COVID-19 LITERATURE BRIEFING
April 14th, 2021: #78

Children's MINNESOTA

Reference(s) of the Week

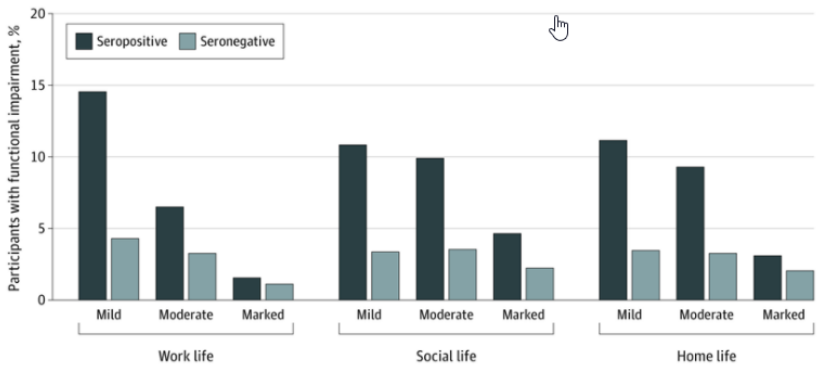
- Bullard J. Infectivity of severe acute respiratory syndrome coronavirus 2 in children compared with adults. Canadian Medical Association Journal. 04.09.2021. https://www.cmaj.ca/content/early/2021/04/09/cmaj.210263 pdf
  Premise/Methods: 1. The role of children in the transmission and community spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is unclear. **2.** Nasopharyngeal swabs were obtained from adult and pediatric cases of coronavirus disease 2019 (COVID-19) and from their contacts who tested positive for SARS-CoV-2 in Manitoba between March and December 2020. **3.** Age stratified comparisons were made of viral growth in cell culture, cycle threshold values from the reverse transcription polymerase chain reaction (RT-PCR) of the SARS-CoV-2 envelope (E) gene and the 50% tissue culture infective dose (TCID50/mL) between adults and children.
  Findings: 1. 97 positive SARS-CoV-2 PCR samples were from children aged 10 years or younger, 78 were from children aged 11–17 years and 130 were from adults (≥ 18 yrs.). **2.** Viral growth in culture was present in 31% of samples, including 18 (19%) samples from children 10 years or younger, 18 (23%) from children aged 11–17 years and 57 (44%) from adults. **3.** The cycle threshold was 25.1 (95% CI 17.7– 31.3) in children 10 years or younger, 22.2 (95% CI 18.3–29.0) in children aged 11–17 years and 18.7 in adults. **4.** The median TCID50/mL was significantly lower in children aged 11–17 years (316, interquartile range [IQR] 178–2125) than adults (5620, IQR 1171 to 17 800, $p < 0.001$).

Compared with adults, children with nasopharyngeal swabs that tested positive for SARS-CoV-2 were less likely to grow virus in culture, and had higher cycle thresholds and lower viral concentrations, suggesting that children are not the main drivers of SARS-CoV-2 transmission. Unfortunately, this information was not available at the start of the pandemic when it was presumed that SARS-CoV-2 resembled influenza in terms of childhood transmission resulting in early school closure.

Other References:

- Havervall S. Symptoms and Functional Impairment Assessed 8 Months After Mild COVID-19 Among Health Care Workers. JAMA network. 04.07.2021. https://jamanetwork.com/journals/jama/fullarticle/2778528 pdf
  Premise/Methods: 1. Approximately 80%of hospitalized patients with COVID-19 report persistent symptoms several months after infection onset but prolonged symptoms in patients with mild disease is not well studied. **2.** Swedish HCWs were invited to participate in a study that focused on seropositive individuals who experienced mild COVID-19. **3.** At the 8-month follow-up (January 11-29, 2021), participants reported via smartphone app the presence, duration (<2 months, ≥2 months, ≥4 months, ≥8 months), and severity (mild, moderate, or severe) of 23 predefined symptoms. **4.** For participants reporting at least 1 symptom persistent for at least 2 months, the Sheehan Disability Scale was used to score functional impairment from present or prior long-term symptoms (0, not at all; 1-3, mild; 4-6, moderate; and 7-10, marked) in 3 interrelated domains (work, social, and home life).
  Findings: 1. 323 seropositive and 1,072 participants completed the 8 month follow-up: seropositive participants who reported no or mild prior symptoms had a median age of 43 (IQR 33-52) years and 268 (83%) were women similar to the seronegative participants; and underlying disease existed in 22% and 24% of seropositive and seronegative participants respectively.
  2. The results of this study showed that a considerable portion of low-risk individuals with mild COVID-19 reported a diversity of long-term symptoms, and that these symptoms disrupted work, social, and home life.

Figure. COVID-19–Related Long-term Functional Impairment



Now we know that individuals with mild COVID-19 are at risk of intermediate term sequelae. Symptoms are for the most part of mild to moderate severity and relatively low frequency but this study underscores the difference of SARS-CoV-2 from other predominantly respiratory viral infections.

