COVID-19 in Children

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CNHS ID ECHO May 24, 2021

Data in Children

CDC estimates in the US as of Feb 2021:

- Children age 0-4 years = 1.9% of COVID-19 diagnoses
- Children age 5-17 years = 9.4% of COVID-19 diagnoses

Lower hospitalization rate compared with adults

- 8 per 100,000 vs 165 per 100,000
- But similar ICU admission once hospitalized (1 in 3)
- Adolescents with more severe disease
- American Indian/Alaska Native children - 5.3 times more likely to be hospitalized than non-Hispanic white children

Children account for <1% of all COVID-19 related deaths in the US

BMJ 2021;372:n385 http://dx.doi.org/10.1136/bmj.n385 Published: 01 March 2021; Centers for Disease Control and Prevention. CDC COVID Data Tracker. 2020. https://covid.cdc.gov/covid-data-tracker/#datatracker-home

Spectrum of COVID-19 in Children

Clinical spectrum of COVID-19 and COVID-19-associated multisystem inflammatory syndromes in children

Acute COVID-19		COVID-19-associated MIS-C		
Mild	**Severe**	**Febrile inflammatory state**	**KD-like illness**	**Severe MIS-C**
In most children, COVID-19 causes no or only mild symptoms.	A small minority of children present with severe acute COVID-19 manifestations, including respiratory failure, ARDS, neurologic symptoms, coagulopathy, and shock. This occurs most commonly in children with underlying medical conditions. Some children with severe acute COVD-19 may develop signs of cytokine storm.	Some children may present with persistent fevers and mild symptoms (eg, headache, fatigue). Inflammatory markers may be elevated, but signs of severe multisystem involvement are lacking.	Some children meet criteria for complete or incomplete KD and do not develop shock and severe multisystem involvement.	Children with severe MIS-C have markedly elevated inflammatory markers and severe multisystem involvement. Cardiac involvement and shock are common.

As more is learned about COVID-19 and MIS-C in children, it is apparent that the spectrum of disease ranges from mild to severe. Our understanding of the full spectrum, including subphenotypes, is evolving. There may be some overlap between these categories. It remains unclear how common each presentation is, how frequently children progress from mild to more severe manifestations, and what the risk factors are for such progression.

COVID-19: coronavirus disease 2019; MIS-C: multisystem inflammatory syndrome in children; KD: Kawasaki disease; ARDS: acute respiratory distress syndrome.

Why is COVID-19 less severe in children?

- Less intense immune response to the virus than adults; Cytokine release syndrome is thought to be important in the pathogenesis of severe COVID-19 infections
- Viral interference in the respiratory tract of young children, which may lead to a lower SARS-CoV-2 viral load;
- Different expression of the angiotensin converting enzyme 2 receptor (the receptor for SARS-CoV-2) in the respiratory tracts of children;
- Pre-existing cross-reactive antibody;
- A vigorous early mucosal immune response, protective off-target effects of live vaccines;
- Relatively healthier blood vessels in children than in adults

UpToDate: COVID-19-Clinical manifestations and diagnosis in children

Asymptomatic COVID-19 in Children

Prospective study **to evaluate the performance of symptom based testing in pediatric population**

Four French hospitals screened 438 consecutively admitted pediatric patients (by PCR)

- 182 had suspected COVID-19 symptoms
- 22 had positive SARS-CoV-2 test (5% positivity)
  - 10 of the 22 had no s/s of suspected COVID-19 (45%)

Symptom based screening for COVID-19 in hospitalized children could miss as much as 45% of transmissible **infections**

Poline J, Gaschignard J, Leblanc C, etal. Systematic SARS-CoV-2 screening at hospital admission in children: A French prospective multicenter study. Clin Infect Dis 2020;ciaa1044. doi: 10.1093/cid/ciaa1044. pmid: 32710743

Symptomatic COVID-19 in Children

Table 1 | Prevalence of symptoms in children with acute SARS-CoV-2 infection, summarised from three meta-analyses

