The Daily COVID-19 Literature Surveillance Summary

January 18, 2021

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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

Epidemiology

- Seroprevalence of SARS-CoV-2 antibodies in over 6000 healthcare workers show increased occupational risk. Physicians and laboratory scientists from Spain conducted a cross-sectional study of 6,038 healthcare workers (HCW) across 4 regions in Spain to assess the seroprevalence of IgG anti-SARS-CoV-2 antibodies. They found 11% of HCW (n=662) had IgG against SARS-CoV-2, with those with high (OR: 2.06; 95%CI: 1.63-2.62) and moderate (OR: 1.77; 95%CI: 1.32-2.37) risk exposures more likely to have antibodies. Because this rate of seropositivity is slightly higher than in the general Spanish population, authors suggest their data confirm the occupational risk of SARS-CoV-2 infection among HCW with working in a clinical environment.

- Epidemiological characteristics and transmission dynamics of pediatric cases with COVID-19 in Hubei province, China aligns with current literature. A multidisciplinary team of researchers conducted a retrospective study of 1369 pediatric patients with COVID-19 in Hubei, China to examine the epidemiological characteristics and severity of cases. Comparison of results to adult patients (n = 68541) found that children had significantly higher number of asymptomatic cases with an epidemic curve lagging behind the adults by 19 days. Authors suggest that decreased severity in children is due to decreased expression of ACE-2 receptors in younger ages and that a lagging spike in cases may be due to differences in transmission and timing of school holidays. Overall, this information suggests that because children often present asymptomatically, prevention of household and school transmission is very important to minimize risk of spread to others.

Understanding the Pathology

- The inhaled steroid Ciclesonide blocks SARS-CoV-2 RNA replication by targeting the viral replication-transcription complex in cultured cells. An in vitro study from the National Institute of Infectious Diseases in Japan evaluates the suppression of coronavirus replication, notably MERS-CoV and SARS-CoV-2, by the inhaled corticosteroid ciclesonide in human bronchial epithelial Calu-3 cells and VeroE6/TMPRSS2 cells. Results show that Ciclesonide reduced SARS-CoV-2 replication in both VeroE6 and Calu-3 cells, and it also suppressed replication (> 90%) in Ciclesonide escape mutants. In light of these results, the authors urge further study evaluating Ciclesonide's mechanism of action and potential clinical utility.

Adjusting Practice During COVID-19

- There was an effect of the COVID-19 pandemic process on STEMI patients' timeline? An interdisciplinary group of cardiology researchers from hospitals in Samsun and Sivas, Turkey, performed a combined observational analysis as well as chart review to assess the effects that the COVID-19 pandemic has had on the management of ST elevation myocardial infarction (STEMI) patients. They concluded that there was a delayed time to first medical contact (61 minutes in non-pandemic times versus 190 minutes during the pandemic), as well as a delayed time for patients to leave their house after their onset of symptoms (30 minutes in non-pandemic times versus 165 minutes during the pandemic). While this implies that there may need to be widespread analysis of medical responses to patients experiencing STEMI, the authors do comment on the fact that the COVID-19 burden in areas studied was relatively small when compared to hotspots around the world. Further investigation is required in areas that can represent a patient population more severely burdened by COVID-19, however these results suggest an opportunity for quality improvement changes to more efficiently manage patients with STEMI during the pandemic and improve outcomes.

- What were the early postoperative outcomes among patients with delayed surgeries after preoperative positive test for SARS-CoV-2? A case-control study conducted by surgeons at the AC Camargo Cancer Center in Sao Paulo, Brazil compared the rate of post-operative complications in 49 patients who had surgery after recovering from asymptomatic SARS-CoV-2 to 98 controls who had surgery but never had COVID-19. Only 14.3% of the control patients and 16.3% of the COVID-recovered patients developed complications within 30 days (OR: 1.17; 95% CI: 0.45–3.0; p=0.74), with 6 controls and 4 COVID-recovered patients developing grade III or higher complications by Clavien-Dindo classification. Authors suggest there is no increased risk of post-operative complications among patients whose elective surgery was delayed due to asymptomatic SARS-CoV-2 positivity.

R&D: Diagnosis & Treatments

- Fluvoxamine when compared to placebo can decrease clinical deterioration in outpatients with symptomatic COVID-19. A double-blind randomized clinical trial, conducted by physicians from Washington University in St. Louis, analyzed the efficacy of fluvoxamine (100 mg 3 times daily for 15 days) against a placebo to decrease clinical deterioration of COVID-19 in non-hospitalized patients with confirmed SARS-CoV-2 infection within 7 days and oxygen saturation 92% or greater.

Clinical deterioration (defined as development of both 1) shortness of breath or hospitalization for shortness of breath or pneumonia and 2) oxygen saturation less than 92% on room air or need for supplemental oxygen to achieve oxygen saturation of 92% or greater) occurred in 0 of 80 patients in the fluvoxamine group and in 6 of 72 patients in the placebo group without a significant increase in adverse events. This clinical trial supports the hypothesis that fluvoxamine administration for COVID-19 in an outpatient setting can decrease events of clinical deterioration, though an increased sample size and length of follow up is needed.

- Repurposed Tocilizumab in patients with severe COVID-19 has shown benefits but need to be further studied. A respective study of 195 hospitalized patients in Wuhan, China found that 65 patients treated with tocilizumab sustained better outcomes compared to 130 matched patients who did not receive the IL-6 inhibitor. The tocilizumab group experienced lower in-hospital death rates, fewer ICU stay days, lower acute respiratory distress syndrome incidence rates, and lower infection related markers (IL-10, CRP). Additionally, T-cell counts were higher in the tocilizumab group, suggesting greater immune system recovery in this group. The authors suggest that, while tocilizumab was able to ameliorate the cytokine release storm associated with mortality in COVID-19, the possibility of negative effects like transaminitis should be further studied and characterized.

TABLE OF CONTENTS

CLIMATE

SCIENCE DENIAL AND COVID CONSPIRACY THEORIES: POTENTIAL NEUROLOGICAL MECHANISMS AND POSSIBLE RESPONSES

Miller BL.. JAMA. 2020 Dec 8;324(22):2255-2256. doi: 10.1001/jama.2020.21332.
Level of Evidence: 5 - Expert Opinion

BLUF

A neurologist from the Memory and Aging Center at the University of California, San Francisco discusses the importance of science literacy in understanding the COVID-19 pandemic. The author suggests that low science literacy underlies the induction of false beliefs, which has lead to incomplete conclusions over COVID-19 treatments and preventative measures and thus a lack of public compliance. He draws a parallel to distortions in neural circuitry as seen in dementia and psychiatric conditions as having a conceptually similar basis. He concludes that greater education on science literacy and public dialogue with experts in scientific fields and politicians will help to ameliorate challenges around science denial and improve science literacy.

DISPARITIES

DISPROPORTIONATE IMPACT OF THE COVID-19 PANDEMIC ON PERCEIVED SOCIAL SUPPORT, MENTAL HEALTH AND SOMATIC SYMPTOMS IN SEXUAL AND GENDER MINORITY POPULATIONS

Moore SE, Wierenga KL, Prince DM, Gillani B, Mintz LJ.. J Homosex. 2021 Jan 5:1-15. doi: 10.1080/00918369.2020.1868184. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

Researchers from Case-Western Reserve University in Cleveland, Ohio conducted a cross-sectional study of 1380 adults from March 23 to June 20, 2020, using social media recruitment and a survey including self-reported demographics, COVID-19 related items (avoiding social situations and/or experienced job loss or financial difficulties), sexual and gender identity, physical symptoms, symptoms of depression and anxiety, perceived social support, and rumination. Results reveled statistically significant higher depression and anxiety scores (reported by PHQ8 and GAD7, respectively) for respondents belonging to sexual and/or gender minority groups compared to non-minority sexual and/or gender groups ($p<0.001$ for both the PHQ8 and GAD7; Table 2). The authors call for additional longitudinal studies looking at the impacts COVID-19 has on sexual and gender minority communities in order to help eliminate the widening disparities of this population during the pandemic, and in health care in general.

ABSTRACT

Deaths from COVID-19 continue to rise, and this virus has asymmetric impacts on marginalized communities though specific impacts on sexual and gender minority communities are not well understood. From March 23 to June 20, 2020, in an online cross-sectional survey among 1380 US adults, we assessed physical symptoms, psychological symptoms, rumination, and perceived social support in order to describe differences between sexual and gender minority (n = 290) and cisgender heterosexual (n = 1090) respondents. Sexual and gender minority respondents had more frequent COVID-19-associated physical symptoms and depression and anxiety symptoms. Sexual and gender minorities had a significantly higher proportion of depression and anxiety scores exceeding the clinical concern threshold. Longitudinal studies on the physical and psychological impacts of COVID-19 among sexual and gender minority communities are needed to inform interventions to eliminate these disparities.

Variable	Sexual or Gender Minority *M (SD)*	Cis-Heterosexual *M (SD)*	Full Sample *M (SD)*	*t*-tests *t*	df	*p*
Physical Symptoms						
Number of physical symptoms experienced in the past month	6.43 (4.30)	4.58 (3.52)	4.97 (3.77)	−6.76	397.79	***<.001***
Number of COVID-19-associated Symptoms experienced in past month [a]	4.33 (2.96)	3.27 (2.51)	3.48 (2.64)	−5.61	406.70	***<.001***
Psychological Symptoms						
Anxiety Symptoms (GAD7)	9.27 (5.90)	5.83 (5.23)	6.56 (5.56)	−9.01	417.84	***<.001***
Depression Symptoms (PHQ8)	10.44 (5.87)	6.29 (5.28)	7.16 (5.67)	−10.91	421.68	***<.001***
Ruminative Responses Scale						
Brooding	10.59 (3.65)	8.73 (3.07)	9.12 (3.29)	−7.90	400.56	***<.001***
Reflection	11.48 (3.42)	9.28 (3.14)	9.74 (3.32)	−9.82	421.31	***<.001***
Medical Outcomes Survey Social Support Scale						
Emotional Support	62.79 (25.47)	69.20 (25.37)	67.85 (25.51)	3.82	1377	***<.001***
Tangible Support	68.75 (31.69)	74.87 (29.74)	73.58 (30.26)	2.96	434.16	***.003***
Affectionate Support	70.75 (30.33)	78.84 (28.05)	77.14 (28.72)	4.10	429.73	***<.001***
Positive Social Interaction Support	69.27 (28.01)	74.87 (26.22)	73.69 (26.69)	3.07	433.28	***.002***
Overall Perceived Social Support	66.59 (23.53)	72.94 (23.05)	71.61 (23.29)	4.15	1377	***<.001***

[a]based on Centers for Disease Control and Prevention reports.

Table 2. Means, standard deviations, independent samples t-tests for symptom & social support variables

EPIDEMIOLOGY

SEROPREVALENCE OF SARS-COV-2 ANTIBODIES IN OVER 6000 HEALTHCARE WORKERS IN SPAIN

Varona JF, Madurga R, Peñalver F, Abarca E, Almirall C, Cruz M, Ramos E, Castellano Vázquez JM.. Int J Epidemiol. 2021 Jan 12:dyaa277. doi: 10.1093/ije/dyaa277. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

Physicians and laboratory scientists from Spain conducted a cross-sectional study of 6,038 healthcare workers (HCW) between April 15-June 30, 2020 across 4 regions in Spain to assess the seroprevalence of IgG anti-SARS-CoV-2 antibodies (Table 1). They found 11% of HCW (n=662) had IgG against SARS-CoV-2, with those with high (OR: 2.06; 95%CI: 1.63-2.62) and moderate (OR: 1.77; 95%CI: 1.32-2.37) risk exposures more likely to have antibodies (defined in summary)(Table 3). Because this rate of seropositivity is slightly higher than in the general Spanish population, authors suggest their data confirm the occupational risk of SARS-CoV-2 infection among HCW with working in a clinical environment.

SUMMARY

The authors classified HCW into the following risk categories:
- High risk: "workers who carry out their activity in a clinical environment and have prolonged direct contact with patients (e.g. nurse, doctor, physiotherapist, porter, etc.)"
- Moderate risk: "those who work in a clinical environment and have non-intense/no patient contact, but are potentially at higher risk of nosocomial exposure (e.g. domestic and laboratory staff)"
- Low risk: "staff who work in a non-clinical environment and have minimal/no patient contact (e.g. office staff/administrative, information technology, secretarial, clerical)"

HCW older than 60 and those with a history of moderate-severe disease had higher antibody titers (median antibody-titre 11.8 and 13.7 AU/mL, respectively) than younger HCW or those with mild or asymptomatic infection (4.2, 6.4, and 5.1 AU/mL)(Figure 2).

ABSTRACT

BACKGROUND: Spain has one of the highest incidences of coronavirus disease 2019 (COVID-19) worldwide, so Spanish health care workers (HCW) are at high risk of exposure. Our objective was to determine severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antibody seroprevalence amongst HCW and factors associated with seropositivity. METHODS: A cross-sectional study evaluating 6190 workers (97.8% of the total workforce of a healthcare-system of 17 hospitals across four regions in Spain) was carried out between April and June 2020, by measuring immunoglobulin G (IgG) -SARS-CoV-2 antibody titres and related clinical data. Exposure risk was categorized as high (clinical environment; prolonged/direct contact with patients), moderate (clinical environment; non-intense/no patient contact) and low (non-clinical environment). RESULTS: A total of 6038 employees (mean age 43.8 years; 71% female) were included in the final analysis. A total of 662 (11.0%) were seropositive for IgG against SARS-CoV-2 (39.4% asymptomatic). Adding available PCR-testing, 713 (11.8%) employees showed evidence of previous SARS-CoV-2 infection. However, before antibody testing, 482 of them (67%) had no previous diagnosis of SARS-CoV-2-infection. Seroprevalence was higher in high- and moderate-risk exposure (12.1 and 11.4%, respectively) compared with low-grade risk subjects (7.2%), and in Madrid (13.8%) compared with Barcelona (7.6%) and Coruna (2.0%). High-risk [odds ratio (OR): 2.06; 95% confidence interval (CI): 1.63-2.62] and moderate-risk (OR: 1.77; 95% CI: 1.32-2.37) exposures were associated with positive IgG-SARS-CoV-2 antibodies after adjusting for region, age and sex. Higher antibody titres were observed in moderate-severe disease (median antibody-titre: 13.7 AU/mL) compared with mild (6.4 AU/mL) and asymptomatic (5.1 AU/mL) infection, and also in older (>60 years: 11.8 AU/mL) compared with younger (<30 years: 4.2 AU/mL) people. CONCLUSIONS: Seroprevalence of IgG-SARS-CoV-2 antibodies in HCW is a little higher than in the general population and varies depending on regional COVID-19 incidence. The high rates of subclinical and previously undiagnosed infection observed in this study reinforce the utility of antibody screening. An occupational risk for SARS-CoV-2 infection related to working in a clinical environment was demonstrated in this HCW cohort.

		All ($n = 6038$)	Positive ($n = 662$)	Negative ($n = 5349$)	Indeterminate ($n = 27$)
Region	Madrid	3920	540 (13.8%)	3363 (85.8%)	17 (0.4%)
	Coruña	1099	22 (2.0%)	1076 (97.9%)	1 (0.1%)
	Barcelona	887	67 (7.6%)	820 (92.4%)	0 (0.0%)
	Other	132	33 (25.0%)	90 (68.2%)	9 (6.8%)
Age, years	<30	909	112 (12.3%)	785 (86.4%)	12 (1.3%)
	30–45	2679	273 (10.2%)	2395 (89.4%)	11 (0.4%)
	46–60	1881	209 (11.1%)	1668 (88.7%)	4 (0.2%)
	>60	569	68 (11.9%)	501 (88.0%)	0 (0.0%)
Sex	Male	1744	195 (11.2%)	1542 (88.4%)	7 (0.4%)
	Female	4294	467 (10.9%)	3807 (88.7%)	20 (0.5%)
Exposure risk	Low-grade	1238	89 (7.2%)	1148 (92.7%)	1 (0.1%)
	Moderate-grade	1014	116 (11.4%)	881 (86.9%)	17 (1.7%)
	High-grade	3786	457 (12.1%)	3320 (87.7%)	9 (0.2%)
COVID-19 Symptoms	Yes	1253	401 (32.0%)	839 (67.0%)	13 (1.0%)
	Fever	318	174 (54.7%)	140 (44.0%)	4 (1.3%)
	Low-grade fever	342	166 (48.5%)	171 (50.0%)	5 (1.5%)
	Cough	543	227 (41.8%)	308 (56.7%)	8 (1.5%)
	Breathlessness	180	86 (47.8%)	93 (51.7%)	1 (0.6%)
	Anosmia	208	161 (77.4%)	41 (19.7%)	6 (2.9%)
	Dysgeusia	194	150 (77.3%)	40 (20.6%)	4 (2.1%)
	Diarrhoea	277	126 (45.5%)	149 (53.8%)	2 (0.7%)
PCR testing[a]	Non-testing	4977	362 (7.3%)	4595 (92.3%)	20 (0.4%)
	Positive	245	194 (79.2%)	49 (20.0%)	2 (0.8%)
	Negative	816	106 (13.0%)	705 (86.4%)	5 (0.6%)
Infection category	No infection	5300	0 (0.0%)	5300 (100.0%)	0 (0.0%)
	Asymptomatic infection	264	261 (98.9%)	2 (0.8%)	1 (0.4%)
	Mild	395	351 (88.9%)	43 (10.9%)	1 (0.3%)
	Moderate–severe	54	50 (92.6%)	4 (7.4%)	0 (0.0%)
	NA[b]	25	0 (0.0%)	0 (0.0%)	25 (100.0%)

[a]PCR testing was performed (prior to serological testing) in 1061 subjects: 763 subjects with COVID-19-compatible symptoms and 298 asymptomatic subjects with close unprotected household or hospital contact with COVID-19 patients.

