COVID-19 Evidence Digest 12/04/20

NYC HEALTH + HOSPITALS | POPULATION HEALTH

Efficacy and Safety of Favipiravir, an Oral RNA-Dependent RNA Polymerase Inhibitor, in Mild-to-Moderate COVID-19: A Randomized, Comparative, Open-Label, Multicenter, Phase 3 Clinical Trial (Int J Infect Dis)

Bottom Line: Favipiravir may be a safe and effective treatment to improve the time to clinical cure in patients with mild to moderate COVID-19.

Details: This study is a randomized, phase 3 clinical trial of the efficacy and safety of favipiravir as treatment in adults (18-75 years) with PCR-confirmed COVID-19 who are asymptomatic or have mild to moderate symptoms. Participants were randomized to a treatment and control group. The treatment group received oral favipiravir with standard care, while the control group received only standard care. The primary outcome was the time it took to see viral shedding to stop, while the secondary outcome was the time it took to see clinical cure. The treatment and control group each included 75 patients. The median time to see the stop of viral shedding was 5 days in the treatment group versus 7 days in the control group. This was not a significant difference. The median time to clinical cure was significant with 3 days in the treatment group versus 5 days in the control group (p=0.030). Adverse events were observed in 36% of patients who received favipiravir and 8% of control patients. Adverse events that were observed were fairly mild, with increases in asymptomatic transient uric acid and liver enzymes being the most common event.

Key Takeaways:

- Favipiravir may be a safe and effective treatment for those with mild to moderate COVID-19 and may improve time to clinical cure
- Additional clinical trials on Favipiravir as treatment is needed to better understand its effectiveness. It is under investigation in many countries as COVID-19 treatment.

A Randomized Trial of Convalescent Plasma in Covid-19 Severe Pneumonia (NEJM)

Bottom line: Treatment with convalescent plasma showed no effect on 30 day clinical status (ranging from recovery to death) or mortality in hospitalized adult patients with severe COVID-19 pneumonia.

Details: A total of 333 hospitalized adult patients with severe COVID-19 pneumonia were randomly assigned to receive an infusion of convalescent plasma (n=228; median titer of 1:3200 of SARS-Cov-2 antibodies) or placebo (n=105). At 30 days post infusion the patient's clinical status was measured on a six-point qualitative clinical scale ranging from 1-death to 6-discharged with full return to baseline physical function. Patients were enrolled in the study a median of 8 days from the onset of symptoms and the most common severity criterion was hypoxemia. The total SARS-Cov2 antibody titers tended to be higher in the convalescent plasma group when measured 2 days after infusion, but were similar at day 7 and 14. The distribution of clinical status at day 30 for the convalescent plasma group was not significantly different from the placebo group (odds ratio, 0.83 (95% confidence interval [CI], 0.52 to 1.35; P=0.46). The mortality rate for the convalescent plasma group was 10.96% and 11.43% in the placebo group. There was no significant differences in the mortality rates (risk difference of −0.46 percentage points (95% CI, −7.8 to 6.8), and both groups had similar adverse events and serious adverse events.

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Key Takeaways:

- Treatment with convalescent plasma (median titer of 1:3200 of SARS-Cov-2 antibodies) on average after 8 days of symptoms in hospitalized adult patients with severe COVID19 pneumonia showed no effect on clinical status or mortality.
- The total SARS-Cov2 antibody titers tended to be higher in the convalescent plasma group when measured 2 days after infusion, but were no different at day 7 or day 14.

Evidence for treatment with estradiol for women with SARS-CoV-2 infection (BMC Medicine)

Bottom Line: In a retrospective analysis of electronic health records for COVID-19 patients, women >50 years old receiving estradiol therapy had a significantly lower fatality risk (OR 0.33, HR 0.29) than women in the same age group not receiving hormone therapy.

Details: This large, international retrospective analysis included 68,466 COVID-19 cases to examine differences in outcomes based on age, sex, and hormone administration. This study found that overall fatality rate was higher in men than women across all age groups. However, premenopausal women (age <50) were found to have a higher incidence of infection with COVID-19 than age-matched men (about 15% higher). This sex-related difference in infection rates decreased among men and women at ages 65 to 80, where infection rates were similar. In order to assess potential effects of exogenous female sex hormones, sub-cohort analysis was performed for women, examining differences in women aged 15-49 years and >50 years between hormone users and non-users. Among women aged 15-49, the dominant form of estrogen use was oral contraceptives, and no significant difference in survival were found. Among women aged >50 years, most usage was post-menopausal estradiol hormone therapy, and a significant survival benefit was found among hormone users (OR 0.33, 95% CI 0.18-0.62; HR 0.29, 95% 0.11-0.76). It was hypothesized that these observed sex and hormone differences across infection and survival may be due to effects of estradiol on ACE2 (increased expression) and IL-6 (inhibitory effect).

Key Takeaways:

- Pre-menopausal women are at a relatively high risk for COVID-19 infection, but the survival probability in this age group is significantly higher in women than in men
- This retrospective analysis showed a decrease in COVID-19 mortality was associated with post-menopausal estradiol use in women aged >50.
- Prospective studies would be needed to further assess potential protective effects of estradiol.

