The Daily COVID-19 Literature Surveillance Summary

July 23, 2020

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COVID-19 Daily Literature Surveillance

COVID19LST

Bringing you real time, distilled information for guiding best practices during the COVID-19 pandemic

LEVEL OF EVIDENCE

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

Question	Step 1 (Level 1*)	Step 2 (Level 2*)	Step 3 (Level 3*)	Step 4 (Level 4*)	Step 5 (Level 5)
How common is the problem?	Local and current random sample surveys (or censuses)	Systematic review of surveys that allow matching to local circumstances**	Local non-random sample**	Case-series**	n/a
Is this diagnostic or monitoring test accurate? (Diagnosis)	Systematic review of cross sectional studies with consistently applied reference standard and blinding	Individual cross sectional studies with consistently applied reference standard and blinding	Non-consecutive studies, or studies without consistently applied reference standards**	Case-control studies, or "poor or non-independent reference standard**	Mechanism-based reasoning
What will happen if we do not add a therapy? (Prognosis)	Systematic review of inception cohort studies	Inception cohort studies	Cohort study or control arm of randomized trial*	Case-series or case-control studies, or poor quality prognostic cohort study**	n/a
Does this intervention help? (Treatment Benefits)	Systematic review of randomized trials or *n*-of-1 trials	Randomized trial or observational study with dramatic effect	Non-randomized controlled cohort/follow-up study**	Case-series, case-control studies, or historically controlled studies**	Mechanism-based reasoning
What are the COMMON harms? (Treatment Harms)	Systematic review of randomized trials, systematic review of nested case-control studies, *n*-of-1 trial with the patient you are raising the question about, or observational study with dramatic effect	Individual randomized trial or (exceptionally) observational study with dramatic effect	Non-randomized controlled cohort/follow-up study (post-marketing surveillance) provided there are sufficient numbers to rule out a common harm. (For long-term harms the duration of follow-up must be sufficient.)**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning
What are the RARE harms? (Treatment Harms)	Systematic review of randomized trials or *n*-of-1 trial	Randomized trial or (exceptionally) observational study with dramatic effect			
Is this (early detection) test worthwhile? (Screening)	Systematic review of randomized trials	Randomized trial	Non -randomized controlled cohort/follow-up study**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning

*** Level may be graded down on the basis of study quality, imprecision, indirectness (study PICO does not match questions PICO), because of inconsistency between studies, or because the absolute effect size is very small; Level may be graded up if there is a large or very large effect size.**

**** As always, a systematic review is generally better than an individual study.**

How to cite the Levels of Evidence Table

OCEBM Levels of Evidence Working Group*. "The Oxford 2011 Levels of Evidence".
Oxford Centre for Evidence-Based Medicine. http://www.cebm.net/index.aspx?o=5653

** OCEBM Table of Evidence Working Group = Jeremy Howick, Iain Chalmers (James Lind Library), Paul Glasziou, Trish Greenhalgh, Carl Heneghan, Alessandro Liberati, Ivan Moschetti, Bob Phillips, Hazel Thornton, Olive Goddard and Mary Hodgkinson*

EXECUTIVE SUMMARY

CLIMATE:

- Authors from Saarland University in Germany propose a method for prioritizing allocation of a SARS-CoV-2 vaccine during a resource shortage. These recommendations include a three-tier preference list for vaccine distribution: beginning with hospital workers and public safety/security officers, followed by immunocompromised/suppressed individuals such as organ transplant recipients, and finally all others in the general population in order from oldest to youngest. This idea highlights one potential method of solving the key issue of vaccine prioritization for individuals with high susceptibility to COVID-19 infection.
- A sharp peak in rates of intestinal obstruction (IO) during the lockdown period in Kerela, India (referred to as "lockdown belly") leads authors to propose four common risk factors:
  - 60 years of age or older
  - prior abdominal surgery
  - strict adherence to lockdown restrictions
  - high fiber diet of jackfruit

  Additionally, the authors suggest at least 75% of IO cases during this time may have been prevented with modifiable risk factors including diet and physical activity.
- This article explores the impact of COVID-19 on immigrants in the United States, with an emphasis on those in Houston, Texas. The most prevalent comorbidities, nationally, include obesity (71.5%), hypertension (HTN, 27.7%), and diabetes (9.6%). Many immigrants are at increased risk for COVID-19 infection as they make up a significant portion of the essential workers work force (20% in Texas) and are more likely to live in large family groups. The unemployment rate increased from 3% to 15% from February to April 2020, and concerns over food insecurity, child support, and healthcare access continue to worsen. Thus, the authors suggest the following policy recommendations in order to better support these disadvantaged communities:
  - Expand Medicaid
  - Eliminate immigration requirements for CHIP
  - Pass registration banning ICE in healthcare
  - Fund COVID-19 testing and treatment for uninsured
  - Provide immigrants and families economic relief packages

UNDERSTANDING THE PATHOLOGY:

- A cross sectional study from Columbia University that analyzed kidney biopsies of SARS-CoV-2 infected patients (n=17), revealed a spectrum of glomerular and tubular injuries, acute kidney injury (88%), and lack of SARS-CoV-2 detection in kidney cells as evidence against direct viral injury as a pathophysiologic mechanism of disease. Authors conclude that the principle nephrogenicity of SARS-CoV-2 likely results from ischemic damage and a dysregulated immune response.
-

TRANSMISSION AND PREVENTION:

- A group of psychologists found that habit reversal training (HRT) was an effective method of treating repetitive behavior problems, such as face touching, and therefore may be an effective strategy for decreasing transmission of SARS-CoV-2. The principles of HRT are centered on mindfulness and behavior modification, and authors include a practical guide to implementing these practices.
-

MANAGEMENT:

- Italian authors describe how the anti-coagulant Defibrotide may be the "drug of choice" for treating the hypercoagulable state associated with severe COVID-19 disease because of its profibrinolytic, antithrombotic, and anti-inflammatory effects. These would theoretically protect from the growing evidence implicating the role of endothelial damage and a hyperinflammatory state in SARS-CoV-2 infection.
- A literature review of 9 studies describes the effect of T cell imbalance, specifically between Treg and Th17, on uncontrolled systemic inflammation in severe COVID-19 cases in pregnancy found that:
  - Treg cells decreased and Th17 cells increased, with a consequent decrease in the Treg/Th17 cell ratio.
  - Treg cells dysregulation in COVID-19 was shown trigger hyperinflammation and tissue damage.
  - Increased Th17 is associated with fetal allograft rejection at the feto-maternal interface.
  - COVID-19 infection puts pregnant persons at higher risk for pregnancy complications.

TABLE OF CONTENTS

CLIMATE

AN EPIDEMIC OF SUB ACUTE INTESTINAL OBSTRUCTION DURING COVID-19 PANDEMIC RELATED LOCKDOWN - 'THE LOCKDOWN BELLY'

Philip S, David A, Kumar KS, Renny RJ, Pillai V, Manda SR.. Br J Surg. 2020 Jul 20. doi: 10.1002/bjs.11803. Online ahead of print.
Level of Evidence: Other - Expert Opinion

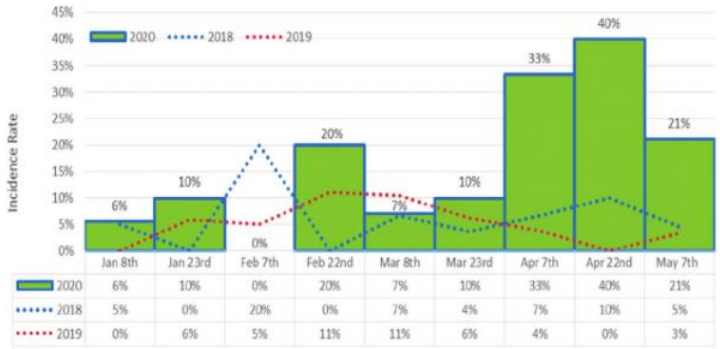
BLUF

In this letter to the editor, the authors hypothesize the reasons for the sharp peak in intestinal obstruction (IO) during the lockdown period (referred to as "lockdown belly") of the COVID-19 pandemic in Kerala, India compared to two years prior (Figure 1). The authors propose four common factors of those presenting with IO during this time including:
- 60 years of age or older
- prior abdominal surgery
- strict adherence to lockdown restrictions
- high fiber diet of jackfruit

In addition to encouraging additional research to better understand the epidemic of “lockdown belly”, the authors suggest at least 75% of IO cases during this time may have been prevented with modifiable risk factors including diet and physical activity.

FIGURES

Fig. 1 Incidence rate of intestinal obstruction by year



	Jan 8th	Jan 23rd	Feb 7th	Feb 22nd	Mar 8th	Mar 23rd	Apr 7th	Apr 22nd	May 7th
2020	6%	10%	0%	20%	7%	10%	33%	40%	21%
2018	5%	0%	20%	0%	7%	4%	7%	10%	5%
2019	0%	6%	5%	11%	11%	6%	4%	0%	3%

Figure 1: Incidence rate of intestinal obstruction by year.

GLOBAL

ALLOCATION CRITERIA FOR AN INITIAL SHORTAGE OF A FUTURE SARS-COV-2 VACCINE AND NECESSARY MEASURES FOR GLOBAL IMMUNITY

Henn W.. Vaccine. 2020 Jul 22;38(34):5396-5397. doi: 10.1016/j.vaccine.2020.06.058. Epub 2020 Jun 23.
Level of Evidence: Other - Opinion

BLUF

An opinion piece from Saarland University in Germany discusses the idea of SARS-CoV-2 vaccine shortages and proposes a three-tier preference list for vaccine distribution: beginning with hospital workers and public safety/security officers, followed by immunocompromised/suppressed individuals such as organ transplant recipients, and finally all others in the general population in order from oldest to youngest. This idea highlights one potential method of solving the key issue of vaccine prioritization for individuals with high susceptibility to COVID-19 infection.

DISPARITIES

RACIAL/ETHNIC DISPARITIES IN DISEASE SEVERITY ON ADMISSION CHEST RADIOGRAPHS AMONG PATIENTS ADMITTED WITH CONFIRMED COVID-19: A RETROSPECTIVE COHORT STUDY

Joseph NP, Reid NJ, Som A, Li MD, Hyle EP, Dugdale CM, Lang M, Betancourt JR, Deng F, Mendoza DP, Little BP, Narayan AK, Flores EJ.. Radiology. 2020 Jul 16:202602. doi: 10.1148/radiol.2020202602. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

A retrospective cohort study from Boston, MA of 326 hospitalized COVID-19 patients from March 27th, 2020 to April 10th, 2020 found that Non-White patients had a higher modified Radiographic Assessment of Lung Edema (mRALE) score on admission chest x-ray compared to White/Non-Hispanic patients (p=0.005, Figure 4). Both had similar adverse outcomes (intubation, ICU admission or deaths) with increasing mRALE scores (p<0.001) with no evidence of interaction (p=0.16). These findings could potentially assist radiologists in identifying at-risk populations to improve outcomes for ethnic and racial minorities.

