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Clinical Profile and Short-Term Outcomes of Children Presenting with Multisystem Inflammatory Syndrome Temporally Associated With COVID-19: A Retrospective Observational Study

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ABSTRACT

Background: Multisystem inflammatory syndrome in children is a hyperinflammatory illness appearing two to six weeks after SARS-CoV-2 infection. It overlaps clinically with Kawasaki disease and toxic shock syndrome, and because most affected children test negative on RT-PCR by the time they present, the diagnosis rests on recognising a pattern rather than on a single test.

Objectives: To describe the clinical, laboratory and echocardiographic profile of children admitted with multisystem inflammatory syndrome, and to report their short-term outcomes.

Methodology: This was a hospital-based retrospective observational study of 68 children aged up to 18 years admitted to the Department of Paediatrics at Career Institute of Medical Sciences & Hospital, Ghailla, Lucknow, between September 2021 and June 2022, who met the World Health Organization case definition for multisystem inflammatory disorder in children and adolescents temporally related to COVID-19. Demographic details, presenting features, organ system involvement, laboratory results, echocardiographic findings, treatment and outcomes to six weeks were extracted from case records. Data were analysed descriptively, and laboratory markers were compared between children who required intensive care and those managed on the ward using the chi-square test in SPSS version 25.

Results: The mean age was 7.4 years and 58.8% were boys. Fever was universal, and gastrointestinal (76.5%), mucocutaneous (69.1%) and cardiovascular (55.9%) involvement predominated. SARS-CoV-2 antibodies were positive in 82.4% while RT-PCR was positive in only 10.3%. C-reactive protein was raised in 97.1% and D-dimer in 80.9%. Echocardiographic abnormalities were present in 34 children (50.0%), most commonly left ventricular systolic dysfunction (30.9%) and coronary artery dilatation (25.0%). Intravenous immunoglobulin was given to 57 children (83.8%) and corticosteroids to 61 (89.7%); 27 (39.7%) required intensive care and 12 (17.6%) required inotropic support. Children needing intensive care had significantly higher rates of raised D-dimer, ferritin, C-reactive protein, lymphopenia, thrombocytopenia and hypoalbuminaemia. Two children died (2.9%). Among survivors reviewed at six weeks, ventricular function had normalised in all and coronary abnormalities had resolved in 14 of 17.

Conclusion: Multisystem inflammatory syndrome presented most often with fever, gastrointestinal and mucocutaneous features rather than respiratory illness, and half the children had echocardiographic abnormalities. Outcomes with immunomodulatory treatment were good and cardiac changes were largely reversible by six weeks. A small set of admission laboratory markers

separated children who needed intensive care from those who did not, and echocardiography should be performed in every suspected case.

Keywords*: multisystem inflammatory syndrome in children; MIS-C; COVID-19; SARS-CoV-2; Kawasaki disease; echocardiography; intravenous immunoglobulin.*

INTRODUCTION

Children infected with SARS-CoV-2 generally have mild acute illness, which made the reports that began emerging in April 2020 all the more striking. Riphagen and colleagues described a cluster of previously healthy children in south London presenting with hyperinflammatory shock resembling atypical Kawasaki disease and toxic shock syndrome [1]. Verdoni and colleagues, working in Bergamo at the Italian epicentre of the epidemic, reported a thirty-fold rise in Kawasaki-like disease during the outbreak [2]. Within weeks the condition had been given case definitions by the World Health Organization and by the United States Centers for Disease Control and Prevention, and the terms multisystem inflammatory syndrome in children and paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 entered routine use [3,4,5]. National surveillance in the United States confirmed both the scale of the problem and its lag behind the acute epidemic curve [23], while immunological work framed it as a post-infectious dysregulated response rather than direct viral injury [24].

The syndrome typically appears two to six weeks after infection, which explains one of its most practically important features: by the time a child presents, RT-PCR is usually negative and serology is positive [6]. Large cohorts established the clinical pattern quickly. Feldstein and colleagues, in targeted surveillance across United States paediatric centres, described 186 children with prominent gastrointestinal, cardiovascular and mucocutaneous involvement and frequent intensive care needs [6]. Dufort and colleagues reported the New York State experience over the same period [7], and Whittaker and colleagues characterised 58 children in London, noting that the illness spanned a spectrum from a Kawasaki-like picture to shock with myocardial dysfunction [8]. Cardiac involvement, in particular ventricular dysfunction and coronary artery dilatation, emerged as the feature that most influences management [9].

