New Research
*note, PREPRINTS have not undergone formal peer review

COVID-19 related publications by Providence caregivers – see Digital Commons

Clinical Syndrome

   
   
   Findings: In this study conducted in five U.S. locations, persons with mild illness seeking clinical care or COVID-19 testing who met simple, standardized screening criteria (reported fever, cough, or shortness of breath of ≤10 day duration) commonly reported other respiratory, gastrointestinal, or systemic symptoms. Although persons with COVID-19 were more likely than those without COVID-19 to report gastrointestinal symptoms (vomiting, diarrhea, or abdominal pain) or other symptoms such as muscle aches or headache, the largest difference was observed in diminished or complete loss of taste or smell, reported by more than half of persons with laboratory-confirmed COVID-19 versus one in five persons without COVID-19. Because of the wide overlap in COVID-19 symptoms with those of other respiratory illnesses, laboratory confirmation of SARS-CoV-2 infection will be critical, not only for limiting disease spread, contact tracing, and monitoring clinical course, but also for assessing the effectiveness of interventions during periods of cocirculation of SARS-CoV-2 and other respiratory viruses, including influenza.

   
   
   Findings: To our knowledge this is the first comprehensive report on COVID-19 in HSCT patients focussing on virological parameters. Compared to immunocompetent patients, prolonged shedding of infectious virus, viremia and high viral loads in respiratory samples, highlights the need of the immune system for viral control, but also indicates virus induced mortality and higher risk for transmission to other patients and medical staff.

Findings: The incidence of UGB in COVID-19 patients attending EDs was lower compared with non-COVID-19 patients. Digestive symptoms predominated over respiratory symptoms, and COVID-19 patients with UGB underwent fewer gastroscopies and endoscopic treatments than the general population with UGB. In-hospital mortality in COVID-19 patients with UGB was increased compared with non-COVID patients with UGB, but not compared with the remaining COVID-19 patients.


Findings: Two-hundred sixty-eight consecutive patients were included in the analysis with a mean age of 58.4 years, 40.3% were female, 44.4% African American, 20.7% Hispanic, and a median APACHE II score of 18. Delirium without coma occurred in 29.1% of patients admitted to the ICU. Delirium persisted for a median of 5 days and was severe. Mechanical ventilation was significantly associated with odds of delirium even after adjustment for sedatives. Clinical attention to manage delirium duration and severity, and deeper understanding of the virus' neurologic effects is needed for patients with coronavirus disease 2019.

**Diagnostics & Screening**


Findings: Our findings indicate that chest CT is sensitive and moderately specific for the diagnosis of COVID-19 in suspected patients, meaning that CT may have limited capability in differentiating SARS-CoV-2 infection from other causes of respiratory illness. However, we are limited in our confidence in these results due to the poor study quality and the heterogeneity of included studies. Because of limited data, accuracy estimates of chest X-ray and ultrasound of the lungs for the diagnosis of suspected COVID-19 cases should be carefully interpreted. Future diagnostic accuracy studies should pre-define positive imaging findings, include direct comparisons of the various modalities of interest on the same participant population, and implement improved reporting practices. Planned updates of this review will aim to: increase precision around the accuracy estimates for chest CT (ideally with low risk of bias studies); obtain further data to inform accuracy of chest X-rays and ultrasound; and obtain data to further fulfil secondary objectives (e.g. 'threshold' effects, comparing accuracy estimates across different imaging modalities) to inform the utility of imaging along different diagnostic pathways.

Findings: In this study, we evaluated and compared 10 commercially-available SARS-CoV-2 rapid serological tests using the STARD methodology (Standards for Reporting of Diagnostic Accuracy Studies). 250 sera from 159 PCR-confirmed SARS-CoV-2 patients (collected from 0 to 32 days after onset of symptoms) were tested with rapid serological tests. Control sera (N = 254) were retrieved from pre-COVID periods from patients with other coronavirus infections (N = 11), positive rheumatoid factors (N = 3), IgG/IgM hyperglobulinemia (N = 9), malaria (n = 5), or no documented viral infection (N = 226). All samples were tested using rapid lateral flow immunoassays (LFIA) from 10 manufacturers. Only four tests achieved ≥98% specificity, with other tests ranging from 75.7%-99.2%. Sensitivities varied by the day of sample collection, from 31.7%-55.4% (Days 0-9), 65.9%-92.9% (Days 10-14), and 81.0%-95.2% (>14 days) after the onset of symptoms, respectively. Only three tests evaluated met French Health Authorities' thresholds for SARS-CoV-2 serological tests (≥90% sensitivity + ≥98% specificity). Overall, the performances between tests varied greatly, with only a third meeting acceptable specificity and sensitivity thresholds. Knowing the analytical performance of these tests will allow clinicians and most importantly laboratorians to use them with more confidence, could help determine the general population's immunological status, and may help to diagnose some patients with false-negative RT-PCR results.

