The Daily COVID-19 Literature Surveillance Summary

January 14, 2021

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COVID-19 Daily Literature Surveillance

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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

- Investigators from the Centers for Disease Control and Prevention (Atlanta, Georgia) and the Louisiana Department of Health (New Orleans, Louisiana) conducted a prospective cohort study of 143 inmates residing in 6 dormitories at an unnamed minimum-security correctional facility in Louisiana between May 7 and June 3, 2020. The 143 inmates were tested for SARS-CoV-2 by RT-PCR with an overall positive rate of 78% (111/143) suggesting a rapid viral outbreak in this population. At the height of the outbreak, 47% (52/111) of positive inmates were asymptomatic, highlighting the importance of early testing for all in congregate settings along with mitigation strategies to reduce rapid viral transmission.

- Gerontologists from Brown University in Rhode Island evaluated risk factors for mortality in 5,256 symptomatic, SARS-CoV-2 positive nursing home residents across 351 US nursing homes between March 16 and September 15, 2020. They found increased odds of all-cause 30-day mortality with increased age, male sex (OR for female sex: 0.69 [95% CI, 0.60-0.80]), impaired cognition (OR: 2.09 [95% CI, 1.68-2.59]), and physical impairment (OR: 1.49 [95% CI, 1.18-1.88]). Authors conclude that understanding these risk factors can help identify high-risk nursing home residents and inform goals of care conversations.

Mental Health & Resilience Needs

- A survey conducted on 2870 adults living in California during July 14 - July 27, 2020 by researchers at University of California - Davis School of Medicine found that fear of personal safety due to violence of others was heightened during the pandemic compared to pre-pandemic concerns. 110,000 individuals purchased a firearm during the pandemic, 47,000 of which were new owners, suggesting that violence-related harm is crucial particularly during the pandemic, and short-term crisis interventions may become key in reducing impulsive violence.

TABLE OF CONTENTS

EPIDEMIOLOGY

SARS-COV-2 SEROPREVALENCE SURVEY ESTIMATES ARE AFFECTED BY ANTI-NUCLEOCAPSID ANTIBODY DECLINE

Bolotin S, Tran V, Osman S, Brown KA, Buchan SA, Joh E, Deeks SL, Allen VG.. J Infect Dis. 2021 Jan 5:jiaa796. doi: 10.1093/infdis/jiaa796. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

Microbiologists from Public Health Ontario and the University of Toronto conducted SARS-CoV-2 serosurveys on 21,676 residual specimens collected between March and August 2020. They found geometric mean concentration (GMCs) for anti-nucleocapsid antibody positive specimens decreased over time (3.7 to 3.1, p=0.015) while the GMC concurrently increased for negative specimens (p=0.0018), indicating an overall decrease in population-level SARS-CoV-2 antibodies (Table 1). Authors suggest though serology may have limited utility in determining individual-level immunity, seroprevalence studies provide important information about population-level exposure and recommend further study into solutions addressing population-level antibody decline.

ABSTRACT

We analyzed 21,676 residual specimens from Ontario, Canada collected between March-August, 2020 to investigate the effect of antibody decline on SARS-CoV-2 seroprevalence estimates. Testing specimens orthogonally using the Abbott (anti-nucleocapsid) and then the Ortho (anti-spike) assays, seroprevalence estimates ranged from 0.4%-1.4%, despite ongoing disease activity. The geometric mean concentration (GMC) of antibody-positive specimens decreased over time (p=0.015), and the GMC of antibody-negative specimens increased over time (p=0.0018). The association between the two tests decreased each month (p<0.001), suggesting anti-N antibody decline. Lowering the Abbott antibody index cut-off from 1.4 to 0.7 resulted in a 16% increase in positive specimens.

