COVID 19 among Children- Clinical Management Challenges The Kerala Scenario

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Setting the scene…

- **COVID 19 data among children**

  State, District, Government Medical Colleges

  Is the data worrisome?
- **Kerala State Guidelines- August 2021**
- **Management challenges in pediatric COVID 19**
- **Management challenges in MIS-c**

Kerala State (DHS)

	Cases			Deaths		
Age group	2020	2021 (till Oct 12)	Total number & (% of total cases in the state)	2020	2021 (till Oct 12)	Total
<5 yrs	21807	124510	146317 (3%)	5	18	23
5-9 yrs	21817	160751	182568 (3.8%)	1	3	4
10-14 yrs	24989	205869	230858 (4.8%)	2	11	13
15-19 yrs	33435	262497	295932 (6.2%)	6	25	31
Total 0-19 yr	102048	753627	855675 (17.8%)	14	57	71

Thiruvananthapuram District (DMO)

	Cases			Deaths		
Age group	2020	2021 (till sep 30)	Total	2020	2021 (till sep 30)	Total
0-9 yrs	4921	25137	30058	4	6	10
10-19 yrs	6342	37666	44008	1	4	5
0-19 yrs	11263 (13.9%)	62803 (17.4%)	74066 (16.8%)	5	10	15 (0.0002%)
All ages	80492	360078	440570	648	3401	4049

SAT Hospital- Pediatric COVID admissions

	2020 (Mar- Dec)	2021 (till Sep 30)	Total
Cat A	235	123	358
Cat B	226 (49)	308 (104)	534 (153 co-m)
Cat C	30 (12)	103 (45)	133 (57 co-m)
MISC	10	13	23
Total	501	547	1048
Deaths	4	6	10 (0.009%)

Government Medical Colleges

- GMC, TVM- 1048 cases, 10 deaths (9 co-m), 0.009%
- GMC, Kottayam- 350 cases, 7 deaths (7 co-m), 0.02%
- GMC, Alappuzha- 379 cases (from 15/10/2020), no deaths
- GMC, Thrissur- 217 cases, 6 deaths (6 co-m), 0.02%
- GMC, Kozhikode- 930 cases, 16 deaths (15 co-m), 0.01%

Table 1: Risk categorisation of patients with acute Covid 19 infection		
Category A	Category B	Category C
Mild sore throat, cough, Rhinorrhea, Diarrhoea, Vomiting	Fever, severe sore throat, increasing cough. Category A patients with comorbidities like Chronic heart, kidney, lung , neurological or liver diseases, obesity*, children on long term steroids, congenital or acquired immunosuppression.	Breathlessness, inability to feed, reduced activity / lethargy, altered sensorium, seizures , breathlessness, cyanosis, hypotension, Respiratory distress, spo2 < 94%,
**Adolescents with obesity are at higher risk of having severe disease.*		

Table 2: Clinical categorization based on severity of illness		
Mild	**Moderate**	**Severe**
Category A & B	Category C	Category C
Uncomplicated URI fever, sore throat, rhinorrhea etc **Without hypoxia or breathlessness.**	**Tachypnea (RR)*** < 2 months: ≥ 60/mt 2–11 months: ≥ 50/mt 1–5 years: ≥ 40/mt > 5 years: >30/mt **Spo2 90- 94%**	**Spo2 < 90%,** **Danger signs** like inability to feed, grunting, lower chest in drawings, altered sensorium,lethargy, seizures, somnolence, hypotension, ARDS, MODS

Mild disease- challenges

- Panic among parents- A, B

  Fever, persistent fever

  Febrile seizure, diarrhea

  Erratic saturation measures
- Panic among doctors-

  Referral to tertiary centre

  Cat A-358, Cat B- 381

ble 3: Treatment Of Acute Covid 19 I
Mild Disease
Home care / CFLTC / CSLTC
Symptomatic treatment Paracetamol 10 -15 mg/kg/dose may repeat 6 hourly (Avoid other NSAIDS) ORS and Zn for Diarrhea

