

## Cardiac Evaluation in Multisystem Inflammatory Syndrome in Children (MIS-C) Associated With COVID-19

Multisystem inflammatory syndrome in children (MIS-C) is notorious for its cardiac involvement. We present a single center data of 71 children, of which 57.7% had myocarditis and 26.8% had coronary artery aneurysms. 45.1% required intensive care support and 29.6% needed inotropes - 91.5% received IVIG. All patients responded to therapy with no mortality.

**Keywords:** Coronary artery aneurysm, Myocarditis.

Multisystem inflammatory syndrome in children (MIS-C) associated with severe acute respiratory syndrome coronavirus (SARS-CoV-2) is a stormy multisystem disease with the brunt of the disease on the heart, causing sudden severe myocarditis, shock and coronary artery aneurysms (CAA) [1].

Patients satisfying the WHO MIS-C criteria admitted at the Institute of Child Health, Kolkata, a tertiary care hospital, between July and December, 2020 were evaluated for cardiac affection clinically, through laboratory investigations and echo-cardiography at admission and post-treatment. Ethical clearance was taken from the Institutional Ethics Committee and written informed consent was taken from the parents/guardians. Treatment protocols and outcomes were noted down. Follow up echo-cardiography was done at 2, 6 weeks, 3 and 6 months. The initial and follow up echocardiographies were performed by a trained pediatric cardiologist.

Seventy-one MIS-C patients with a median age of 6 years were admitted. (Quartile 1 being 3 and quartile 3 being 8, IQR 5). Of these, 41 (57.7%) had myocarditis (disproportionate tachycardia, electrocardiogram changes and echocardiographic changes), and 22 (30.9%) had low ejection fraction (EF) (35-47%). Cardiac symptoms manifested unpredictably around 3 to 7 days of fever and the usual clinical presentation was disproportionate tachycardia and sudden onset hypotension. Intensive care admission was needed by 45.1% and 29.6% required inotropic support. Cardiac affection accounted for the most important cause of intensive care admission. None had any evidence of valvular involvement or heart block.

CAA (>2 z-score) and Kawasaki disease (KD) like manifestations were seen in 26.8%. Four had left anterior descending (LAD) artery dilatation (mean +3.18 z-score), three had left main coronary artery (LMCA) dilatation (mean +2.51 z-score) and four had both (mean LMCA +3.57 z-score and LAD +3.31 z-score). Two had multiple CAAs involving LAD, right coronary artery (RCA), and LMCA. One child had only RCA dilatation (+2.87 z-score), and five had z-score <+2.5 z-score. None had z-scores >5.

Sixty five (91.5%) children received intravenous immunoglobulin (IVIG), mostly at 2g/kg. However, 7 adolescents, because of the need for large dose and consequent financial burden, were administered 1 g/kg along with methylprednisolone (MP). Of these 65 children, 43 also received MP. The remaining 8.5% received MP only. EF improved after 48 to 72 hours of initiation of therapy. Patients presenting with shock and requiring inotropes, were initiated on MP together with IVIG. Fourteen patients required respiratory support (supplemental oxygen, non-invasive ventilation) and four had to be intubated. All patients additionally received 5 mg/kg of aspirin for 6 weeks (Table I).

Following initiation of immunotherapy, inotropes could be tapered off over 48 to 72 hours and all children had normalization of EF within 5 to 7 days. Three patients with CAAs had persistent dilatations at discharge and two had transient increase in size following initial IVIg therapy. 89.5% patients with CAAs had regression by 6 weeks and the remaining dilatations normalized over 6 months.

Since the very first reports and case series on MIS-C, cardiac involvement is reported as the major cause of morbidity [1,2]. Affecting almost half the patients, the lesions range from ventricular dysfunctions, coronary dilatations, arrhythmias to heart blocks and they usually require ICU support [3,4]. The pathogenesis of cardiac dysfunction remains unclear. Post-infectious hyperinflammation is commonly postulated though direct viral injury has also been thought of. MIS-C has some similarities to KD but these are usually older children with higher frequency of ventricular dysfunction, higher NT-pro-BNP and thrombocytopenia. Coronary artery dilatation in MIS-C is mostly mild to moderate but few giant aneurysms have been reported [5,8].