ABSTRACT

Background Disease severity on chest radiographs (CXR) has been associated with higher risk of disease progression and adverse outcomes from COVID-19. Few studies have evaluated COVID-19-related racial/ethnic disparities in radiology. Purpose To evaluate whether Non-White minority patients hospitalized with confirmed COVID-19 infection presented with increased severity on admission CXR compared with White/Non-Hispanic patients. Methods Single-institution, retrospective cohort study approved by the IRB. Patients hospitalized with confirmed COVID-19 infection (3/27/20-4/10/20) were identified using the electronic medical record (EMR) (n=326, mean age: 59 years (SD: 17 years), M:F (188:138). Primary outcome was severity of lung disease on admission CXR, measured by modified Radiographic Assessment of Lung Edema (mRALE) score. Secondary outcome was a composite adverse clinical outcome of intubation, ICU admission, or death. Primary exposure was racial/ethnic category: White/Non-Hispanic versus Non-White [i.e., Hispanic, Black, Asian, Other]. Multivariable linear regression analyses were performed to evaluate the association between mRALE scores and race/ethnicity. Results Non-White patients had significantly higher mRALE scores (median 6.1, 95% CI 5.4-6.7) compared with White/Non-Hispanic patients (median 4.2, 95% CI 3.6-4.9) (unadjusted average difference 1.8, 95% CI 0.9-2.8, p<0.01). For both White (Adjusted HR, 1.3, 95%CI 1.2-1.4, p<0.001) and Non-White patients (Adjusted HR 1.2, 95%CI 1.1-1.3, p<0.001), increasing mRALE scores were associated with a higher likelihood of experiencing composite adverse outcome with no evidence of interaction (p = 0.16). Multivariable linear regression analyses demonstrated that Non-White patients presented with higher mRALE scores on admission CXR versus White/Non-Hispanic patients (adjusted average difference 1.6, 95% CI 0.5-2.7, p<0.01). Adjustment for hypothesized mediators revealed that the association between race/ethnicity and mRALE scores was mediated by limited English proficiency (p<0.01). Conclusion Non-White patients hospitalized with COVID-19 infection were more likely to present with higher severity of disease on admission CXR than White/Non-Hispanic patients, and increased severity was associated with worse outcomes for all patients.

FIGURES

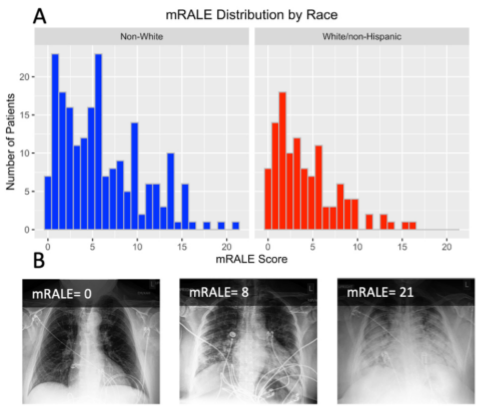


Figure 4 Title: Histogram of mRALE Score Distribution by Race. A) Distribution of mRALE categories on Admission Chest Radiograph by Race/Ethnicity. Non-White/Hispanic patients were more likely to have higher mRALE score categories compared with White/non-Hispanic patients (Coefficient 0.560, 95% CI 0.046 to 1.074 to, p = 0.033). On average, adjusted for potential confounders, Non-White patients presented with higher mRALE scores on admission CXR compared with White patients (average difference 1.60, 95%CI 0.50 to 2.71, p=0.005) in our multiple variable linear regression analyses (B) Examples of modified Radiograph Assessment of Lung Edema (mRALE) annotations for pulmonary disease severity in patients with COVID-19. The top left inset number for each image is the corresponding mRALE score, the average of annotations by multiple raters. A score of 0-4 was categorized as mild, 4.1-10 was moderate, and >10 was severe.

DISPROPORTIONATE IMPACT OF THE COVID-19 PANDEMIC ON IMMIGRANT COMMUNITIES IN THE UNITED STATES

Clark E, Fredricks K, Woc-Colburn L, Bottazzi ME, Weatherhead J.. PLoS Negl Trop Dis. 2020 Jul 13;14(7):e0008484. doi: 10.1371/journal.pntd.0008484. eCollection 2020 Jul.
Level of Evidence: 3 - Local non-random sample

BLUF

This article explores the potential impacts of COVID-19 on immigrants in the United States, with an emphasis on those in Houston, Texas. The most prevalent comorbidities, nationally, include obesity (71.5%), hypertension (HTN, 27.7%), and diabetes (9.6%). Many immigrants are at increased risk for COVID-19 infection as they make up a significant portion of the essential workers work force (20% in Texas) and are more likely to live in large family groups. The unemployment rate increased from 3% to 15% from February to April 2020, and concerns over food insecurity, child support, and healthcare access continue to worsen. Thus, the authors suggest the following policy recommendations in order to better support these disadvantaged communities:
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FIGURES

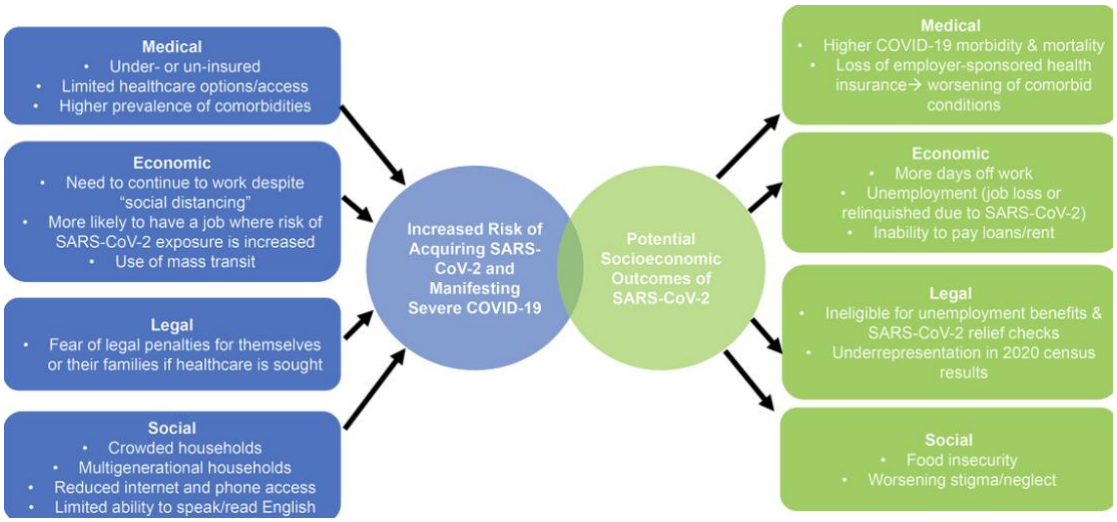


Figure 1: Risk factors and anticipated socioeconomic outcomes for the COVID-19 pandemic in vulnerable immigrant communities.

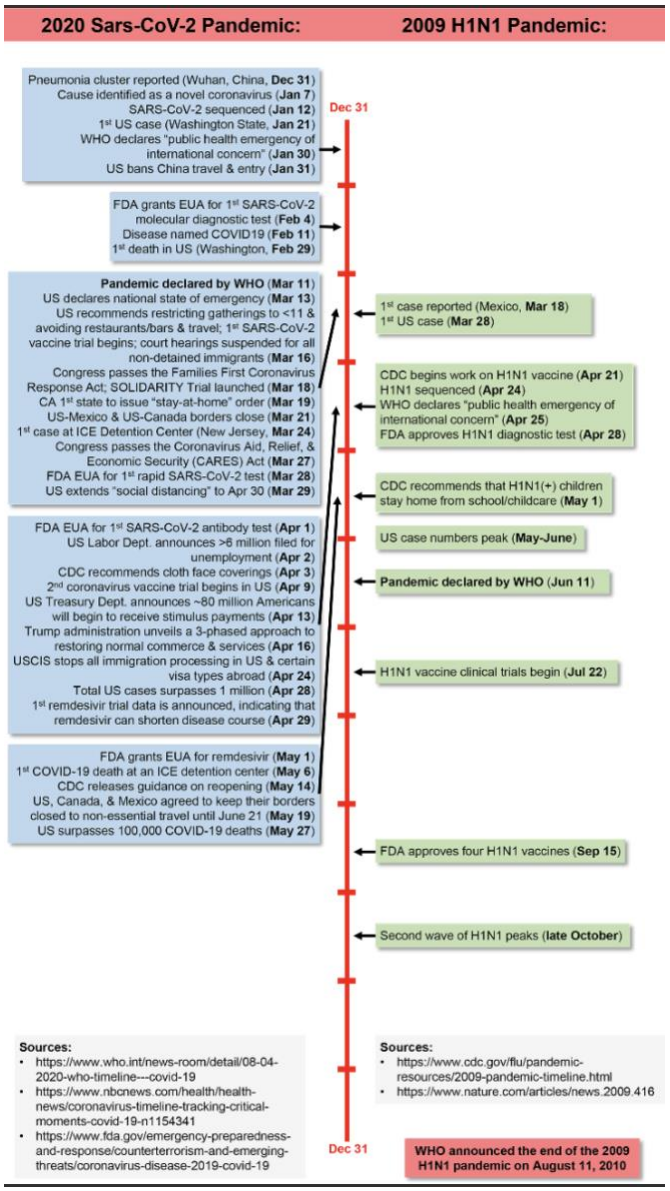


Figure 2: Comparison of COVID-19 and 2009 H1N1 influenza pandemic timelines in the context of events affecting vulnerable immigrant communities in the US. CDC, US Centers for Disease Control and Prevention; EUA, emergency use authorization;

FDA, US Food and Drug Administration; ICE, US Immigration and Customs Enforcement; USCIS, US Citizenship and Immigration Services; WHO, World Health Organization.

COVID-19 AND THE MENTAL HEALTH OF PEOPLE FROM REFUGEE BACKGROUNDS

Rees S, Fisher J.. Int J Health Serv. 2020 Jul 16:20731420942475. doi: 10.1177/0020731420942475. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

Australian researchers conducted a systemically recruited cohort study to investigate the effects of COVID-19 on the mental health of refugee women from conflict-affected backgrounds (violence, insecurity, persecution, and shortage of food and medicine), and report increased stress levels from detainment, limited trust in state-run institutions, and minimal social support from the community. The researchers hope these findings will better inform healthcare providers in order to improve health care delivery to this vulnerable population.