FIGURES

Table 1: Serology test results and geometric mean concentration of Ontario serosurveillance specimens, March – August, 2020

Test results	Specimen collection period				
	March - April	May	June	July	August
Abbott					
Positive n/N (%)	5/827 (0.6%)	20/1,061 (1.9%)	106/7,023 (1.5%)	97/7,001 (1.4%)	90/5,764 (1.6%)
Positive AI GMC (95% CI)*	3.4 (1.9, 6.0)	3.7 (3.0, 4.5)	3.7 (3.4, 4.1)	3.3 (3.0, 3.7)	3.1 (2.8, 3.4)
Negative AI GMC (95% CI)*	0.034 (0.032, 0.037)	0.032 (0.031, 0.034)	0.033 (0.032, 0.033)	0.034 (0.033, 0.035)	0.035 (0.034, 0.035)
Ortho[a]					
Positive n/N (%)	3/5 (60.0%)	15/20 (75.0%)	79/106 (74.5%)	70/97 (72.2%)	64/90 (71.1%)
Positive AI GMC (95% CI)	22 (13, 38)	15 (11, 22)	18 (15, 21)	16 (13, 19)	15 (13, 18)
Negative AI GMC (95% CI)	0.046 (0.0055, 0.38)	0.047 (0.012, 0.18)	0.029 (0.020, 0.042)	0.021 (0.015, 0.030)	0.028 (0.019, 0.042)
Orthogonally positive					
n/N	3/827	15/1,061	79/7,023	70/7,001	64/5,764
% (95% CI)	0.4 (0.1, 1.1)	1.4 (0.7, 2.1)	1.1 (0.9, 1.4)	1.0 (0.8, 1.2)	1.1 (0.8, 1.4)

[a] = only Abbott-positive specimens were tested; GMC = geometric mean concentration; AI = antibody index; CI= confidence interval;* = statistically significant trend across sampling periods

ADULTS

DETECTION OF PULMONARY SHUNTS BY TRANSCRANIAL DOPPLER IN HOSPITALIZED NON-MECHANICALLY VENTILATED CORONAVIRUS DISEASE-19 PATIENTS

Salazar-Orellana JLI, García-Grimshaw M, Valdés-Ferrer SI, Alday-Ramírez SM, Ríos-Argaiz E, Vásquez-Ortiz ZY, Rivero-Sigarroa E, Jiménez-Ruiz A, Chiquete E, Cantú-Brito C, Flores-Silva FD.. Rev Invest Clin. 2021 Jan 11. doi: 10.24875/RIC.20000569. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

Neurologists from the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán in Mexico evaluated 31 adult COVID-19 patients undergoing non-invasive mechanical ventilation (non-IMV) for the presence of pulmonary shunts using transcranial doppler with agitated saline of the middle cerebral artery (Table 1). They found that mortality rates between patients with and without pulmonary shunts were similar. Authors suggest intrapulmonary shunts are not correlated with poorer outcomes in patients receiving non-IMV, but do appear to form at this disease stage, indicating they may not play a prominent pathological role until more severe disease develops.

ABSTRACT

In severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-associated disease coronavirus disease 2019 (COVID-19), hypoxemia mechanisms differ from those observed in acute respiratory distress syndrome. Hypoxemia and respiratory failure in COVID- 19 are attributed to pulmonary angiopathy, increasing physiological pulmonary shunting1-3.

