BCM Infectious Disease COVID19 Literature Review Newsletter: WEEK 11
June 8th-June 12th, 2020

Week 10 Newsletter Prepared by:
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<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</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Texas DSFH</td>
<td>June 11, 2020, 10:30 PM</td>
<td>81,583 (Active cases: 25,567)</td>
<td>15,552</td>
<td>1,920</td>
<td>274</td>
<td>1,370,131 Texas</td>
</tr>
<tr>
<td>2. Johns Hopkins</td>
<td>June 12, 2020, 11:33 AM</td>
<td>82,658 (Active cases: 28,562)</td>
<td>15,864</td>
<td>1,930</td>
<td>N/A</td>
<td>1,206,320 Texas</td>
</tr>
</tbody>
</table>

1 DSFH updated the method of reporting COVID-19 cases in Texas on March 24, 2020 to provide the public with more timely information. The DSFH daily case count now includes all cases reported publicly by local health departments around the state.
2 Data sources from WHO, CDC, ECDC, NHC, DXY, 1point3acres, Worldometers.info, BNO, state and national government health departments, and local media reports.
3 Data represents total tests from private and public labs in Texas, unless otherwise stated. N/A = not available

Source: County health authorities, Houston Chronicle reporting
Please see: CDC Considerations for Youth Sports, Youth Summer Camps and Public pools/water playgrounds during COVID-19

Articles:

Background:
- Convalescent Plasma Therapy
  - Treat patients with infections using plasma collected from recovered patients
  - Used previously in SARS, MERS, Ebola
- Case series from China (Shen, 03/2020; Duan, 04/2020) reported improved outcomes
- US Food and Drug Administration approved the emergency use of convalescent plasma for patients with severe or life-threatening COVID 19
- Limitations: No standardization or evidence-based rationale for --
  - Donor selection
  - Quality control of convalescent plasma
  - Recipient transfusion indications

Methods:
- Open-label, randomized (1:1, stratified based on severity, block randomization) clinical study done from Feb. 14, 2020 - April 1, 2020 at 7 medical centers in China
- Convalescent Plasma with Standard of Care vs Standard of Care Only (antivirals, steroids, human immunoglobulin, antibacterial medications, Chinese herbal medications)
- Limited to severe and life-threatening COVID-19 cases
  - Severe COVID-19
    - Respiratory distress ≥30 breaths/min; in resting state
    - Oxygen saturation of 93% or less on room air; or arterial partial pressure of oxygen (PaO₂)/fraction of inspired oxygen (FiO₂) of 300 or less
  - Life-threatening COVID-19
    - Respiratory failure requiring mechanical ventilation
    - Shock; or other organ failure (apart from lung) requiring intensive care unit (ICU) monitoring
- Procurement of Convalescent Plasma = Laboratory-confirmed COVID-19 diagnosis, who had fully recovered and been discharged from the hospital for more than 2 weeks with a S-RBD-specific IgG antibody titer of at least 1:640
  - Positive correlation between the SARS-CoV-2 viral neutralization titer and the S-RBD-specific IgG titer (r = 0.622, P = .03)
The study was terminated early (March 2020) due to a drop of the number of COVID-19 at Wuhan

**Results:**

- 103 patients were enrolled in RCT
- Median interval between the onset of symptoms and randomization = 30 days (IQR, 20-39 days)

**PRIMARY ENDPOINTS:**

- Time to clinical improvement with 28 days
  - Patient discharged or a reduction of 2 points in a 6 point disease severity scale ranging from 6 - Death to 1 - Hospital Discharge
  - There was *no significant difference* in the time to clinical improvement [51.9% (27/52) in the convalescent plasma group vs 43.1% (22/51) in the control group; P = .26].
    - Signal of possible clinical benefit for convalescent plasma among patients with **severe COVID-19** [in the convalescent plasma group, primary outcome happened in 91.3% (21/23) vs 68.2% (15/22) in the standard of care group P = .03; HR, 2.15 [95% CI, 1.07-4.32]).
      - BUT the test for interaction by disease severity was not statistically significant, so the findings for the severe and life-threatening subgroups should not be interpreted as different.

