BCM Infectious Disease COVID19 Literature Review Newsletter: WEEK 9
May 25th-May 29th, 2020

Week 9 Newsletter Prepared by:
1Amy Spallone, MD @A_Spalloni
1Melanie Goebel @MelanieGoebelMD
1Alison Robinson, MD @Bacteri_Al
1Dierdre Axell-House @AxellHouse
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

The number of COVID-19 confirmed cases, related deaths, and total tests reported for State and County

<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 DSHS</td>
<td>May 28, 2020, 3:30 PM</td>
<td>59,776</td>
<td>11,542</td>
<td>1,601</td>
<td>223</td>
<td>873,218 Texas</td>
</tr>
<tr>
<td>(Active cases: 52,710)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>2. Johns Hopkins</td>
<td>May 29, 2020, 5:32 AM</td>
<td>60,416</td>
<td>11,770</td>
<td>1,611</td>
<td>N/A</td>
<td>873,218 Texas</td>
</tr>
</tbody>
</table>

*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.

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

1 Data represents total tests from private and public labs in Texas, unless otherwise stated. N/A = not available

COVID-19 in the greater Houston area

Source: County health authorities, Houston Chronicle reporting
COVID-19 Literature Review Newsletter Volume #25
Infectious Disease Fellows: Alison Robins, MD and Dierdre Axell-House, MD
Faculty: Jill Weatherhead, MD
May 27th, 2020

Looking for COVID Simulations? Check out NEJM Covid-19 Rx: Treatment Simulations

Articles:
https://www.thelancet.com/action/showPdf?pii=S0140-6736%2820%2931180-6

Background:
- Multiple drugs have been shown to have antiviral properties in vitro, including hydroxychloroquine and chloroquine
- Current in vivo data is limited and inconclusive
- These drugs have been combined with azithromycin, with associated QTc prolongation

Methods:
- Multinational registry to assess use of hydroxychloroquine or chloroquine +/- a macrolide through the Surgical Outcomes Collaborative, a cloud-based health-care data analytics platform which collects data at predetermined intervals from 671 hospitals in 6 continents
- Data collection occurred from Dec 20, 2019 – April 14, 2020 and included hospitalized patients with PCR-confirmed COVID-19 with an available clinical outcome (hospital discharge or death)
- Treatment group: patients who received hydroxychloroquine or chloroquine with or without a macrolide
- Exclusion criteria: negative COVID-19 PCR, treatment initiation after 48h of diagnosis, receipt of Remdesivir, on mechanical ventilation at the time of treatment initiation
- Primary outcome: association of the four treatment regimens with in-hospital mortality
- Secondary outcome: association of the four treatment regimens and clinically significant ventricular arrhythmias during hospitalization, progression to mechanical ventilation, ICU length of stay (LOS)

Results:
- Patient characteristics: 96,032 patients met inclusion, included a total of 14,888 patients within the 4 treatment group (chloroquine only, chloroquine + macrolide, hydroxychloroquine only, hydroxychloroquine + macrolide) and 81,144 in the control group
  - Median age of 53.8 years
  - 46.3% women
  - Obesity: 30.7%
  - Hyperlipidemia: 31.4%
  - Hypertension: 26.9%
  - Diabetes: 13.8%
  - Coronary artery disease (CAD): 12.6%
  - 40.5% of patients received another antiviral treatment (lopinavir + ritonavir, ribavirin, and oseltamivir were the most common with 17.4% getting combination therapy)
- Overall in-hospital mortality of 11.1% with mean LOS of 9.1 days
- Similar baseline characteristics between groups
Both increased in-hospital mortality and ventricular arrhythmias were independently associated with all of the treatment groups.

Multiple characteristics were independent predictors of in-hospital mortality: age, black race or Hispanic ethnicity, CAD, congestive heart failure, history of arrhythmia, diabetes, HTN, HLD, chronic obstructive pulmonary disease, current smoker, and immunocompromised conditions.

Factors associated with reduced risk of in-hospital mortality: female sex, Asian ethnicity, use of ACE inhibitors and statins.

Conclusions/Limitations:

- Use of hydroxychloroquine and chloroquine do not appear to have clinical benefit in patients admitted to the hospital with COVID-19 and have the potential to cause harm.
- Mortality was associated with increased age, black race or Hispanic ethnicity, and obesity.
- Observational study has high risk for confounding variables.

**Currently there are academic discussions on the validity of this data. Please see most up to date literature discussions regarding this article.**


Background:

- No therapeutic agents have been shown to be efficacious for Covid-19.
- This is the publication of the phase 3 Adaptive Covid-19 Treatment Trial (ACTT-1) preliminary results.