[b]NA, not applicable: subjects with indeterminate IgG result and negative or non-tested PCR.

Table 1: "Geographical region, demographic characteristics, exposure grade, previous clinical data and final infection category among all participants (n = 6038), by IgG against SARS-CoV-2 results".

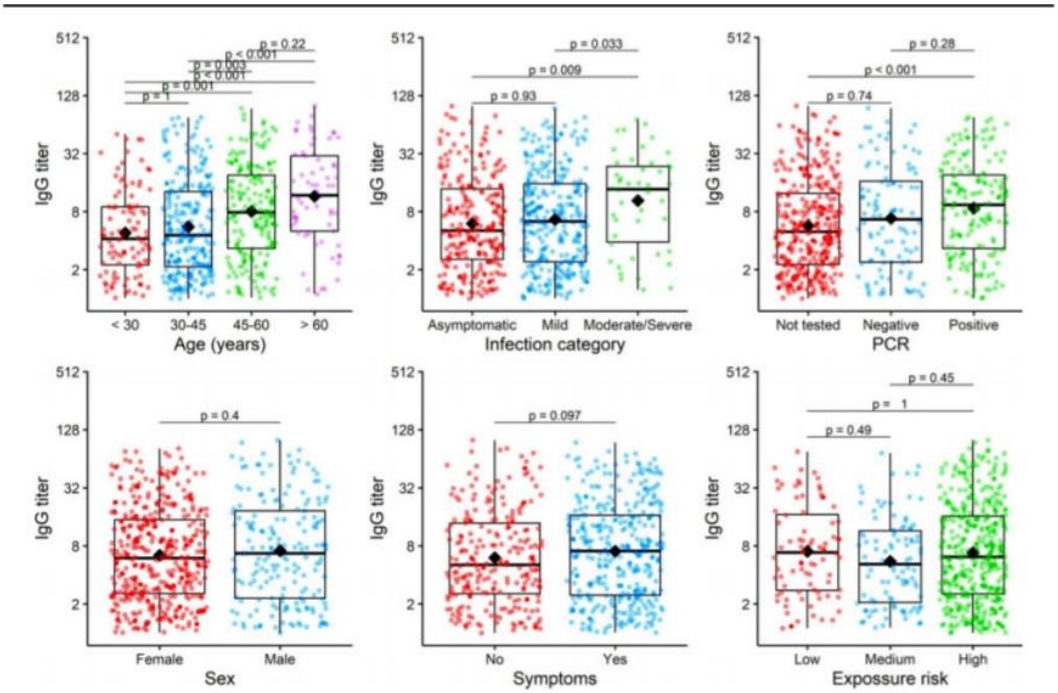

Figure 2 Boxplots of the IgG titre of the IgG-positive subjects grouped by different baseline variables: age, infection category, SARS-Cov-2 PCR result, sex, COVID-19 symptoms and exposure to COVID-19. Black diamonds represent the mean of IgG titre. The IgG titre value of all subjects are presented as jittered points by the grouping variable to help visualization. Mean differences were evaluated by Mann–Whitney U test and *P* values adjusted by Bonferroni method for multiple tests.

Figure 2: "Boxplots of the IgG titre of the IgG-positive subjects grouped by different baseline variables: age, infection category, SARS-Cov-2 PCR result, sex, COVID-19 symptoms and exposure to COVID-19. Black diamonds represent the mean of IgG titre. The IgG titre value of all subjects are presented as jittered points by the grouping variable to help visualization. Mean differences were evaluated by Mann–Whitney U test and P values adjusted by Bonferroni method for multiple tests".

		Univariate model OR (95% CI)	Multivariate model OR (95% CI)
Region	Madrid	1.000 (ref.)	1.00 (ref.)
	Barcelona	0.51 (0.39–0.66)	0.52 (0.40–0.66)
	Coruña	0.13 (0.08–0.19)	0.12 (0.08–0.18)
	Other	2.09 (1.37–3.09)	2.28 (1.51–3.37)
Age, years	<30	1.000 (ref.)	1.00 (ref.)
	30–45	0.80 (0.64–1.01)	0.84 (0.67–1.06)
	46–60	0.83 (0.66–1.06)	0.96 (0.76–1.23)
	>60	0.88 (0.64–1.21)	1.07 (0.77–1.48)
Sex	Female	1.000 (ref.)	1.00 (ref.)
	Male	1.03 (0.86–1.23)	1.02 (0.85–1.21)
Exposure Risk	Low-grade	1.000 (ref.)	1.00 (ref.)
	Moderate-grade	1.67 (1.25–2.23)	1.77 (1.32–2.37)
	High-grade	1.77 (1.41–2.26)	2.06 (1.63–2.62)
COVID-19 Symptoms	No	1.000 (ref.)	
	Yes	8.16 (6.87–9.70)	
Fever	No	1.000 (ref.)	
	Yes	12.95 (10.20–16.48)	
Low-grade fever	No	1.000 (ref.)	
	Yes	9.89 (7.85–12.46)	
Cough	No	1.000 (ref.)	
	Yes	8.36 (6.86–10.17)	
Breathlessness	No	1.000 (ref.)	
	Yes	8.39 (6.18–11.38)	
Anosmia	No	1.000 (ref.)	
	Yes	36.44 (26.21–51.57)	
Dysgeusia	No	1.000 (ref.)	
	Yes	35.50 (25.29–50.81)	
Diarrhea	No	1.000 (ref.)	
	Yes	8.08 (6.27–10.39)	
Infection category	Mild	1.00 (ref.)	
	Moderate–severe	1.57 (0.60–5.37)	

Table 3: "Results of univariate and multivariate logistic regression models for the identification of associated and independently associated factors with a positive result for IgG against SARS-CoV-2".

EMPIRIC EVIDENCE OF ETHNIC DISPARITIES IN CORONAVIRUS POSITIVITY IN WASHINGTON STATE

Pflugeisen BM, Mou J.. Ethn Health. 2021 Jan 11:1-13. doi: 10.1080/13557858.2020.1863922. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

An observational cohort study conducted by researchers from the Multicare Health system in Washington examined the relationship between ethnicity and outcomes of COVID-19 in 18,667 patients tested for COVID-19 with EHR-documented ethnicity (White, Black, Asian, Latinx, and "other"). These researchers found that there was a disproportionate amount of positive COVID-19 tests in Latinx patients (32% of patients who tested positive identified as Latinx while making up 11.2% of the tested population) (Fig. 1). In addition, odds of hospitalization were significantly higher in the Latinx population when compared to White patients (aOR = 2.19); however, this was exclusive to the Latinx population and did not hold true for the other tested ethnicities. This study discovered that many of the Latinx population identified as uninsured which suggests that there may be difficulty for these patients to manage their illness, further highlighting COVID-19 related healthcare disparities in minority populations.

ABSTRACT

OBJECTIVES: Early reports from the initial months of the coronavirus pandemic reveal ethnic disparities in coronavirus incidence, severity, and mortality. This study aimed to evaluate the relationship between ethnicity and outcomes of coronavirus positivity and hospitalization. DESIGN: An observational cohort study using electronic health record (EHR) data from a large community healthcare system in Washington State across the first phase of the pandemic (March 5 - June 7, 2020). RESULTS: A total of 18,667 patients (65.9% of all tested) with EHR-documented ethnicity were included. Overall, 6.4% of patients tested positive for coronavirus. Among Latinx patients, 18.6% of those tested were positive, compared to only 4.0% of tested White patients. Multivariable logistic regression revealed significantly higher odds of positivity for Latinxs (aOR = 4.96, 95% CI 4.19-5.87), Asians (aOR = 2.33, 95% CI 1.74-3.08), Blacks (aOR = 1.82, 95% CI 1.43-2.31), and members of other ethnic minority groups (aOR = 2.34, 95% CI 1.80-2.95), compared to Whites in models adjusting for relevant confounders. Latinxs had a higher percentage of self-pay insurance (22.2%) compared to other ethnic groups (7.9-15.8%) and, among those who tested positive, were the only ethnic subpopulation with significantly higher odds than Whites to be hospitalized for COVID-19 (aOR = 2.19, 95% CI 1.45-3.33). We observed a positive correlation between infection and the percentage of Latinxs (r = 0.61, 95% CI 0.45-0.74), Blacks (r = 0.51, 95% CI 0.32-0.66), or Asians (r = 0.64, 95% CI 0.49-0.76) in a given zip-code. This correlationwas negative for Whites (r = -0.63, 95% CI -0.75, -0.45). CONCLUSIONS: We present empirical evidence of higher rates of coronavirus positivity among People of Color compared to White people in Washington State. Social determinants of health, such as occupation, housing, healthcare access, and community structure, may contribute to health disparities in the coronavirus pandemic. Targeted capture of these variables in electronic health records is warranted to inform health equity analyses.

FIGURES

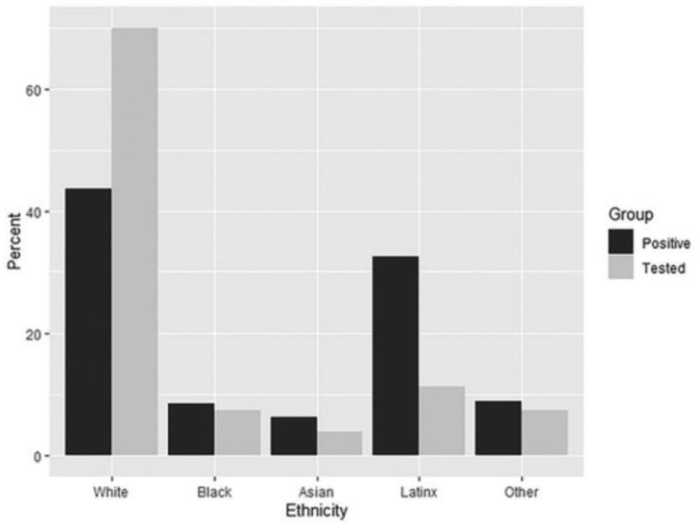

Figure 1. Distributions of the percentage of patients tested in total(black) vs. the percentage of patients that tested positive (grey).

PEDIATRICS

EPIDEMIOLOGICAL CHARACTERISTICS AND TRANSMISSION DYNAMICS OF PAEDIATRIC CASES WITH CORONAVIRUS DISEASE 2019 IN HUBEI PROVINCE, CHINA

Wang M, Nie X, Huang S, Pi W, Wang D, Zhou M, Ma J, Li M, Chen W.. J Paediatr Child Health. 2020 Dec 8. doi: 10.1111/jpc.15287. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

A multidisciplinary team of researchers conducted a retrospective study of 1369 pediatric patients with COVID-19 in Hubei, China to examine the epidemiological characteristics and severity of cases. Comparison of results to adult patients (n = 68541) found that children had significantly higher number of asymptomatic cases (Figure 1) with an epidemic curve lagging behind the adults by 19 days (Figure 2). Authors suggest that decreased severity in children is due to decreased expression of ACE-2 receptors in younger ages and that a lagging spike in cases may be due to differences in transmission and timing of school holidays. Overall, this information suggests that because children often present asymptomatically, prevention of household and school transmission is very important to minimize risk of spread to others.

ABSTRACT

AIM: This study aimed to identify the epidemiological characteristics and transmission dynamics of paediatric cases. METHODS: Information on 1369 paediatric cases with COVID-19 from 8 December 2019 to 7 March 2020 in Hubei province was extracted from the National Infectious Disease Surveillance System. The analysis included epidemic curves, temporal-spatial distribution, clinical classification and interval times between onset and diagnosis. RESULTS: Among 1369 paediatric cases, the median age was 9 years and 58.2% of them were males. The proportion of severe and critical cases in children was lower than that in adults and the proportion of asymptomatic cases in children was five times greater than for adult cases. The first paediatric case was reported on 2 January 2020, and the daily number of new paediatric cases remained high from 1 February through to 22 February. The epidemiological curve of paediatric cases lagged behind that of adults by 19 days, and the first spike of the epidemic curve in senior high school students occurred 1 week earlier than in other paediatric groups. The proportion of clustered cases among children was about twice that for adults. The median of the interval in paediatric cases between onset and diagnosis, isolation and notification were 3, 0 and 3 days, respectively, and all of those were significantly shorter than in adults. CONCLUSIONS: The epidemic curve of child cases lagged behind that of adult cases by 19 days, and the major form of transmission observed was in clusters.

	Children							Adult	
	Total	≤1 year	2–6 years	7–12 years	13–15 years	16–18 years	*P* value †	*n* (%)	*P* value ‡
Number, *n* (%)	1369 (100.0)	227 (16.6)	275 (20.1)	397 (29.0)	220 (16.1)	250 (18.26)	—	68 541 (100.0)	—
Median age, M (25Q, 75Q)	9.0 (3.0, 14.0)	—	—	—	—	—	—	54.0 (41.0, 65.0)	<0.001 §
Gender, *n* (%)							0.097 ¶		<0.001 ¶
Male	797 (58.2)	120 (52.9)	149 (54.2)	238 (60.0)	132 (60.00)	158 (63.20)		33 421 (48.8)	
Female	572 (41.8)	107 (47.1)	126 (45.8)	159 (40.1)	88 (40.0)	92 (36.80)		35 120 (51.2)	
Region, *n* (%)							0.001 ¶		<0.001 ¶
Wuhan city	857 (62.6)	167 (73.6)	180 (65.5)	240 (60.5)	122 (55.45)	148 (59.20)		50 002 (73.0)	
Non-Wuhan city	512 (37.4)	60 (26.4)	95 (34.6)	157 (39.6)	98 (44.6)	102 (40.8)		18 539 (27.1)	
Case							0.000 ¶		<0.001 ¶

Table 1. Basic characteristics of 1369 paediatric cases and 68 541 adult cases with COVID-19 in Hubei province as of 7 March 2020.

Epidemiological characteristics and transmission dynamics of paediatric cases with coronavirus disease 2019 in Hubei province, China

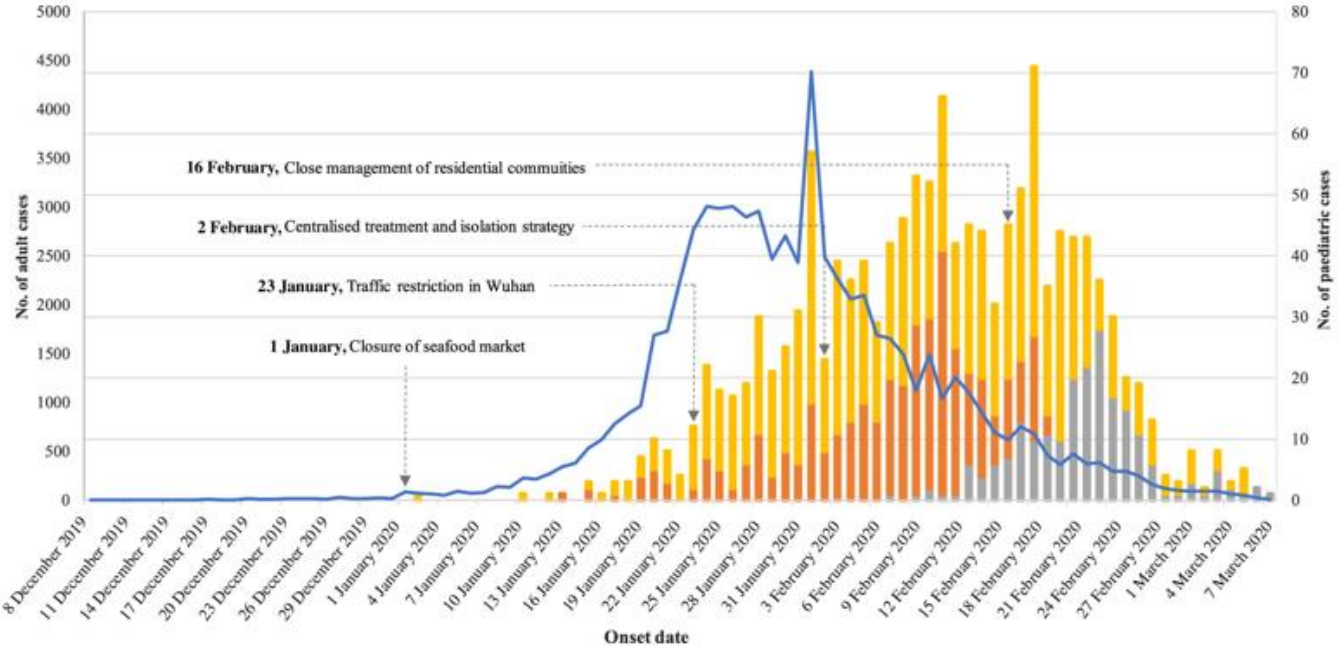

Figure 2. Trend and classification of daily new COVID-19 cases with onset date in paediatric and adult cases as of 7 March 2020.