**Epidemiology & Public Health**


Findings: To determine if SARS-CoV-2 reactive antibodies were present in sera prior to the first identified case in the U.S. on January 19, 2020, residual archived samples from 7,389 routine blood donations collected by the American Red Cross from December 13, 2019 to January 17, 2020, from donors resident in nine states (California, Connecticut, Iowa, Massachusetts, Michigan, Oregon, Rhode Island, Washington, and Wisconsin) were tested at CDC for anti-SARS-CoV-2 antibodies. Of the 7,389 samples, 106 were reactive by pan Ig. Of these 106 specimens, 90 were available for further testing. Eighty four of 90 had neutralizing activity, 1 had S1 binding activity, and 1 had receptor binding domain / Ace2 blocking activity >50%, suggesting the presence of anti-SARS-CoV-2-reactive antibodies. Donations with reactivity occurred in all nine states. These findings suggest that SARS-CoV-2 may have been introduced into the United States prior to January 19, 2020.

8. **Seroprevalence of Novel Coronavirus SARS-CoV-2 at a Community Hospital Emergency Department and Outpatient Laboratory in Northern Orange County, California.** Jason Yamaki, Harry Peled, Sajen Mathews, David Park, Mina Firoozi, Kim Smith, Lee Nguyen [PSJH authors] J
Findings: To estimate the number of infected persons in our community, we conducted a cross-sectional study to estimate seroprevalence of SARS-CoV-2 infection. This cross-sectional study evaluated the presence of immunoglobulin G, antibody for SARS-CoV-2 during the time period of July 15, 2020, to July 27, 2020. Testing was done on serum samples from patients who had visited affiliated outpatient clinics or our emergency department. Additionally, we collected age, gender, ethnicity, race, and location of testing. Eight hundred sixty-five tests were included in the study. The outpatient clinics cohort accounted for 56% of results and emergency department (ED) contributed 44%. The positive percentage of SARS-CoV-2 test was 9.4% (95% CI: 0.08-0.12). The positivity rates of the outpatient (5.6%) and ED (14.2%) setting differed. The prevalence of SARS-CoV-2 IgG was greatest in those that identified as Hispanic/Latino, 18.1% versus 13.4% in other groups. Specifically compared to the non-Hispanic/Latino population, the prevalence was significantly higher, with a relative risk of 2.73 (95% CI: 1.8-4.1), p < 0.0001. The low antibody positivity rate in the community indicates the need for a vaccine. The Hispanic/Latino patient population should be considered for increased education on preventing transmission and acquisition of COVID-19 as well as being considered as a priority for vaccination once a vaccine is available.

Findings: 37 mostly fair-quality cohort and cross-sectional studies, 15 mostly good-quality ecological studies, and data from the Centers for Disease Control and Prevention and APM Research Lab were included. African American/Black and Hispanic populations experience disproportionately higher rates of SARS-CoV-2 infection, hospitalization, and COVID-19-related mortality compared with non-Hispanic White populations, but not higher case-fatality rates (mostly reported as in-hospital mortality) (moderate- to high-strength evidence). Asian populations experience similar outcomes to non-Hispanic White populations (low-strength evidence). Outcomes for other racial/ethnic groups have been insufficiently studied. Health care access and exposure factors may underlie the observed disparities more than susceptibility due to comorbid conditions (low-strength evidence).

10. Infection fatality risk for SARS-CoV-2 in community dwelling population of Spain: nationwide seroepidemiological study. ENE-COVID Study Group. BMJ. 2020 Nov 27;371:m4509. doi: 10.1136/bmj.m4509. https://www.bmj.com/content/371/bmj.m4509
Findings: The overall infection fatality risk was 0.8% for confirmed covid-19 deaths and 1.1% for excess deaths. The infection fatality risk was 1.1% to 1.4% in men and 0.6% to 0.8% in women. The infection fatality risk increased sharply after age 50. The increase in SARS-CoV-2 infection fatality risk after age 50 appeared to be more noticeable in men than in women. Based on the results of this study, fatality from covid-19 was greater than that reported for other common respiratory diseases, such as seasonal influenza.