Symptom	Range[1-3]*
Asymptomatic	**16-19%**
Fever	48-59%
Cough	39-56%
Rhinorrhoea, nasal congestion	7-20%
Myalgia	14-19%
Sore throat	14-18%
Headache	3-13%
Tachypnoea, dyspnoea	8-12%
Diarrhoea	7-10%
Nausea, vomiting	2-9%
Abdominal pain	6-7%
Fatigue	5-8%
Rash	<1%

(Early studies did not specify loss of taste or smell because younger children are not able to report this symptom)

* Hoang et al included 131 studies with 7780 patients; Assaker et al included 28 studies with 1614 patients; Zhang et al included 46 studies with 551 patients

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MIS-C: Complication of COVID-19 in Children

Multisystem inflammatory syndrome in children (MIS-C)

- **Hyperinflammatory syndrome** causing severe illness in children
- **30 deaths among 2060 patients with MIS-C have been reported in the US as of 8 February 2021**
- **Develops 2-6 weeks after SAR-CoV-2 infection** – could have been asymptomatic, mild, moderate or severe infection
- Long-term **outcomes unknown**

Case definition

- Presence of fever for ≥24 hours
- Laboratory evidence of inflammation
  - Including, but not limited to elevated CRP, ESR, fibrinogen, procalcitonin, D-dimer, ferritin, LDH, or IL-6; elevated neutrophils; reduced lymphocytes; low albumin
- Multi-organ dysfunction (≥2 systems: cardiac, dermatological, gastrointestinal, renal, respiratory, hematological, and/or neurological)
- No plausible alternative diagnosis
- Recent or current SARS-CoV-2 infection or exposure

BMJ 2021;372:n385 http://dx.doi.org/10.1136/bmj.n385 Published: 01 March 2021; Centers for Disease Control and Prevention. Health Department-reported cases of multisystem inflammatory syndrome in children (MIS-C) in the United States. https://www.cdc.gov/misc/cases/index.html