Mild disease- challenges

- Diagnostic- delay in RT-PCR results
- Prolonged stay in hospital

  Caretaker positive and not well

  Grandparents at home

  Social reasons

  Demands care till complete recovery
- Zn, Vitamin C, D- 2020

ble 3: Treatment Of Acute Covid 19 I
Mild Disease
Home care / CFLTC / CSLTC
Symptomatic treatment Paracetamol 10 -15 mg/kg/dose may repeat 6 hourly (Avoid other NSAIDS) ORS and Zn for Diarrhea

Co-morbidities-210 patients (20%)

- Malignancies- 51
- Seizures & neuro - 46
- NS- 28, CKD- 8
- CHD- 12, Gastro- 8
- Hematology- 7
- DKA – 5
- Dengue 3

- Febrile seizures – 27
- ADD – 11
- RAD -8
- Pneumonia- 5
- Intussusception -1
- a/c appendicitis-1
- Encephalopathy 1

Cat C (133, 12.6%)

- Seizures- 54
- Co-morbidities -40%
- Supportive care
- Steroids, o2
- 2020- HCQ

Designated District Level Hospital / tertiary care center	
Paracetamol 10 -15 mg/kg/dose may repeat 6 hourly (Avoid other NSAIDS) Maintain fluid and electrolyte balance. Encourage Oral / NG feeds. If not tolerating IV fluids Salbutamol by MDI and face mask with spacer (only if wheeze present) ORS and Zn for Diarrhea Spo2< 94% - Oxygen by prongs, venturi or face mask (Target Spo2 between 94 – 98%)	Amoxycillin in children < 5 years or clinical suspicion of bacterial infection. Steroids if rapid progression and beyond 5 days from onset (any one): Methyl prednisolone 0.5mg/kg/dose BD or Dexamethasone 0.15mg per kg per day OD or

Cat C- severe- ICU

- Remdesivir- 12 pts (2 NB)
- ? Beneficial
- WHO does not recommend -no mortality benefit though reduces duration of hospital stay
- No experience with Tocilizumab, convalescent plasma, mAb (1 pt)

If spo2 < 90% on nasal prongs with minimal work of breathing options include :

Face mask at > 5LPM flow (Fio2 40-60%)

Oxygen hood at > 5LPM flow (Fio2 30 - 90%)

Venturi mask (28-60%Fio2)

Non rebreathing mask at 10 -15LPM (Fio2 80-90%)

High flow nasal cannula

Non invasive ventilation (if no response in 1 hour)

Invasive ventilation ((Low Tidal Volume, Optimal PEEP, Cuffed ET tube, Fluid restriction)

