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3-29-2021

GW Covid-19 Intelligence Reports: March 29, 2021

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Epidemiology and Public Policy

- Mask mandates and restrictions on on-site restaurant dining have been associated with <u>decreases</u> in COVID-19 cases and death rates.
- The CDC published interim <u>public health recommendations</u> for fully vaccinated individuals.
- Student and staff case rates were similar in schools utilizing 3 versus 6 feet of distancing.
- China introduced a <u>digital vaccine passport</u> to track its citizens' international travel.
- The average serial interval of COVID-19 was <u>shown in a systematic review and meta-analysis to be shorter</u> than the average incubation period (5.2 verses 6.5 days, respectively), which suggests that substantial numbers of COVID-19 cases may be attributed to presymptomatic transmission.

Vaccines

First Dose Response

- The <u>first dose</u> of the Pfizer and AstraZeneca vaccines substantially reduced the risk of COVID-19 related hospitalization at 28-34 days post-vaccination in Scotland; effectiveness was 85% and 94% respectively. <u>A single dose</u> of either vaccine was 80% effective at preventing hospitalization; a single dose of the Pfizer vaccine was 85% effective at preventing death. In <u>skilled nursing facility</u> outbreaks, partial vaccination with the Pfizer vaccine was 63% effective against infection.
- The first dose of the Pfizer vaccine resulted in a 30% <u>reduction in COVID-19 infections</u> during the first 1-14 days and a 75% reduction on days 15-28 after vaccination.
- Healthcare workers with prior COVID-19 infection based on serology testing had higher antibody <u>titer</u> <u>responses</u> to a single dose of mRNA vaccine than those who were not previously infected; they generated stronger humoral and cellular responses to one dose of the Pfizer vaccine.

Vaccine Effectiveness

- Vaccinated patients had <u>lower rates of asymptomatic infection</u> in pre-procedural screening and unvaccinated patients (RR=0.44 95% CI: 0.33-0.60; *p*<.0001). The rate of positive molecular tests among asymptomatic post-vaccinated individuals was 1.4% in this study.
- Healthcare workers in Israel who received the Pfizer vaccine had a <u>major reduction in new cases</u>, even when community incidence was high and the B.1.1.7 variant was in up to 80% of cases.

Reactions

- <u>Delayed large local reactions</u> to Moderna vaccine have been seen 4-11 days after the first dose.
- 2% of health care employees had some <u>allergic symptoms</u> after mRNA vaccines; anaphylaxis occured in 2.47 per 100,000 vaccinations, and all recovered without shock or intubation.

Other

- The majority of <u>solid organ transplant</u> recipients did not mount appreciable antibody responses to one mRNA vaccine dose. Patients who were younger, not on antimetabolite maintenance immunosuppression, and receiving the Moderna vaccine were more likely to mount responses.
- Vaccine uptake may improve when <u>public health campaigns</u> provide clear, credible, and shorter messages including benefits and risks of vaccines in language target groups can understand.

Immunogenicity

- An <u>AHRQ Rapid Review</u> discussing the antibody response to SARS-CoV-2 infection suggests that the majority of adults develop IgM and IgG following infection.
- <u>Prior infection</u> was 81.8% protective against reinfection and 84.5% protective against symptomatic infection; protection increased over time for at least 8 months.
- Almost 95% of subjects in one study maintained immune memory at ~6 months after infection. Circulating antibody titers were not predictive of T cell memory.