Methods:

- Enrollment dates: 2/21/20 – 4/19/20
- 60 sites in 10 countries
- Randomization of patients 1:1, remdesivir: placebo
- Dosing: 200mg x1, then 100mg daily for 2-10 days.
- Patients were allowed to receive other treatments in use for Covid-19 on hospital’s “guidelines” or “written policy” but not otherwise
- **1st analysis:** stratified log-rank test of time to recovery, remdesivir v. placebo
- **1st outcome (ordinal category 1-7):** time to recovery during the 28* days after enrollment, “recovery” defined as achieving categories 1, 2 or 3
  - 1: Not hospitalized, and no limitations
  - 2: Not hospitalized, but limitation of activities and/or needing supplemental O₂
  - 3: Hospitalized but not requiring supplemental O₂, no ongoing medical care
  - Groups 4-7 are grades of severity (from 4: Hospitalized+No oxygen+Ongoing medical care to 7: Mechanical Ventilation, ECMO)
- **2nd outcomes:**
  - Improvement in clinical status (by ordinal scale of severity) at day 15
  - Mortality at 14 & 28 days after enrollment
  - Grade 3 and 4 adverse events; serious adverse events
*Mid-trial, (blinded) researchers changed original “15 days” to “28 days” due to developing information on the protracted nature of Covid-19 illness*

Results:

- 1107 patients were assessed for eligibility, 1063 were randomized. Adapted Figure 1:

```
1063 Randomized

Remdesivir
541: Assigned
531: Received

Placebo
522: Assigned
518: Received

180 rec’d all 10 doses
251 rec’d <10

391 completed study
132 in middle of study

538 included in analysis

185 rec’d all 10 doses
225 rec’d <10

340 completed study
169 in middle of study

521 included in analysis
```

- **Demographics/Characteristics:** “No substantial imbalances” (no p-values given)
  - 58.9-years-old (mean age)
  - 64.3% male
  - 79.8% in North America
  - 53.2% white / 23.4% Latinx
  - 52.1% had ≥2 medical conditions
  - 88.7% had severe disease

- **Median # days from symptom onset to randomization:** 9 (IQR 6-12)

- **1° Outcome (Table 2, Fig 2):** Patients receiving remdesivir had shorter time to recovery

- **2° Outcomes:**
  - Odds in improvement in ordinal scale were higher in remdesivir group at 15 days
  - No statistically significant difference in mortality between remdesivir (7.1%) and placebo (11.9%) at day 14.

- **Safety Outcomes:**
  - Serious adverse events in 21.1% of remdesivir and 27.0% of placebo group
  - Grade 3 or 4 adverse events occurred in 28.8% of remdesivir and 33.0% of placebo groups

Discussion:

- A 10-day course of remdesivir may be superior to placebo in hospitalized Covid-19 patients
- Primarily supported by decreased time to recovery in remdesivir group
- In subgroup analysis, the benefit was most apparent in hospitalized patients requiring non-high flow oxygen (ordinal score 5), probably due to larger sample size of that category
***Full analysis of the entire trial population is needed and anticipated, significant number of participants had not met end-point

COVID-19 Literature Review Newsletter Volume #26
Infectious Disease Fellows: Amy Spallone, MD and Melanie Goebel, MD
Faculty: Jill Weatherhead, MD
May 29th, 2020


Articles:


Background: Several papers and reports have highlighted COVID-19’s differences in age- and sex-related health outcomes. More information is needed on the racial and ethnic differences in outcomes from COVID-19.

Methods:
- Retrospective, observational, cohort study
- Performed on patients with COVID-19 (+PCR) within an integrated-delivery health system (Ochsner Health) in Louisiana from March 1 – April 11, 2020
- Ochsner Health population: 31% Black non-Hispanic; 65% White non-Hispanic
- Primary Outcomes: hospitalization and in-hospital death in Black non-Hispanic versus White non-Hispanic patients

Results:
- 3,626 patients tested positive for SARS-CoV-2 during the study period
- 84 were excluded due to missing data on race or ethnicity, 9 identified as Hispanic, 52 identified as Asian or other race/ethnic group.
- Demographics (n=3,481 patients): 60% Female, 70.4% Black non-Hispanic; 29.6% White non-Hispanic
  - Black patients were more likely to be obese, have diabetes, hypertension, and chronic kidney disease than white patients
  - Black patients were 3x likely to have Medicaid insurance and 2x likely to live in low-income areas
- Total of 1,382 (39.7%) of COVID-19 positive patients were hospitalized, 76.9% were black
- Total of 326 patients died from COVID-19 during the study period, 70.6% were black non-Hispanic
- Increased Odds of hospitalization due to COVID-19 (multivariate analysis): Black race, increased age, high Charlson Comorbidity Index, public insurance, residence in a low-income area, and obesity.
- Increased risk of in-hospital mortality due to COVID-19 (adjusted time-to-event analysis): Increased age, increased respiratory rate on presentation, elevated blood levels of lactate, creatinine, or procalcitonin, low blood levels of platelets/lymphocyte count.
  - Black race was not independently associated with higher mortality (hazard ratio for death vs. white
race, 0.89; 95% CI, 0.68 – 1.17)