Empiric antibiotics

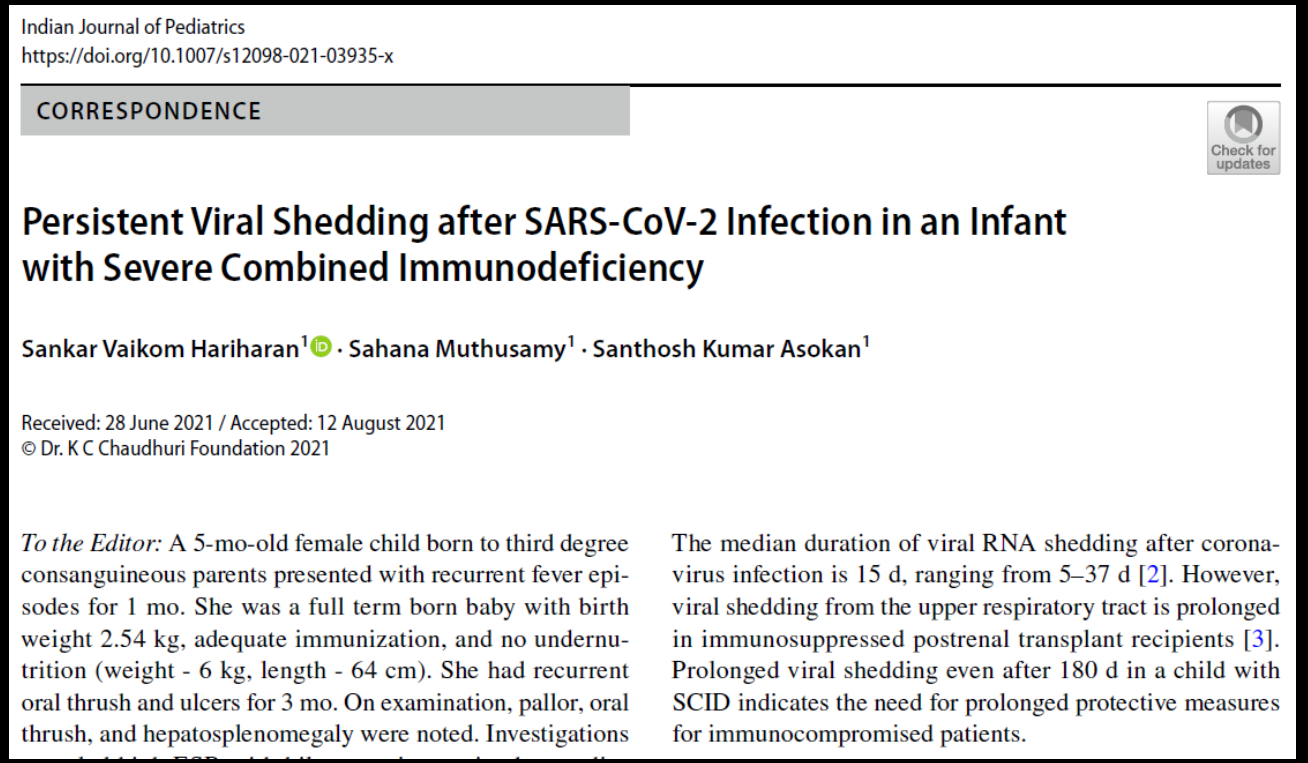
Parenteral Steroids for 5 to 14 days

Methyl prednisolone 1mg/kg/dose BD or Dexamethasone 0.15mg per kg per dose twice daily.

+/- Inj. Remdesivir*

Atypical presentations

- Young strokes- 3 (I/C bleeds)
- Transverse myelitis-2
- Optic neuritis
- Facial palsy
- Acute ataxia
- Orbital abscess



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CORRESPONDENCE

Check for updates

Persistent Viral Shedding after SARS-CoV-2 Infection in an Infant with Severe Combined Immunodeficiency

Sankar Vaikom Hariharan[1] · Sahana Muthusamy[1] · Santhosh Kumar Asokan[1]

Received: 28 June 2021 / Accepted: 12 August 2021

To the Editor: A 5-mo-old female child born to third degree consanguineous parents presented with recurrent fever episodes for 1 mo. She was a full term born baby with birth weight 2.54 kg, adequate immunization, and no undernutrition (weight - 6 kg, length - 64 cm). She had recurrent oral thrush and ulcers for 3 mo. On examination, pallor, oral thrush, and hepatosplenomegaly were noted. Investigations

The median duration of viral RNA shedding after coronavirus infection is 15 d, ranging from 5–37 d [2]. However, viral shedding from the upper respiratory tract is prolonged in immunosuppressed postrenal transplant recipients [3]. Prolonged viral shedding even after 180 d in a child with SCID indicates the need for prolonged protective measures for immunocompromised patients.

- No CAPA, CAM, GBS till date

Severe COVID19 with hyperinflammation

- Severe respiratory symptoms
- + Shock, ARDS, MAS
- Innate Immunity- cytokine storm (within 2 wks of d/s onset)
- Elevated CRP, Ferritin, LDH, D- dimer, IL
- Decreased lymphocytes, platelets and serum albumin
- Complex medical d/s & on immunosuppressives
- Common in adults, rare in children (3/10 deaths)

Severe COVID19 with hyperinflammation

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American College of Rheumatology
Empowering Rheumatology Professionals