Table 1: Baseline characteristics and in-hospital outcomes of COVID-19 patients

	All patients (n = 31)	Without pulmonary shunts (n = 24)	With pulmonary shunts (n = 7)	p-value
Age, mean (±SD), years	44.4 (11.02)	43.83 (10.37)	46.14 (13.83)	0.412
Sex, n (%), male	25 (80.6)	21 (87.5)	4 (57.1)	0.074
Comorbidities, n (%)				
Diabetes	6 (19.4)	5 (20.8)	1 (14.3)	0.7
Hypertension	7 (22.6)	5 (20.8)	2 (28.6)	0.667
Smoking	18 (58.1)	16 (66.7)	2 (28.6)	0.072
Chronic kidney disease	3 (9.7)	1 (4.2)	2 (28.6)	0.055
Obesity, BMI ≥30 kg/m²	13 (41.9)	10 (41.7)	3 (42.9)	0.955
BMI, mean (±SD), kg/m²	30.66 (7.91)	30.67 (7.38)	30.63 (10.19)	0.991
Days from symptom onset, median (IQR)	7 (5-8)	7 (6-8)	6 (2-8)	0.199
Inflammatory response biomarkers, median (IQR)				
D-dimer, ng/dL	639 (462-961)	594 (444-747)	1005 (800-1767)	0.017
Lactic dehydrogenase, U/L	305 (239-354)	310.5 (243.5-376.5)	261 (220-317)	0.317
Ferritin, ng/dL	522.6 (332.3-806.8)	570.7 (317-1335.6)	491.2 (332.3-621.8)	0.417
C-reactive protein, mg/dL	12.39 (5.87-20.01)	15.93 (8.32-21.65)	5.49 (3.26-11.63)	0.017
Neutrophil/lymphocyte ratio	6.7 (4.49-10.62)	6.45 (4.55-9.89)	9.93 (3.86-14.73)	0.563
ABGs, mean (±SD)				
pH	7.45 (0.047)	7.45 (0.05)	7.45 (0.06)	0.882
PaO_2, mmHg	73.25 (20.23)	72.06 (21.92)	77.34 (13.39)	0.552
$PaCO_2$, mmHg	30.96 (4.15)	30.69 (4.27)	31.89 (3.9)	0.513
HCO_3^-, mmol/L	21.62 (2.95)	21.48 (3.09)	22.11 (2.54)	0.624
PaO_2/FiO_2,mmHg	216.74 (57.38)	208 (64)	251 (41)	0.099
Chest CT severity, n (%)				0.531
Mild/moderate, 20–50%	12 (38.7)	10 (41.7)	2 (28.6)	
Severe, >50%	19 (61.3)	14 (58.3)	5 (71.4)	
In-hospital outcomes, n (%)				
IMV	5 (16.1)	5 (20.8)	0	0.187
Days of in-hospital stay	7 (4-11)	7 (4-12)	7 (6-9)	0.661
Death	4 (12.9)	3 (12.5)	1 (14.3)	0.901

SD: standard deviation; BMI: body mass index; IQR: interquartile range; PaO_2: arterial partial pressure of oxygen; $PaCO_2$: arterial partial pressure of carbon dioxide; HCO_3^-: bicarbonate; FiO_2: fraction of inspired oxygen; CT: computed tomography; IMV: Invasive mechanical ventilation; ABGs: Arterial blood gases.

RAPID TRANSMISSION OF SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2 IN DETENTION FACILITY, LOUISIANA, USA, MAY-JUNE, 2020

Wallace M, James AE, Silver R, Koh M, Tobolowsky FA, Simonson S, Gold JAW, Fukunaga R, Njuguna H, Bordelon K, Wortham J, Coughlin M, Harcourt JL, Tamin A, Whitaker B, Thornburg NJ, Tao Y, Queen K, Uehara A, Paden CR, Zhang J, Tong S, Haydel D, Tran H, Kim K, Fisher KA, Marlow M, Tate JE, Doshi RH, Sokol T, Curran KG.. Emerg Infect Dis. 2021 Jan 4;27(2). doi: 10.3201/eid2702.204158. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

Investigators from the Centers for Disease Control and Prevention (Atlanta, Georgia) and the Louisiana Department of Health (New Orleans, Louisiana) conducted a prospective cohort study of 143 inmates residing in 6 dormitories at an unnamed minimum-security correctional facility in Louisiana between May 7 and June 3, 2020. The 143 inmates were tested for SARS-CoV-2 by RT-PCR with an overall positive rate of 78% (111/143) (Figure 2), suggesting a rapid viral outbreak in this population. At the height of the outbreak, 47% (52/111) of positive inmates were asymptomatic, highlighting the importance of early testing for all in congregate settings along with mitigation strategies to reduce rapid viral transmission.

