Evidence-Based Medicine InfoSheet: Clinical Presentation
Updated [09/21/2020]*
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Children Common Presentation

https://www.cdc.gov/mmwr/volumes/69/wr/mm6914e4.htm?s_cid=mm6914e4_w

- Less likely to present with fever, SOB, and cough than adults (18-64)
  - https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7090728/
  - Fever (50%), cough (38%)

http://pediatrics.aappublications.org/lookup/doi/10.1542/peds.2020-0702

- Compared to adult patients, children diagnosed with COVID-19 seem to have less severe disease. In 1 epidemiology study of 2143 children, over 90% of the cases were mild or moderate in nature. Young children, especially infants seemed to be more susceptible to severe disease than older children; 10% of patients under 1 year of age had severe or critical disease. The only death in the series was a 14 year-old male

https://www.nejm.org/doi/10.1056/NEJMc2005073

- In a study of 1391 children, fever was present in 41.5% of the children at any time during the illness. Other common signs and symptoms included cough and pharyngeal erythema. A total of 27 patients (15.8%) did not have any symptoms of infection or radiologic features of pneumonia. A total of 12 patients had radiologic features of pneumonia but did not have any symptoms of infection. During the course of hospitalization, 3 patients required intensive care support and invasive mechanical ventilation; all had coexisting conditions (hydronephrosis, leukemia [for which the patient was receiving maintenance chemotherapy], and intussusception). The most common radiologic finding was bilateral groundglass opacity (32.7%).

https://pediatrics.aappublications.org/content/pediatrics/early/2020/05/11/peds.2020-1056.full.pdf

- 3 patients <60 days present with poor feeding, lethargy, irritability, and fever with no other identifiable source of infection. All 3 infants had an absence of cough, none had respiratory distress. All 3 had lymphopenia and thrombocytosis on initial presentation and 2 had neutropenia.

Liguoro I, Pilotto C, Bonanni M, Ferrari ME, Pusiol A, Nocerino A, Vidal E, Cogo P. SARS-COV-2 infection in children and newborns: a systematic review. Eur J Pediatr. 2020 May 18;. doi: 10.1007/s00431-020-

03684-7. [Epub ahead of print] Review. PubMed PMID: 32424745; PubMed Central PMCID: PMC7234446.

Symptoms

- Children are much less likely to be symptomatic or have severe infection than adults.
- Most common: Fever, cough, sore throat. Less common (<15%): fatigue, diarrhea, vomiting, dyspnea, oxygen desaturation

Labs:

- Elevated CRP, elevated procalcitonin, elevated creatine kinase, elevated ALT, lymphocytopenia

Imaging

- Ground glass opacities & non-specific unilateral & bilateral lesions on chest CT

Risk Factors for Severe Disease & Mortality

- Asthma or other chronic lung disease, congenital heart disease, immunocompromised status, hemato-oncologic disease, prematurity, metabolic disease.
- Mortality <0.1% in a meta-analysis of 7480 children with confirmed COVID-19 infection.

Kawasaki-like presentation

AAP News Release including the CDC's definition and diagnostic criteria for MIS-C
http://www.aappublications.org/news/2020/05/14/covid19inflammatory051420?cct=2287

- An individual under 21 years presenting with fever, laboratory evidence of inflammation and evidence of clinically severe illness requiring hospitalization with multisystem (>2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological);
    - Fever should be at least 38 degrees Celsius for at least 24 hours or a subjective fever lasting 24 hours.
    - Evidence of inflammation could include but is not limited to an elevated C-reactive protein, erythrocyte sedimentation rate, fibrinogen, procalcitonin, d-dimer, ferritin, lactic acid dehydrogenase, or interleukin 6, elevated neutrophils, reduced lymphocytes and low albumin.

  AND

- No alternative plausible diagnoses; AND

- Positive for current or recent SARS-CoV-2 infection by reverse-transcriptase polymerase chain reaction, serology or antigen test; or COVID-19 exposure within the four weeks prior to the onset of symptoms.

https://pediatrics.aappublications.org/content/pediatrics/early/2020/05/19/peds.2020-1711.full.pdf

- 2 patients presented with diarrhea, abdominal pain, high fever, elevated CRP and procalcitonin, lymphopenia. Phase 2: Fever persisted and mucocutaneous involvement appeared (conjunctivitis, fissured lips, acral rash), thrombocytopenia, dec C3 and C4, hepatomegaly, capillary leak syndrome with severely dec albuminemia, diffuse edema. Both developed myocarditis in third phase.

