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Multisystem inflammatory syndrome associated with COVID-19 in children in Pakistan

The knowledge of COVID-19 is evolving with new aspects of the disease continuing to emerge. Children and adolescents younger than 20 years of age constitute 10·6% (24 625 of 231 818) of the total reported confirmed cases of COVID-19 in Pakistan as of July 8, 2020, with a mortality of 0·3% for those aged 10 years or younger and 0·5% for those aged 11–20 years. Multisystem inflammatory syndrome in children (MIS-C), also known as paediatric inflammatory multisystem syndrome temporally associated with severe acute respiratory syndrome coronavirus 2 (PIMS-TS) is being reported primarily from Europe and the USA.[1-8] Many of these children meet the criteria for complete or incomplete Kawasaki disease, but different clinical presentations of this inflammatory disorder are being reported.[1-8] The ethnic origin of reported cases show that Black, Hispanic, and Asian children might be disproportionally affected.[1-8] Similarly, unlike Kawasaki disease, these cases have occurred in older children and adolescents.[9] We report our initial experience from The Children's Hospital Lahore, Pakistan—the first report of this new inflammatory syndrome from south Asia.

Children (aged 0–16 years) with features of this new inflammatory syndrome who fulfilled the WHO criteria[10] for MIS-C and required admission to hospital were prospectively identified, between May 15 and June 30, 2020. Demographic and clinical data were collected from patient records and entered on a predesigned proforma.

There are eight children so far who fulfil the WHO criteria of MIS-C. All eight patients also fulfil the case definition for PIMS-TS. The epidemiological, clinical, laboratory, and echocardiographical features of all eight patients are shown in appendix p 1. One of these patients was admitted through emergency services, another one through outpatient services, and six patients were referred from other paediatric units. All the children were male, except one, and the age range was 5–15 (median 9·5) years. Three patients had a positive PCR for SARS CoV-2 but none of the patients had been symptomatic with classic COVID-19 respiratory symptoms in the 6 weeks prior to admission. No comorbid condition was present in any of the children. SARS-CoV-2 antibodies were positive for all eight of the patients. Despite being clinically unwell, with laboratory evidence of elevated C-reactive protein, ferritin, and D-dimers, no pathological organism was isolated in any of the eight children.

There were two major presentations: one as atypical or typical Kawasaki disease (6 of 8, 75%) and a more severe second one with shock or low cardiac output (2 of 8, 25%). Common presenting features were fever, body aches, and abdominal pain. Patient 2 presented with altered consciousness and signs of meningism, and an initial diagnosis of meningoencephalitis was made. He had cardiopulmonary resuscitation for 10 min and was intubated and ventilated before the diagnosis of MIS-C could be made. This child had acute myocardial dysfunction, became hypotensive and showed clinical signs of vasoplegia. He went into multiorgan failure and died on day 10 of ventilation. Patient 6 also presented with high-grade fever and signs of meningism. He needed inotropic support and volume resuscitation but did not need ventilation and recovered.

The other six children (patients 1, 3, 4, 5, 7, and 8) presented more subacutely with presentation resembling Kawasaki disease; all had at least two features of classic Kawasaki disease. Two of these six patients (patients 7 and 8) had sufficient criteria for typical Kawasaki disease. None of these six children showed evidence of myocardial dysfunction, although pericardial effusion was observed in 3 of 6 children.

Coronary artery dilatation was seen in five (62·5%) patients. A z-score of more than 2·5 in the left anterior descending or right coronary artery was reported in three and 2·0–2·5 in two patients (mean 2·94, SD ± 0·97, 95%CI 1·7–4·16, SE ± 0·44, median 2·6, range +2·06 to +4·27, spread range +2·2). Both children with shock-like presentation had coronary artery involvement, but two patients who fulfilled the Kawasaki disease criteria showed healthy coronary arteries. All children except one (7 of 8, 87·5%) received intravenous immunoglobulin (2 g/kg bodyweight) within the first 2 days of their stay. Three patients received therapeutic anticoagulation (enoxaparin) on the basis of the high risk of thromboembolism and amount of D-dimers. With the exception of the one death discussed already, the other seven children have been discharged home.

Other children with PIMS-TS reported in the literature have presented with acute heart failure and features of acute myocarditis.[3,5,7] This feature has a special notability in our country, because viral myocarditis is a common presentation all year long, and there would be background cases with dilated cardiomyopathy or myocarditis. All children presenting with acute myocarditis in the study period were screened for exposure to SARS-CoV-2 and underwent COVID-19 antibody testing. Only one of six patients admitted with myocarditis during the study period tested positive for COVID-19 antibodies. This child, however, did not show evidence of raised inflammatory markers and is not included in the series.

Our data, although restricted by numbers, show some differences

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from the reported literature on MIS-C. The incidence of coronary artery involvement was high with two-thirds of children showing coronary artery dilatations. This finding is unlike the series from other countries where the incidence of coronary artery involvement was 20% in Italy, 17% in France, 36% in the UK, and 9% in the USA (appendix p2).[2,3,5,8] It has also been observed that Kawasaki disease-like features seem to be predominant in some case series (one in Italy[2] and this Correspondence piece), whereas those reported from France[3] and the UK[8] have more acute presentation with shock. The data reported from these countries comes from intensive care unit admissions rather than paediatric units in general. The US[5] data shows Kawasaki disease-like features in 40% of the patients and is probably a true representative of an overall pattern of presentation.

Presentation of SARS-CoV-2 positive children with hypotension and shock seems to be less common in our patients than in reported case series from France,[3,7] the USA,[5,6] and the UK.[8] With restricted resources, an inability to make an early diagnosis, a poor referral system, and availability of few tertiary care centres with paediatric intensive care facilities, it is possible that some patients did not make it to our institution and that this type of presentation is therefore underestimated. Another limitation is the absence of follow up echocardiography to evaluate the evolution of coronary dimensions since five patients had coronary dilation on admission, which was unchanged at discharge.

The overall infectivity rate of the population aged younger than 20 years is disproportionately high in the Pakistani population (>10%) when compared with the rest of the world.[11] With ongoing spread of this virus in countries such as Pakistan, the paediatric and cardiology communities should be mindful of this emerging disease.

We declare no competing interests. The institutional review board of the Children's Hospital Lahore, Pakistan, approved this study and an informed consent was taken from the parents.

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