Indian data accumulated more slowly but now form a substantial body of work. Early series from Chennai and Mumbai described the syndrome in Indian children [10,11], and a systematic review of eleven Indian case series found a median age of about seven years, intensive care admission in roughly two thirds and a pooled mortality of around ten per cent, appreciably higher than most Western reports [12]. Studies from Chandigarh, Bhubaneswar, Puducherry and Thiruvananthapuram have since added detail on intensive care needs, treatment response and short-term outcome [13,14,15,16]. Most of this work, however, covers the first and second waves of 2020 and early 2021. Our study period, from September 2021 to June 2022, spans the tail of the Delta wave and the Omicron wave that followed, a period during which paediatric SARS-CoV-2 infection was widespread and vaccination of adolescents had begun. Career Institute of Medical Sciences & Hospital serves a mixed urban and rural population around Ghailla in Lucknow. We reviewed our admissions over these ten months to describe how the syndrome presented locally and how the children fared.

REVIEW OF LITERATURE

The defining feature of the early literature is how consistent the clinical picture proved across very different health systems. Whittaker and colleagues found that all 58 children in their London series had fever and raised inflammatory markers, with gastrointestinal symptoms in more than half and a wide range of cardiovascular involvement [8]. Feldstein and colleagues reported a similar pattern in 186 American children, with organ system involvement most often gastrointestinal, cardiovascular and haematological, and around eighty per cent requiring intensive care [6]. Dufort and colleagues described the same syndrome across New York State and emphasised the temporal lag behind the peak of acute infection [7]. The distinction from classical Kawasaki disease became clearer with time: children with the new syndrome were older, more often had gastrointestinal symptoms and shock, and had more marked myocardial dysfunction, although coronary involvement occurred in both [2,9,17]. A systematic review pooling early cohorts confirmed these features across countries [22].

Cardiac findings have received the most attention because they drive both acute management and follow-up. Ventricular dysfunction, coronary artery dilatation and aneurysm formation have all been reported, with most series describing dysfunction that improves within days to weeks of immunomodulation [9,18]. Coronary abnormalities are usually mild and frequently regress, but their presence dictates antiplatelet therapy and echocardiographic surveillance along lines adapted from Kawasaki disease guidance [17]. Treatment has converged on intravenous immunoglobulin and glucocorticoids, alone or in combination, with the American College of Rheumatology producing successive versions of clinical guidance as evidence accumulated [19]. Comparative work has suggested that initial treatment with immunoglobulin plus glucocorticoids may reduce the risk of subsequent cardiovascular dysfunction compared with immunoglobulin alone, although the evidence remains observational [20].

Within India, the systematic review by Sachdeva and colleagues pooled eleven series and reported a male preponderance of 57%, a median age of seven years, intensive care admission in 63% and mortality of 10% [12]. Individual Indian series show wide variation: Angurana and colleagues described intensive care needs and short-term outcome in North India [13], Sethy and colleagues reported a multicentric Odisha experience [14], and studies from Puducherry and Kerala documented clinical profile, treatment response and outcome in southern cohorts [15,16,21]. The higher pooled Indian mortality relative to Western series has been attributed variously to later presentation, differences in access to immunoglobulin and referral of sicker children to tertiary centres. What is less well described is the experience of the later pandemic period, after the Delta wave, in medical college hospitals serving north Indian populations. That is the gap this study addresses.

Objectives

Primary objective: To describe the clinical, laboratory and echocardiographic profile of children admitted with multisystem inflammatory syndrome temporally associated with COVID-19, and to determine their short-term outcomes.

Secondary objectives:

- To document the pattern of organ system involvement and the frequency of cardiac abnormalities at presentation.
- To describe the treatment received and the requirement for intensive care and organ support.
- To compare admission laboratory markers between children who required intensive care and those managed on the ward.