American College of Rheumatology Clinical Guidance for Multisystem Inflammatory Syndrome in Children Associated With SARS–CoV-2 and Hyperinflammation in Pediatric COVID-19: Version 2

Lauren A. Henderson,[1] Scott W. Canna,[2] Kevin G. Friedman,[1] Mark Gorelik,[3] Silvia K. Lapidus,[4] Hamid Bassiri,[5] Edward M. Behrens,[5] Anne Ferris,[6] Kate F. Kernan,[7] Grant S. Schulert,[8] Philip Seo,[9] Mary Beth F. Son,[1] Adriana H. Tremoulet,[10] Rae S. M. Yeung,[11] Amy S. Mudano,[12] Amy S. Turner,[13] David R. Karp,[14] and Jay J. Mehta[5]

Guidance statement	Level of consensus
Medically complex children and those receiving immunosuppressive medications, including moderate-to-high–dose glucocorticoids, may be at higher risk for severe outcomes in COVID-19.	Moderate to high
Children and adults admitted to the hospital with COVID-19 present with similar symptoms, including fever, upper respiratory tract symptoms, abdominal pain, and diarrhea.	Moderate
Children with severe respiratory symptoms due to COVID-19 with any of the following should be considered for immunomodulatory therapy: ARDS, shock/cardiac dysfunction, substantial elevation in LDH, D-dimer, IL-6, IL-2R, CRP, and/or ferritin level, and depressed lymphocyte count, albumin level, and/or platelet count.	Moderate to high
Glucocorticoids should be used as first-tier immunomodulatory treatment in patients with COVID-19 and hyperinflammation.	High
Anakinra appears safe in severe infections and in children with hyperinflammatory syndromes. In children with COVID-19 and hyperinflammation, anakinra (>4 mg/kg/day IV or SC) should be considered for immunomodulatory therapy in patients with refractory disease despite glucocorticoid treatment or in patients with contraindications to steroids. Initiation of anakinra before invasive mechanical ventilation may be beneficial.	High

MIS-c- 140 cases, 1 death - challenges

- Epidemiological link to CoViD19 (-20%)
- Early identification of MIS-c - DDs
- Inflammatory markers mandatory (lab)
- ECHO (cardiologist support)
- Early identification of d/s progression
- IVIG / IVIG+ steroids / steroids alone
- Supportive care in ICU

Kawasaki disease
Bacterial sepses
ADD, Shock
Severe Dengue
Toxic Shock Syndrome
Leptospirosis
Scrub typhus
Surgical abdomen

MIS-c (Suspect ; diagnosis of exclusion!)

Criteria	RCPCH†	CDC	WHO‡
Age	All children (age not defined)	<21 years	0–19 years
Fever	Persistent fever (≥38.5°C)	Temperature ≥38.0°C for ≥24 hours *or* subjective fever for ≥24 hours	Fever for ≥3 days
Clinical symptoms	Both of the following: 1. single or multiorgan dysfunction; *and* 2. additional features	Both of the following: 1. severe illness (hospitalized); *and* 2. ≥2 organ systems involved	At least 2 of the following: 1. rash, conjunctivitis, and mucocutaneous inflammation; 2. hypotension or shock; 3. cardiac involvement; 4. coagulopathy; 5. acute GI symptoms

Lab

- 1st line - CRP, ESR
  CBC, Na, serum albumin
- ECG, ECHO, NT pro-BNP
  D-dimer, PT-INR, L/RFT
- 2nd line- Ferritin, LDH
  Procalcitonin, fibrinogen,
  Trop-T, IL6

ED GUIDELINE | **MIS-C: ED-DIAGNOSTIC/DISPO RECS FOR SUSPECTED MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN (MIS-C) ASSOCIATED WITH COVID-19** (AGE < 21 YEARS)

Children's MINNESOTA

Do Tier 1 labs show all of the following?

1. CRP ≥ 5 mg/dL OR ESR ≥ 40 mm/hr
2. At least 1 of the following
   - ALC < 1000/ul
   - Platelets < 150,000/ul
   - Na < 135 mmol/L
   - Neutrophilia (ANC > 7,700)
   - Albumin < 3

PLUS No alternate probable diagnosis.