UNDERSTANDING THE PATHOLOGY

HOW SARS-COV-2 (COVID-19) SPREADS WITHIN INFECTED HOSTS - WHAT WE KNOW SO FAR

Sanyal S.. Emerg Top Life Sci. 2020 Dec 11;4(4):371-378. doi: 10.1042/ETLS20200165.
Level of Evidence: 5 - Review / Literature Review

BLUF

This review from the University of Oxford summarizes current understanding of the pathogenesis of SARS-CoV-2 with a focus on viral entry into cells, replication, assembly of key proteins, and evasion of host immunity (Figure 1). It concludes with a call to action for additional research into these pathophysiologic mechanisms of disease.

SUMMARY

Key Points:

1. Viral entry via Spike protein-mediated attachment and fusion, as well as ACE2 and TMPRSS2 serine protease activity.
2. Viral replication through its RNA-dependent RNA polymerase (RdRp).
3. Viral assembly, release and cell-to-cell spread via various proposed mechanisms currently still being further studied.
4. Evasion of host immunity via down regulation of the immune response through binding to MHC class I molecules by SARS-CoV-2 viral protein encoding open reading frame 8 (ORF8).

ABSTRACT

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of the ongoing pandemic of coronavirus disease 2019 (COVID-19), belongs to the betacoronavirus genus and shares high homology to the severe acute respiratory syndrome coronavirus (SARS-CoV) that emerged in 2003. These are highly transmissible and pathogenic viruses which very likely originated in bats. SARS-CoV-2 uses the same receptor, angiotensin-converting enzyme 2 (ACE2) as SARS-CoV, and spreads primarily through the respiratory tract. Although several trials for vaccine development are currently underway, investigations into the virology of SARS-CoV-2 to understand the fundamental biology of the infectious cycle and the associated immunopathology underlying the clinical manifestations of COVID-19 are crucial for identification and rational design of effective therapies. This review provides an overview of how SARS-CoV-2 infects and spreads within human hosts with specific emphasis on key aspects of its lifecycle, tropism and immunopathological features.

FIGURES

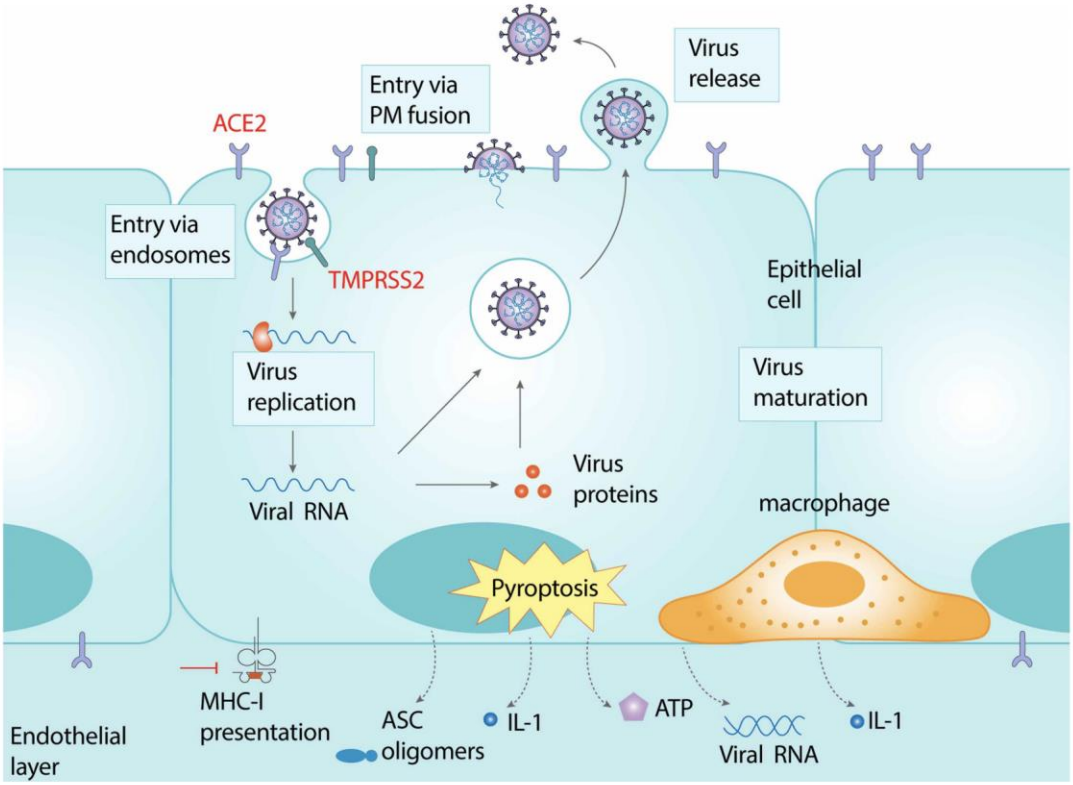

Figure 1. Schematic of the intracellular lifecycle of SARS-CoV-2 and associated immunopathology. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infects cells expressing the surface receptors angiotensinconverting enzyme 2 (ACE2) and TMPRSS2, resulting in entry of the virus via the endocytic machinery or upon fusion at the plasma membrane. The viral genome is released into the cytosol upon fusion of the viral and host membranes and undergoes replication, transcription, translation and assembly to form viral progenies that are released into the extracellular space via unknown mechanisms. Amplification and release of the virus leads to host cell pyroptosis and release of damage-associated molecular patterns, including ATP, nucleic acids and ASC oligomers. This is accompanied by secretion of pro-inflammatory cytokines and chemokines culminating in a cytokine storm. On the other hand MHC-I restricted antigen presentation is downregulated most likely by binding of the viral Orf8 protein, resulting in attenuated T-cell activation, thereby contributing to the common clinical feature of lymphopenia.

IN VITRO

HOST AND VIRAL DETERMINANTS FOR EFFICIENT SARS-COV-2 INFECTION OF THE HUMAN LUNG

Chu H, Hu B, Huang X, Chai Y, Zhou D, Wang Y, Shuai H, Yang D, Hou Y, Zhang X, Yuen TT, Cai JP, Zhang AJ, Zhou J, Yuan S, To KK, Chan IH, Sit KY, Foo DC, Wong IY, Ng AT, Cheung TT, Law SY, Au WK, Brindley MA, Chen Z, Kok KH, Chan JF, Yuen KY.. Nat Commun. 2021 Jan 8;12(1):134. doi: 10.1038/s41467-020-20457-w.
Level of Evidence: 5 - Modeling

BLUF

An interdisciplinary group of researchers from Hong Kong explored the significance of heparan sulfate and sialiac acid in the biological activity of SARS-CoV-2 as well as the significance of the furin-like cleavage site of the SARS-CoV-2 spike protein. They found that heparan sulfate and sialic acid both effect the binding of SARS-CoV-2 (heparan sulfate serves as a binding molecule, while sialiac acid prevents binding), while the endogenous structure of the furin cleavage site is vital for viral binding (experiment details in summary). Authors note that these experiments can next be taken to an in vivo model, to better examine the relationship that these molecules have with the SARS-CoV-2 virus and potentially utilize this information in potential pharmaceutical targeting.

SUMMARY

Firstly, the researchers demonstrated the role of heparan sulfate by pre-treating SARS-CoV-2 with heparan sulfate, and inoculating these treated cells with a line of epithelial lung cells as well as intestinal cells. Following this experiment, the cells themselves were treated with heparanase and further inoculated with the SARS-CoV-2. These experiments confirmed that heparan sulfate is a necessary surface binding site for SARS-CoV-2 to enter into the host cell. Next, three cell lines were treated with neuraminidase to determine the significance of sialiac acid on SARS-CoV-2 binding. The extent of effect was different per cell line, but overall higher levels of sialiac acid were correlated with hindered cell entry, and a smaller amount of viral replication. Finally, the importance of the furin cleavage site on the viral spike protein was examined by comparing its binding ability to different cell lines to a mutant form of the virus where this cell surface area is mutated. The experiments showed increased binding to the cell lines in the non-mutated virus population, demonstrating the importance of the furin cleavage site at the spike protein.

ABSTRACT

Understanding the factors that contribute to efficient SARS-CoV-2 infection of human cells may provide insights on SARS-CoV-2 transmissibility and pathogenesis, and reveal targets of intervention. Here, we analyze host and viral determinants essential for efficient SARS-CoV-2 infection in both human lung epithelial cells and ex vivo human lung tissues. We identify heparan sulfate as an important attachment factor for SARS-CoV-2 infection. Next, we show that sialic acids present on ACE2 prevent efficient spike/ACE2-interaction. While SARS-CoV infection is substantially limited by the sialic acid-mediated restriction in both human lung epithelial cells and ex vivo human lung tissues, infection by SARS-CoV-2 is limited to a lesser extent. We further demonstrate that the furin-like cleavage site in SARS-CoV-2 spike is required for efficient virus replication in human lung but not intestinal tissues. These findings provide insights on the efficient SARS-CoV-2 infection of human lungs.

THE INHALED STEROID CICLESONIDE BLOCKS SARS-COV-2 RNA REPLICATION BY TARGETING THE VIRAL REPLICATION-TRANSCRIPTION COMPLEX IN CULTURED CELLS

Matsuyama S, Kawase M, Nao N, Shirato K, Ujike M, Kamitani W, Shimojima M, Fukushi S.. J Virol. 2020 Dec 9;95(1):e01648-20. doi: 10.1128/JVI.01648-20. Print 2020 Dec 9.

Level of Evidence: 5 - Modeling

BLUF

This in vitro study from the National Institute of Infectious Diseases in Japan evaluates the suppression of coronavirus replication, notably MERS-CoV and SARS-CoV-2, by the inhaled corticosteroid ciclesonide in human bronchial epithelial Calu-3 cells and VeroE6/TMPRSS2 cells. Results show that ciclesonide reduced SARS-CoV-2 replication (Figure 5) in both VeroE6 and Calu-3 cells, and it also suppressed replication (> 90%) in ciclesonide escape mutants (Figure 7). In light of these results, the authors urge further study evaluating ciclesonide's mechanism of action and potential clinical utility.

ABSTRACT

Here, we screened steroid compounds to obtain a drug expected to block host inflammatory responses and MERS-CoV replication. Ciclesonide, an inhaled corticosteroid, suppressed replication of MERS-CoV and other coronaviruses, including SARS-CoV-2, the cause of COVID-19, in cultured cells. The effective concentration (EC90) of ciclesonide for SARS-CoV-2 in differentiated human bronchial tracheal epithelial cells was 0.55 muM. Eight consecutive passages of 43 SARS-CoV-2 isolates in the presence of ciclesonide generated 15 resistant mutants harboring single amino acid substitutions in non-structural protein 3 (nsp3) or nsp4. Of note, ciclesonide suppressed replication of all these mutants by 90% or more, suggesting that these mutants cannot completely overcome ciclesonide blockade. Under the microscope, the viral RNA replication-transcription complex in cells, which is thought to be detectable using antibodies specific for nsp3 and double stranded RNA, was observed to fall in the presence of ciclesonide in a concentration-dependent manner. These observations indicate that the suppressive effect of ciclesonide on viral replication is specific to coronaviruses, highlighting it as a candidate drug for the treatment of COVID-19 patients.IMPORTANCE The outbreak of SARS-CoV-2, the cause of COVID-19, is ongoing. New and effective antiviral agents that combat the disease are needed urgently. Here, we found that an inhaled corticosteroid, ciclesonide, suppresses replication of coronaviruses, including beta-coronaviruses (MHV-2, MERS-CoV, SARS-CoV, and SARS-CoV-2) and an alpha-coronavirus (HCoV-229E), in cultured cells. Ciclesonide is safe; indeed, it can be administered to infants at high concentrations. Thus, ciclesonide is expected to be a broad-spectrum antiviral drug that is effective against many members of the coronavirus family. It could be prescribed for treatment of MERS and COVID-19.

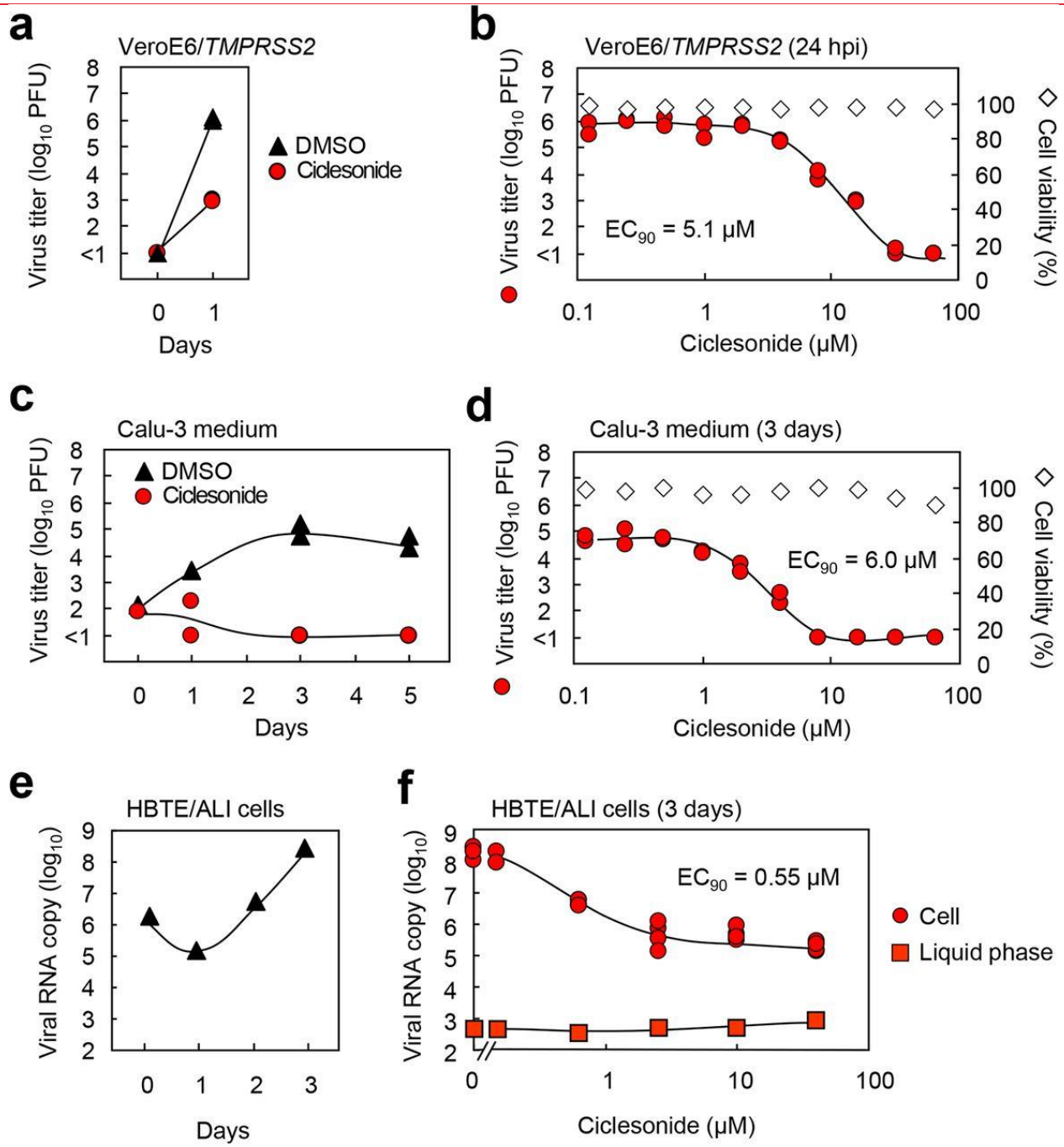

Figure 5. Ciclesonide suppresses the replication of SARS-CoV-2. (a, c, and e) Time course of SARS-CoV-2 propagation. (b, d, and f) Concentration-dependent effects of ciclesonide. VeroE6/TMPRSS2 cells (a and b), Calu-3 cells (c and d), or HBTE/ALI cells (e and f) were infected with SARS-CoV-2 at an MOI of 0.001 in the presence of DMSO or ciclesonide (10 μM) and then incubated for 1, 3, or 5 days. The virus titer in medium was quantified by a plaque assay using VeroE6/TMPRSS2 cells (n = 2 [a and c]); alternatively, the viral RNA in cells or culture medium was quantified by real-time PCR using the E gene primer/probe set (n = 1 [e] or n = 4 [f]). Average cell viability in the absence of virus was quantified using a WST assay (n = 2 [b and d]).