ABSTRACT

To assess transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in a detention facility experiencing a coronavirus disease outbreak and evaluate testing strategies, we conducted a prospective cohort investigation in a facility in Louisiana, USA. We conducted SARS-CoV-2 testing for detained persons in 6 quarantined dormitories at various time points. Of 143 persons, 53 were positive at the initial test, and an additional 58 persons were positive at later time points (cumulative incidence 78%). In 1 dormitory, all 45 detained persons initially were negative; 18 days later, 40 (89%) were positive. Among persons who were SARS-CoV-2 positive, 47% (52/111) were asymptomatic at the time of specimen collection; 14 had replication-competent virus isolated. Serial SARS-CoV-2 testing might help interrupt transmission through medical isolation and quarantine. Testing in correctional and detention facilities will be most effective when initiated early in an outbreak, inclusive of all exposed persons, and paired with infection prevention and control.

FIGURES

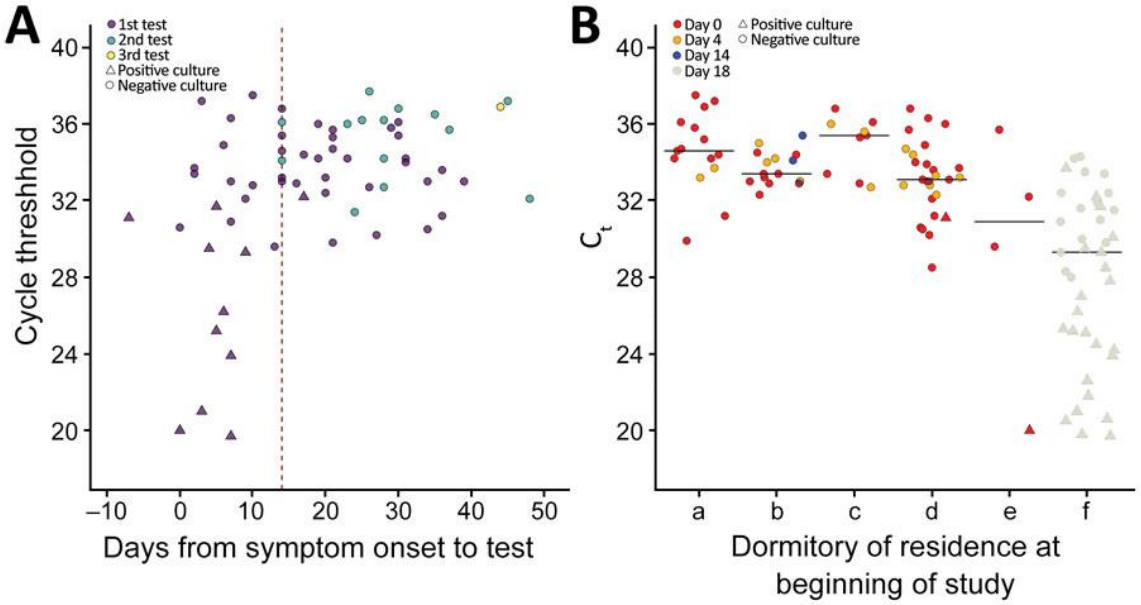


Figure 2. Rapid transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in detention facility, Louisiana, USA, May–June 2020. A) Ct values and viral culture results by days from symptom onset of any symptom in SARS-CoV-2–positive detained persons. Nucleocapsid protein 1 target Ct values and viral culture results of 66 specimens from 51 persons who were positive for SARS-CoV-2 by days from reported symptom onset. Ct values and viral culture results are also shown for 14 of the 51 specimens from persons who were positive a second time, and for 1 specimen that remained positive for a third test. Vertical dashed line indicates day 14 to depict the recommended medical isolation timeframe from symptom onset for persons in congregate settings. Shapes indicate culture results, and colors indicate day of positive test result. One positive test result is not included because Ct values were not reported. B) Ct values and viral culture results for SARS-CoV-2–positive detained persons at the time of first sample collection according to dormitory residence and day of first positive

result. Nucleocapsid protein 1 target Ct values and viral culture results of the first SARS-CoV-2–positive test result for 110 detained persons is shown by dormitory of residence at the time of first sample collection. Horizontal lines indicate median Ct values for first positive samples from residents in each dormitory. One positive test result from a dormitory F resident is not included because Ct value was not reported. Ct , cycle threshold.