Management of MIS-C has been extrapolated from KD and adult studies and is being regularly updated [7,8]. Initially, starting therapy with IVIG with or without steroids was pro-

**Table I Clinical Characteristic and Management in Children With MIS-C (N=71)**

| Characteristics                                 | No (%)    |
|-------------------------------------------------|-----------|
| Myocarditis                                     | 41 (57.7) |
| Low ejection fraction                           | 22 (30.9) |
| Coronary artery dilatation                      | 19 (26.8) |
| <i>Management</i>                               |           |
| Intravenous immunoglobulin ± methylprednisolone | 65 (91.5) |
| Methylprednisolone                              | 6 (8.5)   |
| Intensive care admission                        | 32 (45.1) |
| Inotrope requirement                            | 21 (29.6) |
| Respiratory support <sup>a</sup>                | 14 (19.7) |
| Mechanical ventilation                          | 4 (5.6)   |

MISC: multisystem inflammatory syndrome in children associated with COVID-19. <sup>a</sup>Moist oxygen, non-invasive ventilation.

posed. However, with time, the threshold for instituting steroids has decreased. In unresponsive cases, pulse methylprednisolone is advocated with tapering on follow-up. Aspirin is added in anti-platelet doses. In cases with giant aneurysm or thrombosis enoxaparin is given. Successful usage of interleukin 1 blocker anakinra has been demonstrated. Due to lack of knowledge regarding the long-term complications, moderate to longterm follow-up is required both clinically and echocardiographically.

Acute myocarditis with or without CAA is the predominant cardiac affection seen in MIS-C. Echocardiography is an essential tool in early diagnosis as well as in deciding optimum treatment. Early identification, supportive care by a multidisciplinary team preferably in an intensive care unit, and aggressive immuno-therapy reverts the inflammation rapidly without significant residual lesions.

*Ethics clearance:* IEC, Institute of Child Health; No. EC/250/2021 dated August 25, 2021.

*Contributors:* PL: Case diagnosis, management, preparation of final manuscript; JNB: Case management, preparation and editing the manuscript; MG, PG, HD: Case management, preparation of manuscript; AKS: Case diagnosis, echocardiographic evaluation.

*Funding:* None; *Competing interest:* None stated.

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## NEWS IN BRIEF

### The MELODY trial for RSV

Nirsevimab is a long acting monoclonal antibody against the fusion protein of the respiratory syncytial virus. In the phase III MELODY trial recently published – a single dose of Nirsevimab reduced the incidence of medically attended RSV infections by 74.5%. The other option so far had been Palivizumab, another monoclonal antibody, which could protect infants for only 1 month and needed 5 doses to cover the entire RSV season. The secondary end point of the trial was hospitalizations. This occurred in 6 infants (0.6%) in the nirsevimab group and in 8 infants (1.6%) in the placebo group ( $P=0.07$ ). Nirsevimab has also been used in high risk infants with congenital heart disease and chronic lung disease and shown adequate safety and tolerability.

Since the lifting of curbs after the COVID pandemic, there was a spike in RSV infections in 2021. Nirsevimab may offer a ray of hope, especially to high risk premies. (*NEJM* 3 March 2022)

### Upper age limit for NEET-UG entrance removed

Since 2017, there had been an upper age limit for appearing in the national eligibility-cum-entrance test for undergraduate training (NEET-UG) in India. It was 25 years for unreserved candidates and 30 years for reserved candidates. This has now been scrapped by the National Medical Commission.

Prior to the NEET, the age cut-off in the AIPMT exam applied to only 15% of the seats. When the NEET phased out the AIPMT, this age limit became applicable to all seats. This was challenged in May, 2018 in the Supreme Court. The petitioners felt the rule was unfair to women and candidates from underprivileged backgrounds, who may not be able to follow the same timeline as others. The removal of the age limit will allow more candidates to apply including those who missed the age cutoff due to delay or postponement of examinations, which occurred in 2021 and 2022.

(*The Indian Express* 10th March 2022)

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