**Findings:** We estimated that through the end of September, 1 of every 2.5 hospitalized infections and 1 of every 7.1 non-hospitalized illnesses may have been nationally reported. Applying these multipliers to reported SARS-CoV-2 cases along with data on the prevalence of asymptomatic infection from published systematic reviews, we estimate that 2.4 million hospitalizations, 44.8 million symptomatic illnesses, and 52.9 million total infections may have occurred in the U.S. population from February 27-September 30, 2020. These preliminary estimates help demonstrate the societal and healthcare burdens of the COVID-19 pandemic and can help inform resource allocation and mitigation planning.


**Findings:** A total of 68 911 included individuals, representing 34 million people in the US, provided 79 032 survey responses. The mean age was 39.5 (13.4) years, and 50.7% were women. There were 28 738 individuals, representing 12 million Americans who reported household use of UI benefits in the past week. In adjusted analyses, being in a household that received, vs did not receive, UI benefits was associated with lower risk for unmet health-related social needs, delaying health care, and depressive and anxiety symptoms. Being in a household that received UI was associated with fewer health-related social needs, less health care delay, and better mental health. However, many who reported pandemic-related job loss did not receive UI—particularly Hispanic individuals and those with less education.


**Findings:** Here we analyze the laboratory findings of 1,850 patients to describe the dynamic changes of the total antibody, spike protein (S)-, receptor-binding domain (RBD)-, and nucleoprotein (N)-specific immunoglobulin M (IgM) and G (IgG) levels during SARS-CoV-2 infection and recovery. The generation of S-, RBD-, and N-specific IgG occurs one week later in patients with severe/critical COVID-19 compared to patients with mild/moderate disease, while S- and RBD-specific IgG levels are 1.5-fold higher in severe/critical patients during hospitalization. The RBD-specific IgG levels are 4-fold higher in older patients than in younger patients during hospitalization. In addition, the S- and RBD-specific IgG levels are 2-fold higher in the recovered patients who are SARS-CoV-2 RNA negative than those who are RNA positive.
Lower S-, RBD-, and N-specific IgG levels are associated with a lower lymphocyte percentage, higher neutrophil percentage, and a longer duration of viral shedding. Patients with low antibody levels on discharge might thereby have a high chance of being tested positive for SARS-CoV-2 RNA after recovery.


Findings: Most persons infected with SARS-CoV-2, the virus that causes COVID-19, develop virus-specific antibodies within several weeks, but antibody titers might decline over time. Understanding the timeline of antibody decline is important for interpreting SARS-CoV-2 serology results. Serum specimens were collected from a convenience sample of frontline health care personnel at 13 hospitals and tested for antibodies to SARS-CoV-2 during April 3-June 19, 2020, and again approximately 60 days later to assess this timeline. The percentage of participants who experienced seroreversion, defined as an antibody signal-to-threshold ratio >1.0 at baseline and <1.0 at the follow-up visit, was assessed. Overall, 194 (6.0%) of 3,248 participants had detectable antibodies to SARS-CoV-2 at baseline (1). Upon repeat testing approximately 60 days later (range = 50-91 days), 146 (93.6%) of 156 participants experienced a decline in antibody response indicated by a lower signal-to-threshold ratio at the follow-up visit, compared with the baseline visit, and 44 (28.2%) experienced seroreversion. Participants with higher initial antibody responses were more likely to have antibodies detected at the follow-up test than were those who had a lower initial antibody response. Whether decay in these antibodies increases risk for reinfection and disease remains unanswered. However, these results suggest that serology testing at a single time point is likely to underestimate the number of persons with previous SARS-CoV-2 infection, and a negative serologic test result might not reliably exclude prior infection.


Findings: Patients with profound immunosuppression after undergoing hematopoietic stem-cell transplantation or receiving cellular therapies may shed viable SARS-CoV-2 for at least 2 months. The current guidelines for Covid-19 isolation precautions may need to be revised for immunocompromised patients.

Prognosis


Findings: Complete blood count changes, including new cell activation parameters, from 982 confirmed COVID-19 adult patients from 11 European hospitals were retrospectively analysed
for distinctive patterns based on age, gender, clinical severity, symptom duration and hospital days. The observed haemocytometric patterns formed the basis to develop a multi-
haemocytometric-parameter prognostic score to predict, during the first three days after
presentation, which patients will recover without ventilation or deteriorate within a two-week
timeframe, needing intensive care or with fatal outcome. The prognostic score, with ROC curve
AUC at baseline of 0.753 (95% CI 0.723-0.781) increasing to 0.875 (95% CI 0.806-0.926) on day
3, was superior to any individual parameter at distinguishing between clinical severity. Findings
were confirmed in a validation cohort. Aim is that the score and haemocytometry results are
simultaneously provided by analyser software, enabling wide applicability of the score as
haemocytometry is commonly requested in COVID-19 patients.