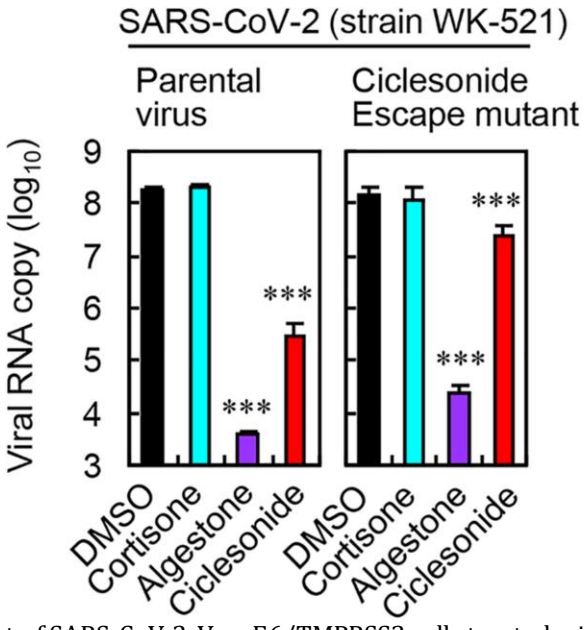

Figure 7. A ciclesonide escape mutant of SARS-CoV-2. VeroE6/TMPRSS2 cells treated with the indicated compounds (each at 10 μM) were infected with parental SARS-CoV-2 or with the ciclesonide escape mutant (MOI = 1). Viral RNA titers in cells were measured at 6.5 hpi. Data are presented as the means ± SD from 4 independent experiments. ***, $P \leq 0.001$.

HOUSEHOLD TRANSMISSION AND INCIDENCE OF POSITIVE SARS-COV-2 RT-PCR IN SYMPTOMATIC HEALTHCARE WORKERS, CLINICAL COURSE AND OUTCOME: A FRENCH HOSPITAL EXPERIENCE

Krastinova E, Garrait V, Lecam MT, Coste A, Varon E, Delacroix I, Si Ali A, Jung C, Smati M, Cherbit M, Maître B, Pairon JC, Andujar P.. Occup Environ Med. 2020 Dec 4:oemed-2020-106866. doi: 10.1136/oemed-2020-106866. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

A group of physicians from Creteil, France investigated the infection rates, clinical characteristics, occupational exposure, and household transmission of SARS-CoV-2 among symptomatic (defined as having cough & dyspnea) health care workers (HCW) from March 17th-April 20th 2020 (Table 2). They found that out of 2188 HCW at Creteil Hospital, 314 were symptomatic, 110 tested positive for SARS-CoV-2 (Figure 1), and 9 were hospitalized for an overall incidence of 5% (110/2188), demonstrating the need for better protection for HCW and a better response to positive tests, including contact tracing and resources to self-isolate.

ABSTRACT

OBJECTIVES: Although healthcare workers (HCWs) have been particularly affected by SARS-CoV-2, detailed data remain scarce. In this study, we investigated infection rates, clinical characteristics, occupational exposure and household transmission among all symptomatic HCWs screened by SARS-CoV-2 RT-PCR between 17 March (French lockdown) and 20 April. METHODS: SARS-CoV-2 RT-PCR was proposed to symptomatic (new cough or dyspnoea) HCWs at Creteil Hospital in one of the Parisian suburbs most severely affected by COVID-19. Data on occupational profile, living situation and household, together with self-isolation and mask use at home were collected, as well as the number of cases in the household. RESULTS: The incidence rate of symptomatic SARS-CoV-2 was estimated to be 5% (110/2188). A total of 110 (35%) of the 314 HCWs tested positive and 9 (8%) were hospitalised. On multivariate analysis, factors independently associated with positive RT-PCR were occupational profile with direct patient facing (OR 3.1, 95% CI 1.1 to 8.8), p<0.03), and presence of anosmia (OR 5.7, 95% CI 3.1 to 10.6), p<0.0001). Being a current smoker was associated with negative RT-PCR (OR 0.3, 95% CI 0.1 to 0.7), p=0.005). Transmission from HCWs to household members was reported in 9 (14%) cases, and 2 deaths occurred. Overall, self-isolation was possible in 52% of cases, but only 31% of HCWs were able to wear a mask at home. CONCLUSION: This is the first study to report infection rates among HCWs during the peak of the SARS-CoV-2 epidemic in France and the lockdown period, highlighting the risk related to occupational profile and household transmission.

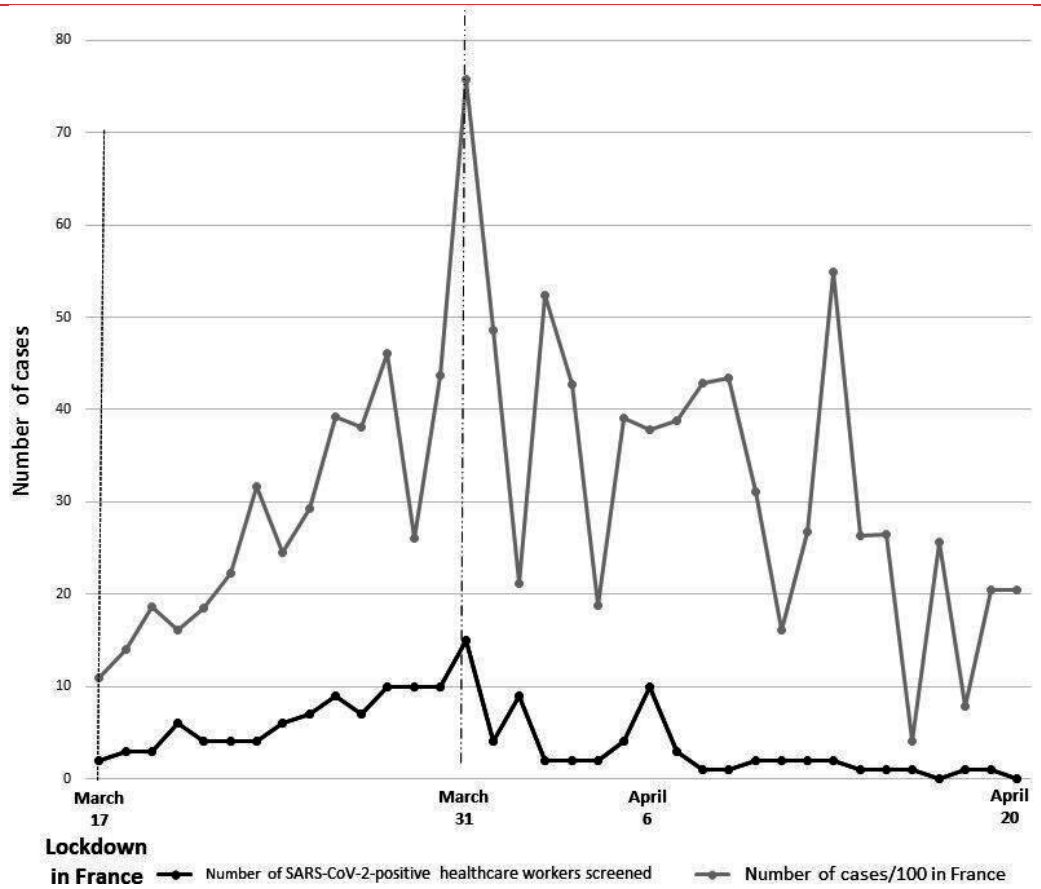

Figure 1. Number of positive SARS-CoV-2 RT-PCR tests per day in the general population in France (divided by 100) and among screened healthcare workers at Creteil Hospital between 17 March and 20 April.

Clinical characteristics	OR 95% CI	P value
Sex (M:F ratio)	0.83 (0.42 to 1.66)	0.6
Age >50 years	1.45 (0.76 to 2.77)	0.2
BMI ≥30 kg/m^2	0.92 (0.62 to 1.63)	0.8
Fever at onset	1.38 (0.51 to 3.73)	0.5
Anosmia at onset	5.57 (3.02 to 10.23)	<0.0001
Occupational profile		
Non-clinical	ref	
At-risk non-patient facing	1.57 (0.5 to 5.31)	0.4
Direct patient facing	3.08 (1.09 to 8.78)	0.03
Smoking status	ref	0.62
Never smokers		
Former smokers	0.83 (0.40 to 1.74)	
Current smokers	0.30 (0.15 to 0.62)	<0.001

BMI, body mass index.

Table 2. Multivariate analyses of factors associated with positive SARS-CoV-2 RT-PCR

"WHEN WILL WE HAVE A VACCINE?" - UNDERSTANDING QUESTIONS AND ANSWERS ABOUT COVID-19 VACCINATION

Bloom BR, Nowak GJ, Orenstein W.. N Engl J Med. 2020 Dec 3;383(23):2202-2204. doi: 10.1056/NEJMp2025331. Epub 2020 Sep 8.
Level of Evidence: 5 - Expert Opinion

BLUF

In this perspective piece published in the New England Journal of Medicine, researchers review some key steps needed before a COVID-19 vaccine can be distributed to the average US citizen, and more importantly, achieve the goal of herd immunity that would allow us to return to pre-pandemic conditions. They ultimately conclude that a safe vaccine will be available after research, engagement, and education efforts have built public trust, and vaccine recommendations are understood and accepted by the majority of the public.

SUMMARY

Key steps include:
-Developing messaging that will foster trust in the vaccine by healthcare professionals and the general public
-Providing easy access to documentation about vaccine safety and side effects
-Creating fair distribution criteria that consider societal values and community needs over politics
-Investing in resources to combat misinformation
-Extensively involving trusted healthcare professionals in vaccine endorsement measures

PREVENTION IN THE HOSPITAL

KN95 AND N95 RESPIRATORS RETAIN FILTRATION EFFICIENCY DESPITE A LOSS OF DIPOLE CHARGE DURING DECONTAMINATION

Yim W, Cheng D, Patel SH, Kou R, Meng YS, Jokerst JV.. ACS Appl Mater Interfaces. 2020 Dec 9;12(49):54473-54480. doi: 10.1021/acsami.0c17333. Epub 2020 Nov 30.
Level of Evidence: 5 - Modeling

BLUF

An experimental study, conducted by engineering professionals at the University of California, San Diego, investigated the filtration efficiency, dipole charge density, and fiber integrity of N95 and KN95 respirators before and after multiple decontamination methods that can be used to help with shortages during the COVID-19 pandemic. The study demonstrated that while there is a significant drop in dipole charge in respirators after VHP (vaporized hydrogen peroxide), IPA (isopropanol), and heat treatment (Figures 5 and 7), fiber integrity remained after heat treatment (Figure 4). Filtration efficiency did not drop substantially after heat or VHP treatment (Figures 5 and 7), though there was a significant drop after IPA treatment. While this experiment is limited in that testing is not perfectly representative of aerosols containing viral particles, it appears that heat and VHP treatment do not have large effects on the structure or efficiency of KN95 and N95 respirators.

ABSTRACT

N95 decontamination protocols and KN95 respirators have been described as solutions to a lack of personal protective equipment. However, there are a few material science studies that characterize the charge distribution and physical changes accompanying disinfection treatments, particularly heating. Here, we report the filtration efficiency, dipole charge density, and fiber integrity of N95 and KN95 respirators before and after various decontamination methods. We found that the filter layers in N95 and KN95 respirators maintained their fiber integrity without any deformations during disinfection. The filter layers of N95 respirators were 8-fold thicker and had 2-fold higher dipole charge density than that of KN95 respirators. Emergency Use Authorization (EUA)-approved KN95 respirators showed filtration efficiencies as high as N95 respirators. Interestingly, although there was a significant drop in the dipole charge in both respirators during decontamination, there was no remarkable decrease in the filtration efficiencies due to mechanical filtration. Cotton and polyester face masks had a lower filtration efficiency and lower dipole charge. In conclusion, a loss of electrostatic charge does not directly correlate to the decreased performance of either respirator.

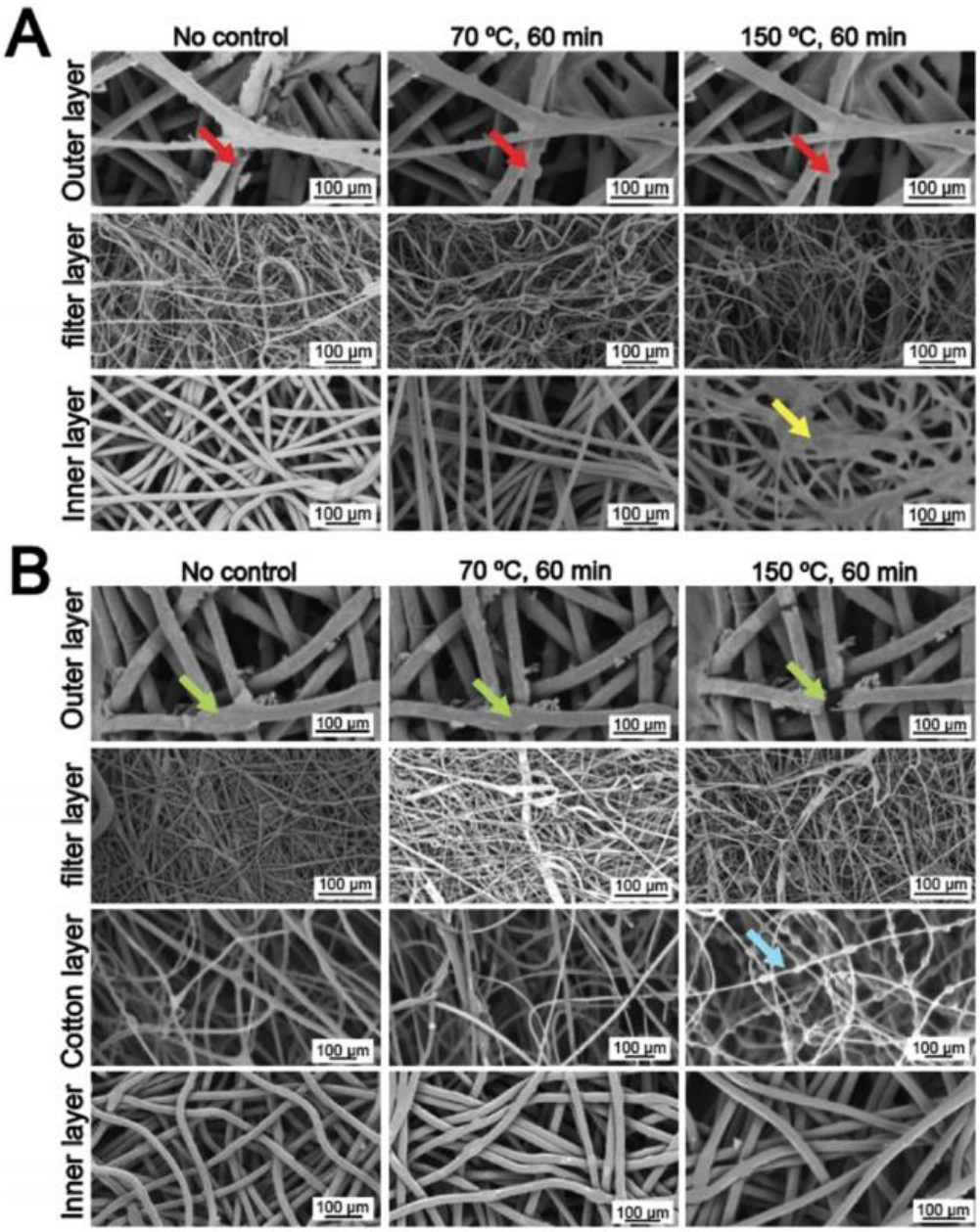

Figure 4. Fiber integrity of N95 (3M 1860) and KN95 (Yomasi) respirators. (A) Red arrows indicate that the particles attached on the outer layer of 3M 1860 are removed after heat treatment. The filter layer has no structural changes, while the inner layer begins to melt when heated at 150 °C (yellow arrow). 3M 8210 and 3M 8511 show similar results (see Figure S6A). (B) Filter layer of Yomasi has no structural deformation; however, a fracture in the outer layer (green arrows) and balloon-shaped fiber expansion in the cotton layer (blue arrow) occur when heated at 150 °C. Decopro, Powecom, and SupplyAID show similar results (see Figure S6B).