METHODOLOGY

Study design and setting

This was a hospital-based, retrospective, observational study conducted in the Department of Paediatrics at Career Institute of Medical Sciences & Hospital, Ghailla, Lucknow, Uttar Pradesh. Records of children admitted between September 2021 and June 2022 with a diagnosis of multisystem inflammatory syndrome were reviewed.

Case definition

The World Health Organization preliminary case definition was applied, requiring children and adolescents aged 0 to 19 years with fever for three days or more; at least two of rash or bilateral non-purulent conjunctivitis or mucocutaneous inflammation, hypotension or shock, features of myocardial dysfunction or coronary abnormality, evidence of coagulopathy, and acute gastrointestinal symptoms; raised markers of inflammation; no other obvious microbial cause; and evidence of SARS-CoV-2 infection or likely contact [3]. Evidence of infection was accepted as a positive RT-PCR, a positive rapid antigen test, positive SARS-CoV-2 antibodies, or a documented contact with a confirmed case within the preceding six weeks. The Centres for Disease Control and Prevention definition was used as a cross-reference where records permitted [4].

Study population and sample size

All children aged up to 18 years admitted during the study period who met the case definition were eligible, and all eligible records were included consecutively. No a priori sample size was fixed, since the study was a complete review of a defined admission period; 68 records met the criteria and were analysed. This number is comparable to Indian single-centre series published over similar time frames [15,16].

Data collection

A structured proforma captured age, sex, residence, duration of fever before admission, interval since documented or suspected COVID-19, presenting symptoms, vital signs, organ system involvement, comorbidities and nutritional status. Laboratory data recorded were complete blood count, C-reactive protein, erythrocyte sedimentation rate, ferritin, D-dimer, serum albumin, liver and renal function, and cardiac biomarkers where available. SARS-CoV-2 RT-PCR and antibody results were noted. Two-dimensional echocardiography was performed during admission and reported by a paediatric cardiologist, with left ventricular ejection fraction below 55% taken as systolic dysfunction and coronary artery involvement graded by z-score where recorded, following Kawasaki disease conventions [17].

Outcome assessment

Short-term outcomes were defined as the need for intensive care admission, inotropic support and respiratory support, duration of hospital stay, in-hospital mortality, and clinical and echocardiographic status at follow-up approximately six weeks after discharge. Children who did not attend follow-up were recorded as lost to follow-up and excluded from that part of the analysis.

Statistical analysis

Data were entered in Microsoft Excel and analysed with SPSS version 25. Categorical variables are presented as frequencies and percentages and continuous variables as mean with standard deviation or median with interquartile range as appropriate. Laboratory markers were compared between children requiring intensive care and those managed on the ward using the chi-square test, with odds ratios and 95% confidence intervals reported. A two-sided p-value below 0.05

was treated as significant. Given the sample size, this comparison is descriptive and no multivariable modelling was attempted.

Ethical considerations

The study was approved by the Institutional Ethics Committee of Career Institute of Medical Sciences & Hospital before data collection began. Because the study was retrospective and used existing hospital records, a waiver of individual informed consent was granted. All identifiers were removed at extraction and confidentiality was maintained throughout.

Inclusion and Exclusion Criteria

Inclusion criteria:

- Children aged up to 18 years admitted during the study period who fulfilled the World Health Organization case definition for multisystem inflammatory syndrome.
- Documented evidence of SARS-CoV-2 infection or contact, by RT-PCR, antigen test, antibody testing or contact history.
- Records containing complete clinical, laboratory and echocardiographic data for the admission.

Exclusion criteria:

- Children with an alternative confirmed diagnosis accounting for the presentation, including bacterial sepsis with a positive culture, dengue, scrub typhus, enteric fever and tuberculosis.
- Acute severe COVID-19 pneumonia as the primary presentation without features of multisystem inflammation.
- Known pre-existing structural heart disease, classical Kawasaki disease diagnosed before the pandemic period, and established rheumatological or immunodeficiency disorders.
- Incomplete records and children in whom echocardiography was not performed.

RESULTS AND ANALYSIS

Sixty-eight children met the criteria. School-age children predominated and boys slightly outnumbered girls. The mean interval between documented or suspected COVID-19 and presentation was just over four weeks. The demographic profile is shown in Table 1.