Conclusions
- In a large cohort of COVID-19 patients in Louisiana, 76.9% of those hospitalized and 70.6% of those who died were black however blacks comprise only 31% of the Ochner Health population. 
- More studies are needed to assess the racial and ethnic disparities leading to these outcomes

https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2766227

Background: Healthcare workers (HCW) are at high risk for COVID-19. Transmission from asymptomatic HCW may contribute to nosocomial spread within hospitals.

Methods:
- Single-center retrospective case series of HCW with symptomatic COVID-19 in Wuhan, China
- 335 asymptomatic medical staff were randomly tested for SARS-CoV-2 by nasopharyngeal PCR
  - 135 first-line HCW (worked in fever clinics or wards with COVID patients)
  - 200 non-first-line HCW (cared for non-COVID patients)
- Environmental samples from fever clinics and wards were tested by PCR

Results:
- **110/9684 HCW were diagnosed with COVID-19 (infection rate 1.1%)**
  - Demographics
    - 71.8% women, median age 36 years
    - 56.4% nurses, 23.6% physicians, 20% healthcare assistants
    - 15.5% worked in fever clinics or wards, 66.4% worked in other clinical departments, 18.2% did not interact with patients
    - Factors associated with increased risk of infection: age < 45, nurses, working in clinical department other than fever clinic or wards
    - Infection rate 0.5% among first-line HCW vs 1.6% among other HCW groups (P < 0.001)
  - 60% were infected during early stage of COVID outbreak
- Clinical features
  - 12.7% had comorbidities
  - Median (IQR) incubation period: 5 (3-8) days
  - Most common symptoms: fever (60.9%), fatigue (60%), cough (56%), sore throat (50%), muscle aches (45.5%)
  - 93 (84%) had non-severe disease, 4 (3.6%) had critical illness, 1 (0.9%) died
- Exposure
  - Contact with indexed patients (59%)
  - Contact with infected colleagues (10.9%)
  - Community acquired infection (12.7%)
- Prevalence of asymptomatic infection: 3/335 (0.9%)
  - 1/135 (0.7%) first-line HCW vs 2/200 (1.0%) non-first-line (p=0.81)

Conclusions:
Non-first-line HCW working in “low-contagion” areas had a higher infection rate than first-line HCW. Most infected HCW were young adults with mild disease. Consider routine screening of HCW to identify asymptomatic infection.

Limitations: recall bias, no details about treatment provided, results may not be generalizable to healthcare settings in other count


Background: Initial reports suggested that patients with a history of or active malignancy might be at increased risk of contracting the virus and developing severe COVID-19. There is minimal data describing the impact of COVID-19 on patients with cancer.

Methods:
- Retrospective, COVID-19 and Cancer Consortium (CCC19) registry database, formed March 15th, 2020 to evaluate the clinical characteristics and course of illness among patients with current or past diagnosis of cancer.
- Evaluated patients entered into registry from March 17th-April 16th, 2020 that had follow up data until May 7th, 2020
- Inclusion: confirmed +SARS-CoV-2 by PCR, > 18 years old, invasive or hematologic malignancy at any time and a resident of the USA, Canada, or Spain
- Outcome: all-cause mortality within 30 days of diagnosis

Results:
- 928 patients met inclusion criteria
  - Median age 66 years, 50% male
  - 50% white non-Hispanic, 16% black non-Hispanic, 16% Hispanic
  - Most prevalent malignancies: 82% had solid tumors, 22% had hematologic malignancies (overlap present)
  - 45% remission or no evidence of disease, 60% had not had anti-cancer therapy in the last 4 weeks
- As of May 7th, 2020 13% of patients had died
  - Increased 30-day all-cause mortality (partial adjustment, multivariable model): increasing age, male sex, smoking status, cancer status (present, stable or responding to treatment and present, progressive disease), ECOG performance status, treatment with hydroxychloroquine + azithromycin, >2 co-morbidities (wide CI)

Discussion:
- Increased risk of death in patients with a history of or current cancer associated with active cancer status. Patient’s in remission have lower risk of mortality.
- Limitations: retrospective review, observational nature induces bias, regional differences in cancer care and COVID-related care, preliminary results as analysis of entire cohort has not been completed as of May 7th, 2020