New Research

*note, PREPRINTS have not undergone formal peer review

Retracted Articles - see also Retraction Watch

   

   

Basic Science / Virology / Pre-clinical

   
   Original: https://www.medrxiv.org/content/10.1101/2020.05.31.20114991v1.full.pdf

   
   Original: https://www.medrxiv.org/content/10.1101/2020.03.11.20031096v2.full.pdf

Findings: both preprints #3 and 4 finding an association between type A blood and severe COVID-19 symptoms.
Clinical Syndrome


Findings: Studies reported the occurrence of venous thromboembolism and stroke in approximately 20% and 3% of patients, respectively. A higher frequency seems to be present in severely ill patients, in particular those admitted to intensive care units. The thrombotic risk is elevated despite the use of anticoagulant prophylaxis but optimal doses of anticoagulation are not yet defined. Although an increase of biomarkers such as D-dimer has been consistently reported in severely ill COVID-19, the optimal cut-off level and prognostic value are not known. A number of pressing issues were identified by this review, including defining the true incidence of VTE in COVID patients, developing algorithms to identify those susceptible to develop thrombotic complications and severe disease, determining the role of biomarkers and/or scoring systems to stratify patients' risk, designing adequate and feasible diagnostic protocols for PE, establishing the optimal thromboprophylaxis strategy, and developing uniform diagnostic and reporting criteria.


Findings: Neurological manifestations are common in hospitalized COVID-19 patients. In our series, more than half of patients presented some form of neurological symptom. Clinicians need to maintain close neurological surveillance for prompt recognition of these complications. The investigation of the mechanisms and emerging consequences of SARS-CoV-2 neurological involvement require further studies.


Findings: Gastrointestinal manifestations are common presenting features of COVID-19, occurring in 25% of our patient population. This finding supports the theory of SARS-CoV-2 gastrointestinal entry and infection via the ACE2 receptor. GI symptoms were not associated with increased rates of ICU admission, intubation, LOS or mortality, suggesting that they do not portend a more severe disease course.


Findings: This cohort study found that higher thromboses rates were associated with TEG results outside reference ranges among patients with COVID-19 who were critically ill. Risk
associated with TEG results outside reference ranges manifested as a 62% thrombosis event rate, 2-fold the thrombosis event rates that have been previously reported, despite our use of recommended deep vein thrombosis prophylaxis.

**Diagnostics & Screening**

Findings: Our study shows the clinical usefulness of tongue, nasal, or mid-turbinate samples collected by patients as compared with nasopharyngeal samples collected by health care workers for the diagnosis of Covid-19. Adoption of techniques for sampling by patients can reduce PPE use and provide a more comfortable patient experience.

https://jamanetwork.com/journals/jama/fullarticle/2767023  
Findings: The CDC recommends that health care workers dispose of N95s after a single patient encounter. However, it recommends N95 extended use and limited reuse during critical PPE shortages. There are limited data regarding N95 reuse and extended use. We examined the prevalence of N95 fit test failure while reusing 2 common types of N95 masks. This study found duckbill N95s had a high failure rate. Failure of dome-shaped masks was associated with increased use. N95 failure may contribute to SARS-CoV-2 transmission despite PPE use and deserves further study. Based on these preliminary data, health systems should closely evaluate N95 fit during extended use or reuse and limit duckbill mask use if alternatives are available.

https://www.acpjournals.org/doi/10.7326/M20-2854  
Findings: This article discusses key use cases for SARS-CoV-2 antibody detection tests and their application to serologic studies, reviews currently available assays, highlights key areas of ongoing research, and proposes potential strategies for test implementation.


**Epidemiology & Public Health**

https://www.acpjournals.org/doi/10.7326/M20-2223
Findings: This analysis reveals that critical structural inequities and health care gaps have historically contributed to and continue to compound disparate health outcomes among communities of color. Shifting from this context to the present, this article frames a discussion of racial health disparities through a resilience approach rather than a deficit approach and offers a blueprint for approaching the COVID-19 crisis and its afterlives through the lens of health equity.