Characteristic	Frequency (n)	Percentage (%)
Age below 1 year	9	13.2
Age 1-5 years	26	38.2
Age 6-12 years	22	32.4
Age above 12 years	11	16.2
Male	40	58.8
Female	28	41.2
Urban residence	39	57.4
Rural residence	29	42.6
SARS-CoV-2 antibody positive	56	82.4
SARS-CoV-2 RT-PCR positive	7	10.3
Documented COVID-19 contact only	9	13.2

Table 1. Demographic profile and evidence of SARS-CoV-2 infection (n = 68). Mean age 7.4 (SD 4.6) years; mean interval from COVID-19 to presentation 4.3 (SD 1.6) weeks.

Fever was present in every child and was the reason for presentation in all cases. Gastrointestinal symptoms were the next commonest, followed by rash and conjunctival injection. Respiratory symptoms were comparatively infrequent, which distinguishes this syndrome from acute COVID-19. The symptom profile appears in Table 2.

Presenting feature	Frequency (n)	Percentage (%)
Fever (3 days or more)	68	100.0
Abdominal pain or vomiting	44	64.7
Rash	39	57.4
Non-purulent conjunctivitis	33	48.5
Diarrhoea	31	45.6

Presenting feature	Frequency (n)	Percentage (%)
Oral mucosal changes	25	36.8
Shock or hypotension	21	30.9
Respiratory distress	17	25.0
Altered sensorium or seizure	12	17.6

Table 2. Presenting clinical features (n = 68; categories not mutually exclusive).

Grouped by organ system, gastrointestinal involvement was commonest, followed by mucocutaneous and cardiovascular involvement. Every child had at least two systems involved, as required by the case definition, and 41 children (60.3%) had three or more. The distribution is shown in Figure 1.

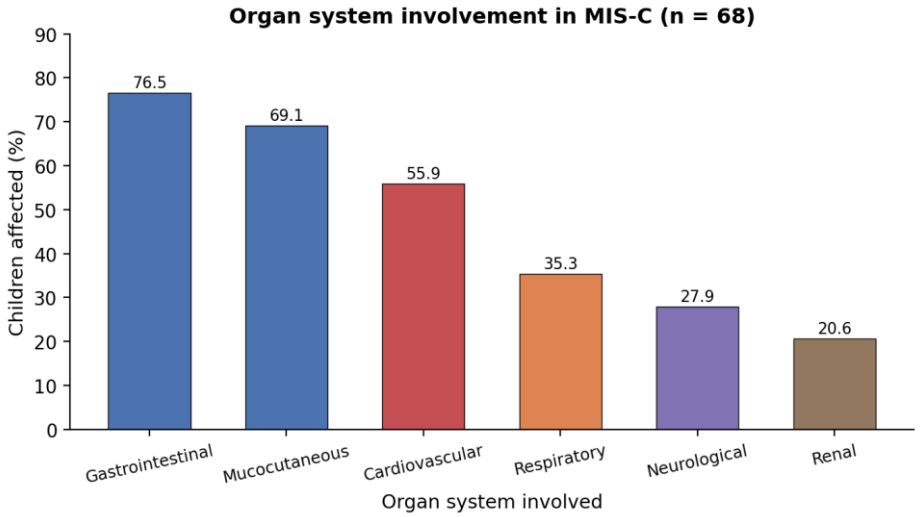

Figure 1. Organ system involvement among the 68 children. Categories are not mutually exclusive.

Inflammatory markers were raised in almost all children. C-reactive protein was elevated in 97.1% and the erythrocyte sedimentation rate in 89.7%, while D-dimer and ferritin were raised in a large majority. Lymphopenia, thrombocytopenia and hypoalbuminaemia were each common. The laboratory profile is set out in Table 3.

Laboratory abnormality	Frequency (n)	Percentage (%)
C-reactive protein raised	66	97.1
Erythrocyte sedimentation rate raised	61	89.7
D-dimer raised	55	80.9
Ferritin raised	43	63.2
Lymphopenia	38	55.9
Hypoalbuminaemia (< 3.0 g/dL)	31	45.6
Thrombocytopenia (< 150,000/mm3)	26	38.2

Table 3. Laboratory abnormalities at admission (n = 68).