Labs suggestive of MIS-C?

Most patients have ≥ 4 abnl markers of inflammation

- **Evidence of inflammation:** CRP > 5 mg/dL, ESR > 40 mm/h, ferritin > 500 ng/mL, ANC > 7700, ALC < 1000, platelet < 150k, D-Dimer > 2 mg/L, fibrinogen > 400 mg/dL, albumin < 3 g/dL, anemia, ALT > 40 U/L, INR > 1.2
- **Other:** AKI, hyponatremia, high LDH, high troponin, BNP > 400 pg/mL, prolonged PT or PTT

Rx- MIS-c

Shock & organ dysfn

IVIG 2g/kg over 12 h

+ IV MP 2 mg/kg/d

36hrs-

IV MP 30mg/kg/d x 5d

oral pred 2mg/kg/d x 3w


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American College of Rheumatology Clinical Guidance for Multisystem Inflammatory Syndrome in Children Associated With SARS–CoV-2 and Hyperinflammation in Pediatric COVID-19: Version 2

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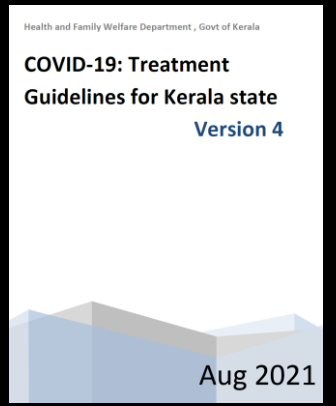

Enoxaparin- Warf (3 mo)

Thrombosis

EF<35%, CAA z >10

Aspirin

3-5mg/kg/d x 4-6 w

MIS-C- SATH (TVM), AIMS (Kochi)+ BMH (Calicut)

RESEARCH PAPER

Clinical Profile and Short-Term Outcome of Children With SARS-CoV-2 Related Multisystem Inflammatory Syndrome (MIS-C) Treated With Pulse Methylprednisolone

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Received: February 07, 2021; Initial review: February 25, 2021; Accepted: April 19, 2021.

Objective: To study the clinical profile and outcome of children with MIS-C treated with methylprednisolone pulse therapy and /or intravenous immunoglobulin (IVIG). **Method:** This prospective observational study included children satisfying CDC MIS-C criteria admitted from September to November, 2020. Primary outcome was persistence of fever beyond 36 hours after start of immunomodulation therapy. Secondary outcomes included duration of ICU stay, mortality, need for repeat immunomodulation, time to normalization of CRP and persistence of coronary abnormalities at 2 weeks. **Results:** Study population included 32 patients with MIS-C with median (IQR) age of 7.5 (5-9.5) years. The proportion of children with gastrointestinal symptoms was 27 (84%), cardiac was 29 (91%) and coronary artery dilatation was 11 (34%). Pulse methylprednisolone and intravenous immunoglobulin were used as first line therapy in 26 (81%), and 6 (19%) patients, respec-tively. Treatment failure was observed in 2/26 patients in methylprednisolone group and 2/6 patients in IVIG group. C-reactive protein levels less than 60mg/L by day 3 was seen in 17(74%) in methylprednisolone group and 2 (25%) in IVIG group (P=0.014). There was no mortality. At 2 weeks follow-up coronary artery dilatation persisted in 4 in methylprednisolone group and 1 in IVIG group. **Conclusion:** In patients with SARS-CoV-2 related MIS-C, methylprednisolone pulse therapy was associated with favorable short-term outcomes.