Variants

- CD4+ and CD8+ T cell responses in convalescent COVID-19 subjects of mRNA vaccines <u>were not substantially affected</u> by mutations found in variants.
- The <u>P1 variant</u> that caused a second wave of COVID-19 infections in Manaus, Brazil, was found to be 1.4 to 2.2 times more transmissible than other local strains, and 25-60% of individuals previously infected with COVID-19 may be susceptible to reinfection with this strain.
- The <u>B.1.1.7 variant</u> emerging in England is estimated to have a 43-90% higher reproduction number than other variants. It was shown to have higher RNA loads and longer persistence in another study.
- A two-dose regimen of the Oxford vaccine did not show protection against mild-to-moderate COVID-19 due to the <u>B.1.351 variant</u>.
- <u>Studies</u> have shown that the B.1.1.7 variant is susceptible to <u>neutralizing antibodies</u> elicited by existing vaccines, that polyclonal antibodies from individuals infected in early 2020 <u>remain active</u> against most mutated spike pseudotypes, and that serum samples collected following mild illness are less resilient to spike variation than those following severe illness. Infection- and vaccine-elicited antibodies were found against <u>B.1, B.1.1.7</u>, and <u>N501Y</u> variants. The E484K mutation, a newly emergent Variant of Concern, led to <u>more substantial loss</u> of neutralizing activity by vaccine-elicited antibodies.
- A laboratory study showed that the <u>B.1.351 and P.1 variants</u> may be resistant to antibodies used for treatment and less efficiently inhibited by plasma from prior patients and by the Pfizer vaccine.
- A double mutant variant with E484Q and L452R mutations was detected in India.

Outcomes and Associations

Long COVID

- A comprehensive <u>review of post-acute COVID-19</u> includes a framework for identification and management. <u>A model</u> was developed to identify individuals at risk of long COVID. A study of whole body [18F]FDG <u>PET/CT</u> supports underlying systemic inflammation and the multi-organ nature of long COVID.
- A <u>systematic review</u> showed fatigue, reduced lung function, and carditis were the most common intermediate and long-term sequelae of COVID-19 in formerly healthy adults under 50 years old. Four months after hospitalization for COVID-19, a <u>cohort</u> of patients reported new fatigue, cognitive symptoms, and dyspnea; 63% had lung abnormalities on CT.

Risk Factors

- <u>Chronic respiratory disease</u> in COVID-19 patients was associated with the risk of needing invasive ventilation or ICU admission but not with death in one study.
- <u>Asthma</u> in COVID-19 patients was associated with similar risk of hospitalization and mechanical ventilation but a lower risk of mortality compared to patients without asthma.
- Higher Vitamin D level was associated with decreased risk of testing positive for COVID in Blacks.
- Most studies show correlation between Vitamin D deficiency and risk of SARS CoV-2 infection, severity and

- mortality; evidence is inconsistent for ICU admission, inflammation, hospitalization, and lung involvement.
- There is some evidence of lack of increased unfavorable outcomes in patients with <u>prior exposure to</u> corticosteroids who are hospitalized for COVID-19.
- A modified-simplified <u>pulmonary embolism severity index</u> can predict the need for intensive care in hospitalized COVID-19 patients.

Diagnostics

Testing Modalities

- Saliva samples from the oral region were shown to provide high sensitivity and specificity.
- Sensitivity of <u>antigen tests</u> is highest in the 1st week of symptom onset when viral loads are high.

Imaging

- <u>Lung ultrasound</u> was shown to be an inexpensive and reliable tool for rapid screening and diagnosis of COVID-19 in symptomatic patients; it may help in resource-limited environments when RT-PCR availability is limited.
- <u>Chest CT and ultrasound</u> were sensitive for the diagnosis of COVID-19; they may be more useful for excluding COVID-19 than for differentiating the cause of respiratory infection.

Other

- An EUA was granted for a test, built with machine learning, that uses <u>signals from T cells</u> to detect past COVID-19 infections.
- Monitoring with <u>EEG, MRI and clinical status</u> combined may better identify and guide treatment for patients with COVID-19 related encephalopathy.

Therapeutics

Steroids

- The European Respiratory Society recommends <u>systemic corticosteroids</u> in patients requiring supplementary oxygen or ventilatory support and anticoagulation in hospitalized patients.
- The <u>LIVING Project</u> found very low certainty evidence that corticosteroids may reduce the risk of death, serious adverse events, and mechanical ventilation; that remdesivir might reduce the risk of serious adverse events; that IVIG might reduce the risk of death and serious adverse events; that tocilizumab might reduce the risk of serious adverse events and mechanical ventilation; and that bromhexine might reduce the risk of non-serious adverse events.
- <u>Dexamethasone</u> resulted in lower 28-day mortality in hospitalized patients with COVID-19 receiving invasive mechanical ventilation or oxygen but not for those not on respiratory support.