ADVANCED AGE

RISK FACTORS ASSOCIATED WITH ALL-CAUSE 30-DAY MORTALITY IN NURSING HOME RESIDENTS WITH COVID-19

Panagiotou OA, Kosar CM, White EM, Bantis LE, Yang X, Santostefano CM, Feifer RA, Blackman C, Rudolph JL, Gravenstein S, Mor V.. JAMA Intern Med. 2021 Jan 4. doi: 10.1001/jamainternmed.2020.7968. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

Gerontologists from Brown University in Rhode Island evaluated risk factors for mortality in 5,256 symptomatic, SARS-CoV-2 positive nursing home residents across 351 US nursing homes between March 16 and September 15, 2020. They found increased odds of all-cause 30-day mortality with increased age (see summary), male sex (OR for female sex: 0.69 [95% CI, 0.60-0.80]), impaired cognition (OR: 2.09 [95% CI, 1.68-2.59]), and physical impairment (OR: 1.49 [95% CI, 1.18-1.88])(Figure 3, Table 2). Authors conclude that understanding these risk factors can help identify high-risk nursing home residents and inform goals of care conversations.

SUMMARY

Compared to those aged 75-79, odds of death increased with age :
Age 80-84: 1.46 (95% CI, 1.14-1.86)
Age 85-89: 1.59 (95% CI, 1.25-2.03)
Age >90: 2.14 (95% CI, 1.70-2.69)

ABSTRACT

Importance: The coronavirus disease 2019 (COVID-19) pandemic has severely affected nursing homes. Vulnerable nursing home residents are at high risk for adverse outcomes, but improved understanding is needed to identify risk factors for mortality among nursing home residents. Objective: To identify risk factors for 30-day all-cause mortality among US nursing home residents with COVID-19. Design, Setting, and Participants: This cohort study was conducted at 351 US nursing homes among 5256 nursing home residents with COVID-19-related symptoms who had severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection confirmed by polymerase chain reaction testing between March 16 and September 15, 2020. Exposures: Resident-level characteristics, including age, sex, race/ethnicity, symptoms, chronic conditions, and physical and cognitive function. Main Outcomes and Measures: Death due to any cause within 30 days of the first positive SARS-CoV-2 test result. Results: The study included 5256 nursing home residents (3185 women [61%]; median age, 79 years [interquartile range, 69-88 years]; and 3741 White residents [71%], 909 Black residents [17%], and 586 individuals of other races/ethnicities [11%]) with COVID-19. Compared with residents aged 75 to 79 years, the odds of death were 1.46 (95% CI, 1.14-1.86) times higher for residents aged 80 to 84 years, 1.59 (95% CI, 1.25-2.03) times higher for residents aged 85 to 89 years, and 2.14 (95% CI, 1.70-2.69) times higher for residents aged 90 years or older. Women had lower risk for 30-day mortality than men (odds ratio [OR], 0.69 [95% CI, 0.60-0.80]). Two comorbidities were associated with mortality: diabetes (OR, 1.21 [95% CI, 1.05-1.40]) and chronic kidney disease (OR, 1.33 [95%, 1.11-1.61]). Fever (OR, 1.66 [95% CI, 1.41-1.96]), shortness of breath (OR, 2.52 [95% CI, 2.00-3.16]), tachycardia (OR, 1.31 [95% CI, 1.04-1.64]), and hypoxia (OR, 2.05 [95% CI, 1.68-2.50]) were also associated with increased risk of 30-day mortality. Compared with cognitively intact residents, the odds of death among residents with moderate cognitive impairment were 2.09 (95% CI, 1.68-2.59) times higher, and the odds of death among residents with severe cognitive impairment were 2.79 (95% CI, 2.14-3.66) times higher. Compared with residents with no or limited impairment in physical function, the odds of death among residents with moderate impairment were 1.49 (95% CI, 1.18-1.88) times higher, and the odds of death among residents with severe impairment were 1.64 (95% CI, 1.30-2.08) times higher. Conclusions and Relevance: In this cohort study of US nursing home residents with COVID-19, increased age, male sex, and impaired cognitive and physical function were independently associated with mortality. Understanding these risk factors can aid in the development of clinical prediction models of mortality in this population.