**SECONDARY ENDPOINTs:**

- 28 Day Mortality = There was *no significant difference* [15.7% in the convalescent plasma group vs 24.0% in the control group; P = .30]
- Duration of hospitalization = There was *no significant difference* [(51.0% in the convalescent plasma group vs 36.0% in the control group were discharged by day 28; P = .12)]
- Negative conversion of nasopharyngeal swab viral PCR results
  - Convalescent plasma treatment was associated with **HIGHER rates of negative SARS-CoV-2 viral PCR results** from nasopharyngeal swabs at 24, 48, and 72 hours
  - Convalescent plasma versus Standard of Care only (44.7%vs 15.0%, P = .003 at 24 hours; 68.1% vs 32.5%, P = .001 at 48 hours; 87.2%vs 37.5%, P < .001 at 72 hours)
- **ADVERSE EVENTS:** 2 adverse events happened, one was a definite non-severe allergic transfusion reaction and another was a possible severe transfusion associated dyspnea

**Conclusions:**

- Among patients with severe or life-threatening COVID-19, convalescent plasma therapy added to standard treatment, compared with standard treatment alone, did not significantly improve the time to clinical improvement within 28 days.
Convalescent plasma treatment was associated with higher rates of negative COVID19 NP tests, but the effect was not seen clinically.
Limitations: early termination of study, small samples, delayed initiation of treatment (average 30 days after symptom onset)


Background:
- Detection of SARS-CpV-2 in asymptomatic individuals suggests subclinical active infection may be important in viral transmission
- Understanding cumulative prevalence of SARS-CoV2 infection using the presence of antibodies will help understand the epidemiology of the outbreak

Methods:
- Test: IgM and IgG antibody using recombinant antigen containing nucleoprotein, spike peptide
  - Internally validated:
    - 447 patients with end-stage kidney disease (samples from June 2019), 100% specificity for IgM and IgG antibodies
    - 242 patients COVID-19 confirmed by RT-PCR, cumulative seroprevalence of IgM and IgG 95% on day 20 post symptom onset
- Population: 17,368, four different geographic locations in China between March 9th-April 10th, 2020
- Cross-section, seroprevalence study

Results:
- Wuhan (Hubei Province) Seroprevalence: healthcare workers 3.8%, hotel staff members 3.8%, family members of healthcare workers 3.2%
- Jinzhou and Honghu (Hubei Province) Seroprevalence: healthcare workers 1.3%, hospital visitors for routine hemodialysis 3.6%
- Chongqing (further west of Wuhan) Seroprevalence: healthcare workers 3.1-3.8%
- Chengdu (Sichuan Province) Seroprevalence: community residents 0.58%
- Guangzhou and Foshan (south of Wuhan) Seroprevalence: patients undergoing hemodialysis 2.8%, healthcare workers 1.2%, factory workers 1.4%

Discussion
- Seropositive rates in different geographic areas were consistent with early SARS-CoV-2 spread
- Limitations: sampling were not randomly selected leading to sampling bias, cross-sectional design could have missed individuals who had not developed antibody yet, outbreak was contained early so results may not be reflective of impact in other areas of the world, assay was not externally validated

COVID-19 Literature Review Newsletter Volume #30
Infectious Disease Fellows: Amy Spallone, MD
Faculty: Jill Weatherhead MD
June 12th, 2020
In the News: Lung Transplant for COVID-19 Patient Performed in US

Articles:
https://www.thelancet.com/journals/lanhiv/article/PIIS2352-3018(20)30164-8/fulltext

Background:
- Information about the incidence, clinical characteristics, and outcomes of HIV-infected individuals with SARS-CoV-2 infection is scarce.
- HIV-infected individuals might represent a population at increased risk of SARS-CoV-2 infection or severe disease.
- Regular use of ART (protease inhibitors[PI], nucleoside reverse transcriptase inhibitors [NRTI], or non-nucleoside reverse transcriptase inhibitors[NNRTI]) might modify infection with SARS-CoV-2 and clinical presentation in this population

Methods:
- This study was an observational prospective study conducted at a Hospital Universitario Ramón y Cajal in Madrid, Spain
- Inclusions: adult patients with HIV who had suspected or confirmed COVID-19 as of April 30, 2020.
- Compared HIV-patients with COVID-19 to a historical cohort (n=1288) of HIV-patients that were described before the pandemic.