Findings: People with IDD had higher prevalence of specific comorbidities associated with poorer COVID-19 outcomes. Distinct age-related differences in COVID-19 trends were present among those with IDD, with a higher concentration of COVID-19 cases at younger ages. In addition, while the overall case-fatality rate was similar for those with IDD (5.1%) and without IDD (5.4%), these rates differed by age: ages ≤17 – IDD 1.6%, without IDD <0.01%; ages 18–74 – IDD 4.5%, without IDD 2.7%; ages ≥75 – IDD 21.1%, without IDD, 20.7%.

Findings: This paper provides the first nationally representative estimates of vulnerability to severe complications from COVID-19 overall and across race-ethnicity and socioeconomic status.

Findings: Asymptomatic persons seem to account for approximately 40% to 45% of SARS-CoV-2 infections, and they can transmit the virus to others for an extended period, perhaps longer than 14 days. Asymptomatic infection may be associated with subclinical lung abnormalities, as detected by computed tomography. Because of the high risk for silent spread by asymptomatic persons, it is imperative that testing programs include those without symptoms. To supplement conventional diagnostic testing, which is constrained by capacity, cost, and its one-off nature, innovative tactics for public health surveillance, such as crowdsourcing digital wearable data and monitoring sewage sludge, might be helpful.

Healthcare Delivery & Healthcare Workers

Findings: After palliative care intervention in the ED, most patients and their surrogates opted to forgo mechanical ventilation and/or CPR, and that tendency further increased on discharge. We believe timely GOC conversations by the palliative care team helped avoid unwanted LSTs for patients with a poor prognosis.


   Findings: The rapid onset and intensity of this pandemic has left society, and health care systems in particular, reeling from the effects and wondering how they could be so unprepared. While it feels unprecedented in many ways, the Covid-19 pandemic itself is not the primary cause of the current chaos in health care. Pandemics have occurred before and will certainly occur again; the new variable during this one is the deeply interconnected world in which we live in today. Network phenomena are the new reality, and they are only going to become increasingly prevalent. Changing old ways of communicating and making decisions, considering ways to reduce employee burnout and encourage professional development, and most critically, prioritizing leadership throughout an organization, will enable health care organizations to transform and emerge from this pandemic stronger than when they entered it.


   Findings: Between March 11 and April 21, 2020, 42% fewer patients were admitted to VA inpatient facilities compared with the preceding 6 weeks, including for conditions generally requiring emergency treatment. The percentage decrease in admissions for conditions generally requiring emergency treatment was greater or similar in magnitude to the decrease in admissions overall and is unlikely to be attributable to declines in elective surgeries or disease incidence related to reduced stress or lower exposure to other pathogens or pollution. Rather, many patients may be avoiding hospitals to minimize risk of SARS-CoV-2 infection.

**Laboratory Results**


   Findings: This study showed that all COVID-19 patients were seropositive to SARS-CoV-2 even at the early stage of illness, and a significant neutralizing antibody response was observed in
convalescent patients. Neutralizing antibody levels depends on time after onset of symptoms, age and the severity of disease.


Findings: Using data for 20,912 patients from two large academic health systems, we analyzed the frequency of SARS-CoV-2 RT-PCR test-discordance among individuals initially testing negative by nasopharyngeal swab who were retested on clinical grounds within 7 days. The frequency of subsequent positivity within this window was 3.5% and similar across institutions.

**Prognosis**


Findings: There were a total of 3099 patients from 24 studies. Meta-analysis showed that patients with poor outcome have a lower lymphocyte count compared to those with good outcome. Lymphopenia was associated with severe COVID-19. Meta-regression showed that the association between lymphocyte count and composite poor outcome was affected by age. This meta-analysis showed that lymphopenia on admission was associated with poor outcome in patients with COVID-19.


Findings: Advanced age and an increasing number of comorbidities are independent predictors of in-hospital mortality for COVID-19 patients. NSAIDs and ACE-I/ARB use prior to admission is not associated with renal failure or increased mortality.