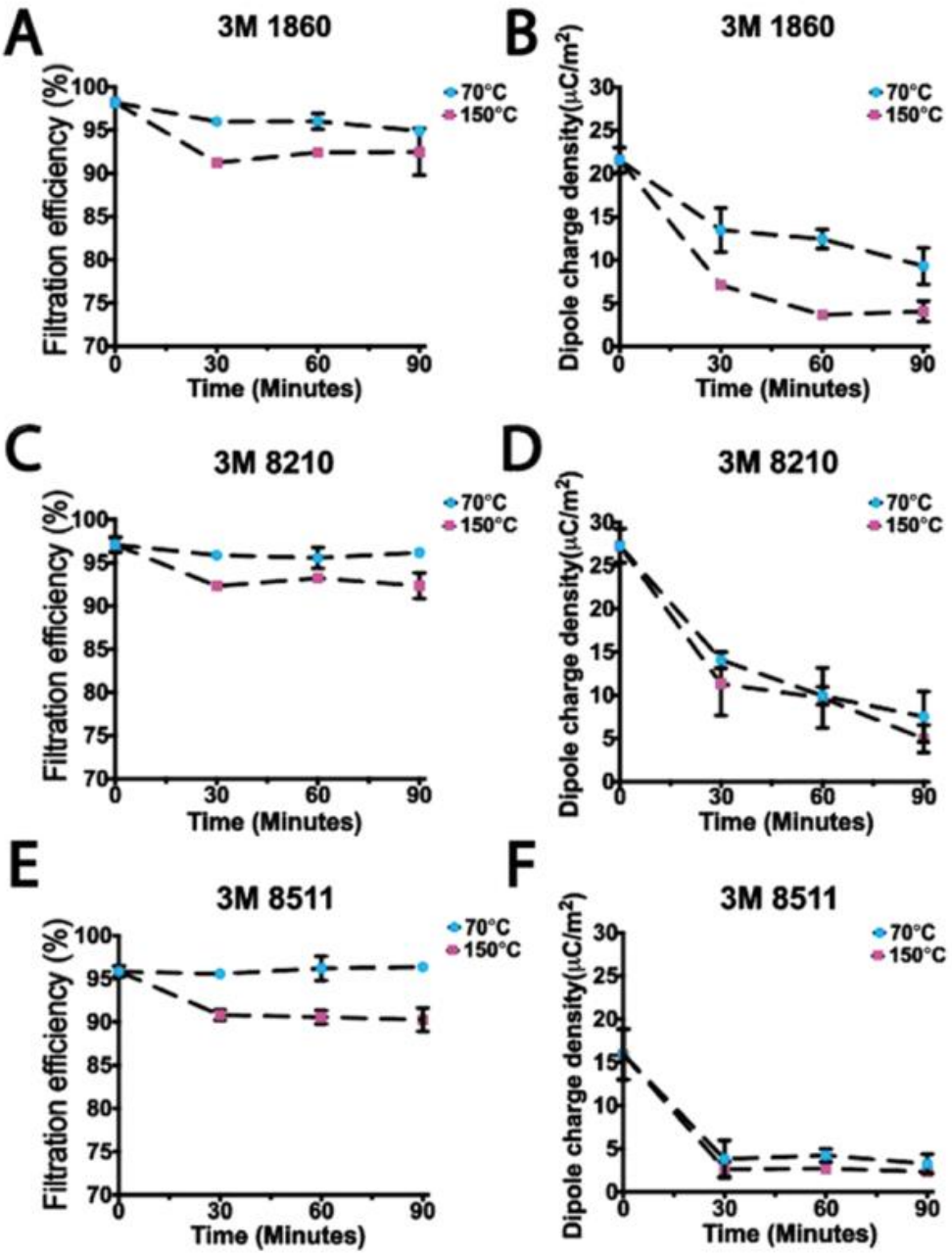

Figure 5. Filtration efficiency and dipole charge density of N95 respirators during heat treatment. Filtration efficiency of (A) 3M 1860, (C) 3M 8210, and (E) 3M 8511. Dipole charge density of (B) 3M 1860, (D) 3M 8210, and (F) 3M 8511. Dipole charge density decreases during heat treatments, but there is no remarkable drop in filtration efficiency. The error bars represent the standard deviation of five measurements.

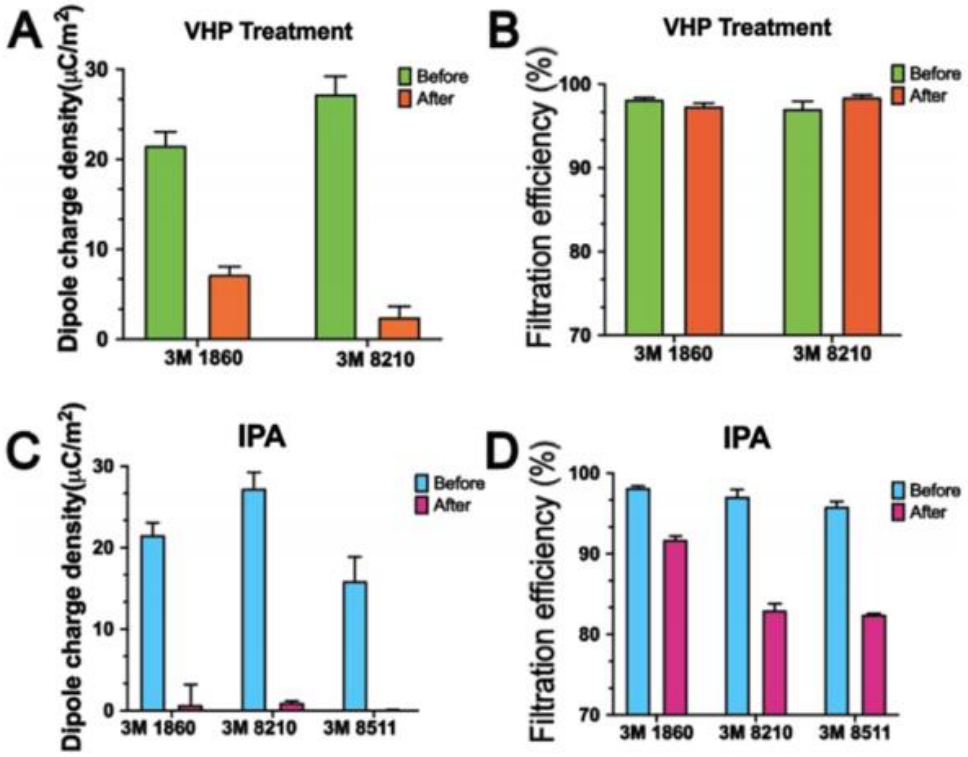

Figure 7. Dipole charge density and filtration efficiency of N95 respirators after VHP and IPA treatments. (A) Loss of dipole charge density occurs after VHP treatment. (B) N95 respirators still have high filtration efficiency after VHP treatment. (C) IPA method completely removes all dipole charges. (D) Filtration efficiencies of N95 respirators before and after IPA treatment. Filtration efficiencies of the charge-free KN95 respirators are shown in Figure S10. The error bars represent the standard deviation of five measurements.

OPTIMIZING COVID-19 SURVEILLANCE IN LONG-TERM CARE FACILITIES: A MODELLING STUDY

Smith DRM, Duval A, Pouwels KB, Guillemot D, Fernandes J, Huynh BT, Temime L, Opatowski L; AP-HP/Universities/Inserm COVID-19 research collaboration.. BMC Med. 2020 Dec 8;18(1):386. doi: 10.1186/s12916-020-01866-6.

Level of Evidence: 5 - Modeling

BLUF

A study conducted in France by Insitut Pasteur, Universite Paris-Saclay, and University of Oxford involved a model to simulate transmission of SARS-CoV-2 in contact networks similar to patient-staff interactions in a 170 bed long-term care facility (LTCF) (Figure 1), given that testing upon patient admission to LTCFs misses potential infection introductions from staff. They found high testing capacity (10 tests/100 beds/day) was most effective in detecting outbreaks prior to nosocomial infection (19-36%) or onset of symptoms (26-46%); however, with limited resources and low testing capacity (2 tests/100 beds/day), group pooling testing strategies were best able to detect outbreaks prior to symptom onset (16-27%) (Figure 2). Due to emerging outbreaks in LTCFs, increased testing capacity and updated surveillance protocols are essential in limiting SARS-CoV-2 transmission.

ABSTRACT

BACKGROUND: Long-term care facilities (LTCFs) are vulnerable to outbreaks of coronavirus disease 2019 (COVID-19). Timely epidemiological surveillance is essential for outbreak response, but is complicated by a high proportion of silent (non-symptomatic) infections and limited testing resources. METHODS: We used a stochastic, individual-based model to simulate transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) along detailed inter-individual contact networks describing patient-staff interactions in a real LTCF setting. We simulated distribution of nasopharyngeal swabs and reverse transcriptase polymerase chain reaction (RT-PCR) tests using clinical and demographic indications and evaluated the efficacy and resource-efficiency of a range of surveillance strategies, including group testing (sample pooling) and testing

cascades, which couple (i) testing for multiple indications (symptoms, admission) with (ii) random daily testing. RESULTS: In the baseline scenario, randomly introducing a silent SARS-CoV-2 infection into a 170-bed LTCF led to large outbreaks, with a cumulative 86 (95% uncertainty interval 6-224) infections after 3 weeks of unmitigated transmission. Efficacy of symptom-based screening was limited by lags to symptom onset and silent asymptomatic and pre-symptomatic transmission. Across scenarios, testing upon admission detected just 34-66% of patients infected upon LTCF entry, and also missed potential introductions from staff. Random daily testing was more effective when targeting patients than staff, but was overall an inefficient use of limited resources. At high testing capacity (> 10 tests/100 beds/day), cascades were most effective, with a 19-36% probability of detecting outbreaks prior to any nosocomial transmission, and 26-46% prior to first onset of COVID-19 symptoms. Conversely, at low capacity (< 2 tests/100 beds/day), group testing strategies detected outbreaks earliest. Pooling randomly selected patients in a daily group test was most likely to detect outbreaks prior to first symptom onset (16-27%), while pooling patients and staff expressing any COVID-like symptoms was the most efficient means to improve surveillance given resource limitations, compared to the reference requiring only 6-9 additional tests and 11-28 additional swabs to detect outbreaks 1-6 days earlier, prior to an additional 11-22 infections. CONCLUSIONS: COVID-19 surveillance is challenged by delayed or absent clinical symptoms and imperfect diagnostic sensitivity of standard RT-PCR tests. In our analysis, group testing was the most effective and efficient COVID-19 surveillance strategy for resource-limited LTCFs. Testing cascades were even more effective given ample testing resources. Increasing testing capacity and updating surveillance protocols accordingly could facilitate earlier detection of emerging outbreaks, informing a need for urgent intervention in settings with ongoing nosocomial transmission.

FIGURES

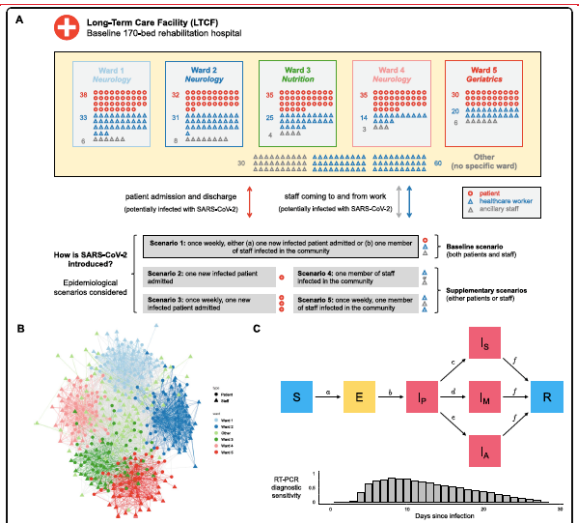

Fig. 1 Characteristics of the SARS-CoV-2 transmission model. a A diagram of the baseline LTCF, showing the average weekly number of patients and staff in each ward, including “Other” staff not primarily in any one specific ward. Below the LTCF is a description of the epidemiological scenarios considered for how SARS-CoV-2 was introduced into the LTCF. b A snapshot of the simulated dynamic contact network, showing all patients (PA, circles) and staff (PE, triangles) present in the baseline LTCF as nodes, and inter-individual contacts aggregated over one randomly selected day as edges. Nodes and edges are coloured by ward, with grey edges representing contacts across wards. c A diagram of the modified SEIR process used to characterize COVID-19 infection (S, susceptible; E, exposed; IP, infectious pre-symptomatic; IA, infectious asymptomatic; IM, infectious with mild symptoms; IS, infectious with severe symptoms; R, recovered), with transitions between states a to f (see Additional File 1: Table S1). Below, diagnostic sensitivity of RT-PCR for detecting SARS-CoV-2 in a true positive specimen was modelled as a function of time since infection

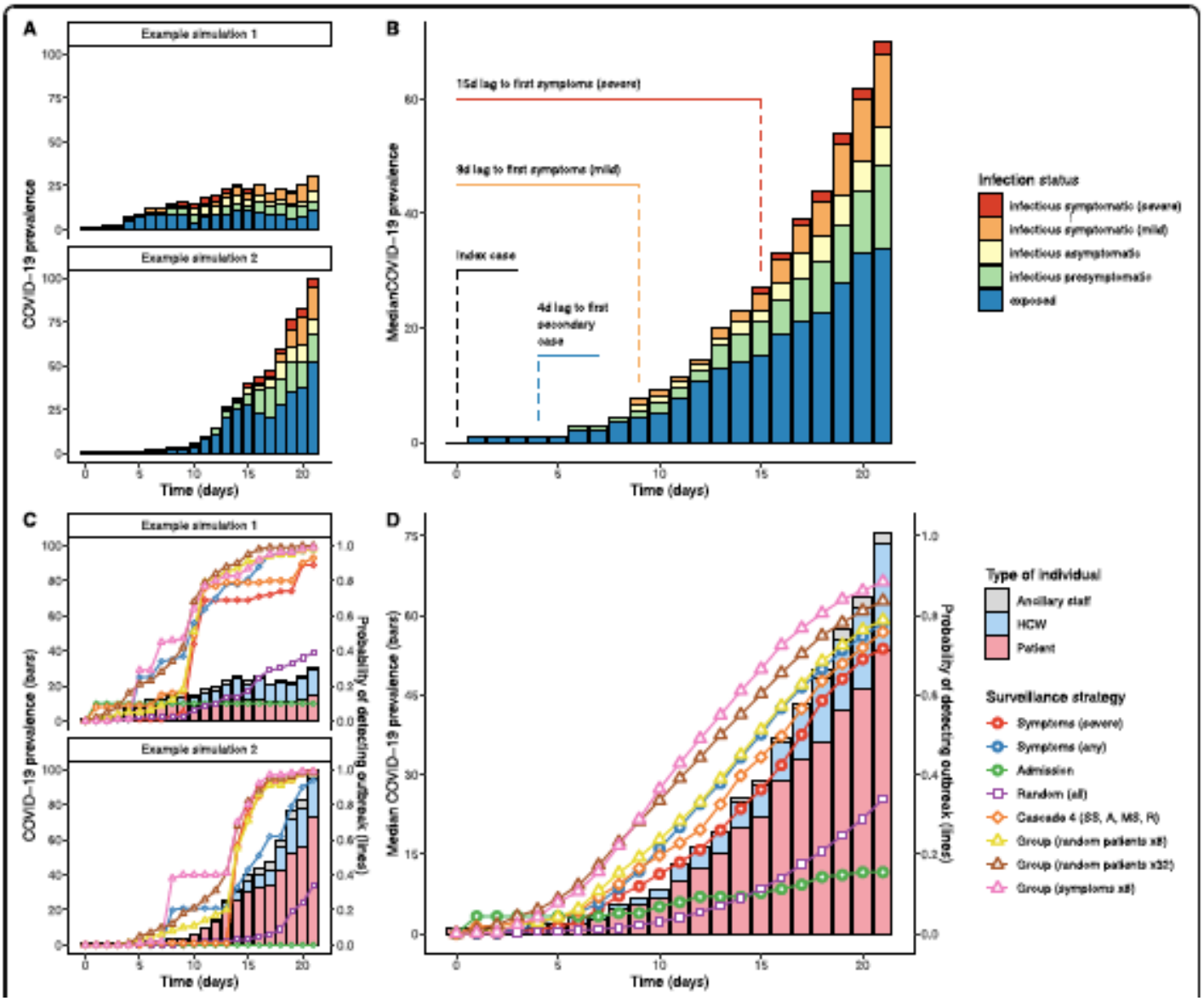

Fig. 2 Epidemic curves of COVID-19 infection resulting from random introductions of SARS-CoV-2 into a 170-bed LTCF. Symptomatic cases represent just the "tip of the iceberg" in nascent outbreaks. a Two examples of epidemic simulations, demonstrating variation in outbreak velocity and lags until first onset of COVID-19 symptoms. b The median epidemic curve across all simulations for the baseline scenario, with dotted lines demarcating median time lags to selected events. Bars represent the median number of individuals in each infection class over time, and do not necessarily total to the median number infected (e.g. there is a median 1 infection at t = 0 but a median 0 infections in each class, as each index case had an equal 1/3 probability of being exposed, pre-symptomatic or asymptomatic). For the same simulation examples (c) and median (d), the probability of detecting outbreaks varied over time for different surveillance strategies (coloured lines), depending on how many, and which types of individuals became infected over time (vertical bars); here, testing capacity = 1 test/day

LIVER MANIFESTATIONS IN COVID-19 AND THE INFLUENCE OF PRE-EXISTING LIVER DISEASE IN THE COURSE OF THE INFECTION

Guerra Veloz MF, Cordero Ruiz P, Rios Villegas MJ, Del Pino Bellido P, Bravo-Ferrer J, Galves Cordero R, Cadena Herrera ML, Vias Parrado C, Bellido Muñoz F, Vega Rodriguez F, Caunedo Álvarez Á, Rodriguez-Baño J, Carmona Soria I.. Rev Esp Enferm Dig. 2021 Jan 4;113. doi: 10.17235/reed.2020.7627/2020. Online ahead of print.
Level of Evidence: 4 - Case-series or case-control studies, or poor quality prognostic cohort study

BLUF

An interdisciplinary group of researchers from Spain conducted a retrospective single center cohort study to assess the course of SARS-CoV-2 infection in patients with chronic liver disease (CLD). This study included 447 RT-PCR positive SARS-Cov-2 patients between March 23 to April 30, 2020 in Virgen Macarena University Hospital in Seville, Spain and results suggest that patients with CLD (n=28) who tested positive for SARS-CoV-2 were more likely to be hospitalized than patients without CLD but found no significant difference in mortality rate. The authors note that these COVID-19 patients with CLD also higher prevalence of comorbidities currently known to be associated with poor COVID-19 outcomes such as cardiovascular disease, cancer, diabetes, obesity, and COPD, but they believe that these results suggest that CLD should be recognized as a risk factor for more severe COVID-19 requiring hospital admission.