Results:
- 51 out of 2873 HIV-infected adult patients with COVID-19 (69% lab confirmed). The population was predominantly middle-aged males (84%). More than half of the patients (55%) required hospitalization.
- CD4 and age was similar to the historic control; however, 63% with COVID-19 has at least one comorbidity (HTN, DM2, chronic liver disease, chronic kidney disease) compared to 38% in the control group (p-value 0.00059).
- In a post-hoc analysis on lab-confirmed cases, higher BMI, comorbidities, and the use of tenofovir before COVID-19 pandemic were associated with diagnosis of COVID-19.
- Clinical, analytical, and radiological presentations of COVID-19 in HIV-infected individuals was similar to that described in the general population.
- Six patients were critically ill, two had CD4 <200 cells/μL, and two died.
  - Age, gender, comorbidities, ART regimen and years of HIV infection were not significantly different from patients with non-critical disease
- SARS-CoV-2 RT-PCRs remained positive after median of 40 days from symptoms onset in 6 patients (32% of PCR positive patients)
  - Most of the patients in this group had severe disease or low CD4 counts

Conclusions/Limitations:
- Patients with HIV who contract COVID-19 should receive the same treatment and management approach as the general population.
- Small numbers, observational study. More robust studies are needed.

Background:
- Few data available are available on COVID-19 in younger, healthier persons in the US.
- In March 2020, the USS Theodore Roosevelt arrived at port in Guam after numerous US service members onboard developed COVID-19. 1000 service members were determined to be infected with SARS-CoV-2.
- The outbreak was characterized by widespread transmission with relatively mild symptoms and asymptomatic infection among the convenience sample of young, healthy adults occupying close quarters.

Methods:
- 382 service members were evaluated between April 20th-24th, 2020 (27% of the 1417 service members)
  - Collected serum and NP swab (70%) when available
- Participants completed a questionnaire eliciting information on the following: demographics, exposure, COVID-19 protective behaviors, health history, and symptoms
  - Participants also reported whether they had had a previous positive COVID-19 test since deployment but before this investigation.

Results:
- 382 service members voluntarily completed questionnaires and provided serum specimens.
  - 75% males, median age 30 years old (IQR: 24-35 years), 58.4% non-Hispanic white, 7.3% reported medical history of asthma, diabetes, or immunosuppression.
  - 1/3 of participants reported fever, myalgia, and chills.
  - Participants reporting anosmia (loss of sense of smell) or ageusia (loss of sense of taste) had 10 times the odds of having infection, compared with those who did not.
- 228 (59.7%) had positive ELISA, among these 135 (59.2%) had positive microneutralization test.
Prevalence of previous or current infection was higher among participants who:
- reported contact with someone known to have COVID-19 (64.2%), compared with those who did not (41.7%) (OR = 2.5; 95% CI = 1.1–5.8).
- reported sharing the same sleeping berth with a crewmember who had positive test results (65.6%), compared with those who did not (36.4%) (OR = 3.3; 95% CI = 1.8–6.1).

Service members who reported taking preventive measures had a lower infection rate than did those who did not report taking these measures:
- wearing a face covering, 55.8% versus 80.8%
- avoiding common areas, 53.8% versus 67.5%
- observing social distancing, 54.7% versus 70.0%

Discussion
- In this convenience sample of young, healthy U.S. service members experiencing close contact aboard an aircraft carrier those with COVID-19 experienced mild illness overall, and nearly 20% were asymptomatic.
• The presence of neutralizing antibodies against SARS-CoV-2 among the majority (59.2%) of those with antibody responses is a promising indicator of at least short-term immunity.
• Limitations:
  • Convenience sampling, self-reporting, and increased likelihood of selection and recall bias were the primary limitations of this paper.