Findings: This is a retrospective observational study of all patients admitted with COVID-19 to Huo Shen Shan Hospital. Among 2877 hospitalized patients, 29.5% (850/2877) had a history of hypertension. After adjustment for confounders, patients with hypertension had a two-fold increase in the relative risk of mortality as compared with patients without hypertension. Patients with a history of hypertension but without antihypertensive treatment (n = 140) were associated with a significantly higher risk of mortality compared with those with antihypertensive treatments (n = 730). While hypertension and the discontinuation of antihypertensive treatment are suspected to be related to increased risk of mortality, in this retrospective observational analysis, we did not detect any harm of RAAS inhibitors in patients...
infected with COVID-19. However, the results should be considered as exploratory and interpreted cautiously.


Findings: Based on the large-scale retrospective study, we demonstrated that in-hospital use of ACEIs/ARBs was associated with a lower risk of 28-day death among hospitalized patients with COVID-19 and co-existing hypertension, CAD, and hypertension combined with CAD. These data suggested that patients with hypertension and CAD might obtained the highest benefits from taking ACEIs/ARBs compared to the non-ACEIs/ARBs in the setting of COVID-19. Notably, in-hospital usage of ACEIs trended to have a higher incidence and risk of 28-day COVID-19 mortality than those taking ARBs, but the difference was not statistically significant.


Findings: Elevation of blood glucose level predicted worse outcomes in hospitalized patients with COVID-19. Our findings may provide a simple and practical way to risk stratify COVID-19 inpatients for hierarchical management, particularly where medical resources are in severe shortage during the pandemic.

**Therapecutic**


Findings: We conducted a randomized, double-blind, placebo-controlled trial across the United States and parts of Canada testing hydroxychloroquine as postexposure prophylaxis. We enrolled 821 asymptomatic participants. Overall, 87.6% of the participants (719 of 821) reported a high-risk exposure to a confirmed Covid-19 contact. After high-risk or moderate-risk exposure to Covid-19, hydroxychloroquine did not prevent illness compatible with Covid-19 or confirmed infection when used as postexposure prophylaxis within 4 days after exposure.


Findings: In this randomized clinical trial that included 103 patients and was terminated early, the hazard ratio for time to clinical improvement within 28 days in the convalescent plasma group vs the standard treatment group was 1.40 and was not statistically significant. Among
patients with severe or life-threatening COVID-19, convalescent plasma therapy added to standard treatment did not significantly improve the time to clinical improvement within 28 days, although the trial was terminated early and may have been underpowered to detect a clinically important difference.

Findings: Older patients who developed COVID-induced pneumonitis may benefit from LDRT to the whole lung, to improve their quality of life and survival. This cost-effective treatment should be tested as a clinical trial for all countries to decrease the burden of the hospital system which is currently being overwhelmed by the increased number of infected patients.

Findings. In this systematic review and network meta-analysis that included 25 studies and 3804 patients with acute hypoxemic respiratory failure, compared with standard oxygen therapy there was a statistically significant lower risk of death with helmet noninvasive ventilation (risk ratio, 0.40) and face mask noninvasive ventilation (risk ratio, 0.83).

Findings: To date, persuasive evidence of important benefit in COVID-19 does not exist for any antiviral treatments, although for each treatment evidence has not excluded important benefit. Additional randomized controlled trials involving patients with COVID-19 will be needed before such treatments can be administered with confidence.

Findings: Corticosteroid might have a negative effect on lung injury recovery in non-severe COVID-19 pneumonia patients, however the results of this study must be interpreted with caution because of confounding factors.

Transmission / Infection Control
https://www.cdc.gov/mmwr/volumes/69/wr/mm6922e2.htm
Findings: Nonpharmaceutical interventions (NPI) introduced among 10,579 basic trainees at Joint Base San Antonio-Lackland limited COVID-19 incidence to five cases (47 per 100,000 persons), three of which were in persons who were contacts of the first patient.

Findings: The coronavirus pandemic has created worldwide shortages of N95 respirators. We analyzed 4 decontamination methods for effectiveness in deactivating severe acute respiratory syndrome coronavirus 2 virus and effect on respirator function. Our results indicate that N95 respirators can be decontaminated and reused, but the integrity of respirator fit and seal must be maintained.

Findings: The findings of this systematic review and meta-analysis support physical distancing of 1 m or more and provide quantitative estimates for models and contact tracing to inform policy. Optimum use of face masks, respirators, and eye protection in public and health-care settings should be informed by these findings and contextual factors. Robust randomised trials are needed to better inform the evidence for these interventions, but this systematic appraisal of currently best available evidence might inform interim guidance.