SUMMARY

"liver disease" was determined to be chronic hepatitis B or C, alcohol related liver disease, autoimmune hepatitis, primary biliary cholangitis, primary sclerosis cholangitis, and non-alcoholic fatty liver disease.

ABSTRACT

Patients with advanced chronic liver disease (CLD) may be at an increased risk of a severe course due to cirrhosis-associated immune dysfunction. The aim of this study was to determine the prevalence of CLD in COVID-19 patients and to analyze the course of the infection, compared with patients with non-liver disease. Material This was a retrospective single center study of all patients with a positive SARS-Cov2 polymerase chain reaction (PCR) test from March 23 to April 30, 2020. Clinical and biochemical data of patients with and without CLD and COVID-19 were collected from the medical records. Result 447 patients with a SARS-Cov2 positive PCR were included, 6.3% had CLD. 69.7% of patients with CLD were male, with a median age of 65.5 years and active alcohol consumption and smoking 75% had non-advanced liver fibrosis and most were Non-alcoholic Fatty Liver Disease (NAFLD). The hospital admission rate (92.9% vs 47.7% p<0.001), concomitant comorbidities (diabetes 38.5 vs 16.5% p=0.011; obesity 30.8 vs 8.5% p=0.033; cancer 23.1 vs 5% p=0.027 and COPD 19.2 vs 9% p=0.009) and concomitant antibiotics treatment (19.3 vs 5%; p= 0.018) were higher in patients with CLD than those without CLD. In-patient hospital mortality rate were similar in both groups (30.8 vs 19.6% p=0.289). The presence of CLD was not associated with mortality (OR= 1.06; 95% IC= 0.35- 3.18; p=0.924). However, patients with CLD and COVID-19 who were male, obese or under concomitant antibiotic treatment had the highest risk of mortality according to the univariate analysis. Conclusion Patients with CLD had a higher risk of hospital admission, with worse outcomes during the COVID-19 infection associated to other concomitant comorbidities and a suspicion of bacterial co-infection.

EMERGENCY MEDICINE

A SIMPLE LUNG ULTRASOUND PROTOCOL FOR THE SCREENING OF COVID-19 PNEUMONIA IN THE EMERGENCY DEPARTMENT

Dacrema A, Silva M, Rovero L, Vertemati V, Losi G, Piepoli MF, Sacchi R, Mangiacotti M, Nazerian P, Pagani L, Tinelli V, Poggiali E, Bastoni D, Vercelli A, Magnacavallo A.. Intern Emerg Med. 2021 Jan 11. doi: 10.1007/s11739-020-02596-6. Online ahead of print.
Level of Evidence: 3 - Non -randomized controlled cohort/follow-up study

BLUF

A retrospective cohort study conducted in a Community Hospital in northern Italy between February 21 to March 15, 2020 included 131 patients who presented to the Emergency Department and subsequently underwent 6-scan lung ultrasound (US) protocol for COVID-19 pneumonia diagnosis (LUSCOP) in addition to high resolution computed tomography (HRCT) (See Figure 3). COVID-19 diagnosis was then confirmed in these patients by RT-PCR nasopharyngeal swabs, and their results suggest that LUSCOP was able to correctly screen/identify 130/131 COVID-19 pneumonia patients (99.2% sensitivity), indicating consistency with HRCT screening sensitivity (See Table 2). These findings suggest the use of LUSCOP protocol as a rapid, simplified, and reliable screening tool for detecting COVID-19 pneumonia that is feasible to be performed quickly by many operators and allows for prompt isolation of suspected patients to optimize safety and minimize infection transmission in the emergency department.

ABSTRACT

The most relevant manifestation of coronavirus disease 2019 (COVID-19) is interstitial pneumonia. Several lung ultrasound (US) protocols for pneumonia diagnosis are used in clinical practice, but none has been proposed for COVID-19 patients' screening in the emergency department. We adopted a simplified 6-scan lung US protocol for COVID-19 pneumonia diagnosis (LUSCOP) and compared its sensitivity with high resolution computed tomography (HRCT) in patients suspected for COVID-19, presenting to one Emergency Department from February 21st to March 15th, 2020, during the outbreak burst in northern Italy. Patients were retrospectively enrolled if both LUSCOP protocol and HRCT were performed in the Emergency Department. The sensitivity of LUSCOP protocol and HRCT were compared. COVID-19 pneumonia's final diagnosis was based on real-time reverse-transcription polymerase chain reaction from nasal-pharyngeal swab and on clinical data. Out of 150 suspected COVID-19 patients, 131 were included in the study, and 130 had a final diagnosis of COVID-19 pneumonia. The most frequent lung ultrasonographic features were: bilateral B-pattern in 101 patients (77%), B-pattern with subpleural consolidations in 26 (19.8%) and lung consolidations in 2 (1.5%). LUSCOP Protocol was consistent with HRCT in correctly screening 130 out of the 131 COVID-19 pneumonia cases (99.2%). In one case COVID-19 pneumonia was excluded by both HRCT and lung US. LUSCOP protocol showed optimal sensitivity and can be proposed as a simple screening tool for COVID-19 pneumonia diagnosis in the context of outbreak burst areas where prompt isolation of suspected patients is crucial for patients' and operators' safety.

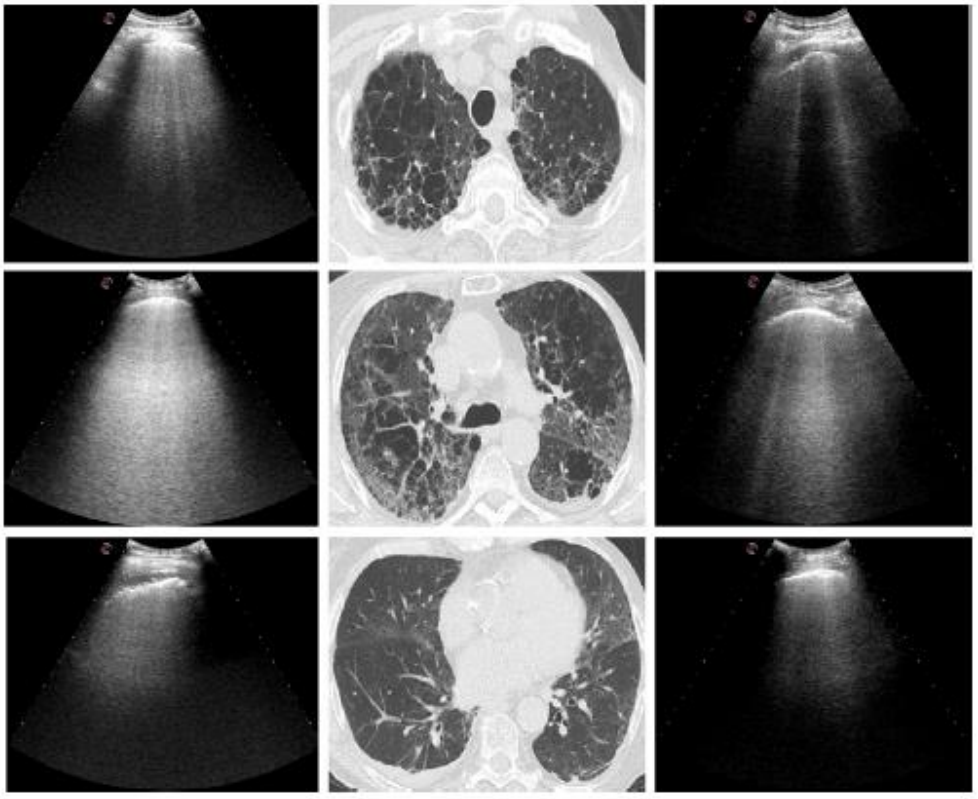

Fig. 3 Comparison between HRCT and lung US according to LUSCOP protocol. From top to bottom: upper, medium, and lower fields are shown both in HRCT slices and in the corresponding right and left lung US. HRCT shows diffuse pulmonary emphysema mostly in upper and medium fields, associated with COVID-19 bilateral dorsal, subpleural ground-glass opacities, and consolidations. In the upper fields, B-lines at the lung US correspond to areas of mild interstitial involvement. In the middle fields, lung ultrasound shows confluent B-lines with pleural thickening. In the lower fields, pleural effusion is detected by lung US in the right side, associated with pleural thickening and irregularity; the left lung US shows a predominantly A-pattern corresponding to relatively spared parenchyma.

Table 2 Confusion matrix comparing the frequency of positive and negative diagnoses according to lung US (rows) and HRCT (columns)

Lung US	HRCT (Standard)	
	Positive	Negative
Positive	129	0
Negative	1	1

Lung US lung ultrasound, *HRCT* high resolution computed tomography

Confusion matrix comparing the frequency of positive and negative diagnoses according to lung US (rows) and HRCT (columns)

NEUROSURGERY

ISCHEMIC STROKE IN COVID-19-POSITIVE PATIENTS: AN OVERVIEW OF SARS-COV-2 AND THROMBOTIC MECHANISMS FOR THE NEUROINTERVENTIONALIST

Zakeri A, Jadhav AP, Sullenger BA, Nimjee SM.. J Neurointerv Surg. 2020 Dec 9:neurintsurg-2020-016794. doi: 10.1136/neurintsurg-2020-016794. Online ahead of print.
Level of Evidence: 5 - Review / Literature Review

BLUF

A team of American neurosurgeons conducted a review to understand the correlation between SARS-CoV-2 infection and arterial/venous thrombosis. Authors suggest that COVID-19-associated coagulopathy begins with the cytokine storm, which increases expression of endothelial cell tissue factor that initiates the clotting cascade to produce fibrin and activate platelets (Figure 2). Authors believe these coagulopathies may be the reason for COVID-19-associated stroke and that understanding these mechanisms are important for prophylaxis and management.

ABSTRACT

Coronavirus disease 2019 (COVID-19) results from infection by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It was first reported in Wuhan, China in patients suffering from severe pneumonia and acute respiratory distress syndrome and has now grown into the first pandemic in over 100 years. Patients infected with SARS-CoV-2 develop arterial thrombosis including stroke, myocardial infarction and peripheral arterial thrombosis, all of which result in poor outcomes despite maximal medical, endovascular, and microsurgical treatment compared with non-COVID-19-infected patients. In this review we provide a brief overview of SARS-CoV-2, the infectious agent responsible for the COVID-19 pandemic, and describe the mechanisms responsible for COVID-19-associated coagulopathy. Finally, we discuss the impact of COVID-19 on ischemic stroke, focusing on large vessel occlusion.

FIGURES

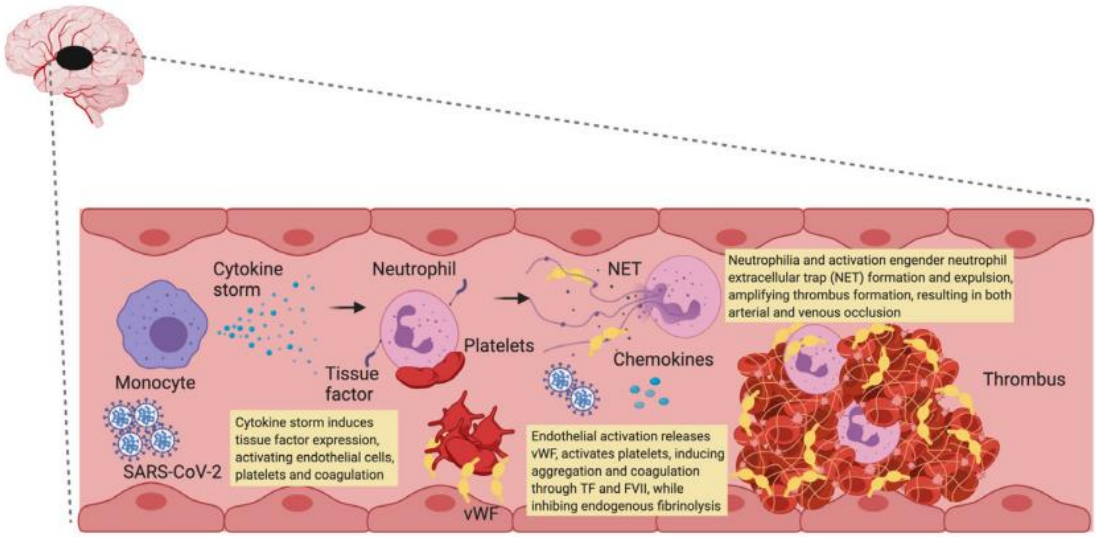

Figure 2. Summary of COVID-19-associated coagulopathy (CAC). Viral infection activates monocytes, releasing a proinflammatory cytokine storm. This results in neutrophil recruitment and tissue factor (TF) activation. TF then binds to coagulation factor VII (FVII) activating coagulation. SARS-CoV-2 infection also induces an endotheliopathy, releasing von Willebrand factor (vWF) and activating platelets, which together further amplify coagulation.
Persistent neutrophil recruitment promotes neutrophil extracellular trap (NET) formation which further facilitates thrombosis. NET formation and platelet aggregation both inhibit endogenous mechanisms of fibrinolysis including tissue factor pathway inhibitor (TFPI). These processes represent the best data describing CAC.

ADJUSTING PRACTICE DURING COVID-19

ACUTE CARE

EFFECT OF COVID-19 PANDEMIC PROCESS ON STEMI PATIENTS TIMELINE

Soylu K, Coksevim M, Yanık A, Cerik IB, Aksan G.. Int J Clin Pract. 2021 Jan 5:e14005. doi: 10.1111/ijcp.14005. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

An interdisciplinary group of cardiology researchers from hospitals in Samsun and Sivas, Turkey, performed a combined observational analysis as well as chart review to assess the effects that the COVID-19 pandemic has had on the management of ST elevation myocardial infarction (STEMI) patients. They concluded that there was a delayed time to first medical contact (61 minutes in non-pandemic times versus 190 minutes during the pandemic), as well as a delayed time for patients to leave their house after their onset of symptoms (30 minutes in non-pandemic times versus 165 minutes during the pandemic). While this implies that there may need to be widespread analysis of medical responses to patients experiencing STEMI, the authors do comment on the fact that the COVID-19 burden in areas studied was relatively small when compared to hotspots around the world. Further investigation is required in areas that can represent a patient population more severely burdened by COVID-19, however these results suggest an opportunity for quality improvement changes to more efficiently manage patients with STEMI during the pandemic and improve outcomes.