ABSTRACT

Approximately 1 in 10 of the current 26 million people who are refugees reside in high-income countries. They have commonly experienced trauma related to violence, insecurity, persecution and shortage of food and medicine. Our research suggests that COVID-19 and its health and social sequalae may be triggering past traumatic reactions, exacerbating mental health problems and undermining functioning. The purpose of this article is to promptly communicate these anecdotal findings to general health practitioners to ensure informed and sensitive health care delivery to this vulnerable population.

HEALTH LITERACY AND COVID-19

Spring H.. Health Info Libr J. 2020 Jul 16. doi: 10.1111/hir.12322. Online ahead of print.
Level of Evidence: Other - Opinion

BLUF

This editorial argues health literacy to be a social determinant of health and promotes health literacy to empower communities to be informed and participate in their care, to address disparities, and build community resilience. The novelty of COVID-19 and social distancing has isolated people, and many have chosen to ignore the recommendations over time. The author suggests that health literacy may help to overcome these barriers and promote community safety.

ABSTRACT

In early 2020, the world experienced an unprecedented health crisis. When the pandemic of coronavirus was declared by the World Health Organization, it brought with it sudden and dramatic changes to everyday life. In the UK, the key message from the Government was to 'Stay at home, protect the NHS, save lives', sending out a clear warning that failing to stay at home would put other lives and the ability of the NHS to cope at risk. This editorial discusses COVID-19, how society responded and the vital role that health literacy plays in saving lives during a global health emergency.

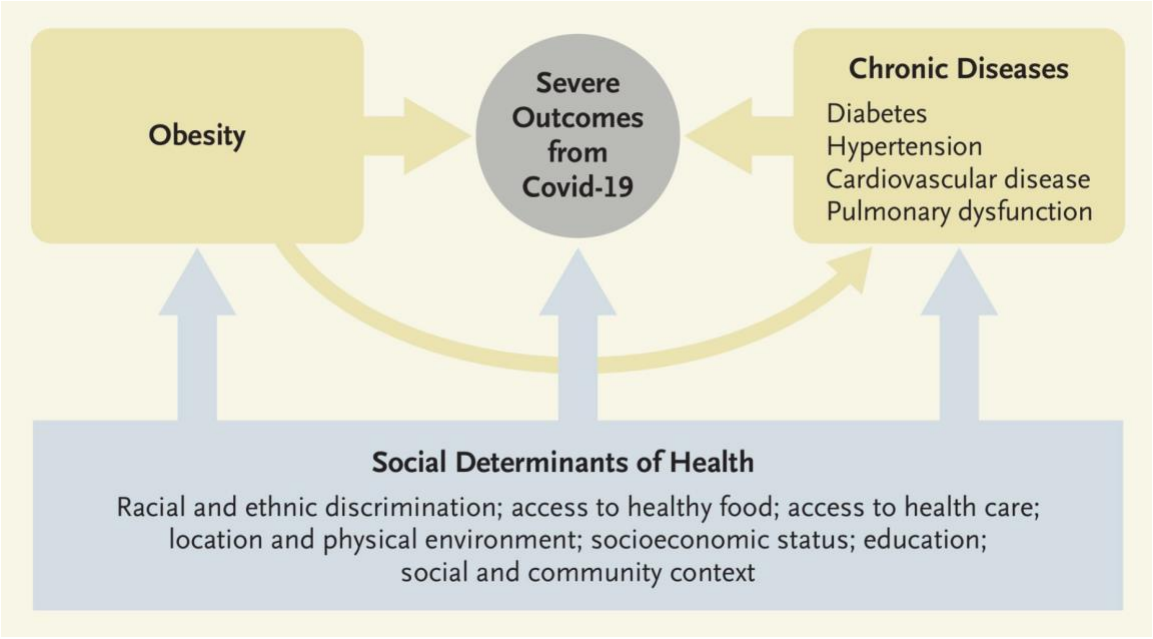
COVID-19 AND DISPARITIES IN NUTRITION AND OBESITY

Belanger MJ, Hill MA, Angelidi AM, Dalamaga M, Sowers JR, Mantzoros CS.. N Engl J Med. 2020 Jul 15. doi: 10.1056/NEJMp2021264. Online ahead of print.
Level of Evidence: Other - Opinion

BLUF

Public health activists remark that the socioeconomic, environmental, and educational gaps between populations (notably, Black, Latinx, and Native American households) may be contributing to disparities in nutrition, obesity, and overall worse outcomes from COVID-19 (Figure 1). The authors recommend that the U.S. health care system needs to address strategies to eliminate these health inequities in order to minimize the toll of the COVID-19 pandemic and ensure high-quality, affordable health care.

FIGURES


Obesity
Severe Outcomes from Covid-19
Chronic Diseases
Diabetes
Hypertension
Cardiovascular disease
Pulmonary dysfunction
Social Determinants of Health
Racial and ethnic discrimination; access to healthy food; access to health care; location and physical environment; socioeconomic status; education; social and community context

PREGNANT PERSONS

THIRD TRIMESTER PLACENTAS OF SARS-COV-2-POSITIVE WOMEN: HISTOMORPHOLOGY, INCLUDING VIRAL IMMUNOHISTOCHEMISTRY AND IN SITU HYBRIDIZATION

Smithgall MC, Liu-Jarin X, Hamele-Bena D, Cimic A, Mourad M, Debelenko L, Chen X.. Histopathology. 2020 Jul 21. doi: 10.1111/his.14215. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

A study comparing placental histopathology using in-situ hybridization (ISH) and immunohistochemistry (IHC) of 51 SARS-CoV-2 positive and 25 negative persons presenting in third-trimester labor at Columbia University Irving Medical Center from 23 March to 29 April 2020 found nonspecific maternal/fetal malperfusion with evidence of subchorionic thrombi (p=0.026, Figure 1A), intervillous thrombi (Figure 1B), infarction (Figure 1C), segmental avascular-villi (Figure 1D), fetal thrombotic vasculopathy (Figure 1E), and villous agglutination (p=0.003, Figure 1F). There was no evidence of direct viral changes in placental tissue with ISH (Figure 1G) or IHC (Figure 1H), and all infants born to SARS-CoV-2 positive mothers subsequently tested negative for the virus, suggesting no evidence for vertical transmission.

ABSTRACT

AIMS: The wide-variety of affected organ-systems associated with SARS-CoV-2 infection highlights the need for tissue-specific evaluation. We compared placentas from SARS-CoV-2-positive and negative women in our hospital in New York City, which became the epicenter of the COVID-19 pandemic in March 2020. While some limited studies have been published on placentas from SARS-CoV-2-positive women to date, this study, in addition to describing histomorphology, utilizes in-situ hybridization (ISH) for the S-gene encoding the spike-protein and immunohistochemistry (IHC) with the monoclonal-SARS-CoV-2 spike-antibody 1A9 for placental evaluation. METHODS AND RESULTS: In this study, 51 singleton, third-trimester placentas from SARS-CoV-2-positive women and 25 singleton, third-trimester placentas from SARS-CoV-2-negative women were examined histomorphologically using the Amsterdam Criteria as well as with ISH and/or IHC. Corresponding clinical findings and neonatal outcomes also were recorded. While no specific histomorphologic changes related to SARS-CoV-2 were noted in the placentas, evidence of maternal/fetal vascular malperfusion was identified, with placentas from SARS-CoV-2-positive women significantly more likely to show villous agglutination (p=0.003) and subchorionic thrombi (p=0.026) than placentas from SARS-CoV-2-negative women. No evidence of direct viral involvement was identified using ISH and IHC. CONCLUSIONS: In this study, third trimester placentas from SARS-CoV-2-positive women were more likely to show evidence of maternal/fetal vascular malperfusion; however, no evidence of direct viral involvement or vertical transmission was noted by ISH and IHC.

FIGURES

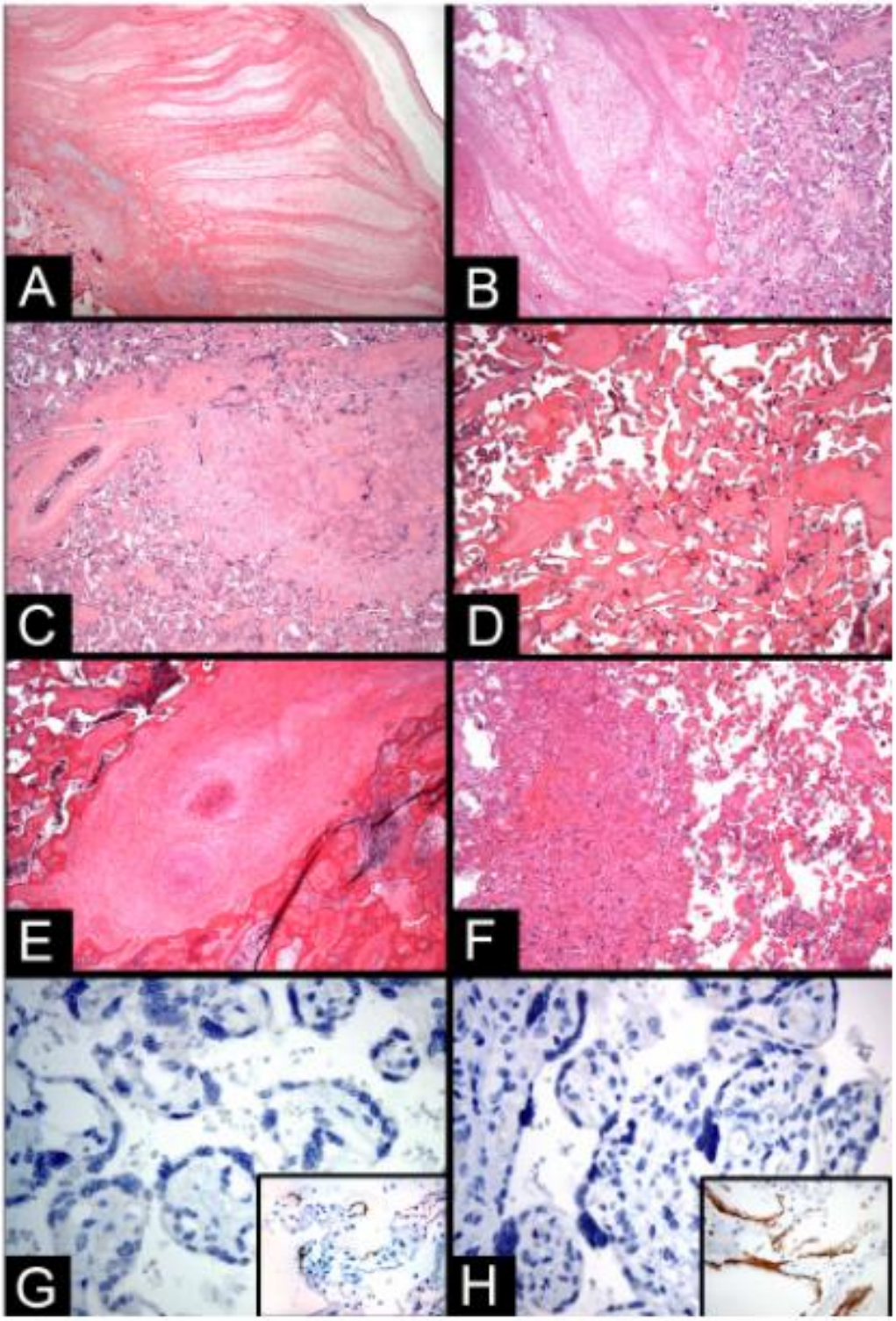


Figure 1: Subchorionic thrombi (A), intervillous thrombi (B), infarction (C), chorangiosis, segmental avascular-villi (D), fetal thrombotic vasculopathy (E), and villous agglutination (F). ISH (G) and IHC (H).