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31094-1/fulltext

- Case series of 8 children: All had unrelenting fever, variable rash, conjunctivitis, peripheral edema, generalized extremity pain with significant GI symptoms progressing to warm, vasoplegic shock, refractory to volume resuscitation and eventually requiring noradrenaline and milrinone for hemodynamic support. Most children had no respiratory involvement, but 7/8 required mechanical ventilation for cardiovascular stabilization. Other notable features besides persistent fever and rash included development of small pleural pericardial and ascitic effusions suggestive of diffuse inflammatory process. All 8 tested negative for SARS-COV2 upon admission, and only 2 tested positive after discharge (one was post mortem).

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31103-X/fulltext

- Between Feb 8 and April 20,2020 - 10 patients diagnosed with Kawasaki disease. Serologies in all patients available April 13 - 8/10 were IgG positive and 3/10 also IgM positive. Only 1 had a negative serology for COVID
    - 5/10 presented with classic form
        - Presenting with non-exudative conjunctivitis, hand and feet anomalies (ie, erythema or firm induration, or both), and polymorphic rash. Four (80%) of five patients had associated changes of the lips or oral cavity, or both; patient 7 also had laterocervical lymphadenopathy
    - 5/10 presented with incomplete form

        - presenting with three or fewer clinical criteria associated with additional laboratory criteria (n=1) or an abnormal echocardiography (n=4)
    - 5/10 had minimal mono or bilateral infiltrates
    - 5/10 met criteria for KDSS (Kawaski Disease Shock Syndrome) because of hypotension and clinical signs of hypoperfusion (of note, none of the patients diagnosed with Kawaski in the past 5 years had signs of hypoperfusion, hypotension or atypical symptoms).
    - Labs: Neutrophilia in 8/10; Lymphopenia in 8/10; thrombocytopenia in 8/10 patients. Hyponatremia 8/10 patients, and slight increase in transaminases in 7/10 patients. Hypertriglyceridemia in 7/8 tested patients, fibrinogen high in 9/10 patients and high D-dimer in 8/10 patients, proBNP elevated in all 10 patients.
    - Italty reports a 30 fold increase in the diagnosis of Kawasaki-like disease presentation (0-3 diagnosed per month prior to COVID; 10 per month now)

https://www.aappublications.org/news/2020/05/20/covid19inflammatorysyndrome052020?cct=2287

- UK Cohort Study: 5% of the patients experienced shock, 59.5% had diarrhea, 57% had abdominal involvement, 54% had a rash, 51% had myocardial involvement, 51% required oxygen, 38% had acute kidney injury and 32% had respiratory symptoms
- New York Cohort study: 7% of patients had gastrointestinal symptoms, 76% had shock, 70% had acute kidney injury, 58% had neurocognitive symptoms, 58% had myocardial involvement, 52% required oxygen, 52% had respiratory symptoms, 48% had coronary artery abnormalities.
    - 64% met criteria for Kawasaki
- Labs: elevated C-reactive protein, fibrinogen, procalcitonin, d-dimer, ferritin and lactic acid dehydrogenase and neutrophils and reduced lymphocytes

ITP in SARS-CoV-2 Positive Pediatric Patient

https://pediatrics.aappublications.org/content/pediatrics/early/2020/05/19/peds.2020-1419.full.pdf

- Case presentation of patient who tested positive for SARS-CoV-2 with severe thrombocytopenia and wet purpura in setting of suspected ITP.

Symptom frequency

https://www.cdc.gov/mmwr/volumes/69/wr/mm6924e2.htm

Age Group
</= 9 Yrs

-Fever: 46%
-cough: 37
-myalgia 10%
Sore throat 12
Headache 15
Diarrhea 14%
OThers: </=10% SOB, Runny Nose, N/V, abdominal pain, loss of taste/smell

10-19yrs
-fever 35%
-cough 41%
SOB 16%
Myalgia 30%
Sore throat 29%
Headache 42%
Diarrhea 14%
Others: runny nose, abdominal pain, loss of smell/taste

Uncommon presentations

Uncommon presentations include a case presentation of a patient who tested positive for SARS-CoV-2 with severe thrombocytopenia and wet purpura in the setting of suspected ITP.

https://pediatrics.aappublications.org/content/pediatrics/early/2020/05/19/peds.2020-1419.full.pdf

Vertical transmission

Coronavirus Disease 2019 (COVID-19) in Children: Vulnerable or Spared? A Systematic Review
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7305578/

- There is no confirmed data yet regarding the vertical transmission of COVID-19