



## Multisystem Inflammatory Syndrome in Children (MIS-C): Does it have a Long-Term Impact?

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Multisystem Inflammatory Syndrome in Children (MIS-C) is a rare, serious complication associated with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection. Its acute outcomes are extensively described and are excellent [1]. Evidence on the long-term outcome of MIS-C is limited and yet to be known. The article by Kapoor et al. published in *IJP* addressed some aspects of this issue in which they reported a one-year follow-up of MIS-C [2].

MIS-C is characterized by multisystem involvement; most children had involvement of  $\geq 2$  organ systems [1, 3]. In the study by Kapoor et al., at baseline, all children had  $>3$  organ involvement; cardiovascular system (CVS) involvement was 85%, including coronary artery dilation in one child. On day 7, 98% had normal echocardiography (ECHO) and inflammatory markers and it was completely resolved by 6-mo of follow-up [2]. However, they did not mention the outcome of other organ systems, especially respiratory and central nervous system (CNS). Knowing the outcome of other organ systems would also be interesting. A simple test like spirometry and a 6-min walk test (6MWT) would help to know the cardiorespiratory outcome.

CVS is the commonly reported organ in most studies. A multicentric study by Feldstein et al. in 539 MIS-C observed CVS involvement in 67% of children at enrolment, including decreased left ventricular ejection fraction (LVEF) in 34.2% and coronary artery aneurysm (CAA) in 13.4%, of which 99.4% of LVEF and 100% of CAA normalized by 90 d [3]. In another study by Awasthi et al., with a median follow-up of 5 (3–6) mo, coronary artery dilation was present in 22.5% in the acute phase, which improved significantly on follow-up and only one child had persistent dilatation after eight

months [4]. Other authors also noted the normalization of LVEF and cardiac biomarkers by six months. In contrast, in a cohort study with a one-year follow-up, CAA persisted in 5 out of 19 children [5].

Although, ECHO is usually good for monitoring CVS function. American College of Rheumatology (ACR) recommends cardiac MRI, 2–6 mo after MIS-C diagnosis in children with moderate to severe LVEF, as it can also detect myocardial fibrosis and scarring. Similarly, cardiac CT should be performed where CAA is suspected in the distal branch that could be missed on ECHO [1].

The time to complete resolution varies in different studies. It depends on the type and severity of the underlying organ involvement. Zuccotti et al., in 33 children with MIS-C, observed that most complications improved in the initial few weeks only; however, insulin resistance and CNS symptoms persisted in 21.2% and 27.3%, respectively, at six months of follow up [6]. In another one-year follow-up study, authors reported a deranged blood count in 2%, abnormal D-dimer in 25%, and ferritin level in 17% of MIS-C [7]. Penner et al., in a 6-mo follow-up study in MIS-C, found that most gastrointestinal symptoms and radiological findings resolved, but emotional lability persisted in 15% of children. In 6MWT, 45% of the children completed a distance below the 3rd percentile [8].

In conclusion, the long-term outcome of MIS-C is still evolving. The available evidence suggests a complete resolution of most complications on follow-up. There is an urgent need for prospective, multicentric long-term longitudinal follow-up in children with MIS-C, especially from developing countries.

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## Declarations

**Conflict of Interest** None.

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