Interleukin Inhibitors and Antibodies

- Evidence for Tocilizumab is conflicted. In one study, it reduced all-cause mortality and slightly reduced serious adverse events but did not cause clinical improvement at day 28; evidence for sarilumab and other IL-6 agents was uncertain. Another study showed the use of tocilizumab in hospitalized patients with severe COVID-19 pneumonia did not result in significantly better clinical status or lower mortality at 28 days. Another did not support routine use in hospitalized patients with moderate to severe disease. Yet another showed tocilizumab can improve outcomes for patients with bilateral pulmonary lesions and elevated IL-6.
- Treatment with <u>interleukin-6 receptor antagonists</u> (tocilizumab and sarilumab) improved outcomes, including survival, in critically ill patients with COVID-19 receiving organ support. Another trial did not show efficacy of <u>sarilumab</u> in COVID-19 hospitalized patients on oxygen.
- Early aggressive use of tocilizumab and corticosteroids improved outcomes in hospitalized patients with

COVID-19.

- <u>Baricitinib</u> combined with remdesivir <u>decreased</u> recovery time, accelerated improvement, and had fewer serious adverse events in hospitalized COVID pneumonia patients.
- HHS discontinued <u>Bamlanivimab</u> distribution due to increased variants that are resistant to the drug when administered alone. When coadministered with remdesivir, <u>Bamlanivimab did not demonstrate</u> efficacy among hospitalized patients who had Covid-19 without end-organ failure.
- A Phase 3 trial showed that <u>Regeneron</u> reduced hospitalization or death by 70% in non-hospitalized COVID-19 and shortened the duration of symptoms by 4 days.

Existing Medications

- <u>Convalescent plasma</u> in early COVID-19 <u>did not benefit</u> mortality, length of hospitalization, or mechanical ventilation compared to use in deteriorating patients. An NIH trial of convalescent plasma in emergency department patients with mild symptoms <u>was halted</u> due to lack of benefit.
- Aspirin was associated with decreased mechanical ventilation, ICU care, and in-hospital mortality.
- The use of <u>intermediate-dose prophylactic anticoagulation</u> or was not supported for unselected COVID-19 ICU patients. <u>Therapeutic anticoagulation</u> (versus thromboprophylaxis) did not improve survival or need for organ support in patients with severe COVID-19.
- An RCT supported continued treatment with ACEi or ARBs during hospitalization for COVID-19.
- A WHO living guideline recommended against <u>hydroxychloroquine</u> to prevent COVID-19.
- <u>Ivermectin</u> for mild COVID-19 did not significantly improve the time to resolution of symptoms.
- Antibiotics may be excessively and <u>unnecessarily prescribed</u> for COVID-19 patients.

Trial Treatments

- A Phase 2a trial of <u>molnupiravir</u>, an investigational oral antiviral agent, showed a reduction in time to negativity of infectious virus in patients with symptomatic infection.
- Early intervention with <u>sulodexide</u> in COVID-19 patients was shown to reduce hospital admissions and oxygen support requirements but not length of hospital stay.
- A Phase 2 trial of <u>pegylated interferon alfa-2b</u> showed significant improvement in clinical status on day 15 likely due to faster viral reduction.
- Pfizer initiated a Phase 1 trial of PF-07321332, an <u>oral protease inhibitor</u> with potent anti-viral activity against SARS-CoV-2 in in-vitro studies.

Special Populations

- <u>COVID-19 infection in pregnancy</u> may be associated with increased risks of preeclampsia, preterm birth, stillbirth, and severe disease with other adverse pregnancy outcomes.
- <u>mRNA vaccines administered during pregnancy</u> induced adequate maternal serologic response and efficient transplacental transfer, indicating maternal and neonatal protection.
- Testing using a SAMBA-II machine was acceptable for pregnant women requiring admission.
- <u>Pediatric patients with MIS-C</u> were shown to be more likely than those with severe COVID-19 to be 6 to 12 years old, non-Hispanic Black, and have severe cardiovascular or mucocutaneous involvement and more extreme inflammation.
- Neurologic involvement was common in hospitalized children and adolescents with COVID-19.

This edition of the COVID-19 Intelligence Report was produced by Dr. Laura Sigman with support from the Himmelfarb Librarian team and the entire GW Intelligence Unit led by Dr. Lawrence "Bopper" Deyton.

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