[https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7685686/](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7685686/)

Findings: We investigated relationships between IS, AD, and outcomes in patients hospitalized with COVID-19. Data on consecutive admissions for COVID-19 were extracted retrospectively from medical records. Patients were assigned to one of four cohorts, according to whether or not they had an AD (AD and NAD) or were immunosuppressed (IS and NIS). The primary endpoint was development of severe acute respiratory distress syndrome (ARDS); secondary endpoints included death, and a composite of mechanical ventilation (MV) or death. A total of 789 patients were included: 569 (72.1%) male, 76 (9.6%) with an AD, and 63 (8.0%) with IS. Relative to the NIS-NAD cohort, patients in the IS-AD cohort had a significantly reduced risk of severe ARDS (adjusted hazard ratio [aHR] 0.42; 95% confidence interval [CI] 0.23-0.80; p = 0.008). No significant relationships between IS or AD status and either death or the composite of MV and death were identified, although a trend towards higher mortality was identified in the IS-NAD cohort (aHR vs NIS-NAD 1.71; 95% CI 0.94-3.12; p = 0.081). Patients in this cohort also had higher median serum levels of interleukin-6 compared with IS-AD patients (98.2 vs 21.6 pg/mL; p = 0.0328) and NIS-NAD patients (29.1 pg/mL; p = 0.0057). In conclusion, among patients hospitalized with COVID-19, those receiving immunosuppressive treatment for an AD may have a reduced risk of developing severe ARDS.

**Survivorship & Rehabilitation**


Findings: Of the 180 participants (96.3% of the 187 eligible COVID-19 patients), 53.1% reported persistence of at least one symptom after a mean of 125 days after symptoms onset, 33.3% reported one or two symptoms and 19.4% three or more symptoms. At the last follow-up, 46.7% were asymptomatic compared with 4.4 % during the acute phase. The most prevalent persistent symptoms were fatigue, loss of smell and taste, and arthralgias. Our results show
that it might take months for symptoms to resolve, even among non-hospitalized persons with mild illness course in the acute phase. Continued monitoring for long COVID is needed.

**Therapeutics**


Findings: A total of 228 patients were assigned to receive convalescent plasma and 105 to receive placebo. The median time from the onset of symptoms to enrollment in the trial was 8 days, and hypoxemia was the most frequent severity criterion for enrollment. The infused convalescent plasma had a median titer of 1:3200 of total SARS-CoV-2 antibodies. No patients were lost to follow-up. At day 30 day, no significant difference was noted between the convalescent plasma group and the placebo group in the distribution of clinical outcomes according to the ordinal scale. Overall mortality was 10.96% in the convalescent plasma group and 11.43% in the placebo group, for a risk difference of −0.46 percentage points. Total SARS-CoV-2 antibody titers tended to be higher in the convalescent plasma group at day 2 after the intervention. Adverse events and serious adverse events were similar in the two groups. No significant differences were observed in clinical status or overall mortality between patients treated with convalescent plasma and those who received placebo.

**Transmission / Infection Control**


Findings: Five identified studies found that a low proportion of reported global SARS-CoV-2 infections have occurred outdoors (<10%) and the odds of indoor transmission was very high compared to outdoors (18.7 times; 95% CI 6.0, 57.9). Five studies described influenza transmission outdoors and two described adenovirus transmission outdoors. There was high heterogeneity in study quality and individual definitions of outdoor settings which limited our ability to draw conclusions about outdoor transmission risks. In general, factors such as duration and frequency of personal contact, lack of personal protective equipment and occasional indoor gathering during a largely outdoor experience were associated with outdoor reports of infection. Existing evidence supports the widely-held belief that the risk of SARS-CoV-2 transmission is lower outdoors but there are significant gaps in our understanding of specific pathways.


Findings: The analysis included 2314 healthy contacts of 672 index case patients with Covid-19 who were identified between March 17 and April 28, 2020. A total of 1116 contacts were randomly assigned to receive hydroxychloroquine and 1198 to receive usual care. Results were similar in the hydroxychloroquine and usual-care groups with respect to the incidence of PCR-confirmed, symptomatic Covid-19 (5.7% and 6.2%, respectively; risk ratio, 0.86 [95% confidence interval, 0.52 to 1.42]). In addition, hydroxychloroquine was not associated with a lower incidence of SARS-CoV-2 transmission than usual care (18.7% and 17.8%, respectively). The incidence of adverse events was higher in the hydroxychloroquine group than in the usual-care group (56.1% vs. 5.9%), but no treatment-related serious adverse events were reported. Postexposure therapy with hydroxychloroquine did not prevent SARS-CoV-2 infection or symptomatic Covid-19 in healthy persons exposed to a PCR-positive case patient.