KIDNEY BIOPSY FINDINGS IN PATIENTS WITH COVID-19

Kudose S, Batal I, Santoriello D, Xu K, Barasch J, Peleg Y, Canetta P, Ratner LE, Marasa M, Gharavi AG, Stokes MB, Markowitz GS, D'Agati VD.. J Am Soc Nephrol. 2020 Jul 17:ASN.2020060802. doi: 10.1681/ASN.2020060802. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

A cross sectional study conducted in New York, United States between 13 March to 1 June 2020 by authors at Columbia University Irving Medical Center found kidney biopsies of SARS-CoV-2 infected patients (n=17; Table 1) revealed a spectrum of glomerular and tubular injuries (Figure 1, Table 3), acute kidney injury in 15 participants (88%), and lack of SARS-CoV-2 detection in kidney cells as evidence against a direct viral infection mechanism. Authors suggest SARS-CoV-2 has the potential to influence immune responses (innate and adaptive) that lead to new glomerular disease (podocytopathies and anti-glomerular basement membrane nephritis) or alloimmune conditions (lupus nephritis, membranous glomerulopathy, and allograft rejection), as well as acute tubular injury (ATI).

ABSTRACT

BACKGROUND: Coronavirus disease 2019 (COVID-19) is thought to cause kidney injury by a variety of mechanisms. To date, pathologic analyses have been limited to patient reports and autopsy series. METHODS: We evaluated biopsy samples of native and allograft kidneys from patients with COVID-19 at a single center in New York City between March and June of 2020. We also used immunohistochemistry, in situ hybridization, and electron microscopy to examine this tissue for presence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). RESULTS: The study group included 17 patients with COVID-19 (12 men, 12 black; median age of 54 years). Sixteen patients had comorbidities, including hypertension, obesity, diabetes, malignancy, or a kidney or heart allograft. Nine patients developed COVID-19 pneumonia. Fifteen patients (88%) presented with AKI; nine had nephrotic-range proteinuria. Among 14 patients with a native kidney biopsy, 5 were diagnosed with collapsing glomerulopathy, 1 was diagnosed with minimal change disease, 2 were diagnosed with membranous glomerulopathy, 1 was diagnosed with crescentic transformation of lupus nephritis, 1 was diagnosed with anti-GBM nephritis, and 4 were diagnosed with isolated acute tubular injury. The three allograft specimens showed grade 2A acute T cell-mediated rejection, cortical infarction, or acute tubular injury. Genotyping of three patients with collapsing glomerulopathy and the patient with minimal change disease revealed that all four patients had APOL1 high-risk gene variants. We found no definitive evidence of SARS-CoV-2 in kidney cells. Biopsy diagnosis informed treatment and prognosis in all patients. CONCLUSIONS: Patients with COVID-19 develop a wide spectrum of glomerular and tubular diseases. Our findings provide evidence against direct viral infection of the kidneys as the major pathomechanism for COVID-19-related kidney injury and implicate cytokine-mediated effects and heightened adaptive immune responses.

FIGURES

Pt	Age	Sex	Race	Comorbidities	IS	Temperature, °C	SpO_2 on RA	BP	Edema	COVID-19 Manifestations	Renal Presentation/ Biopsy Indications
1	46	M	B	OSA, obesity (BMI=44)	N	37.1	94	144/100	Y	Cough, fever, sore throat	AKI, NS
2	62	M	B	HTN, prostate carcinoma	N	37.2	98	126/79	Y	Fever, myalgia, weakness	AKI on CKD, NS
3	62	M	B	HTN, DM, prostate carcinoma	N	36.8	91	122/82	N	Fever, hypoxemia, bilateral perihilar and basilar infiltrates on CXR	AKI, NRP
4	57	M	B	HTN, untreated hepatitis C virus	N	38.1	97	173/92	N	Flu-like symptoms with ground glass opacities and patchy consolidation on CXR	AKI on CKD, NRP
5	61	M	B	HTN, obesity (BMI=31.1)	N	38.5	99	134/79	N	Cough, fever	AKI, NRP
6	25	M	B	Obesity (BMI=32.2)	N	38.5	95	117/79	Y	Cough, fever, myalgia, infiltrates on CXR	AKI, NS
7	43	F	B	DM, HLD, streptococcal infection, obesity (BMI=52.5)	N	37.6	96	107/67	N	Cough, fever, sore throat, weakness, patchy LUL infiltrates on CXR	AKI
8	28	M	B	None	N	38.6	96 (on O_2)	143/62	N	Cough, fever, hypoxemia, bilateral infiltrates on CXR, elevated troponin and CPK	AKI
9	67	M	W	HTN, gout, history of tobacco use, obesity (BMI=34.9)	N	36.5	95	135/75	N	Cough, diarrhea, lethargy, multifocal infiltrates on CXR	AKI on CKD
10	51	M	B	HTN, DSA+ OHTx for NICM 1 yr ago, atrial fibrillation, CVA, BPH, HLD	Y	36.8	96	117/81	N	Predominantly nausea, vomiting, abdominal pain, with cough	AKI on CKD
11	72	M	W	HTN, DM, HLD, gout, spinal stenosis, atrial fibrillation	N	36.8	97 (on O_2)	125/73	Y	Cough, pleural effusion on CT	NS
12	70	F	B	HTN, CAD, PVD, cervical carcinoma, GERD, HLD, obesity (BMI=39.4)	N	38.1	92	118/58	Y	Cough, fever, shortness of breath	AKI, NRP
13	27	F	A	SLE with class 2 lupus nephritis	Y	36.9	93	130/80	Y	Cough, fever, shortness of breath, hypoxemia, bilateral infiltrates on CXR, required intubation and ICU admission	AKI, NS
14	48	F	B	GERD, history of tobacco use, obesity	N	37.6	98	185/80	N	Cough, myalgia, infiltrates on CXR	AKI
15	54	M	W	ESKD secondary to IgAN s/p DSA+ LURTx 1 mo ago, HTN, obesity (BMI=30.7)	Y	36.8	99	116/75	N	Asymptomatic	AKI
16	22	M	B	ESKD likely secondary to PLA2R+ MGN s/p DDRTx 2 years ago, HTN	Y	37.7	95	178/127	N	Cough, fever, bilateral infiltrates on CXR, required intubation and ICU admission	CKD
17	54	F	H	ESKD secondary to PCKD s/p DDRTx 2 months ago, HTN	Y	98.8	100	104/70	N	Fever, dry throat	AKI

BP is in millimeters of Hg. Pt, patient; IS, immunosuppression at presentation; SpO_2, oxygen saturation (percentage); RA, room air; M, man; B, black; OSA, obstructive sleep apnea; BMI, body mass index; N, no; Y, yes; NS, nephrotic syndrome; HTN, hypertension; AKI on CKD, AKI superimposed on CKD; DM, diabetes mellitus; CXR, chest x-ray; NRP, nephrotic-range proteinuria; F, woman; HLD, hyperlipidemia; LUL, left upper lobe; O_2, oxygen; CPK, creatine phosphokinase; W, white; DSA, donor-specific antibody; OHTx, orthotopic heart transplantation; NICM, nonischemic cardiomyopathy; CVA, cerebrovascular accident; BPH, benign prostatic hyperplasia; CT, computed tomography; CAD, coronary artery disease; PVD, peripheral vascular disease; GERD, gastroesophageal reflux disease; A, Asian; ICU, intensive care unit; IgAN, IgA nephropathy; s/p, status post; LURTx, living unrelated renal transplantation; MGN, membranous glomerulopathy; DDRTx, deceased donor renal transplantation; H, Hispanic; PCKD, polycystic kidney disease.

Table1. Clinical findings in patients with COVID-19 who underwent kidney biopsy.

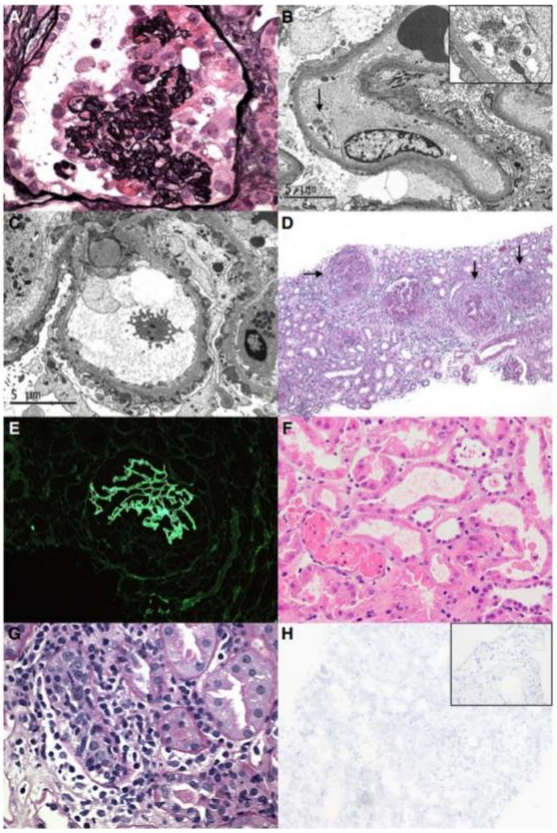


Figure 1. Kidney biopsy findings in patients with COVID-19. (A) Light microscopy demonstrates a lesion of collapsing glomerulopathy characterized by hyperplasia of glomerular epithelial cells and collapse of the underlying glomerular capillaries. Jones methanamine silver. Magnification, x 600. (B) Diffuse foot process effacement and endothelial TRIs (arrow and inset) in a patient with minimal change disease. Electron micrograph. Magnification, X 8000. (C) Subepithelial electron dense deposits in PLA2R-associated membranous glomerulopathy Electron micrograph. Magnification, X15,000. (D) Multiple glomeruli with circumferential cellular crescents (arrows) in a patient with class 4+5 lupus nephritis.Periodic acid–Schiff.Magnification, X100(E) A glomerulus compressed by a crescent with global linear GBM staining for IgG in a patient with

anti-GBM nephritis. Immunofluorescence for IgG. Magnification, X400. (F) Tubular simplification and focal shedding of degenerating epithelial cells into the tubular lumina in a patient with isolated ATI.Hematoxylin and eosin. Magnification, X 400. (G) Severe lymphocytic tubulitis in a patient with acute T cell-mediated rejection. Periodic acid–Schiff. Magnification, X 600 (H)ISH for the virus by automated method showing undetectable viral RNA in the kidney (inset shows positive lung control). Automated ISH with hematoxylin counterstain. Magnification, X 400.