Keywords: *Coronary artery, COVID-19, IVIG, Kawasaki disease.*

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- 32pts (Sep- Nov 2020), 0 deaths
- IV MP (2/26), IV IG (2/6)

BMJ Paediatrics Open

COVID-19 related multisystem inflammatory syndrome in children (MIS-C): a hospital-based prospective cohort study from Kerala, India

Arun Tiwari ,[1] Suma Balan ,[1] Abdul Rauf,[2] Mahesh Kappanayil,[3] Sajith Kesavan,[4] Manu Raj ,[5] Suchitra Sivadas,[5] Anil Kumar Vasudevan,[6] Pranav Chickermane,[1] Ajay Vijayan,[2] Shaji Thomas John,[2] Sasidharan CK,[2] Raghuram A Krishnan,[7] Abish Sudhakar[3]

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ABSTRACT

Objectives To study (1) epidemiological factors, clinical profile and outcomes of COVID-19 related multisystem inflammatory syndrome in children (MIS-C), (2) clinical profile across age groups, (3) medium-term outcomes and (4) parameters associated with disease severity.

Design Hospital-based prospective cohort study.

Setting Two tertiary care centres in Kerala, India.

Participants Diagnosed patients of MIS-C using the case definition of Centres for Disease Control and Prevention.

Statistical analysis Pearson χ^2 test or Fisher's exact test was used to compare the categorical variables and independent sample t-test or Mann-Whitney test was used to compare the continuous variables between the subgroups categorised by the requirement of mechanical ventilation. Bonferroni's correction was used for multiple comparisons.

Results We report 41 patients with MIS-C, mean age was 6.2 (4.0) years, and 33 (80%) were previously healthy. Echocardiogram was abnormal in 23 (56%), and coronary abnormalities were noted in 15 (37%) patients. Immunomodulatory therapy was administered to 39 (95%), steroids and IVIg both were used in 35 (85%) and only steroids in 3 (7%) patients. Intensive care was required

What is known about the subject?

- Multisystem inflammatory syndrome in children (MIS-C) is a rare but critical association of COVID-19 infection in children.
- MIS-C is known to present as a hyperinflammatory state with fever, gastrointestinal, mucocutaneous symptoms, atypical Kawasaki disease-like phenotype and macrophage activation syndrome.

What this study adds?

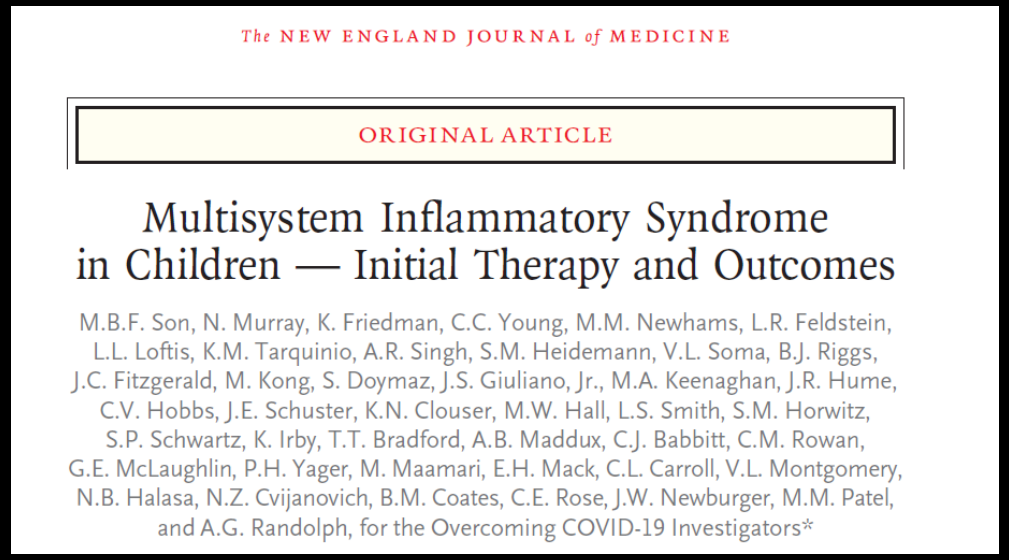
- In our cohort of MIS-C, patients presented at a younger age with more frequent mucocutaneous changes and lesser comorbidities as compared with western studies.
- The medium-term outcome of patients with MIS-C is excellent; however, we need to monitor echocardiogram at subsequent follow-up visits in selected patients.
- We were able to associate hyperferritinaemia with requirement of mechanical ventilation in patients with MIS-C.