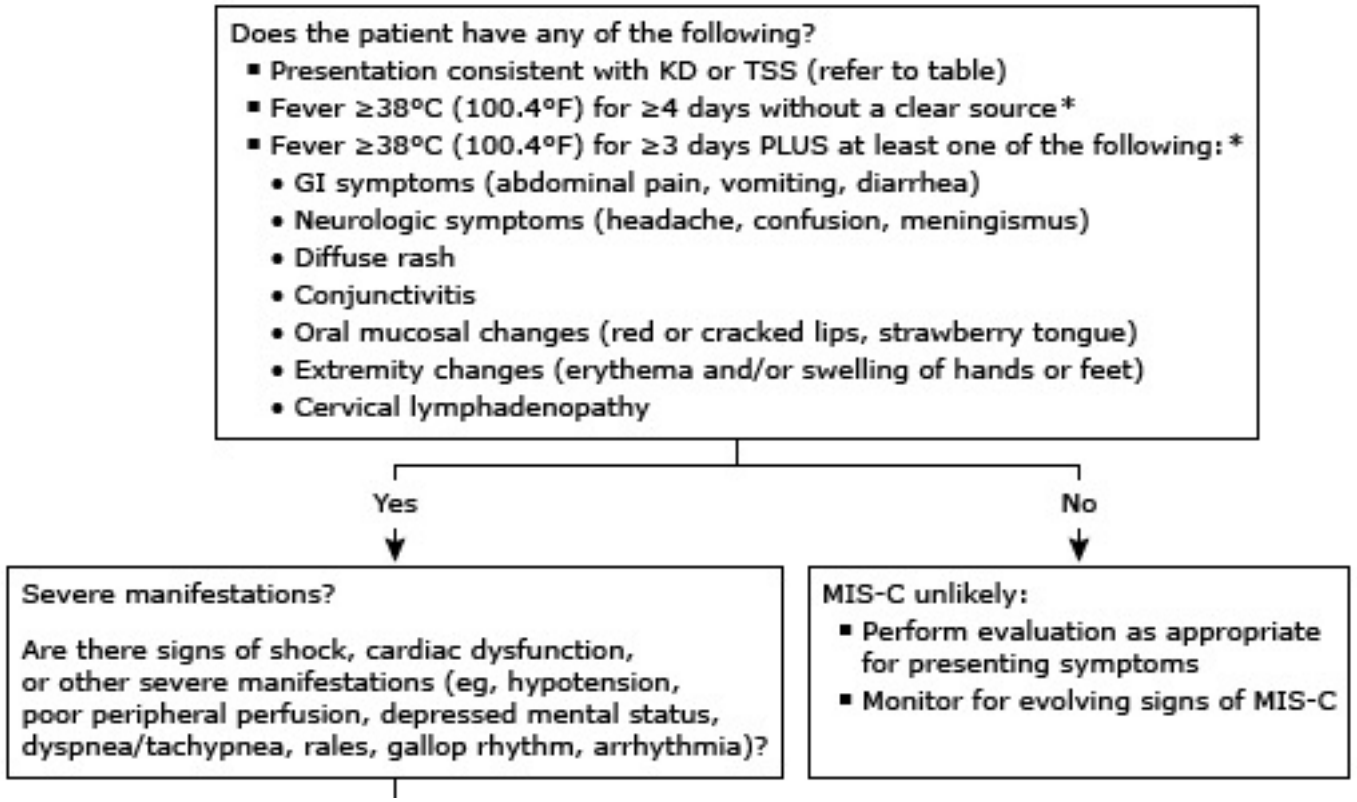
MIS-C Symptoms

Presenting symptoms	Frequency* (%)
•Persistent fevers (median duration 4 to 6 days)	100
•Gastrointestinal symptoms (abdominal pain, vomiting, diarrhea)	60 to 100
•Rash	45 to 76
•Conjunctivitis	30 to 81
•Mucous membrane involvement	27 to 76
•Neurocognitive symptoms (headache, lethargy, confusion)	29 to 58
•Respiratory symptoms (tachypnea, labored breathing)	21 to 65
•Sore throat	10 to 16
•Myalgias	8 to 17
•Swollen hands/feet	9 to 16
•Lymphadenopathy	6 to 16

*Frequencies represent the proportion of patients with each finding among those tested or assessed for the finding. Not all patients were tested or assessed for each.