Findings: Carbapenem-resistant Acinetobacter baumannii (CRAB) causes health care–associated infections that are challenging to contain and often linked to infection prevention and control (IPC) breaches. A New Jersey hospital reported a cluster of 34 CRAB cases that peaked during a surge in COVID-19 hospitalizations. Strategies to preserve continuity of care led to deviations in IPC practices; CRAB cases decreased when normal operations resumed. Hospitals managing surges of patients with COVID-19 might be vulnerable to outbreaks of multidrug-resistant organism (MDRO) infections. Maintaining IPC best practices (e.g., MDRO surveillance and hand hygiene and environmental cleaning audits) to the extent possible could mitigate spread.

Vaccine

To reduce the spread of SARS-CoV-2, the virus that causes coronavirus disease 2019 (COVID-19) and its associated impacts on health and society, COVID-19 vaccines are essential. The U.S. government is working to produce and deliver safe and effective COVID-19 vaccines for the entire U.S. population. The Advisory Committee on Immunization Practices (ACIP)* has broadly outlined its approach for developing recommendations for the use of each COVID-19 vaccine authorized or approved by the Food and Drug Administration (FDA) for Emergency Use Authorization or licensure (1). ACIP’s recommendation process includes an explicit and transparent evidence-based method for assessing a vaccine’s safety and efficacy as well as consideration of other factors, including implementation (2). Because the initial supply of vaccine will likely be limited, ACIP will also recommend which groups should receive the earliest allocations of vaccine. The ACIP COVID-19 Vaccines Work Group and consultants with expertise in ethics and health equity considered external expert committee reports and published literature and deliberated the ethical issues associated with COVID-19 vaccine allocation.
decisions. The purpose of this report is to describe the four ethical principles that will assist ACIP in formulating recommendations for the allocation of COVID-19 vaccine while supply is limited, in addition to scientific data and implementation feasibility: 1) maximize benefits and minimize harms; 2) promote justice; 3) mitigate health inequities; and 4) promote transparency. These principles can also aid state, tribal, local, and territorial public health authorities as they develop vaccine implementation strategies within their own communities based on ACIP recommendations.

Women & Children


Findings: We present population-based data highlighting a disproportionate burden of MIS-C among Black and Hispanic children in NYC. It is unclear whether this finding represents a phenomenon distinct from the increased burden of COVID-19 in Black and Hispanic communities, because we also observed a disproportionate burden of COVID-19 hospitalizations among Black and Hispanic children. This analysis is limited by missing race/ethnicity data for most confirmed, nonhospitalized, and nonfatal COVID-19 cases in NYC, which prohibits evaluating the excess burden of MIS-C and COVID-19 hospitalizations among children of color. Furthermore, some patients meeting the MIS-C criteria may have been misclassified or not reported. Larger studies are needed to explore the relationship between MIS-C and race/ethnicity and to elucidate the impact of structural racism in perpetuating health disparities.


Findings: Seventy-four children were recruited. Sixty-one percent met MIS-C definition. MIS-C patients were older than non-MIS-C patients: 9.4 years vs 3.4 years. A higher proportion of them had no previous medical history of interest. Non-MIS-C patients presented more frequently with respiratory distress. MIS-C patients showed higher prevalence of fever, diarrhea, vomits, fatigue, shock and cardiac dysfunction. MIS-C group had a lower lymphocyte count and LDH but higher neutrophil count, neutrophil/lymphocyte ratio, C-reactive protein and procalcitonin. Patients in the MIS-C group were less likely to receive invasive ventilation but were more often treated with vasoactive drugs, corticosteroids and immunoglobulins. Most patients were discharged from PICU by the end of data collection with a median length of stay of 5 days in the MIS-C group. Three patients died, none of them belonged to the MIS-C group. MIS-C seems to be the most frequent presentation among critically ill children with SARS-CoV-2 infection. MIS-C patients are older and usually healthy. They show a higher prevalence of
gastrointestinal symptoms and shock and are more likely to receive vasoactive drugs and immunomodulators and less likely to need mechanical ventilation than non-MIS-C patients.

GUIDELINES & CONSENSUS STATEMENTS


FDA / CDC / NIH / WHO Updates

**CDC** - Considerations for Inpatient Obstetric Healthcare Settings, updated Dec 1, 2020.


**NIH** - Fourth iteration of the Adaptive COVID-19 Treatment Trial (ACTT-4) has begun to enroll hospitalized adults with coronavirus disease 2019 (COVID-19) who require supplemental oxygen.


Commentary / Press Releases


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