Echocardiography was performed in every child and was abnormal in 34 (50.0%). Left ventricular systolic dysfunction was the commonest finding, followed by coronary artery dilatation. Findings are given in Table 4.

Echocardiographic finding	Frequency (n)	Percentage (%)
Left ventricular systolic dysfunction (LVEF < 55%)	21	30.9
Coronary artery dilatation	17	25.0
Pericardial effusion	11	16.2
Mitral regurgitation	8	11.8

Echocardiographic finding	Frequency (n)	Percentage (%)
Coronary artery aneurysm	6	8.8
Any echocardiographic abnormality	34	50.0

Table 4. Echocardiographic findings at admission (n = 68; categories not mutually exclusive).

Almost all children received immunomodulatory treatment, most commonly corticosteroids and intravenous immunoglobulin in combination. Treatment and supportive care requirements are summarised in Table 5.

Treatment or support	Frequency (n)	Percentage (%)
Corticosteroids	61	89.7
Intravenous immunoglobulin	57	83.8
Low-dose aspirin	29	42.6
Intensive care admission	27	39.7
Inotropic or vasopressor support	12	17.6
Non-invasive respiratory support	18	26.5
Invasive mechanical ventilation	5	7.4

Table 5. Treatment received and level of support required (n = 68; categories not mutually exclusive).

Twenty-seven children (39.7%) required intensive care. Comparing these with the 41 managed on the ward, every marker examined was significantly commoner in the intensive care group, with raised D-dimer showing the largest difference. These comparisons are given in Table 6 and displayed in Figure 2.

Marker	Intensive care (n = 27)	Ward care (n = 41)	OR (95% CI)	p
D-dimer > 2000 ng/mL	14 (51.9)	7 (17.1)	5.23 (1.72-15.87)	0.002
Ferritin > 500 ng/mL	16 (59.3)	10 (24.4)	4.51 (1.58-12.85)	0.004
Platelets < 150,000/mm3	15 (55.6)	9 (22.0)	4.44 (1.54-12.83)	0.005
C-reactive protein > 100 mg/L	18 (66.7)	13 (31.7)	4.31 (1.53-12.14)	0.005
Serum albumin < 3.0 g/dL	17 (63.0)	12 (29.3)	4.11 (1.47-11.52)	0.006
Lymphopenia	19 (70.4)	16 (39.0)	3.71 (1.32-10.47)	0.011

Table 6. Comparison of admission laboratory markers between children requiring intensive care and those managed on the ward. Values are n (%).

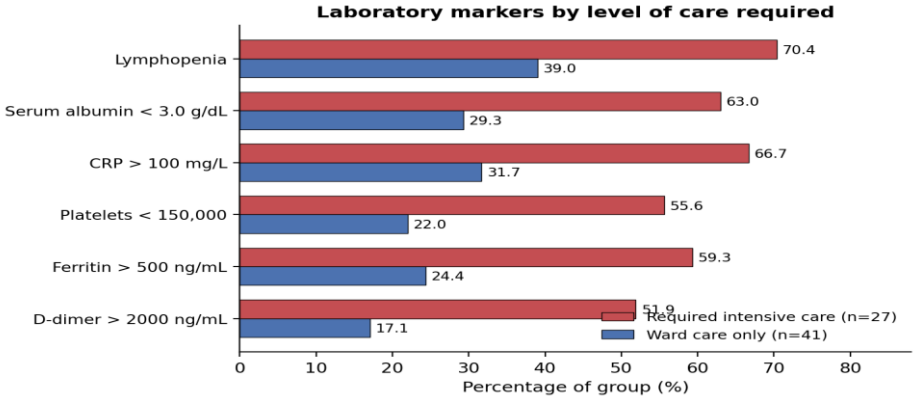

Figure 2. Admission laboratory markers by level of care required.

The median hospital stay was 8 days (interquartile range 6 to 12). Two children died (2.9%), both presenting late with refractory shock and multi-organ dysfunction. Of the 66 survivors, 59 attended follow-up at approximately six weeks. Left ventricular function had normalised in all children in whom it had been impaired. Of 17 children with coronary artery dilatation or aneurysm at admission who returned, abnormalities had resolved in 14, and 3 had persisting mild dilatation requiring continued surveillance and antiplatelet therapy. No child had a documented recurrence during the follow-up period.