- Adelman MW. Secondary Bacterial Pneumonias and Bloodstream Infections in Patients Hospitalized with COVID-19. Annals of American Thoracic Society. 04.05.2021. https://www.atsjournals.org/doi/abs/10.1513/AnnalsATS.202009-1093RLhttps://www.atsjournals.org/doi/abs/10.1513/AnnalsATS.202009-1093RL pdf
  Premise/Methods: 1. Initial reports of patients hospitalized with COVID-19 indicated that 10-33% develop bacterial pneumonia and 2-6% develop bloodstream infections. **2.** This is a descriptive study to identify the prevalence, microbiology, and outcomes of secondary pneumonias and BSIs in patients hospitalized with COVID-19. **3.** PCR + patients hospitalized from 02/15 – 05/16/2020 from 4 adult Atlanta hospitals affiliated with Emory University were included for data extraction.

  Findings: 1. 774 COVID-19 hospitalized patients were included in the study: median age 62 years (IQR 50-73); 49.7% female and 66.6% Black; 75.5% hypertension and 45.7% diabetes mellitus; 335 (43%) required ICU; 238 (30.7%) required mechanical ventilation; and 120 (15.5%) died. **2.** Among non-intubated patients limited respiratory microbial diagnostics were performed and few pathogens isolated (1-staph aureus). **3.** Among 201 intubated patients with respiratory cultures 65 (27.3%) had a positive culture: s aureus 34.5%; p aeruginosa 19%; klebsiella 16.7%; and 1 with aspergillus. **4.** 4.7% (36/588) cultured patients had a non-contaminant BSI: s aureus 16.7%; candida 16.7%; coag negative staph 11.9%; and 28.6% were gram negative. **5.** Isolation of a respiratory bacterial/fungal pathogen had no effect on mortality whereas mortality was 50% in patients with BSI versus 13.8% without (p<0.0001).
  This study determined that secondary bacterial/fungal infections were more related to hospitalization and intensive care than any intrinsic risk associated with COVID-19.

- Pfizer. Pfizer and BioNTech Confirm High Efficacy and No Serious Safety Concerns Through Up to Six Months Following Second Dose in Updated Topline Analysis of Landmark COVID-19 Vaccine Study. Press Release.04.01.2021. https://www.businesswire.com/news/home/20210401005365/en/
  Subject: Efficacy and safety under "real world conditions" measured 7 days up to 6 months after the second dose:
  1. 12,000 vaccinated participants having at least 6 months follow-up after their second dose in more than 46,307 participants 16 years and older.
  2. Vaccine was 100% effective in preventing COVID-19 cases in South Africa where the B.1.351 strain is present.
  3. 927 confirmed symptomatic cases of COVID-19: 850 cases in the placebo group and 77 cases in the vaccination group for an efficacy of 91.3%.
  4. The vaccine is 100% efficacious against severe disease by CDC definition and 95.3% efficacious by FDA definition.
  5. No serious safety concerns were observed in trial participants up to six months after the second dose. Side effects were generally consistent with previously reported result.

- Faqihi F. Therapeutic plasma exchange [TPE] in patients with life-threatening COVID-19: a randomized control clinical trial. Int J of Antimic Agents. 04.07.2021. https://www.sciencedirect.com/science/article/pii/S0924857921000716
  Premise/Methods: 1. Apart from dexamethasone, therapies with major impact on the course of hospitalized COVID-19 are lacking. **2.** TPE hypothetically could suppress cytokine release syndrome, ameliorate thrombosis, and lessen multisystem organ failure. **3.** This single center, open label, randomized clinical study enrolled critically ill COVID-19 patients admitted to King Saud Medical City (Riyadh, Saudi Arabia) between July 1 and October 1, 2020. **4.** Inclusion criteria included intubated adults with life-threatening COVID-19 with the primary outcome being mortality 35-days post ICU-admission and the safety of TPE in life-threatening COVID-19.
  Findings: 1. 87 critically ill COVID-19 patients were randomized to the TPE group or control group in a 1:1 fashion: mean age 49 years (IQR: 34-63); 82.8% males with median BMI 26 (IQR: 21-31); and there were no significant differences within PaO2/FiO2, age, sex, BMI, comorbidities, symptom onset, or APACHE II/SOFA scores. **2.** The duration of MV (p = 0.007) and ICU stay (p = 0.02) were significantly lower in the TPE group versus controls. The mortality on day 35 post-ICU admission was lower in the TPE group (20.9%) compared to the control group (34.1%), but did not reach statistical significance (p = 0.09). **3.** There were no adverse events recorded in either group. Specifically, TPE patients did not experience any allergic reactions, fever, coagulopathy, cardiac and/or renal failure.
  This initial study with limited numbers suggests that TPE unlike convalescent plasma has a beneficial effect not through antibody infusion but removal of inflammatory and pro-coagulant factors. Similar preliminary findings have been seen in patients with septic shock and early multi-system organ failure without COVID-19.