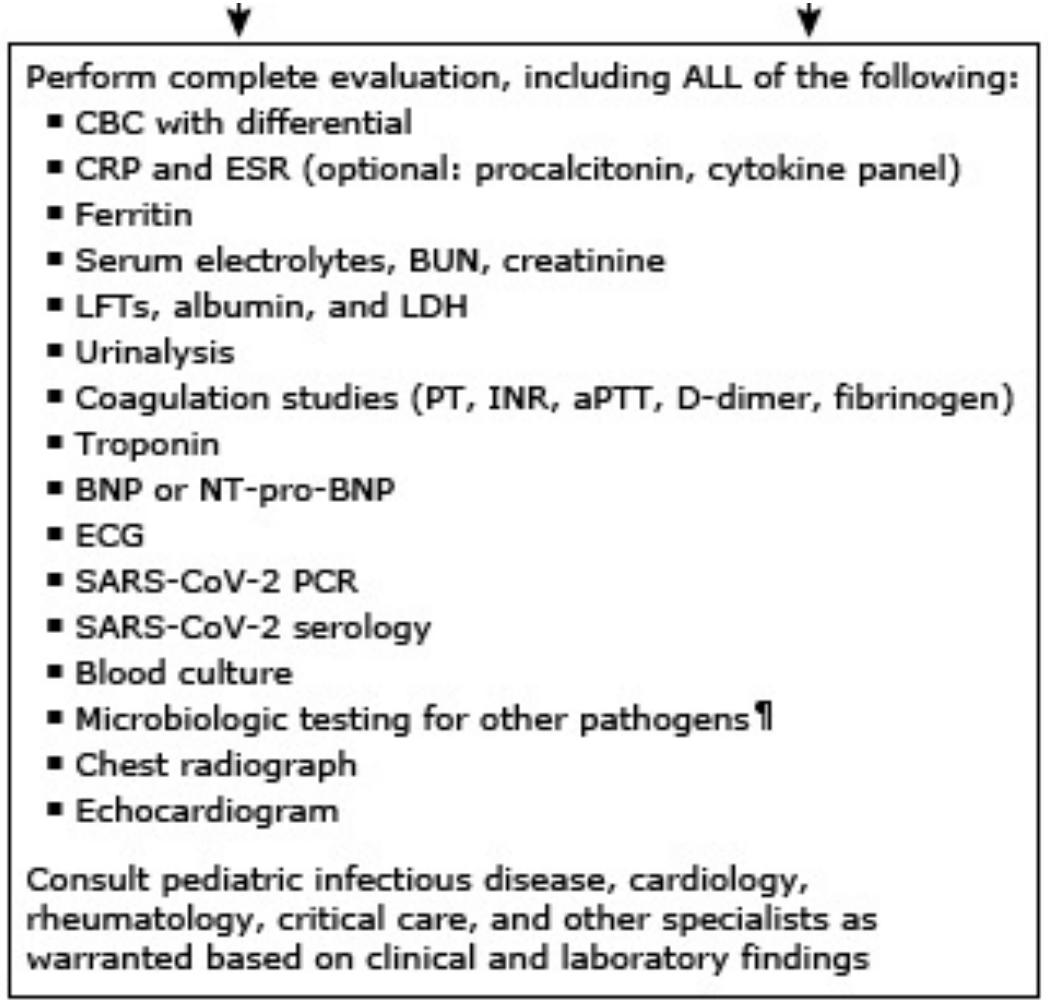
uptodate.com: Clinical Manifestations of COVID-19-associated MIS-C, Graphic 128294 Version 7.0

Evaluation of the Patient



uptodate.com: Suggested Approach to Evaluation of Patients with Suspected MIS-C, Graphic 129371 Version 1.0

Work-up



uptodate.com: Suggested Approach to Evaluation of Patients with Suspected MIS-C, Graphic 129371 Version 1.0

Laboratory findings	Frequency* (%)
Abnormal blood cell counts	
•Lymphocytopenia	80 to 95
•Neutrophilia	68 to 90
•Mild anemia	70
•Thrombocytopenia	31 to 80
Elevated inflammatory markers	
•C-reactive protein	90 to 100
•Erythrocyte sedimentation rate	75 to 80
•D-dimer	67 to 100
•Fibrinogen	80 to 100
•Ferritin	55 to 76
•Procalcitonin	80 to 95
•Interleukin-6	80 to 100
Elevated cardiac markers	
•Troponin	50 to 90
•BNP or NT-pro-BNP	73 to 90
Other	
•Hypoalbuminemia	48 to 95
•Mildly elevated liver enzymes	62 to 70
•Elevated lactate dehydrogenase	10 to 60
•Hypertriglyceridemia	70

*Frequencies represent the proportion of patients with each finding among those tested or assessed for the finding. Not all patients were tested or assessed for each.

Management of MIS-C

Based on organ system involvement
IVIG
Corticosteroids
Broad-spectrum antibiotics: Vancomycin + Ceftriaxone
Aspirin
Specialty Center with pediatric infectious disease and rheumatology
Prognosis is uncertain and long-term complications from MIS-C are unknown

UpToDate: COVID-19: Multisystem inflammatory syndrome in children (MIS-C) management and outcome

References

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- UpToDate:
  - COVID-19: Multisystem inflammatory syndrome in children (MIS-C) management and outcome
  - COVID-19: Clinical manifestations and diagnosis in children
  - COVID-19: Multisystem inflammatory syndrome in children (MIS-C) clinical features, evaluation, and diagnosis