DISCUSSION AND INTERPRETATION

Three points stand out from this series. The syndrome presented as a febrile, gastrointestinal and mucocutaneous illness rather than a respiratory one. Half the children had echocardiographic abnormalities, and cardiac involvement drove much of the management. And outcomes were good, with mortality of 2.9% and cardiac changes largely reversible by six weeks. Our clinical profile closely matches the established literature. Fever was universal, as in the London series of Whittaker and colleagues and the American surveillance data of Feldstein and colleagues [6,8], and gastrointestinal symptoms were the commonest non-febrile feature, present in 64.7% of our children. The relative scarcity of respiratory symptoms, at 25%, is the finding that most clearly separates this syndrome from acute COVID-19 and is the reason it is so easily missed: a child presenting with fever and abdominal pain several weeks after an unremarkable or unrecognised infection does not obviously suggest a COVID-related diagnosis. The serological pattern reinforces this, with antibodies positive in 82.4% but RT-PCR positive in only 10.3%, consistent with the two to six week post-infectious interval described since the earliest reports [1,6,7]. A mean interval of 4.3 weeks in our series falls squarely within that window.

Echocardiographic abnormalities in half our children are within the reported range, and the balance between ventricular dysfunction at 30.9% and coronary involvement at 25.0% mirrors what other series describe [9,18]. This dual pattern is one of the ways the syndrome differs from classical Kawasaki disease, where coronary changes dominate and myocardial dysfunction is less prominent [2,17]. The practical consequence is that echocardiography cannot be reserved for children with murmurs or shock; a substantial proportion of our children with abnormal studies were haemodynamically stable at the time. That every case had an echocardiogram in this series reflects a deliberate departmental policy, and our data support continuing it.

The comparison between children needing intensive care and those managed on the ward is descriptive rather than predictive, given the sample size, but the direction is consistent and clinically recognisable. Raised D-dimer, ferritin, C-reactive protein, lymphopenia, thrombocytopenia and hypoalbuminaemia all clustered in the sicker group, with odds ratios between three and five. These are the same markers that reflect the intensity of the hyperinflammatory and prothrombotic response, and they are all available from the admission bloods. In a district or medical college hospital deciding whether a child needs a higher level of monitoring, this pattern is useful, though it should be read alongside clinical assessment rather than in place of it.

Our mortality of 2.9% is markedly lower than the 10% pooled across eleven Indian series by Sachdeva and colleagues [12] and closer to Western figures. Several explanations are plausible and not mutually exclusive. Our study period, from September 2021 to June 2022, came after the first and second waves, by which time recognition of the syndrome had improved considerably, immunomodulation was being started earlier, and national and international guidance was established [19]. Almost all our children received corticosteroids and most received immunoglobulin, in line with the combination approach that observational comparisons have suggested may reduce subsequent cardiovascular dysfunction [20]. The earlier Indian series, drawn largely from 2020 and early 2021, were assembled when the condition was newly described and many children reached tertiary centres late. Referral patterns may also differ, since some of the pooled series came from tertiary intensive care units receiving the sickest transfers. The reversibility we observed, with ventricular function normalising in all followed-up children and coronary changes resolving in 14 of 17, matches the generally favourable short-term cardiac trajectory reported elsewhere [9,18,21] and supports the practice of continuing surveillance in the small group with persisting abnormalities rather than assuming permanent damage.

CONCLUSION

Multisystem inflammatory syndrome in this north Indian cohort presented as a febrile illness dominated by gastrointestinal and mucocutaneous features, appearing a little over four weeks after SARS-CoV-2 infection that was usually detectable only on serology. Half the children had echocardiographic abnormalities and two fifths required intensive care, yet mortality was low at 2.9% and cardiac changes had largely resolved by six weeks. Two practical conclusions follow. Echocardiography should be performed in every child meeting the case definition, regardless of how well they appear, because a meaningful proportion of abnormalities occurred in haemodynamically stable children. And a small panel of admission markers, particularly D-dimer, ferritin, C-reactive protein, platelet count and albumin, identifies children more likely to need intensive care and can support early escalation decisions. For hospitals serving Lucknow and comparable settings, maintaining a low threshold for considering this diagnosis in a febrile child with abdominal symptoms weeks after a COVID-19 wave remains the single most important step towards timely treatment.