- 41 pts (Mar- April 2021), 2 deaths
- Steroids+ IV IG (35), Steroids (3)

IVIG + steroids vs IVIG alone vs steroids alone

- 58 US hospitals, 518 pts
- Shock/CV dysfn > D2
- 17% vs 31% (June 2021)

- 32 countries, 614 (208, 246, 99)
- Inotrope/MV>D2, score
- No difference in outcomes

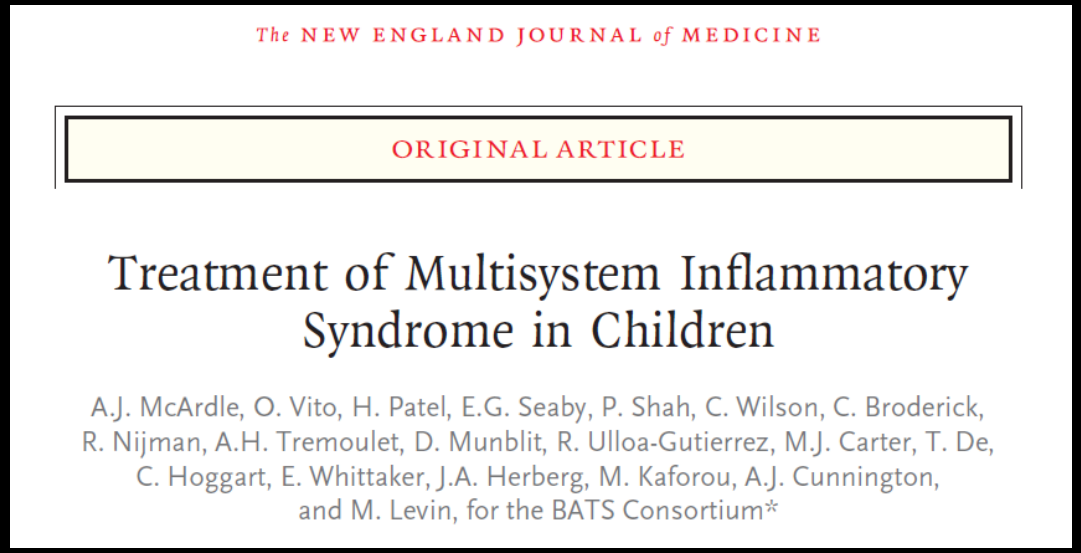


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Multisystem Inflammatory Syndrome in Children — Initial Therapy and Outcomes

M.B.F. Son, N. Murray, K. Friedman, C.C. Young, M.M. Newhams, L.R. Feldstein, L.L. Loftis, K.M. Tarquinio, A.R. Singh, S.M. Heidemann, V.L. Soma, B.J. Riggs, J.C. Fitzgerald, M. Kong, S. Doymaz, J.S. Giuliano, Jr., M.A. Keenaghan, J.R. Hume, C.V. Hobbs, J.E. Schuster, K.N. Clouser, M.W. Hall, L.S. Smith, S.M. Horwitz, S.P. Schwartz, K. Irby, T.T. Bradford, A.B. Maddux, C.J. Babbitt, C.M. Rowan, G.E. McLaughlin, P.H. Yager, M. Maamari, E.H. Mack, C.L. Carroll, V.L. Montgomery, N.B. Halasa, N.Z. Cvijanovich, B.M. Coates, C.E. Rose, J.W. Newburger, M.M. Patel, and A.G. Randolph, for the Overcoming COVID-19 Investigators*



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Treatment of Multisystem Inflammatory Syndrome in Children

A.J. McArdle, O. Vito, H. Patel, E.G. Seaby, P. Shah, C. Wilson, C. Broderick, R. Nijman, A.H. Tremoulet, D. Munblit, R. Ulloa-Gutierrez, M.J. Carter, T. De, C. Hoggart, E. Whittaker, J.A. Herberg, M. Kaforou, A.J. Cunnington, and M. Levin, for the BATS Consortium*

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