Pt	Diagnosis		Light Microscopy									Electron Microscopy		
	Diagnosis	Other Findings	No. Glom	No. GS	No. Collapse	No. Noncollapsed FSGS	Hypercellularity	Microcysts	II	IFTA	VS	FPE	TRI	Viral Particles
1	Collapsing FSGS	ATI	20	0	14	0	N	Y	Focal	Mild	Mild	NA[a]	NA[a]	N
2	Collapsing FSGS	ATI	8	3	2	0	N	Y	Focal	Moderate	Moderate to severe	100	Y	N
3	Collapsing FSGS	ATI	18	4	4	1	N	Y	None	Moderate	Moderate	30	N	N
4	Collapsing FSGS	ATI	10	1	5	0	N	N	Focal	Severe	Mild	NA	NA	NA
5	Collapsing FSGS	ATI	11	3	7	0	N	Y	Focal	Severe	Moderate to severe	90	N	N
6	MCD	ATI	17	0	0	0	N	Y	None	None	None	100	Y	N
7	ATI		15	0	0	0	N	N	Focal	None	Mild	15	Y	N
8	ATI	Pigment casts	22	0	0	0	N	N	None	None	Mild	10	Y	N
9	ATI		2	1	0	0	N	N	None	Mild	Moderate	NA[a]	NA[a]	N
10	ATI		8	0	0	0	N	N	None	None	Moderate	5	N	N
11	MGN	PLA2R stain positive[b]	15	3	0	4	N	N	Focal	Mild	Mild to moderate	100	N	N
12	MGN	PLA2R stain negative[b]	3	2	0	0	N	Y	Focal	Moderate	Moderate to severe	30	Y	N
13	LN class 4+5		35	9	0	0	Mes, Endo, Crescents	N	Diffuse	Mild	Mild	90	Y	N
14	Anti-GBM GN	ATI, RBC casts	32	1	0	0	Crescents	Y	Diffuse	Mild	Moderate	NA[a]	NA[a]	N
15	TCMR grade 2A		11	1	0	0	N	N	Focal	None	Mild	NA	NA	NA
16	Infarction[c]		NA	NA	NA	NA	NA	N	Focal	Severe	NA	NA	NA	NA
17	ATI		20	1	0	0	N	N	None	None	Mild	NA	NA	NA

Pt, patient; glom, No., number; glomerulus or glomeruli; GS, global sclerosis; II, interstitial inflammation; IFTA, tubular atrophy and interstitial fibrosis; VS, vascular sclerosis; FPE, foot process effacement (percentage); N, no; Y, yes; NA, not available; MCD, minimal change disease; LN, lupus nephritis; Mes, mesangial hypercellularity; Endo, endocapillary hypercellularity; RBC, red blood cell; TCMR, T cell–mediated rejection.
[a]All glomeruli were involved by crescents in the patient with anti-GBM GN, and no glomeruli were available for ultrastructural examination in two patients with native kidney biopsies.
[b]Performed by tissue staining.
[c]Nephrectomy specimen.

Figure 1. Kidney biopsy findings in patients with COVID-19. (A) Light microscopy demonstrates a lesion of collapsing glomerulopathy characterized by hyperplasia of glomerular epithelial cells and collapse of the underlying glomerular capillaries. Jones methanamine silver. Magnification, x 600. (B) Diffuse foot process effacement and endothelial TRIs (arrow and inset) in a patient with minimal change disease. Electron micrograph. Magnification, X 8000. (C) Subepithelial electron dense deposits in PLA2R-associated membranous glomerulopathy Electron micrograph. Magnification, X15,000. (D) Multiple glomeruli with circumferential cellular crescents (arrows) in a patient with class 4+5 lupus nephritis.Periodic acid–Schiff.Magnification, X100(E) A glomerulus compressed by a crescent with global linear GBM staining for IgG in a patient with anti-GBM nephritis. Immunofluorescence for IgG. Magnification, X400. (F) Tubular simplification and focal shedding of degenerating epithelial cells into the tubular lumina in a patient with isolated ATI.Hematoxylin and eosin. Magnification, X 400. (G) Severe lymphocytic tubulitis in a patient with acute T cell-mediated rejection. Periodic acid–Schiff. Magnification, X 600 (H)ISH for the virus by automated method showing undetectable viral RNA in the kidney (inset shows positive lung control). Automated ISH with hematoxylin counterstain. Magnification, X 400.

VIRUSES AND ASTHMA: THE ROLE OF COMMON RESPIRATORY VIRUSES IN ASTHMA AND ITS POTENTIAL MEANING FOR SARS-COV-2

Novak N, Cabanillas B.. Immunology. 2020 Jul 20. doi: 10.1111/imm.13240. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

A review study conducted by allergy experts in Bonn, Germany and Madrid, Spain discussed how patients with asthma may have reduced capacity to fight off respiratory viruses due to increased Th2 inflammation and production of IL-4, IL-5, and IL-13, reduced levels of Type 1 Interferons, and increased quantities of pro-Th2 epithelial-derived cytokines (Figures 1 and 2). This authors suggest that patients with asthma who develop COVID-19 be monitored and followed up on to evaluate the sequelae and long term effects from infection with SARS-CoV-2. To note, most of the data in this publication was acquired prior to the onset of the SARS-CoV-2 pandemic.

SUMMARY

Additional points discussed:
-Asthmatic patients can have increased levels of mast cells which permit replication of respiratory viral infections.
-Two cohort studies in Wuhan found the prevalence of asthma in COVID-19 patients was not greater than that of the general population. However, a prospective cohort study in the United Kingdom found the prevalence of asthma in COVID-19 patients was 17.9% which is greater than that of the general population.
-Certain viruses may be capable of producing IgE which can exacerbate asthma symptoms.

ABSTRACT

Viral infections and atopic diseases are closely related and contribute to each other. The physiological deficiencies and immune mechanisms that underlie atopic diseases can result in a suboptimal defense against multiple viruses and promote a suitable environment for their proliferation and dissemination. Viral infections, on the other hand, can induce per se several immunological mechanisms involved in allergic inflammation capable to promote the initiation or exacerbation of atopic diseases such as atopic asthma. In a world that is affected more and more by factors that significantly impact the prevalence of atopic diseases, coronavirus disease 2019 (COVID-19) induced by the novel coronavirus severe acute respiratory syndrome (SARS-CoV-2) is having an unprecedented impact with still unpredictable consequences. Therefore, it is of crucial importance to revise the available scientific literature regarding the association between common respiratory viruses and asthma, as well as the newly emerging data about the molecular mechanisms of SARS-CoV-2 infection and its possible relation with asthma, to better understand the interrelation between common viruses and asthma and its potential meaning on the current global pandemic of COVID-19.

FIGURES

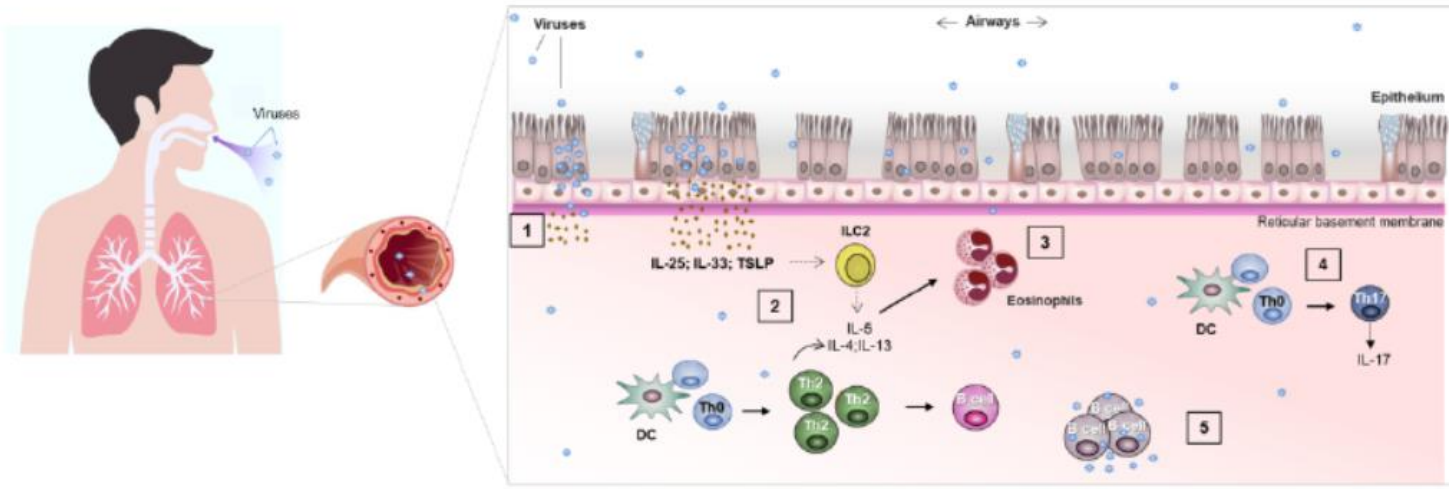


Figure 1. Mechanisms involved in the infection of respiratory viruses that can promote asthma development. Respiratory viruses can induce immunological and morphological changes that can contribute to the development of asthmatic processes. (1) Respiratory viruses replicate in the airway epithelium, which can alter the epithelial barrier integrity. (2 and 3) Infected epithelial cells promote the production of pro-inflammatory cytokines such as IL-25, IL-33, and TSLP, which induce the activation of ILC2s, DCs, Th2 cells, increasing Th2 inflammation linked to atopic asthma. (4) During respiratory viral infections, the cytokine IL-17, a proinflammatory cytokine produced by Th17 cells and linked to asthma, can increase. (5) Respiratory viruses can infect immune cells such as B cells, macrophages, or T cells which may contribute to viral replication and propagation. ILC2: group 2 innate lymphoid cells; DC: myeloid dendritic cell; TSLP: thymic stromal lymphopoietin.