Limitations of the Study

- The retrospective design depends on the completeness of case records, and some laboratory and clinical details were variably documented; cardiac biomarkers in particular were not measured in all children.
- This was a single-centre study of 68 children over ten months, so the sample was too small for multivariable analysis and the comparison between intensive care and ward groups should be read as descriptive rather than predictive.
- Case ascertainment depended on the syndrome being suspected and the case definition applied, so milder cases managed as undifferentiated fever were probably missed, and the profile may be skewed towards more severe disease.
- Follow-up extended only to about six weeks and seven survivors did not attend, so medium and long-term cardiac outcomes, including late coronary changes, could not be assessed.
- SARS-CoV-2 variant sequencing was not available, so the contribution of the Delta and Omicron waves to the case mix could not be determined, and treatment was not randomised, so the comparative effectiveness of immunoglobulin and corticosteroids cannot be inferred from these data.

REFERENCES

1. Riphagen S, Gomez X, Gonzalez-Martinez C, Wilkinson N, Theocharis P. Hyperinflammatory shock in children during COVID-19 pandemic. Lancet. 2020;395(10237):1607-1608. doi:10.1016/S0140-6736(20)31094-1.
2. Verdoni L, Mazza A, Gervasoni A, Martelli L, Ruggeri M, Ciuffreda M, et al. An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study. Lancet. 2020;395(10239):1771-1778. doi:10.1016/S0140-6736(20)31103-X.
3. World Health Organization. Multisystem inflammatory syndrome in children and adolescents temporally related to COVID-19: scientific brief. Geneva: World Health Organization; 15 May 2020.
4. Centers for Disease Control and Prevention. Multisystem inflammatory syndrome in children (MIS-C) associated with coronavirus disease 2019 (COVID-19). CDC Health Advisory HAN00432. Atlanta: CDC; 14 May 2020.
5. Nakra NA, Blumberg DA, Herrera-Guerra A, Lakshminrusimha S. Multi-system inflammatory syndrome in children (MIS-C) following SARS-CoV-2 infection: review of clinical presentation, hypothetical pathogenesis, and proposed management. Children (Basel). 2020;7(7):69. doi:10.3390/children7070069.
6. Feldstein LR, Rose EB, Horwitz SM, Collins JP, Newhams MM, Son MBF, et al. Multisystem inflammatory syndrome in U.S. children and adolescents. N Engl J Med. 2020;383(4):334-346. doi:10.1056/NEJMoa2021680.
7. Dufort EM, Koumans EH, Chow EJ, Rosenthal EM, Muse A, Rowlands J, et al. Multisystem inflammatory syndrome in children in New York State. N Engl J Med. 2020;383(4):347-358. doi:10.1056/NEJMoa2021756.
8. Whittaker E, Bamford A, Kenny J, Kaforou M, Jones CE, Shah P, et al. Clinical characteristics of 58 children with a pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2. JAMA. 2020;324(3):259-269. doi:10.1001/jama.2020.10369.
9. Kaushik S, Aydin SI, Derespina KR, Bansal PB, Kowalsky S, Trachtman R, et al. Multisystem inflammatory syndrome in children associated with severe acute respiratory syndrome coronavirus 2 infection (MIS-C): a multi-institutional study from New York City. J Pediatr. 2020;224:24-29. doi:10.1016/j.jpeds.2020.06.045.
10. Dhanalakshmi K, Venkataraman A, Balasubramanian S, Madhusudan M, Amperayani S, Putilibai S, et al. Epidemiological and clinical profile of pediatric inflammatory multisystem syndrome - temporally associated with SARS-CoV-2 (PIMS-TS) in Indian children. Indian Pediatr. 2020;57(11):1010-1014. doi:10.1007/s13312-020-2025-1.
11. Jain S, Sen S, Lakshmivenkateshiah S, Bobhate P, Venkatesh S, Udani S, et al. Multisystem inflammatory syndrome in children with COVID-19 in Mumbai, India. Indian Pediatr. 2020;57(11):1015-1019. doi:10.1007/s13312-020-2026-0.
12. Sachdeva M, Agarwal A, Sra HK, Rana M, Pradhan P, Singh M, et al. Multisystem inflammatory syndrome associated with COVID-19 in children (MIS-C): a systematic review of studies from India. Indian Pediatr. 2022;59(7):563-569. doi:10.1007/s13312-022-2559-5.
13. Angurana SK, Awasthi P, Thakur A, Randhawa MS, Nallasamy K, Kumar MR, et al. Intensive care needs and short-term outcome of multisystem inflammatory syndrome in children (MIS-C): experience from North India. J Trop Pediatr. 2021;67(3):fmab055. doi:10.1093/tropej/fmab055.
14. Sethy G, Mishra B, Jain MK, Patnaik S, Mishra R, Behera JR, et al. Clinical profile and immediate outcome of multisystem inflammatory syndrome in children associated with COVID-19: a multicentric study. J Glob Infect Dis. 2021;13(4):159-163. doi:10.4103/jgid.jgid_85_21.
15. Sugunan S, Bindusha S, Geetha S, Niyas HR, Santhosh Kumar A. Clinical profile and short-term outcome of children with SARS-CoV-2 related multisystem inflammatory syndrome (MIS-C) treated with pulse methylprednisolone. Indian Pediatr. 2021;58(8):718-722. doi:10.1007/s13312-021-2277-4.
16. Karunakar P, Ramamoorthy JG, Anantharaj A, Parameswaran N, Biswal N, Dhodapkar R, et al. Clinical profile and outcomes of multisystem inflammatory syndrome in children (MIS-C): hospital-based prospective observational study from a tertiary care hospital in South India. J Paediatr Child Health. 2022;58(11):1964-1971. doi:10.1111/jpc.16129.