Findings: Between March 10th and April 4th, 2020, 14,000 quarantined people were tested for SARS-CoV-2; 49 were positive. Of these, 30 participated in the study: 13(43%) never had symptoms and 17(57%) were symptomatic. 17(57%) participants acquired their infection outside Vietnam. Compared with symptomatic individuals, asymptomatic people were less likely to have detectable SARS-CoV-2 in NTS samples collected at enrolment (8/13 (62%) vs. 17/17 (100%) P=0.02). Asymptomatic SARS-CoV-2 infection is common and can be detected by analysis of saliva or NTS. NTS viral loads fall faster in asymptomatic individuals, but they appear able to transmit the virus to others.

Findings: Aerosol generating procedures are an important consideration for HCWs during the COVID-19 pandemic. There is not any evidence demonstrating an increased infection risk related to AGPs in SARS-CoV-2, but in related viruses a risk has been shown associated specifically with intubation of infected patients and it is possible that other AGPs convey a risk as well. There is a significant knowledge gap in this area and the risk HCWs face has not been established. Guidelines are necessary to ensure HCWs are aware of this fact and that their practice is consistent, appropriate and safe.

Findings: Governments around the world are responding to the novel coronavirus (COVID-19) pandemic with unprecedented policies designed to slow the growth rate of infections. Many actions, such as closing schools and restricting populations to their homes, impose large and visible costs on society, but their benefits cannot be directly observed and are currently understood only through process-based simulations. Here, we compile new data on 1,717 local, regional, and national non-pharmaceutical interventions deployed in the ongoing pandemic across localities in China, South Korea, Italy, Iran, France, and the United States (US). We estimate that across these six countries, interventions prevented or delayed on the order of 62 million confirmed cases, corresponding to averting roughly 530 million total infections. These findings may help inform whether or when these policies should be deployed, intensified, or lifted, and they can support decision-making in the other 180+ countries where COVID-19 has been reported.

Findings: We estimate that, across all 11 countries, between 12 and 15 million individuals have been infected with SARS-CoV-2 up to 4th May, representing between 3.2% and 4.0% of the population. Our results show that major non-pharmaceutical interventions and lockdown in particular have had a large effect on reducing transmission. Continued intervention should be considered to keep transmission of SARS-CoV-2 under control.

Findings: An Internet panel survey identified gaps in knowledge about safe preparation, use, and storage of cleaners and disinfectants. Approximately one third of survey respondents engaged in nonrecommended high-risk practices with the intent of preventing SARS-CoV-2 transmission, including using bleach on food products, applying household cleaning and disinfectant products to skin, and inhaling or ingesting cleaners and disinfectants.

Findings: SARS-CoV-2 RNA was not detectable by air sampler which suggests that airborne route is not the predominant mode of transmission of COVID-19. Wearing of surgical mask, appropriate hand hygiene and thorough environmental disinfection are sufficient infection control measures for COVID-19 patients isolated singly in AIIR. But this may not apply during aerosol generating procedures or in cohort wards with large number of COVID-19 patients nursed together.

**Women & Children**


Findings: In this case series of 50 children and adolescents hospitalized with COVID-19 infection, respiratory symptoms, while common, were not always present. Children hospitalized with COVID-19 commonly had comorbidities, infants had less severe disease, those with obesity were likely to receive mechanical ventilation, and elevated markers of inflammation at admission and during hospitalization were associated with severe disease. Expanded testing, maintaining a high suspicion for severe acute respiratory syndrome coronavirus infection given the variable presentation of COVID-19, risk stratification, and recognition of findings suggestive of immune dysregulation are crucial to effective COVID-19 management in children.

44. **Kawasaki-like multisystem inflammatory syndrome in children during the covid-19 pandemic in Paris, France: prospective observational study.** Toubiana J, Poirault C, Corsia A, et al. *BMJ* 2020; 369 :m2094 [https://www.bmj.com/content/369/bmj.m2094](https://www.bmj.com/content/369/bmj.m2094)

Findings. The ongoing outbreak of Kawasaki-like multisystem inflammatory syndrome among children and adolescents in the Paris area might be related to SARS-CoV-2. In this study an unusually high proportion of the affected children and adolescents had gastrointestinal symptoms, Kawasaki disease shock syndrome, and were of African ancestry.


