary dilatations and thrombocytosis were supplemented with aspirin to prevent any major cardiac or neural event. One patient receiving mechanical ventilation expired (4%). Majority of the cases were discharged as Kawasaki phenotype (44%).

DISCUSSION

A temporal association of MIS-C to an antecedent or past COVID infection has been described in all the cases included in our study. As described by Riphagen et al., hyperinflammatory shock is a common element in MIS-C [17]. The literature reports that MIS-C typically manifests 3-4 weeks after SARS-CoV-2 infection[18]. The clinical and the laboratory features of hyperinflammation, the timing of onset in relation to SARS-CoV-2 infection, and the similarities with the disease pattern in adults with Covid-195 support the hypothesis that MISC is a consequence of immune-mediated injury triggered by SARS-CoV-2 infection[19]. Findings in our study suggest an extraordinary immunological response in the affected children, although active and supportive management has been successful in curbing the symptoms and providing a sense of well-being. Abdominal pain, which is sometimes severe enough to mimic appendicitis warranting surgery (as found in our study), gives a prospect of using this symptom as a distinguishing feature from an active COVID infection. Fever and leukocytosis was common, respecting WHO definition. The findings in this study are comparable to the study done by Khalate et. al, in Western Maharashtra, where mean age was 5 years, 100% cases presented with fever, 100% had raised CRP. The striking predominance of myocardial involvement in our study, provides a new field for further research. Distinguishing feature in contrast to acute COVID infection is the overlap of a cardiorespiratory syndrome rather than respiratory symptoms alone. To add, the rapid decline in cardiac symptoms post treatment also mandates further probing on the pathophysiology of the disease. Epidemiological enrichment for males in our study might be the explanation of a possible genetic shield for females. Overlapping features of Kawasaki are addressed by the affected age group disparity, probable male predilection, and the specificity of coronary aneurysms as cardiac involvement. Findings in our study have not shown much light upon the outcome of children with known comorbidities, as we studied only two such cases, and one of them had expired (VSD with PAH). Paucity of neurological involvement in our study might be a case of epidemiological advantage, although further studies are prudent. To date, the molecular pathophysiological mechanisms in MISC are insufficiently studied, although publications measuring serological and inflammatory responses have shown some initial insights [20,21]. A better understanding of the highly variable spectrum of this clinical entity will give us better screening protocols, more tailored treatment and better vigilance of clinicians. Our study is limited by the number of subjects included, and a restricted time frame for follow up. Large scale follow up via cardiac imaging is required to comment on the long term myocardial implications. Until more is known about long-term cardiac sequelae of MIS-C, providers could consider following Kawasaki's disease guidelines for follow-up, which recommend repeat echocardiographic imaging at 1 to 2 weeks and 4 to 6 weeks after treatment for patients whose disease course is uncomplicated and more frequent echocardiography for patients with coronary-artery z scores of 2.5 or higher. [22]

CONCLUSION

MIS-C is still a clinical entity with a scope for better understanding in the future via further studies. Probing into the molecular level of pathogenesis is vital, since only a handful of children with antecedent or past COVID infection show features of this hyperinflammatory syndrome. Cardiorespiratory predominance of the symptoms seek the urge of researchers to probe into the immunological backdrop of this phenomenon, in view of which, current Indian guidelines suggest a regular follow up of cardiac status of these children. Further studies are required for any genetic predilection, epidemiological risk factors and better prognostication.

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