17. McCrindle BW, Rowley AH, Newburger JW, Burns JC, Bolger AF, Gewitz M, et al. Diagnosis, treatment, and long-term management of Kawasaki disease: a scientific statement for health professionals from the American Heart Association. Circulation. 2017;135(17):e927-e999. doi:10.1161/CIR.0000000000000484.
18. Capone CA, Subramony A, Sweberg T, Schneider J, Shah S, Rubin L, et al. Characteristics, cardiac involvement, and outcomes of multisystem inflammatory disease of childhood (MIS-C) associated with SARS-CoV-2 infection. J Pediatr. 2020;224:141-145. doi:10.1016/j.jpeds.2020.06.044.
19. Henderson LA, Canna SW, Friedman KG, Gorelik M, Lapidus SK, Bassiri H, et al. American College of Rheumatology clinical guidance for multisystem inflammatory syndrome in children associated with SARS-CoV-2 and hyperinflammation in pediatric COVID-19: version 3. Arthritis Rheumatol. 2022;74(4):e1-e20. doi:10.1002/art.42062.
20. Son MBF, Murray N, Friedman K, Young CC, Newhams MM, Feldstein LR, et al. Multisystem inflammatory syndrome in children: initial therapy and outcomes. N Engl J Med. 2021;385(1):23-34. doi:10.1056/NEJMoa2102605.
21. Balagurunathan M, Natarajan T, Karthikeyan J, Palanisamy V. Clinical spectrum and short-term outcomes of multisystem inflammatory syndrome in children in a south Indian hospital. Clin Exp Pediatr. 2021;64(10):531-537. doi:10.3345/cep.2021.00374.
22. Hoste L, Van Paemel R, Haerynck F. Multisystem inflammatory syndrome in children related to COVID-19: a systematic review. Eur J Pediatr. 2021;180(7):2019-2034. doi:10.1007/s00431-021-03993-5.
23. Godfred-Cato S, Bryant B, Leung J, Oster ME, Conklin L, Abrams J, et al. COVID-19-associated multisystem inflammatory syndrome in children - United States, March-July 2020. MMWR Morb Mortal Wkly Rep. 2020;69(32):1074-1080. doi:10.15585/mmwr.mm6932e2.
24. Rowley AH. Understanding SARS-CoV-2-related multisystem inflammatory syndrome in children. Nat Rev Immunol. 2020;20(8):453-454. doi:10.1038/s41577-020-0367-5.