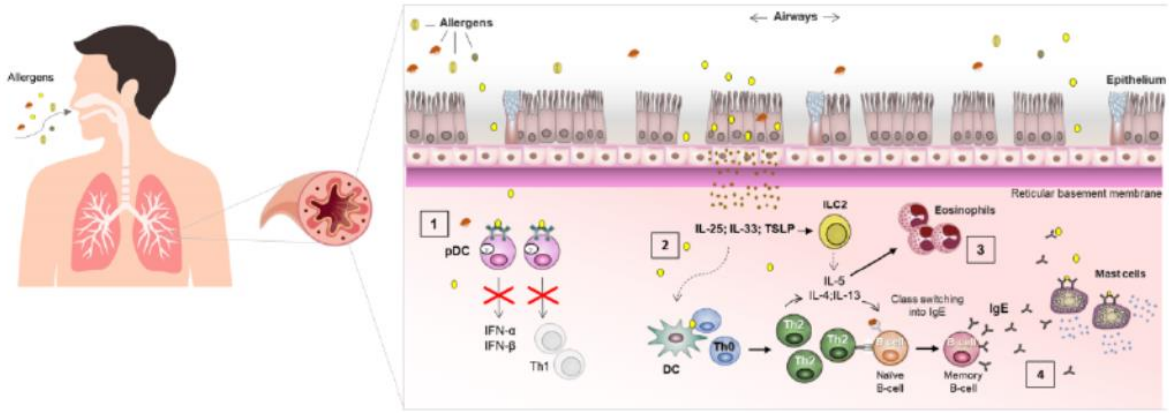


Figure 2. Pathophysiologic mechanisms of asthma that may act as facilitators of respiratory viral infections. (1) An impaired production of type I interferons (IFN-a/IFN-B) has been found in a high proportion of asthmatic patients. One of the mechanisms involves crosslinking of IgE bound to the high-affinity receptor of IgE (FCeRI) by allergens in pDCs that result in decreased TLR expression and a decline in type I interferons production. (2) Th2 inflammation in asthma linked to the production of IL-4, IL-5, and IL-13 by Th2 cells and ILC2s has been related to reduced protection against viruses. Furthermore, allergen exposure can induce production in the epithelium of cytokines that can synergistically interact with respiratory viruses. (3) Asthma is characterized by abundant infiltration of immune cells that can act as infective targets for respiratory viruses. (4) In the context of Th2 polarization in atopic asthma high amounts of specific IgE against different allergens is produced. Recent studies have proposed that specific IgE against certain viruses can also be produced. pDCs: plasmacytoid dendritic cells; ILC2: group 2 innate lymphoid cells; DC: myeloid dendritic cell; TSLP: thymic stromal lymphopoietin.

IN SILICO

ACE2 GENE VARIANTS MAY UNDERLIE INTERINDIVIDUAL VARIABILITY AND SUSCEPTIBILITY TO COVID-19 IN THE ITALIAN POPULATION

Benetti E, Tita R, Spiga O, Ciolfi A, Birolo G, Bruselles A, Doddato G, Giliberti A, Marconi C, Musacchia F, Pippucci T, Torella A, Trezza A, Valentino F, Baldassarri M, Brusco A, Asselta R, Bruttini M, Furini S, Seri M, Nigro V, Matullo G, Tartaglia M, Mari F; GEN-COVID Multicenter Study, Renieri A, Pinto AM.. Eur J Hum Genet. 2020 Jul 17. doi: 10.1038/s41431-020-0691-z. Online ahead of print.

Level of Evidence: Other - Mechanism-based reasoning

BLUF

To examine the interaction between angiotensin converting enzyme 2 (ACE2) variants and the SARS-CoV-2 spike protein, Italian investigators conducted molecular dynamics simulations of databased genomes of non-Finnish European and Italian COVID-19 patients in March 2020. Investigators identified the following:

- Several specific ACE2 variants were present in Italian/non-Finnish European populations but absent in East Asian populations that affected key interactions with SARS-CoV-2 spike protein binding to ACE2.
- When compared to an Italian control group, Italian COVID-19 patients had an overall lower degree of ACE2 gene variability.
- In support of previous studies, a genetic component to COVID-19 susceptibility was also found, proposing that inheritance of certain ACE2 variants and variable gene expression through X-inactivation could account for differential COVID-19 morbidity among sexes and ethnic groups.
- The study was limited by a narrow number of simulated ACE2-SARS-CoV-2 interactions due to technological constraints.

ABSTRACT

In December 2019, an initial cluster of interstitial bilateral pneumonia emerged in Wuhan, China. A human-to-human transmission was assumed and a previously unrecognized entity, termed coronavirus disease-19 (COVID-19) due to a novel coronavirus (SARS-CoV-2) was described. The infection has rapidly spread out all over the world and Italy has been the first European country experiencing the endemic wave with unexpected clinical severity in comparison with Asian countries. It has been shown that SARS-CoV-2 utilizes angiotensin converting enzyme 2 (ACE2) as host receptor and host proteases for cell surface binding and internalization. Thus, a predisposing genetic background can give reason for interindividual disease susceptibility and/or severity. Taking advantage of the Network of Italian Genomes (NIG), here we mined whole-exome

sequencing data of 6930 Italian control individuals from five different centers looking for ACE2 variants. A number of variants with a potential impact on protein stability were identified. Among these, three more common missense changes, p.(Asn720Asp), p.(Lys26Arg), and p.(Gly211Arg) were predicted to interfere with protein structure and stabilization. Rare variants likely interfering with the internalization process, namely p.(Leu351Val) and p.(Pro389His), predicted to interfere with SARS-CoV-2 spike protein binding, were also observed. Comparison of ACE2 WES data between a cohort of 131 patients and 258 controls allowed identifying a statistically significant (P value < 0.029) higher allelic variability in controls compared with patients. These findings suggest that a predisposing genetic background may contribute to the observed interindividual clinical variability associated with COVID-19, allowing an evidence-based risk assessment leading to personalized preventive measures and therapeutic options.

FIGURES

Table 2 Predicted changes in ACE2 protein stability as consequence of residues changes.

Wild Residue	Residue position	Mutant Residue	Predicted ΔΔG	Interaction Network around (5 Å)	Outcome
V	506	A	-2,456	*Y180, L456, R460, P500, A501, S502, L503, F504, H505, N506, S507*	*Highly Destabilizing*
V	209	G	-2,353	*Y207, E208, V209, N210, G211, V212, Y215, D216, Y217, P565, T567*	*Highly Destabilizing*
G	377	E	-2,231	*H373,* H374, E375, M376, G377, H378, I379, A380, Y381, F315, H401, V404, G405, M408	*Highly Destabilizing*
A	264	G	-1,555	*L262, P263, A264, H265, L266, L267, W271, W478, V487, V488, E489, P490, W165*	*Destabilizing*
C	498	R	-1,539	*Y497, C498, D499, P500, A501, S502, G173, R177, L176, Y180, W459, W473, M474*	*Destabilizing*
A	246	T	-1,454	*A242, Y243, V244, R245, A246, K247, L248, M249*	*Destabilizing*
G	377	W	-1,318	*H373 .* H374, E375, M376, G377, H378, I379, A380, Y381, F315, H401, V404, G405, M408	*Destabilizing*
L	351	V	-1,173	*W349, D350, L351, G352 ,* D355, R357, Y41, S44, L45, W48	*Destabilizing*
P	389	H	-1,161	*A387, Q388, P389, F390, L391, L392,* N33, T92. Q96	*Destabilizing*
T	55	A	-0,948	N53, I54, T55, E56, E57, N58, V59	*Destabilizing*
D	206	G	-0,87	*W203, G205, D206, Y207, A396, N397, E398, G399*	*Destabilizing*
K	26	R	-0,79	*E22, E23, Q24, A25, K26, T27, L29, N90, V93*	*Destabilizing*
N	580	D	-0,629	*M579, N580, V581, R582, P583, Q524*	*Destabilizing*
S	547	C	-0,611	*I544, S545 ,* N546, S547, T548, E549, A550, G551	*Destabilizing*
A	65	V	-0,423	*N61, M62, N63, N64, A65, G66, D67, K68, Q42, S43, S44, A46*	*Destabilizing*
H	505	R	-0,345	*L503, F504, M505, F512, Y515, Y510, S511, R273*	*Destabilizing*
T	92	V	-0,322	N90, L91, T92, V93, L95, Q96, P389, L392, S563, E564	*Destabilizing*
E	329	G	-0,302	*Q325, G326, F327, W328, E329, N330, S331*	*Destabilizing*
G	211	R	-0,283	*V209, N210, G211, V212, D213, D216*	*Destabilizing*
T	92	I	-0,155	N90, L91, T92, V93, L95, Q96, P389, L392, S563, E564	*Destabilizing*
D	494	V	-0,041	*H493, D494, E495, T496, Y497*	*Destabilizing*
Q	102	P	0,036	Q98, A99, Q102, N103, G104	(Stabilizing)

DUET program results that display predicted change in folding free energy upon ACE2 missense variant (ΔΔG in kcal/mol). In the first three columns are reported single missense variants with specific position on ACE2 protein. The residues in the first column highlighted in gray are involved in N-glycosylation pattern NxT/S, therefore those missense variants determine the loss glycosylation of Asparagine 53 and 90, respectively. In the fourth column is reported ΔΔG analysis predict effects of missense variants on protein stability using an integrated computational approach. The column "Interaction Network around (5 Å)" shows for each single missense variant the residues around 5 Å. In this column, we highlight in green residues involved in spike SARS-CoV protein interaction, in yellow residues involved in Zinc coordination and finally in magenta residues of Asn involved in N-glycosylation. The last column defines the outcome of protein stability for each single missense variant. An increasing negative value for the ΔΔG is correlated with a higher destabilizing effect, while a positive value is associated with a variant predicted as stabilizing.

A SURFACE COATING THAT RAPIDLY INACTIVATES SARS-COV-2

Behzadinasab S, Chin A, Hosseini M, Poon LLM, Ducker WA.. ACS Appl Mater Interfaces. 2020 Jul 13. doi: 10.1021/acsami.0c11425. Online ahead of print.
Level of Evidence: 5 - Mechanism-based reasoning

BLUF

A collaborative basic research study investigates SARS-CoV-2 viral titer loads on glass and stainless steel surfaces when coated with cuprous oxide (Cu2O) and found a 99.9% reduction of viral loads after one hour and retained potency after multiple exposures (Table 1), suggesting use of Cu2O as a preventative measure of coating for regularly used items.

