BCM Infectious Disease COVID19 Literature Review Newsletter: WEEK 12
June 15th-June 19th, 2020

Week 12 Newsletter Prepared by:
1Amy Spallone, MD @A_Spallonii
2Margaret Taylor, MD
2Catherine Foster, MD
1Alison Robins, MD @Bacteri_Al
1,2,3Jill Weatherhead, MD @JillWeather

1Department of Medicine, Section of Infectious Diseases, Baylor College of Medicine, Houston, TX
2Department of Pediatrics, Section of Infectious Diseases, Baylor College of Medicine, Houston, TX
3National School of Tropical Medicine, Baylor College of Medicine, Houston, TX

<table>
<thead>
<tr>
<th>Data Source</th>
<th>Last Updated</th>
<th>COVID-19 cases in Texas</th>
<th>COVID-19 cases in Harris County</th>
<th>COVID-19 related deaths in Texas</th>
<th>COVID-19 related deaths in Harris County</th>
<th>Total tests performed a</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Texas DSHS a</td>
<td>June 18, 2020, 4:15 PM</td>
<td>99,851 (Active cases: 33,834)</td>
<td>18,157</td>
<td>2,105</td>
<td>298</td>
<td>1,576,925 Texas</td>
</tr>
<tr>
<td>2. Johns Hopkins a</td>
<td>June 19, 2020, 5:33 AM</td>
<td>101,259 (Active cases: 37,447)</td>
<td>18,552</td>
<td>2,129</td>
<td>N/A</td>
<td>1,407,741 Texas</td>
</tr>
</tbody>
</table>

a DSHS updated the method of reporting COVID-19 cases in Texas on March 24, 2020 to provide the public with more timely information. The DSHS daily case count now includes all cases reported publicly by local health departments around the state.

b Data sources from WHO, CDC, ECDC, NHC, DXY, 1point3acres, Worldometers.info, BNO, state and national government health departments, and local media reports.

c Data represents total tests from private and public labs in Texas, unless otherwise stated. N/A = not available
COVID-19 Literature Review Newsletter Volume #31
Pediatric Infectious Disease Fellow: Margaret Taylor, MD
Pediatric Infectious Disease Faculty: Catherine Foster, MD & Jill Weatherhead, MD
June 15th, 2020

Vaccine Update:
- Moderna mRNA-127:
  - Moderna mRNA-1273 is currently in Phase II (Started May 29th, 2020).

Articles:

Background:
Early reports of children with COVID-19 infection describe higher rates of asymptomatic cases or mild-moderate respiratory illnesses compared to adults
  o Data in United States are lacking

Methods:
• Patients were identified from Texas Children’s Hospital Infection Control and Prevention line list:
  o March 10-April 18, 2020
  o Positive nasopharyngeal swabs for SARS-CoV-2 by RT-PCR
  o 3 hospitals (TCH Medical Center, West campus, Woodlands), 11 urgent care centers, and 50 Texas Children’s Pediatrics clinics in Houston, TX
• Demographic data, clinical outcomes, laboratory and radiographic findings, and rates of viral co-infections were recorded

Results:
• 57 children identified March 10-April 18, 2020
  o 30/57 (53 %) in ambulatory setting, 19/57 (33 %) ED, 8/57 (14 %) hospitalized
  o Median age 10.7 yrs (range 0.1-20.2 years)
• 54 % had laboratory-confirmed COVID-19 household contact
• Most patients (83 %) presented with either fever or cough
  o Fever reported in 53 % ambulatory, 90 % ED, and 25 % hospitalized patients
• Most common underlying conditions were asthma (7/57) and sickle cell disease (4/57)
  o All hospitalized patients (N = 8) had additional diagnoses:
    ▪ 2 with DKA
    ▪ 1 vaso-occlusive crisis
    ▪ 1 acute chest syndrome
    ▪ 1 asthma exacerbation
    ▪ 1 hypernatremia with altered mental status
    ▪ 1 reactive arthritis
    ▪ 1 appendicitis
• 19/57 (33 %) had testing for other viral pathogens:
  o 3/19 (15.7 %) w/ co-viral pathogens: 1 rhinovirus, 2 human metapneumovirus
• Outcomes of 8 hospitalized patients
  o Median length of stay = 2 days (range 1-10 days)
  o 4/8 (50 %) required supplemental oxygen via nasal cannula
  o No mechanical ventilation, no deaths
  o None treated with antiviral therapeutic agents
Conclusions:

- Most children presented in the ambulatory setting and were mildly symptomatic
  - Fever (61%) and cough (67%) were the most frequently reported symptoms
- Approximately half of cases had known household exposure to COVID-19
- Hospitalized patients had underlying medical conditions and generally did well
  - No mechanical ventilation needed
  - No antiviral treatment used
  - No deaths
- **Impact:** Mild disease presentation in children may mean that reopening daycares and schools could significantly impact disease transmission and community spread
- **Limitations:** Small retrospective cohort study conducted during early quarantine phase in Houston, TX over 5 weeks
https://hosppeds.aappublications.org/content/early/2020/06/06/hpeds.2020-000208?cct=2287

Background:
• Prior reports of children infected with SARS-CoV-2 suggest milder disease course compared to adults
  o Data in the UK are lacking

Methods:
• Retrospective case series of hospitalized patients with positive PCR for SARS-CoV-2 from March 14-April 24, 2020
• Demographic, clinical, laboratory, and radiological data were obtained

Results:
• 45 children hospitalized during study period (12% positivity rate, 45/389 children)
  o Median age 3.5 years (range 0.7-12 years)
• Fever (67 %) and cough (55 %) were most common symptoms
• Most (29/45, 64 %) hospitalized children had other medical conditions
  o 44 % were “extremely vulnerable” – ie receiving chemotherapy, s/p stem cell transplant, CF, severe asthma, inborn error of metabolism, receiving immunosuppressive meds, etc
• Lab findings:
  o CRP >10 mg/L in 19/28 (68 %)
  o Lymphopenia (<1.2 x 10⁹/L) in 9/40 (23 %), but possibly related to other medical conditions in 6/9
• Clinical outcomes:
  o 9/45 (20 %) supplemental oxygen (5 simple nasal cannula, 2 high flow nasal cannula, 1 NIPV, 1 mechanical ventilation)
  o Median length of stay 3 days (range 2-7 days)
  o None with multi-system hyperinflammation, Kawasaki disease, or shock
  o No deaths

Conclusions:
• Most hospitalized children had mild disease course, including those with significant co-morbidities and considered “extremely vulnerable”
• Fever (67 %) and cough (55 %) were most common symptoms
• Limitations: small case series conducted over 6-week time period in UK, did not examine outcomes or incidence of children seen in ambulatory or ED settings, did not do contact tracing of households

Additional Resources:
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7235572/

COVID-19 Literature Review Newsletter Volume #32
Infectious Disease Fellows: Amy Spallone, MD and Alison Robins, MD
In the News: RECOVERY Trial demonstrates dexamethasone reduces death by up to one third in hospitalized patients with severe respiratory complications of COVID-19. Published June 16th, 2020.

https://www.recoverytrial.net/files/recovery_dexamethasone_statement_160620_v2final.pdf

- Data not yet published
- Reduced death in ventilated patients (rate ratio 0.65) and patients receiving oxygen only (rate ratio 0.80) but had no impact on patients who did not require respiratory support

Articles:


https://academic.oup.com/ofid/article/7/6/ofaa199/5851740

Background:

• The true community burden of COVID-19 is unknown due to mild infections and inadequacies in testing
• Common symptoms of COVID-19 include fever, cough, dyspnea, malaise, myalgia, and GI disturbance.
• Olfactory dysfunction (OD) has been reported in COVID-19 patients
• This study aimed to quantitate OD in COVID-19 patients and compared to healthy controls

Methods:

• This study was an observational cohort study conducted at Queen Mary Hospital and Pamela Youde Nethersole Eastern Hospital in Hong Kong
• Patients were between 18-60 years old admitted with mild (did not require supplemental oxygen) COVID-19 infections
  o COVID-19 was diagnosed by RT-PCR from nasopharyngeal and throat swabs
• All patients received standard of care and were compared in a 1:1 ratio with healthy, age-matched controls (volunteer student or healthcare providers with no symptoms of upper respiratory infections).
• Quantitative assessment of olfactory function was screened with the butanol threshold test (BTT) and each participant received a final average score of both nostrils.
  o The smell identification test (SIT) was performed as a confirmatory and discriminatory test of olfactory function
• Patients with COVID-19 patients with OD received CT scans of the sinuses and chest and given a score of rhinosinusitis per the Lund-Mackay (LM) score.
• Nasoendoscopy was performed on COVID-19 patients with OD and biopsy was obtained at the discretion of the surgeon.

Results:

• 18 patients and 18 controls were enrolled in this study, demographic were similar between groups
• Olfactory symptoms were reported in 67% of COVID-19 patients compared with 0/18 controls (P < 0.001).
• Median time from symptoms onset to olfactory symptoms was 0.5 days (IQR 0 – 4.75 days).
  o Two patients were asymptomatic except for impaired sense of smell
• Mean BTT of COVID-19 patients was 4.1 (SD = 2.2), the controls were 5.9 (SD = 1.1) \((P = 0.004; \text{differences in means 1.8 with 95\%CI = 0.6 — 2.9)}.\)
  o Younger COVID-19 patients (<22 years) performed worse in the BTT compared to other age groups \((P = 0.002)\) and controls \((P = <0.001).\)
• CT was performed in 6 patients with confirmed OD but no radiologic evidence of sinusitis was found.
• No endoscopic evidence of obstruction, polyps, or sinusitis was found.
  o Biopsies were performed in 3 patients, 1 specimen was positive for SARS-CoV-2 by RT-PCR, H&E staining showed minimal inflammatory changes

Conclusions:
• OD is a characteristic symptom of COVID-19, which was reported in a significant number (67%) \(o\) The authors found that a subset of patients suffered from profound OD in the absence of typical respiratory and systemic symptoms.
• Etiology of OD in COVID-19 patients remains unknown as mechanical obstruction and inflammation of the nasal mucosa was not found to be significant in this cohort.
• Alternative hypothesis is direct invasive of the olfactory neurons by SARS-CoV-2
• Limitations: small sample size, nasal biopsy and imaging was not performed on all patients, and biopsies did not include assessment of olfactory neuroepithelium.


Background:
• Neurologic symptoms have been reported in patients with COVID-19, including headache, altered mental status, and anosmia

Methods:
• Standard autopsy with brain sampling of 18 patients with SARS-CoV-2
• Patients were hospitalized and died between April 14 and April 29, 2020
  o All had positive RT-PCR for SARS-CoV-2 from nasopharyngeal swabs

Results:
• 78\% male, median age of 62, 67\% with diabetes mellitus, 61\% with hypertension, 27.8\% with cardiovascular disease, 27.8\% with hyperlipidemia, 22.2\% with chronic kidney disease, 22.2\% with prior stroke, and 22.2\% with dementia
• Median hospital length of stay prior to death was 6 days with 61\% of patients receiving mechanical ventilation, with median 2 days of symptoms prior to hospital presentation
• Atherosclerotic disease was present on autopsy in 77.8\% of patients, without findings of acute stroke, herniation, or olfactory bulb damage
• 100\% of patients had findings of acute hypoxic injury, without thrombi or vasculitis
• RT-PCR for SARS-CoV-2 was performed in varying numbers of samples between patients, and was detected in 5 patients (3 sections of the medulla and 3 sections from the frontal lobes and olfactory nerves), with equivocal results in 2 patients
  o Immunohistochemical stains were negative

Conclusion:
• The predominant finding on neuropathologic exam on patients who died from COVID-19 was acute hypoxic injury but no evidence of encephalitis or other specific brain changes secondary to the virus
• Although there was SARS-CoV-2 detected by RT-PCR in 5 patients, immunohistochemical staining was negative.
• Limitations: small sample size, few patients presented with neurologic symptoms which may impact results.