ABSTRACT

OBJECTIVE: Delayed revascularization in patients with ST-segment elevation myocardial infarction (STEMI) is associated with poor prognosis. The aim of this study is to investigate how the timeline in STEMI treatment was affected during the Covid-19 outbreak. METHOD: Consecutive 165 STEMI patients were enrolled in the study during the Covid-19 pandemic period (Pandemic period) and the pre-pandemic period (Control period). The time period until patients' leaving their current position after the onset of pain (home-delay), the time from the onset of pain to the first medical contact (FMC delay), door-to-balloon time, procedure time and hospitalization time were recorded. RESULTS: A total of 165 patients, 82 in the Pandemic period and 83 in the Control period, were included in the study. When compared with the control period, home-delay [30 (5-6912) min versus 165 (10-360) min, p <0.001] and FMC delay [61 (20-6932) min versus 190 (15-3660) min, p <0.001] were significantly prolonged during the pandemic period. In addition, non-IRA PCI rate (8.8% versus 19.3% p = 0.043) and hospitalization time [71 (15-170) versus 74.2 (37-329) hours, p = 0.045] were decreased. CONCLUSION: During the Covid-19 pandemic period, prolonged pre-hospital time parameters were observed in STEMI patients. Therefore, additional measures may be required to prevent unfavorable delays in STEMI patients during the outbreak.

SURGICAL SUBSPECIALTIES

EARLY POSTOPERATIVE OUTCOMES AMONG PATIENTS WITH DELAYED SURGERIES AFTER PREOPERATIVE POSITIVE TEST FOR SARS-COV-2: A CASE-CONTROL STUDY FROM A SINGLE INSTITUTION

Baiocchi G, Aguiar S Jr, Duprat JP, Coimbra FJF, Makdissi FB, Vartanian JG, Zequi SC, Gross JL, Nakagawa SA, Yazbek G, Diniz TP, Gonçalves BT, Zurstrassen CE, Campos HGDA, Joaquim EHG, França E Silva IA, Kowalski LP.. J Surg Oncol. 2021 Jan 11. doi: 10.1002/jso.26377. Online ahead of print.
Level of Evidence: 4 - Case-series, case-control studies, or historically controlled studies

BLUF

A case-control study conducted by surgeons at the AC Camargo Cancer Center in Sao Paulo, Brazil compared the rate of post-operative complications in 49 patients who had surgery after recovering from asymptomatic SARS-CoV-2 to 98 controls who had surgery but never had COVID-19 between April 22 and July 2, 2020 (Figure 1). Only 14.3% of the control patients and 16.3% of the COVID-recovered patients developed complications within 30 days (OR: 1.17; 95% CI: 0.45–3.0; p=0.74)(Table 2), with 6 controls and 4 COVID-recovered patients developing grade III or higher complications by Clavien-Dindo

classification (Table 3). Authors suggest there is no increased risk of post-operative complications among patients whose elective surgery was delayed due to asymptomatic SARS-CoV-2 positivity.

ABSTRACT

BACKGROUND: There are limited data on surgical complications for patients that have delayed surgery after severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. We aimed to analyze the surgical outcomes of patients submitted to surgery after recovery from SARS-CoV-2 infection. METHODS: Asymptomatic patients that had surgery delayed after preoperative reverse-transcription polymerase chain reaction (RT-PCR) for SARS-CoV-2 were matched in a 1:2 ratio for age, type of surgery and American Society of Anesthesiologists to patients with negative RT-PCR for SARS-CoV-2. RESULTS: About 1253 patients underwent surgical procedures and were subjected to screening for SARS-CoV-2. Forty-nine cases with a delayed surgery were included in the coronavirus disease (COVID) recovery (COVID-rec) group and were matched to 98 patients included in the COVID negative (COVID-neg) group. Overall, 22 (15%) patients had 30-days postoperative complications, but there was no statistically difference between groups -16.3% for COVID-rec and 14.3% for COVID-neg, respectively (odds ratio [OR] 1.17:95% confidence interval [CI] 0.45-3.0; p = .74). Moreover, we did not find difference regarding grades more than or equal to 3 complication rates - 8.2% for COVID-rec and 6.1% for COVID-neg (OR 1.36:95%CI 0.36-5.0; p = .64). There were no pulmonary complications or SARS-CoV-2 related infection and no deaths within the 30-days after surgery. CONCLUSIONS: Our study suggests that patients with delayed elective surgeries due to asymptomatic preoperative positive SARS-CoV-2 test are not at higher risk of postoperative complications.

FIGURES

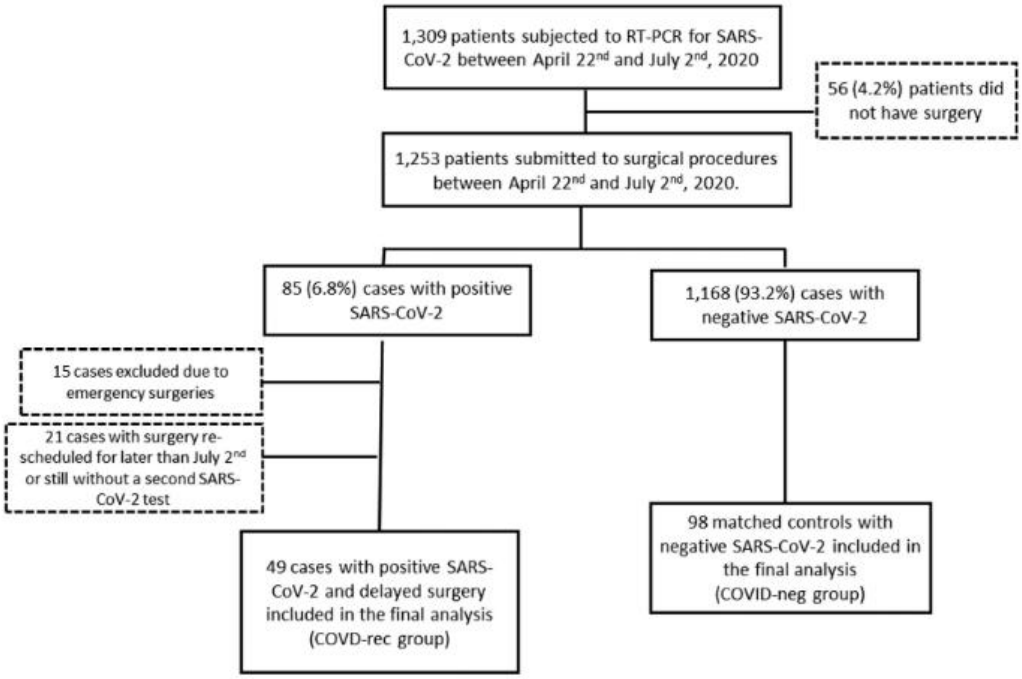

FIGURE 1 Flow-chart of the 147 patients included in the study. COVID, coronavirus disease; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2

TABLE 2 Clinical and demographic characteristics of the 147 patients submitted to surgical procedures from April 22 to July 2, 2020

Variable		COVID-neg[a] group $n = 98$ (%)	COVID-rec[b] group $n = 49$ (%)	p value	Total 147 (%)
Age, mean; median (range) year		49.8; 51 (16–81)	50.1; 52 (13–81)	.86	49.9; 51 (13–81)
Body mass index, mean; median (range) kg/m^2		26.8; 25.9 (16.9–53.9)	27.6; 27.5 (18.8–43)	.33	27.1; 26.6 (16.9–53.9)
Surgical time length, mean; median (range) (min)		119.0; 100 (10–670)	110.2; 79 (10–362)	.54	116.1; 93 (10–670)
Hospital stay length, mean; median (range) (days)		3.48; 1.0 (0–62)	3.08; 1.0 (0–47)	.28	3.35; 1.0 (0–62)
Gender	Male	40 (40.8)	16 (33.3)	.38	56 (38.4)
	Female	58 (59.2)	32 (66.7)		90 (61.6)
ASA[c]	1 and 2	82 (83.7)	44 (89.8)	.31	126 (85.7)
	3 and 4	16 (16.3)	5 (10.2)		21 (14.3)
ECOG[d]	0 and 1	83 (84.7)	42 (85.7)	.87	125 (85.0)
	2 and 3	15 (15.3)	7 (14.3)		22 (15.0)
Surgical type	Oncological	53 (54.1)	25 (51.0)	.72	78 (53.1)
	Nononcological	45 (45.9)	24 (49.0)		69 (46.9)
Surgical Department	Gastrointestinal	17 (17.3)	10 (20.4)	.73	27 (18.4)
	Gynecology	16 (16.3)	10 (20.4)		26 (17.7)
	Breast	21 (23.5)	5 (14.3)		26 (17.7)
	Skin Cancer	14 (14.3)	5 (10.2)		19 (12.9)
	Urology	12 (12.2)	7 (14.3)		19 (12.9)
	Head and Neck	11 (11.2)	7 (14.3)		18 (12.2)
	Others[e]	8 (8.2)	4 (8.2)		12 (8.2)
Intensive care unit	No	92 (93.9)	41 (85.4)	.12	133 (91.1)
	Yes	6 (6.1)	7 (14.6)		13 (8.9)
Morbidity (Clavien–Dindo[f])	none	84 (85.7)	41 (83.7)	.74	125 (85.0)
	I	1 (1.0)	2 (4.1)		3 (2.0)
	II	7 (7.1)	2 (4.1)		9 (6.1)
	IIIa	3 (3.1)	3 (6.1)		6 (4.1)
	IIIb	1 (1.0)	1 (2.0)		2 (1.4)
	IVa	1 (1.0)	0 (0)		1 (0.7)
	IVb	1 (1.0)	0 (0)		1 (0.7)

[a]COVID-neg: patients that had surgeries after a negative RT-PCR test for SARS-CoV-2.

[b]COVID-rec: asymptomatic patients that had surgeries delayed due to positive RT-PCR test for SARS-CoV-2.

[c]ASA: American Society of Anesthesiologists risk classification.[10]

[d]ECOG: Eastern Cooperative Oncology Group Performance Status.

[e]Others: Vascular surgery, Intervention Radiology, Neurosurgery and Reconstructive Surgery.

[f]Clavien–Dindo: Clavien–Dindo classification of surgical complications.[11]

TABLE 3 Characteristics of the 10 patients with Clavien–Dindo[a] Grades III and IV submitted to surgical procedures from April 22 to July 2, 2020

Group	Age (year)	ASA[b]	Oncological surgery	Surgical procedure	Clavien–Dindo[a]	Complication type	Treatment	ICU[c]
COVID-rec	57	3	No	Splenic embolization	IIIa	Abdominal abscess	Guide drainage[d]	No
COVID-rec	76	2	Yes	Skin resection	IIIa	SS[e] infection	Local suture	No
COVID-rec	68	3	Yes	Pulmonary lobectomy	IIIa	Pleural effusion	Pleural drainage	No
COVID-rec	61	2	No	Biliary drainage	IIIb	Biliary leakage	Re-drainage	No
COVID-neg	49	2	Yes	Rectal amputation	IIIa	Abdominal abscess	Guide drainage	No
COVID-neg	52	2	No	Hysterectomy	IIIa	Abdominal abscess	Guide drainage	No
COVID-neg	48	3	No	Biliary drainage	IIIa	SS bleeding	Local suture	No
COVID-neg	48	2	Yes	Total gastrectomy	IIIb	Small bowel obstruction	Laparotomy	No
COVID-neg	55	3	No	Ileostomy closure	IVa	Anastomotic leakage	Laparotomy	Yes
COVID-neg	55	3	No	Implantable venous catheter	IVb	Catheter infection	Catheter removal	Yes

FLUVOXAMINE VS PLACEBO AND CLINICAL DETERIORATION IN OUTPATIENTS WITH SYMPTOMATIC COVID-19: A RANDOMIZED CLINICAL TRIAL

Lenze EJ, Mattar C, Zorumski CF, Stevens A, Schweiger J, Nicol GE, Miller JP, Yang L, Yingling M, Avidan MS, Reiersen AM.. JAMA. 2020 Dec 8;324(22):2292-2300. doi: 10.1001/jama.2020.22760.
Level of Evidence: 2 - Randomized trial or observational study with dramatic effect

BLUF

A double-blind randomized clinical trial, conducted by physicians from Washington University in St. Louis from 10 April to 5 August 2020 analyzed the efficacy of fluvoxamine (100 mg 3 times daily for 15 days) against a placebo to decrease clinical deterioration of COVID-19 in non-hospitalized patients with confirmed SARS-CoV-2 infection within 7 days and oxygen saturation 92% or greater. Clinical deterioration (defined as development of both 1) shortness of breath or hospitalization for shortness of breath or pneumonia and 2) oxygen saturation less than 92% on room air or need for supplemental oxygen to achieve oxygen saturation of 92% or greater) occurred in 0 of 80 patients in the fluvoxamine group and in 6 of 72 patients in the placebo group (Table 2) without a significant increase in adverse events (Table 3). This clinical trial supports the hypothesis that fluvoxamine administration for COVID-19 in an outpatient setting can decrease events of clinical deterioration, though an increased sample size and length of follow up is needed.

ABSTRACT

Importance: Coronavirus disease 2019 (COVID-19) may lead to serious illness as a result of an excessive immune response. Fluvoxamine may prevent clinical deterioration by stimulating the sigma-1 receptor, which regulates cytokine production. Objective: To determine whether fluvoxamine, given during mild COVID-19 illness, prevents clinical deterioration and decreases the severity of disease. Design, Setting, and Participants: Double-blind, randomized, fully remote (contactless) clinical trial of fluvoxamine vs placebo. Participants were community-living, nonhospitalized adults with confirmed severe acute respiratory syndrome coronavirus 2 infection, with COVID-19 symptom onset within 7 days and oxygen saturation of 92% or greater. One hundred fifty-two participants were enrolled from the St Louis metropolitan area (Missouri and Illinois) from April 10, 2020, to August 5, 2020. The final date of follow-up was September 19, 2020. Interventions: Participants were randomly assigned to receive 100 mg of fluvoxamine (n = 80) or placebo (n = 72) 3 times daily for 15 days. Main Outcomes and Measures: The primary outcome was clinical deterioration within 15 days of randomization defined by meeting both criteria of (1) shortness of breath or hospitalization for shortness of breath or pneumonia and (2) oxygen saturation less than 92% on room air or need for supplemental oxygen to achieve oxygen saturation of 92% or greater. Results: Of 152 patients who were randomized (mean [SD] age, 46 [13] years; 109 [72%] women), 115 (76%) completed the trial. Clinical deterioration occurred in 0 of 80 patients in the fluvoxamine group and in 6 of 72 patients in the placebo group (absolute difference, 8.7% [95% CI, 1.8%-16.4%] from survival analysis; log-rank P = .009). The fluvoxamine group had 1 serious adverse event and 11 other adverse events, whereas the placebo group had 6 serious adverse events and 12 other adverse events. Conclusions and Relevance: In this preliminary study of adult outpatients with symptomatic COVID-19, patients treated with fluvoxamine, compared with placebo, had a lower likelihood of clinical deterioration over 15 days. However, the study is limited by a small sample size and short follow-up duration, and determination of clinical efficacy would require larger randomized trials with more definitive outcome measures. Trial Registration: ClinicalTrials.gov Identifier: NCT04342663.

	Fluvoxamine (n = 80)	Placebo (n = 72)	Absolute difference (95% CI)[a]	*P* value[b]
Primary end point				
Clinical deterioration (met both criteria), No. (%)[c]	0	6 (8.3)	8.7 (1.8 to 16.4)	.009
Secondary end points				
Clinical status on 7-point scale, No. (%)[d]				
0 (none)	80 (100)	66 (91.7)	8.3 (0.6 to 18.4)	.009
Any nonzero value	0	6 (8.3)	−8.3 (−18.4 to −0.6)	.009
1 (shortness of breath and oxygen saturation <92% but no supplemental oxygen needed)	0	2 (2.8)	−2.8 (−10.8 to 3.5)	.15
3 (oxygen saturation <92% plus supplemental oxygen needed and hospitalization related to dyspnea or hypoxia)	0	3 (4.2)	−4.2 (−13.2 to 2.0)	.07
5 (oxygen saturation <92% plus supplemental oxygen needed and hospitalization related to dyspnea or hypoxia plus ventilator support needed for ≥3 days)	0	1 (1.4)	−1.4 (−8.4 to 4.4)	.36
Clinical status on 7-point scale, mean (SD)	0	0.22 (0.84)	−0.22 (−0.41 to −0.04)	.02
Clinical deterioration, No. of days[e]	NA	NA	NA	NA
Most severe baseline symptom change score (difference between baseline and final rating)[f]	−5.6	−5.8	0.3 (−0.8 to 1.4)	.63
Nonprespecified end points				
30-d post trial observation events (emergency department visit, hospitalization, or both)[g]	1 (1.3)	1 (1.4)	−0.1 (−6.7 to 5.1)	>.99

Abbreviation: NA, not applicable (see footnote "e" for explanation).