ABSTRACT

SARS-CoV-2, the virus that causes the disease COVID-19, remains viable on solids for periods of up to one week, so one potential route for human infection is via exposure to an infectious dose from a solid. We have fabricated and tested a coating that is designed to reduce the longevity of SARS-CoV-2 on solids. The coating consists of cuprous oxide (Cu2O) particles bound with polyurethane. After one hour on coated glass or stainless steel, the viral titer was reduced by about 99.9% on average compared to the uncoated sample. An advantage of a polyurethane-based coating is that polyurethane is already used to coat a large number of everyday objects. Our coating adheres well to glass and stainless steel, as well as everyday items that people may fear to touch during a pandemic, such as a doorknob, a pen, and a credit card keypad button. The coating performs well in the cross-hatch durability test and remains intact and active after 13 days immersed in water, or after exposure to multiple cycles of exposure to virus and disinfection.

FIGURES

condition	comparison	% reduction	log reduction	95% CI*	*p*-value	Figure no.
Cu_2O/PU coating on glass	glass	>99.98	>3.64	99.95	5×10^{-4}	2
Cu_2O/PU coating on stainless steel	stainless steel	99.90	2.97	98.51	8×10^{-3}	2
PU coating on glass	glass	10	0.04	-164	0.22	S7
Cu_2O/PU on glass, stored 13 days underwater	glass†	99.96	3.39	99.56	8×10^{-4}	S10
Cu_2O/PU glass, high contact angle	glass	99.89	2.97	99.22	2×10^{-6}	S8
Cu_2O/PU glass, 5× disinfection	glass	99.89	2.95	99.79	4×10^{-8}	3

* 95% confidence limit lower bound. Upper bound set at 100%. Calculated for one-tail, assuming heteroscedastic.

† Comparison sample not stored under water.

p-values for Student's t-test calculated for one-tail, assuming heteroscedastic.

Table 1. Average reduction of SARS-CoV-2 titer on Cu_2O/PU coated solid in 1 h compared to titer on uncoated solid in 1h.

REDUCING RISKY BEHAVIOR WITH HABIT REVERSAL: A REVIEW OF BEHAVIORAL STRATEGIES TO REDUCE HABITUAL HAND-TO-HEAD BEHAVIOR

Heinicke MR, Stiede JT, Miltenberger RG, Woods DW.. J Appl Behav Anal. 2020 Jul 20. doi: 10.1002/jaba.745. Online ahead of print.

Level of Evidence: Other - Guidelines and Recommendations

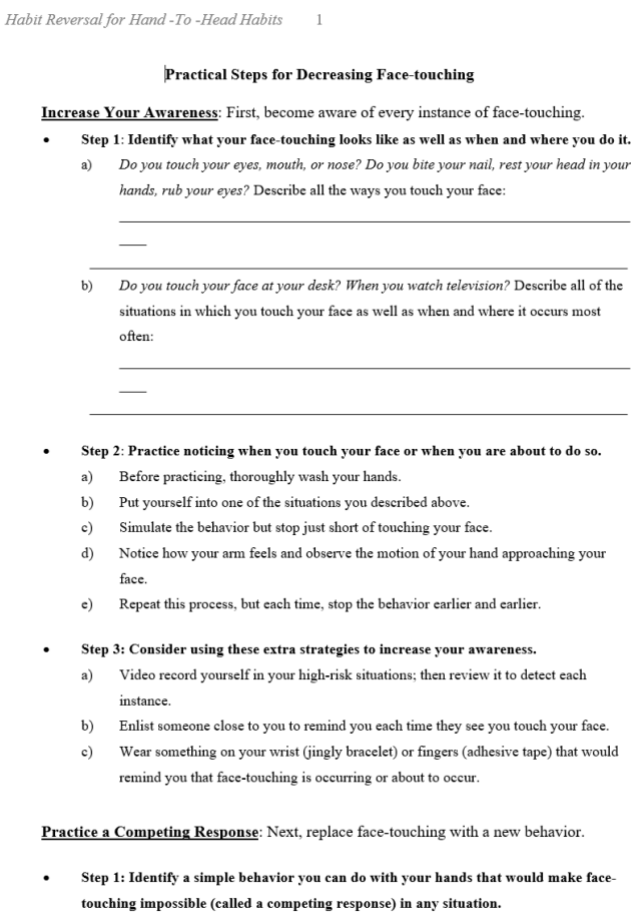
BLUF

This review by authors in psychology assessed efficacy of habit reversal training (HRT) in treating repetitive behavior problems and found HRT (increased awareness and practicing a competing response) to be effective in reducing hand-to-face or head contact, as shown in 35/39 studies examined. Authors advocate for self-administration of HRT in a wide distribution during the COVID-19 pandemic, providing recommendations/instructions for practical application (Worksheets 1 and 2) to achieve decreased face-touching and reduced disease transmission.

ABSTRACT

Habit reversal training (HRT) has been a mainstay of behavior analysts' repertoire for nearly the last 50 years. HRT has been effective in treating a host of repetitive behavior problems. In the face of the current coronavirus pandemic, HRT has practical public health importance as a possible intervention for reducing hand-to-head behaviors that increase the risk of viral infection. The current paper provides a brief review of HRT for hand-to-head habits that is designed for a broad audience and concludes with practical suggestions, based on HRT, for reducing face-touching behaviors.

FIGURES



Habit Reversal for Hand -To -Head Habits 1

Practical Steps for Decreasing Face-touching

Increase Your Awareness: First, become aware of every instance of face-touching.

- **Step 1**: **Identify what your face-touching looks like as well as when and where you do it.**
  a) *Do you touch your eyes, mouth, or nose? Do you bite your nail, rest your head in your hands, rub your eyes?* Describe all the ways you touch your face:

  _____

  ___

  _____

  b) *Do you touch your face at your desk? When you watch television?* Describe all of the situations in which you touch your face as well as when and where it occurs most often:

  _____

  ___

  _____

- **Step 2**: **Practice noticing when you touch your face or when you are about to do so.**
  a) Before practicing, thoroughly wash your hands.
  b) Put yourself into one of the situations you described above.
  c) Simulate the behavior but stop just short of touching your face.
  d) Notice how your arm feels and observe the motion of your hand approaching your face.
  e) Repeat this process, but each time, stop the behavior earlier and earlier.

- **Step 3: Consider using these extra strategies to increase your awareness.**
  a) Video record yourself in your high-risk situations; then review it to detect each instance.
  b) Enlist someone close to you to remind you each time they see you touch your face.
  c) Wear something on your wrist (jingly bracelet) or fingers (adhesive tape) that would remind you that face-touching is occurring or about to occur.

Practice a Competing Response: Next, replace face-touching with a new behavior.

- **Step 1: Identify a simple behavior you can do with your hands that would make face-touching impossible (called a competing response) in any situation.**

Worksheet 1. Habit reversal training (HRT) guidelines.

Would it be possible to make a fist and hold it in your lap? Sit on your hands? Fold your hands or arms? Describe your competing response for each situation:

_____

_____

- **Step 2: Practice your competing response.**
  a) Simulate face-touching and then immediately interrupt the behavior and use your competing response for 60 seconds.
  b) Repeat this process, but each time, interrupt the movement of your hand earlier and earlier and immediately use your competing response.ss

- **Step 3: Make the competing response a new habit in your everyday life.**
  a) Practice the exercises until you catch every movement of your hand toward your face.
  b) Continue to use the competing response during all waking hours.

- **Step 4: Consider using these extra strategies to use your competing response consistently.**
  a) Keep a tally sheet with you in high-risk situations. Each time you touch your face, mark it in first column, and each time you use your competing response before touching your face, mark it in the second column.

Continue to enlist your support person to remind you to use your competing response.

Worksheet 2. Habit reversal training (HRT) guidelines.

MANAGEMENT

ACUTE CARE

MULTIFACTORIAL PATHOGENESIS OF COVID-19-RELATED COAGULOPATHY. CAN DEFIBROTIDE HAVE A ROLE IN THE EARLY PHASES OF COAGULATION DISORDERS?

Macciò A, Madeddu C, Caocci G, La Nasa G.. J Thromb Haemost. 2020 Jul 21. doi: 10.1111/jth.15021. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

A letter written by members of the Department of Medical Sciences and Public Health at the University of Cagliari in Italy discusses the connection between infection with the SARS-CoV-2 virus and endothelial damage, platelet aggregation, and systemic inflammation associated with coagulation. The authors suggest the potential use of defibrotide in the early stages of COVID-19 due to its antithrombotic and anti-inflammatory effects, in an attempt to improve prognosis via preventing disease progression.

ABSTRACT

Thrombotic complications emerged as an important issue in patients with coronavirus disease 2019 (COVID-19). Consolidated reports regarding the clinical and laboratory findings in COVID-19 patients reveal thrombocytopenia, elevated D-dimer, prolonged prothrombin time, disseminated intravascular coagulation, and pulmonary intravascular coagulation (PIC). Recently, some authors emphasized the potential role of antiphospholipid antibodies in the pathogenesis of thrombotic events in patients with severe COVID-19.

COVID-19: WHAT TYPE OF CYTOKINE STORM ARE WE DEALING WITH?

Monneret G, Benlyamani I, Gossez M, Martin JB, Martín-Fernandez M, Sesques P, Wallet F, Venet F.. J Med Virol. 2020 Jul 18. doi: 10.1002/jmv.26317. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

An expert opinion from the Immunology Laboratory at Edouard Herriot Hospital, France discusses the use of toclizumab, a monoclonal antibody against the interleukin-6 (IL-6) receptor, in patients diagnosed with COVID-19. Though mean and median levels of IL-6 for COVID-19-positive patients are similar to those in patients with inflammatory diseases (chronic infection, rheumatoid arthritis, Crohn's disease, etc), they were found to still be lower when compared to diseases more often linked to a cytokine storm where tocilizumab would be more effective, like sepsis or cytokine release syndrome (Figure 1). However, the authors still advocate for its cautious use on an individualized basis for patients with COVID-19 based on extent of lymphopenia, presence of ARDS, disease chronology, and IL-6 level stratification.

ABSTRACT

We read with great interest the comment published by Andrianopoulos et al. in which the authors advocate for cautious use of tocilizumab in COVID-19 patients 1 . Tocilizumab is a monoclonal antibody against the interleukin-6 receptor which has immunosuppressive properties. Whereas accumulating results from uncontrolled trials present tocilizumab as an effective agent blocker of disease progression, some contrasting studies also progressively appear in COVID-19 literature 2-5 . This muddies the waters and makes the situation more confused. This article is protected by copyright. All rights reserved.