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Race/Ethnicity among Children with COVID-19–Associated Multisystem Inflammatory Syndrome (JAMA)*

Bottom Line: Findings from this study suggest a disproportionate burden of COVID-19–associated multisystem inflammatory syndrome in children (MIS-C) among Black and Hispanic children in NYC.

Details: This cohort study (n=223 patients) included data reported to the New York City (NYC) Health Department from March 1 to June 30, 2020. The study looked at the incidence rates of hospitalized patients under the age of 20 with MIS-C and COVID-19 by race and ethnicity. The median age was 7 years and 57% (n=127) were male. 22% (n=50) of patients had 1 or more underlying conditions, with asthma and obesity being the most common (14% and 9%, respectively). SARS-CoV-2 infection and/or antibodies against SARS-CoV-2 were found in 79% (n=175) of patients. All other patients (21%) were included based on epidemiological criteria. Race/ethnicity data were available for 83% (n=184) of patients. The incidence rate of MIS-C was 11.4 per 100,000. 34% of children with MIS-C were Black, though they only made up 20% of COVID-19 hospitalizations among patients <20 years and 22% of NYC's population. 30% of MIS-C cases were in Hispanic children, which was similar to the NYC population (36%), and lower than the 40% of Hispanic patients <20 years of age hospitalized with COVID-19. White and Asian/Pacific Islander individuals had lower MIS-C and COVID-19 hospitalization rates (12.8% and 5.5%, respectively, and 13.8% and 3.2%, respectively) relative to their proportion of NYC's population (26.1% and 12.8%, respectively).

Key Takeaways:

- There is a disproportionate burden of MIS-C among Black and Hispanic children compared to White children; however, it is not clear if the burden is unique from the disproportionate burden of COVID-19 also observed.
- Larger studies can help explain the relationship between MIS-C and race/ethnicity and the role of structural racism in exacerbating health disparities.

COVID-19 Infection among People with HIV in New York City: A Population-Level Analysis of Linked Surveillance Data (CID)*

Bottom Line: In this study matching reported COVID-19 cases to people with HIV (PWH) in NYC, a greater proportion of PWH with COVID-19 experienced adverse outcomes compared to COVID-19 cases overall.

Details: This study linked HIV and COVID-19 surveillance data in New York City (NYC) to describe socio-demographic characteristics and clinical outcomes of people with HIV (PWH) with COVID-19 and identify differences in COVID-19 outcomes between people with and without HIV infection. Lab-confirmed COVID-19 case and death data reported to the Health Department were matched against the city's HIV surveillance registry. Of 204,583 COVID-19 cases reported through June 2nd, 2,410 PWH (1.06%) were matched; comparison groups were New Yorkers with COVID-19 (n=202,012) and PWH (n=113,907). Compared to individuals with COVID-19 and PWH, a greater proportion of

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PWH with COVID-19 were male, older, Black or Latino, and living in high-poverty neighborhoods. A higher proportion of PWH with COVID-19 had at least one underlying condition (58.9% (excluding immunodeficiency) vs 35.4% for COVID-19 cases). Compared to all COVID-19 cases, a higher proportion of PWH with COVID-19 were hospitalized (42% vs. 26%), admitted to the ICU (5% vs. 3%), and died (13% vs. 8%). PWH admitted to the ICU or who died had lower CD4 counts (CD4 <500 cells/μL).

Key Takeaways:

- While PWH were not overrepresented among COVID-19 cases in NYC, a greater proportion of PWH with COVID-19 experienced adverse outcomes compared to COVID-19 cases overall; this may be due to PWH in NYC having similar characteristics/experiences to people with COVID-19 who experienced adverse outcomes.
- More research is needed to ascertain whether HIV infection is an independent risk factor for adverse COVID-19-related outcomes.
- Racial/ethnic inequities in the COVID-19 pandemic are echoed in outcomes among PWH with COVID-19, necessitating the need for robust services and support for this population.

Serologic Testing of U.S. Blood Donations to Identify SARS-CoV-2-Reactive Antibodies: December 2019-January 2020 (CID)

Bottom Line: In this study, SARS-CoV-2 antibodies were found in blood donations collected in the US from mid-December to mid-January.

Details: On January 19th, 2020, the first US case of SARS-CoV-2 was identified. In order to determine if antibodies against SARS-CoV-2 were present in blood collected prior to that date, Samples from 7,389 unique donations collected from 12/13/19-1/17/20 in 9 US states were tested at the CDC. Of 7,389 samples, 106 (1.4%) were reactive by pan-immunoglobulin (pan Ig) enzyme linked immunosorbent assay (ELISA) against the virus' spike protein, with the earliest reactive samples collected between 12/13-12/16 from Washington, Oregon, and California. 90/106 underwent further testing to distinguish whether reactivity was to common coronaviruses or SARS-CoV-2; 84/90 (93%) had neutralizing antibody activity against SARS-CoV-2, and 2 others had activity suggesting the presence of antibodies against SARS-CoV-2. These reactive samples were from all 9 states.

Key Takeaways:

- Findings suggest that SARS-CoV-2 may have been introduced into the United States prior to January 19, 2020 or that a small portion of the population has pre-existing antibodies that bind to SARS-CoV-2's spike protein.

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