[a] For outcomes reported as No. (%), the absolute difference is a difference in proportions. For other variables, the difference between group means is reported. Most analyses were conducted using BinomCI from the R package ExactCIdiff.

[b] Most were calculated using the exact.test from the R package Exact. The log-rank χ^2 was used ($\chi^2 = 6.8$) for the primary end point. The *t* test was used for clinical status on 7-point scale ($t = -2.4$) and the most severe baseline symptom change ($t = 0.5$).

[c] Shortness of breath or hospitalization for shortness of breath or pneumonia and oxygen saturation dropped below 92% or supplemental oxygen was required to keep oxygen saturation at or above 92%. The prespecified primary outcome analysis was determined instead by survival analysis (time to clinical worsening). The absolute difference and 95% CI are for the Kaplan-Meier estimate of the placebo group at day 15. The test of difference is the log-rank statistic ($\chi^2 = 6.8$).

[d] No study participants were rated 2 (shortness of breath and oxygen saturation <92% plus supplemental oxygen needed), 4 (oxygen saturation <92% plus supplemental oxygen needed and hospitalization related to dyspnea or hypoxia plus ventilator support needed for <3 days), or 6 (death).

[e] The protocol included a plan to examine number of days (1) requiring oxygen, (2) requiring hospitalization, and (3) requiring ventilator support. This type of outcome measure turned out to be invalid for this study because few patients required these interventions; therefore, a statistical analysis comparing the number of days was not appropriate.

[f] Change from day 0 to day 15. The mean of the highest daily symptom score for each participant that was reported most severe at baseline (62 for fluvoxamine group and 54 for placebo group). This analysis was not pursued further because the curves showed no substantial differences and because the baseline most severe symptom was heterogeneous across participants (Table 1) and likely did not adequately capture overall symptom burden. eFigure 1 in Supplement 2 is a box and whisker plot of the symptom data over the 15 days.

[g] During the 30-day observation period after the 15-day randomized clinical trial, 1 participant from the fluvoxamine group was hospitalized for post-COVID headache and 1 participant from the placebo group had an emergency department visit for chest pain (costochondritis COVID-19 sequela). Details appear in eResults 2 in Supplement 2.

Table 2. Primary, Secondary, and Nonprespecified Outcomes

	No. of adverse events (%)[a]	
	Fluvoxamine (n = 80)	Placebo (n = 72)
Pneumonia	3 (3.8)	6 (8.3)
Shortness of breath	2 (2.5)	4 (5.6)
Headache or head pain	2 (2.5)	1 (1.4)
Gastroenteritis, nausea, or vomiting	1 (1.3)	5 (6.9)
Muscle aches	1 (1.3)	0
Bacterial infection	1 (1.3)	0
Vasovagal syncope	1 (1.3)	0
Teeth chattering	1 (1.3)	0
Dehydration	1 (1.3)	0
Low oxygen saturation or hypoxia	0	6 (8.3)
Chest pain or tightness	0	2 (2.8)
Fever	0	2 (2.8)
Acute respiratory failure	0	1 (1.4)
Hypercapnia	0	1 (1.4)
Flank pain	0	1 (1.4)
By No. of patients		
Serious adverse events[b]	1 (1.3)	5 (6.9)
Other adverse events[c]	11 (13.8)	6 (8.3)

[a] In some cases, there was more than 1 symptom or problem that occurred as part of 1 adverse event. Additional details of adverse events appear in eResults 1 in Supplement 2.

[b] One patient in the placebo group had more than 1 serious adverse event. The total No. of serious adverse events was 1 in the fluvoxamine group and 6 in the placebo group.

[c] There were patients in the placebo group who had more than 1 other adverse event. The total No. of other adverse events was 11 in the fluvoxamine group and 12 in the placebo group.

Table 3. Adverse Events

REPURPOSED TOCILIZUMAB IN PATIENTS WITH SEVERE COVID-19

Tian J, Zhang M, Jin M, Zhang F, Chu Q, Wang X, Chen C, Yue H, Zhang L, Du R, Zhao D, Zeng Z, Zhao Y, Liu K, Wang M, Hu K, Miao X, Zhang H.. J Immunol. 2020 Dec 9:ji2000981. doi: 10.4049/jimmunol.2000981. Online ahead of print.
Level of Evidence: 3 - Non-randomized controlled cohort/follow-up study

BLUF

A respective study of 195 hospitalized patients in Wuhan, China found that patients treated with tocilizumab (n=65) sustained better outcomes compared to matched patients who did not receive the IL-6 inhibitor (n=130) (Figure 1). The tocilizumab group experienced lower in-hospital death rates, fewer ICU stay days, lower acute respiratory distress syndrome incidence rates, and lower infection related markers (IL-10, CRP). Additionally, T-cell counts were higher in the tocilizumab group, suggesting greater immune system recovery in this group (Figure 2). The authors suggest that, while tocilizumab was able to ameliorate the cytokine release storm associated with mortality in COVID-19, the possibility of negative effects like transaminitis should be further studied and characterized.

ABSTRACT

The coronavirus disease 2019 (COVID-19) has caused a global pandemic, resulting in considerable morbidity and mortality. Tocilizumab, an inhibitor of IL-6, has been widely repurposed as a treatment of severely ill patients without robust evidence supporting its use. In this study, we aimed to systematically describe the effectiveness of treatment and prevention of the cytokine storms in COVID-19 patients with tocilizumab. In this multicentered retrospective and observational cohort study, 65 patients with COVID-19 receiving tocilizumab and 130 not receiving tocilizumab were propensity score matched at a ratio of 2:1 based on age, sex, and comorbidities from January 20, 2020 to March 18, 2020 in Wuhan, China. After adjusting for confounding, the detected risk for in-hospital death was lower in the tocilizumab group versus nontocilizumab group (hazard ratio = 0.47; 95% confidence interval = 0.25-0.90; p = 0.023). Moreover, use of tocilizumab was associated with a lower risk of acute respiratory distress syndrome (odds ratio = 0.23; 95% confidence interval = 0.11-0.45; p < 0.0001). Furthermore, patients had heightened inflammation and more dysregulated immune cells before treatment, which might aggravate disease progression. After tocilizumab administration, abnormally elevated IL-6, C-reactive protein, fibrinogen, and activated partial thromboplastin time decreased. Tocilizumab may be of value in prolonging survival in patients with severe COVID-19, which provided a novel strategy for COVID-19-induced cytokine release syndrome. Our findings could inform bedside decisions until data from randomized, controlled clinical trials become available.

FIGURES

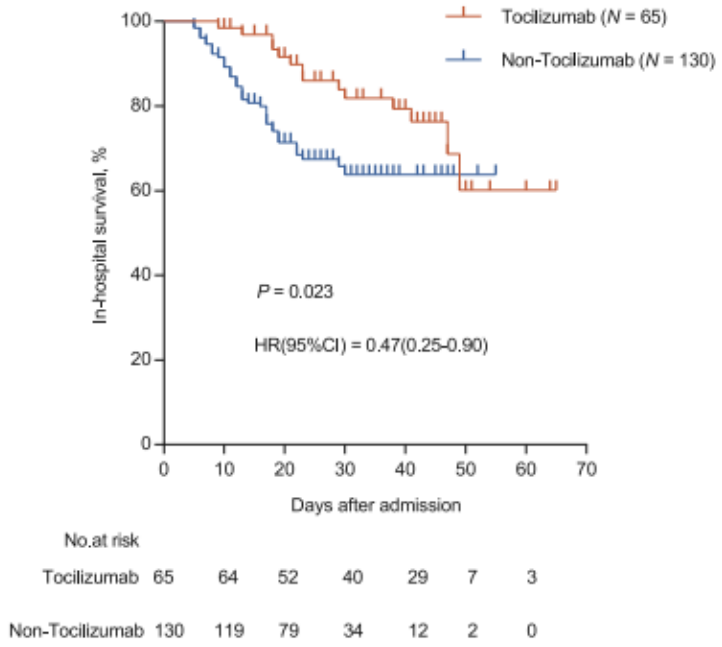

FIGURE 1. Survival of COVID-19 patients during hospitalization. Kaplan–Meier curves for cumulative p value of COVID-19 mortality during follow up duration in tocilizumab or non-tocilizumab cohort among 195 patients within Cox proportional hazards model

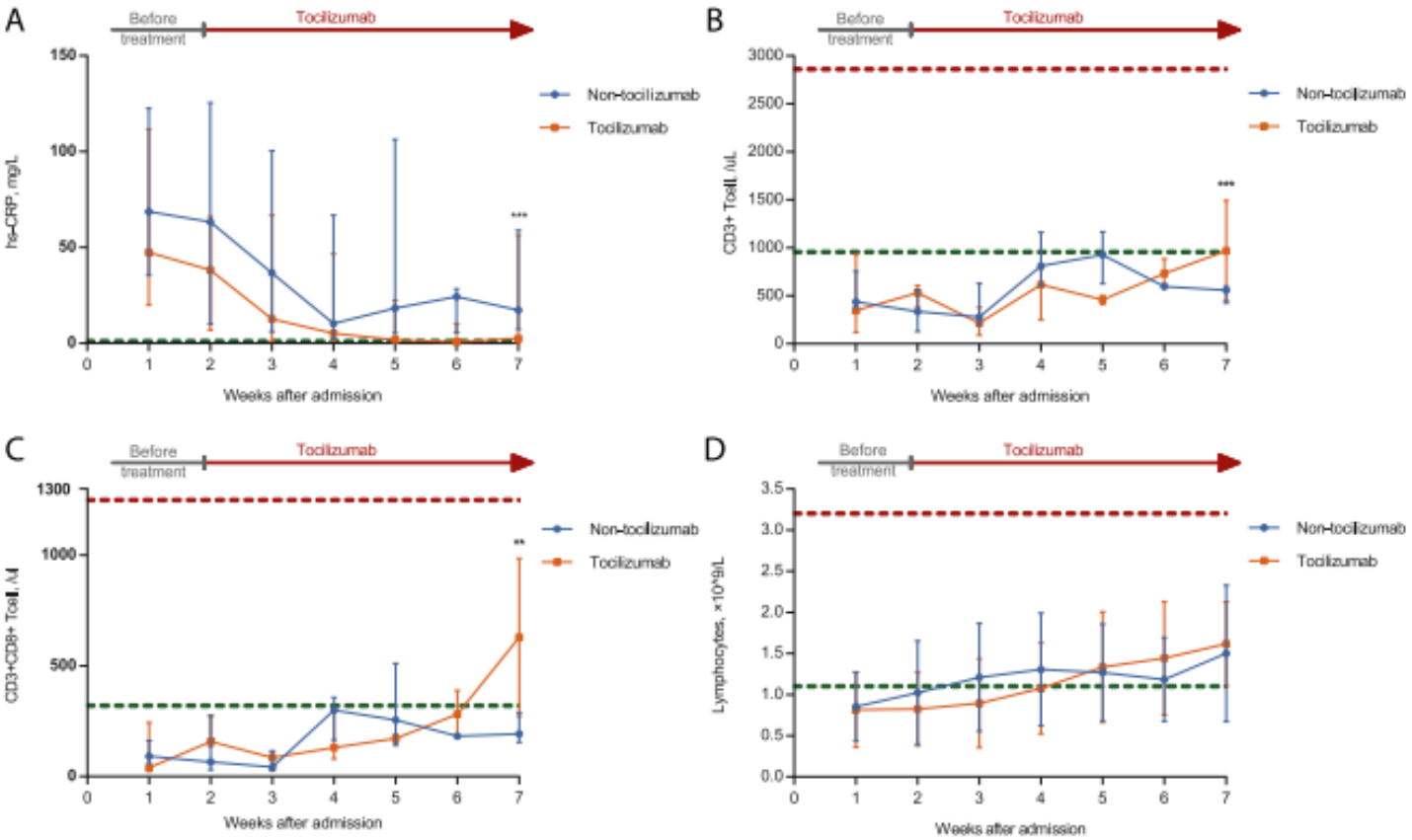

FIGURE 2. Temporal changes in laboratory parameters in COVID-19 patients after admission. The temporal changes of hypersensitive CRP (hs-CRP) (A), CD3+ T cell (B), CD8+ T cell (C), and lymphocyte (D) in tocilizumab group and nontocilizumab group. These parameters were measured at 1, 2, 3, 4, 5, 6, and 7 wk after admission. The green dotted line represents the lower limit of normal, and the red dotted line represents the upper limit of normal. The levels of these parameters at each point were expressed as median and IQR.
**p , 0.01, ***p , 0.001 were calculated by Mann–Whitney U test for last examination.

IMPACT OF LOCKDOWN DUE TO COVID-19 ON THE MODALITIES OF INTOXICATED PATIENTS PRESENTING TO THE EMERGENCY ROOM

Fayed MM, Sharif AF.. Prehosp Disaster Med. 2021 Jan 5:1-44. doi: 10.1017/S1049023X20001533. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

A five-year retrospective, comparative cross-sectional study from Tanta Poison Control Center (TPCC) in Tanta, Egypt investigating the impact of the COVID-19 lockdown on the patterns of toxic exposure cases referred to TPCC. The authors analyzed 1,916 acutely intoxicated patients admitted to TPCC from March through May from 2016-2020 and found higher reported phosphides ($p<0.001$) and antipsychotics ($p<0.001$) exposures during the lockdown period and significant delays to access to emergency services ($p<0.001$), with lower recovery rates and higher death rates (Table 13). This highlights the need for greater awareness regarding handling hazardous pesticides and establishment of better mental health counseling services.

ABSTRACT

INTRODUCTION: Coronavirus disease 2019 (COVID-19) pandemic influences health care facilities world-wide. The flow rate, type, and severity of cases presented to emergency departments varied during the pandemic in comparison to the past years. However, this change has not been well-described among the cases of hospital admission due to toxic exposure. STUDY OBJECTIVE: Recognition of the pattern of toxic exposure among the cases refereed to Tanta Poison Control Center (TPCC; Tanta, Egypt) during the past five years, and furthermore, exploration of the impact of lockdown due to the COVID-19 pandemic on the pattern of presented cases. METHODS: The current study is a five-year retrospective, comparative cross-sectional study carried out among acutely intoxicated patients admitted to TPCC during the spring months (March through May) of 2016-2020. A total of 1,916 patients with complete medical records were recruited. The type and manner of toxic exposure, demographic, clinical data, and outcomes were analyzed. RESULTS: The current study noted that there were delays in time from toxic exposure to emergency services during the lockdown period. This was reflected in significant lower recovery rates (884.8/1,000 population; $z = -3.0$) and higher death rates (49.4/1,000 population; $z = 2.1$) despite the marked decrease in the total number of hospital admissions in comparison to the past four years. The lockdown period showed significantly higher phosphides ($z = 3.5$; $chi2 = 34.295$; $P < .001$) and antipsychotics exposure ($z = 3.6$; $chi2 = 21.494$; $P < .001$) than the previous years. However, predominance of female exposure and intentional self-poisoning was maintained over the past five years, including the lockdown. CONCLUSION: COVID-19-associated lockdown greatly reformed the usual intoxication pattern of the cases admitted to emergency room. Also, it played a role in delaying time of hospital arrival, which was reflected as lower recovery rates and higher death rates.

FIGURES

	Recovery Rate (per 1,000 population)	Death Rate (per 1,000 population)	ICU Admission Rate (per 1,000 population)	Hospital Admission Rate (per 1,000 population)
2016	(296/311) * 1000 = 951.8	(3/311) * 1000 = 9.7	(12/311) * 1000 = 38.6	(311/1916) * 1000 = 162.3
2017	(428/449) * 1000 = 953.2	(16/449) * 1000 = 35.6	(12/449) * 1000 = 26.7	(449/1916) * 1000 = 234.3
2018	(498/533) * 1000 = 934.3	(14/533) * 1000 = 26.3	(24/533) * 1000 = 45.0	(533/1916) * 1000 = 278.2
2019	(342/380) * 1000 = 900.0	(15/380) * 1000 = 39.5	(39/380) * 1000 = 102.6	(380/1916) * 1000 = 198.3
2020	(215/243) * 1000 = 884.8	(12/243) * 1000 = 49.4	(30/243) * 1000 = 123.5	(243/1916) * 1000 = 126.8
Among Past 5 Years	(1779/1916) * 1000 = 928.5	(60/1916) * 1000 = 31.3	(117/1916) * 1000 = 61.1	(1916/1916) * 1000 = 1000.0

Table 13. Recovery, Death, ICU Admission, and Hospital Admission Rates of the Cases Admitted to Tanta Poison Center According to the Outcome Over the Period (March through May) of 2016-2020. Abbreviation: ICU, intensive care unit.

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