Findings: Acute myocarditis with intense systemic inflammation and atypical Kawasaki disease is an emerging severe pediatric disease following SARS-CoV-2 infection. Early recognition of this
disease is needed and referral to an expert center is recommended. A delayed and inappropriate host immunological response is suspected. While underlying mechanisms remain unclear, further investigations are required to target an optimal treatment.


Findings: Analysis provides pediatric-specific dosing suggestions for hydroxychloroquine and remdesivir and raises concerns regarding hydroxychloroquine use for COVID-19 treatment because concentrations were less than those needed to mediate an antiviral effect.


Findings: As many countries begin to lift some of the restrictions to contain COVID-19 spread, lack of evidence of transmission in the school setting remains. We examined Irish notifications of SARS-CoV2 in the school setting before school closures on 12 March 2020 and identified no paediatric transmission. This adds to current evidence that children do not appear to be drivers of transmission, and we argue that reopening schools should be considered safe accompanied by certain measures.


Findings: COVID-19-positive pregnant women present with fewer symptoms than the general population and may be RT-PCR negative despite having signs of viral pneumonia. The incidence of preterm births, low birth weight, C-section, NICU admission appear higher than the general population.

49. **Characteristics and outcomes of pregnant women admitted to hospital with confirmed SARS-CoV-2 infection in UK: national population based cohort study.** Knight M, Bunch K,Vousden N, et al. *BMJ* 2020; 369 :m2107 [https://www.bmj.com/content/369/bmj.m2107](https://www.bmj.com/content/369/bmj.m2107)

Findings: Most pregnant women admitted to hospital with SARS-CoV-2 infection were in the late second or third trimester, supporting guidance for continued social distancing measures in later pregnancy. Most had good outcomes, and transmission of SARS-CoV-2 to infants was uncommon. The high proportion of women from black or minority ethnic groups admitted with infection needs urgent investigation and explanation.

Findings: This study describes 17 previously healthy children and adolescents who developed an inflammatory phenotype related to COVID-19. Features overlapped with, but were distinct from, those of KD and TSS. The observed pattern of cytokine expression suggests an interferon signaling component, along with IL-6 and IL-10 production, seen in KD5 and acute pulmonary COVID-19 infection. The lack of elevated TNF-α or IL-13 levels may differ from acute pulmonary COVID infections. The occurrence of abnormal cardiac findings suggests the need for long-term surveillance.


Findings: In this case series of hospitalized children who met criteria for PIMS-TS, there was a wide spectrum of presenting signs and symptoms and disease severity, ranging from fever and inflammation to myocardial injury, shock, and development of coronary artery aneurysms. The comparison with patients with Kawasaki disease (KD) and KD shock syndrome provides insights into this syndrome, and suggests this disorder differs from other pediatric inflammatory entities.

GUIDELINES & CONSENSUS STATEMENTS


FDA / CDC / NIH / WHO Updates

**CDC - Collection and Submission of Postmortem Specimens from Deceased Persons with Known or Suspected COVID-19 Interim Guidance**

**CDC - Use Personal Protective Equipment when caring for Patients with Confirmed or Suspected COVID**

**FDA - Coronavirus (COVID-19) Update: FDA Reissues Emergency Use Authorizations Revising Which Types of Respirators Can Be Decontaminated for Reuse**

**WHO - Advice on the use of masks in the context of COVID-19**

Commentary

Open letter advocating for an anti-racist public health response to demonstrations against systemic injustice occurring during the COVID-19 pandemic.

**Ethical Challenges Arising in the COVID-19 Pandemic: An Overview From the Association of Bioethics Program Directors (ABPD) Task Force.**


Concerns regarding the statistical analysis and data integrity. Open letter to MR Mehra, SS Desai, FRuschitzka, and AN Patel, authors of “Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis”.

Response to Widespread Reaction to Recent Lancet Article on Hydroxychloroquine.

Kaiser Health News and The Guardian: Lost On The Frontline

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