FIGURES

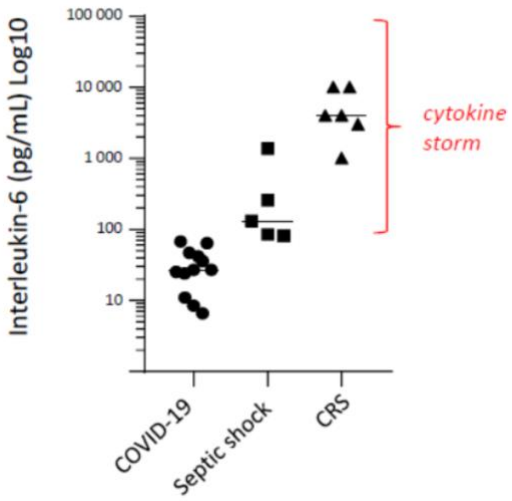


Figure 1: Median/Mean IL-6 Values in COVID-19, septic shock and cytokine release syndrome (CRS).

COVID-19 AND TREG/TH17 IMBALANCE: POTENTIAL RELATIONSHIP TO PREGNANCY OUTCOMES

Muyayalo KP, Huang DH, Zhao SJ, Xie T, Mor G, Liao AH.. Am J Reprod Immunol. 2020 Jul 14:e13304. doi: 10.1111/aji.13304. Online ahead of print.
Level of Evidence: 2 - Review / Literature Review

BLUF

A literature review summarizes the effect of Treg/Th17 cell imbalance on uncontrolled systemic inflammation in severe COVID-19 cases in pregnancy pooled from nine studies found that:
In COVID-19 positive pregnant patients:
- Treg cells decreased and Th17 cells increased, with a consequent decrease in the Treg/Th17 cell ratio.
- Treg cells dysregulation in COVID-19 was shown trigger hyperinflammation and tissue damage.
- Increased Th17 is associated with fetal allograft rejection at the feto-maternal interface.
- COVID-19 infection puts pregnant persons at higher risk for pregnancy complications.

ABSTRACT

Caused by a novel type of virus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), coronavirus disease 2019 (COVID-19) constitutes a global public health emergency. Pregnant women are considered to have a higher risk of severe morbidity and even mortality due to their susceptibility to respiratory pathogens and their particular immunological state. Several studies assessing SARS-CoV-2 infection during pregnancy reported adverse pregnancy outcomes in patients with severe conditions, including spontaneous abortion, preterm labor, fetal distress, cesarean section, preterm birth, neonatal asphyxia, neonatal pneumonia, stillbirth, and neonatal death. However, whether these complications are causally related to SARS-CoV-2 infection is not clear. Here, we reviewed the scientific evidence supporting the contributing role of Treg/Th17 cell imbalance in the uncontrolled systemic inflammation characterizing severe cases of COVID-19. Based on the recognized harmful effects of these CD4+ T cell subset imbalances in pregnancy, we speculated that SARS-CoV-2 infection might lead to adverse pregnancy outcomes through the deregulation of otherwise tightly-regulated Treg/Th17 ratios, and to subsequent uncontrolled systemic inflammation. Moreover, we discuss the possibility of vertical transmission of COVID-19 from infected mothers to their infants, which could also explain adverse perinatal outcomes. Rigorous monitoring of pregnancies and appropriate measures should be taken to prevent and treat early eventual maternal and perinatal complications.

DEVELOPMENTS IN DIAGNOSTICS

LUNG ULTRASOUND FOR TREATMENT OF PATIENTS WITH COVID-19: PLEASE REPORT YOUR SETTINGS AND MECHANICAL INDEX

Rosado-Mendez IM, Smargiassi A, Inchingolo R, Soldati G, Muller M, Demi L.. J Ultrasound Med. 2020 Jul 21. doi: 10.1002/jum.15389. Online ahead of print.
Level of Evidence: 5 - Mechanism-based reasoning

BLUF

A mechanism based reasoning study conducted by experts in Italy, Mexico, and the United States discussed the utilization of lung ultrasound (LUS) to evaluate acute respiratory distress syndrome (ARDS) and SARS-CoV-2 pneumonia, suggesting that this imaging could be beneficial for accurate diagnosis particularly in low-income and resource-poor settings. However, healthcare providers must be careful to avoid cavitation and tissue damage by minimizing the acoustic energy and scanning time without compromising diagnostic value.

PAN-FAMILY ASSAYS FOR RAPID VIRAL SCREENING: REDUCING DELAYS IN PUBLIC HEALTH RESPONSES DURING PANDEMICS

Erlichster M, Chana G, Zantomio D, Goudey B, Skafidas E.. Clin Infect Dis. 2020 Jul 20:ciaa1028. doi: 10.1093/cid/ciaa1028. Online ahead of print.
Level of Evidence: 5 - Mechanism-based reasoning

BLUF

An in silico study conducted in Australia using pan-family assays derived from 60 species of coronavirus indicates that these assays would "be expected to be sufficiently specific for a novel pathogen to allow for broad population screening" due to recognition of highly conserved regions of the viral genome (Figure 1). The authors suggest that the development of these pan-family assays would help detect SARS-CoV-2 with adequate sensitivity and specificity to be practical in largely affected areas with limited testing options. The utility of pan-family assays could prove useful not only for COVID-19, but also in any future pandemics.

ABSTRACT

BACKGROUND: COVID-19 has highlighted deficiencies in the testing capacity of many developed countries during the early stages of pandemics. Here we describe a strategy utilizing pan-family viral assays to improve early accessibility of large-scale nucleic acid testing. METHODS: Coronaviruses and SARS-CoV-2 were used as a case-study for assessing utility of pan-family viral assays during the early stages of a novel pandemic. Specificity of a pan-coronavirus (Pan-CoV) assay for a novel pathogen was assessed using the frequency of common human coronavirus (HCoV) species in key populations. A reported Pan-CoV assay was assessed to determine sensitivity to 60 reference coronaviruses, including SARS-CoV-2. The resilience of the primer target regions of this assay to mutation was assessed in 8893 high-quality SARS-CoV-2 genomes to predict ongoing utility during pandemic progression. RESULTS: Due to common HCoV species, a Pan-CoV assay would return false positives for as few as 1% of asymptomatic adults, but up to 30% of immunocompromised patients with respiratory disease. Half of reported Pan-CoV assays identify SARS-CoV-2 and with small adjustments can accommodate diverse variation observed in animal coronaviruses. The target region of one well established Pan-CoV assay is highly resistant to mutation compared to species-specific SARS-CoV-2 RT-PCR assays. CONCLUSIONS: Despite cross-reactivity with common pathogens, pan-family assays may greatly assist management of emerging pandemics through prioritization of high-resolution testing or isolation measures. Targeting highly conserved genomic regions make pan-family assays robust and resilient to mutation. A strategic stockpile of pan-family assays may improve containment of novel diseases prior to the availability of species-specific assays.

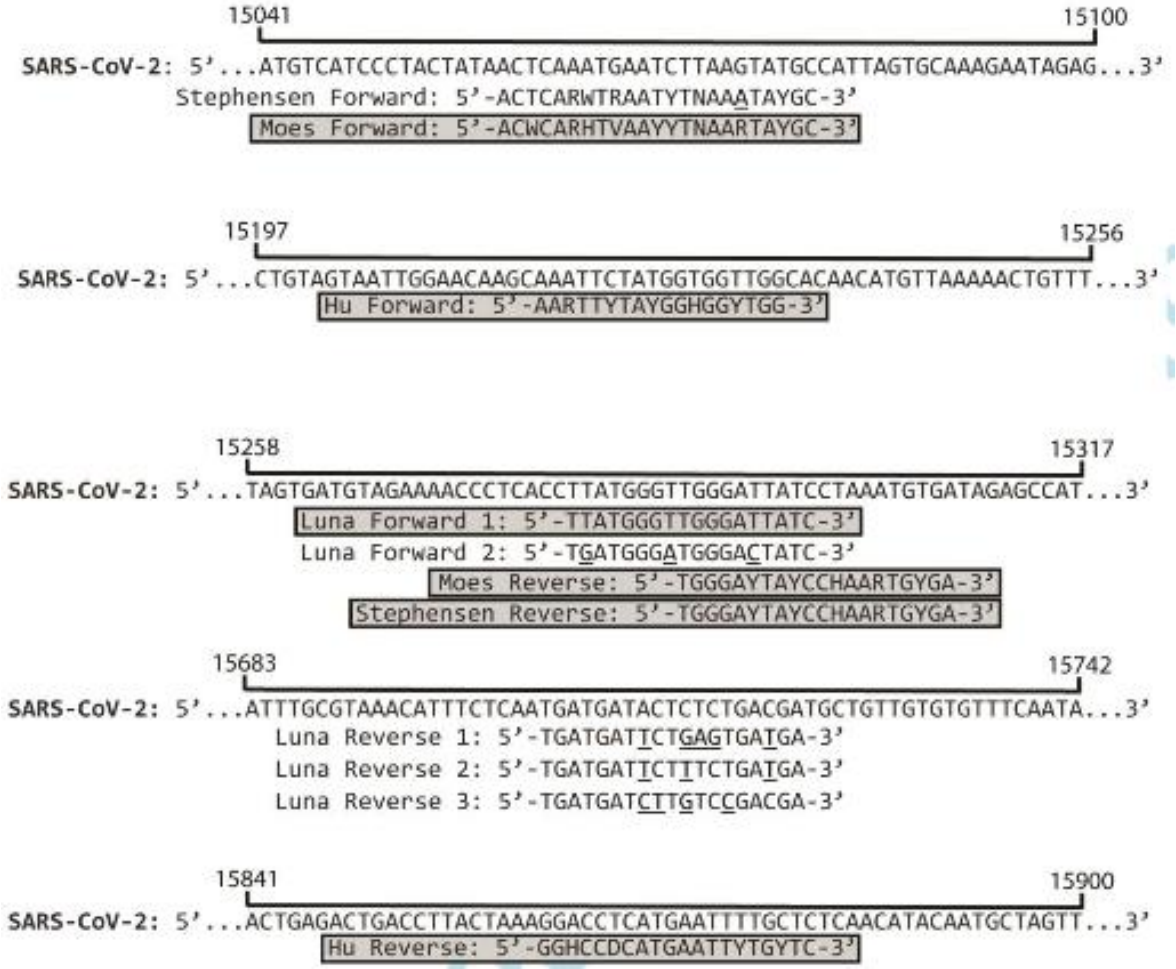


Figure 1. Alignment of 4 Reported Pan-Coronavirus Primer Targets and the SARS-CoV-2 Genome. IUPAC nucleotide code used where degenerate primers are reported. Each of the 5 rows shows a different region of the SARS2 genome. Primers targets with a 100% match to the SARS-CoV-2 genome highlighted with a gray box. Primers with mismatches between target sites and SARS-CoV-2 genome are not highlighted, with mismatched underlined.

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