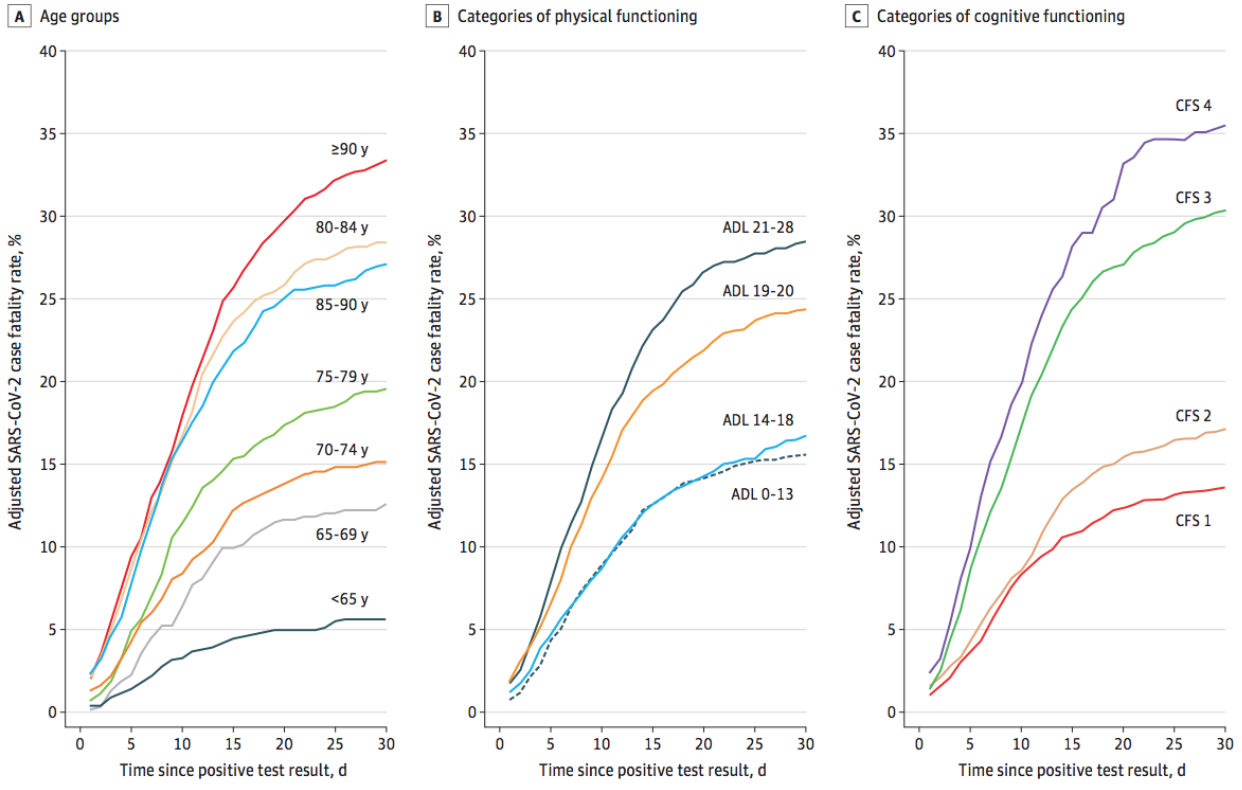
Table 2. Associations Between Clinical Risk Factors and 30-Day All-Cause Mortality in Symptomatic Nursing Home Residents Who Tested Positive for SARS-CoV-2

Risk factor	Patients with COVID-19, No.	Deaths, No. (%)	Odds ratio (95% CI)	
			Univariable	Multivariable
Age group, y				
<65	765	44 (6)	0.24 (0.16-0.37)	0.23 (0.15-0.34)
65-69	539	67 (12)	0.57 (0.41-0.80)	0.56 (0.40-0.78)
70-74	687	108 (16)	0.74 (0.54-1.02)	0.74 (0.55-1.01)
75-79	697	138 (20)	1 [Reference]	1 [Reference]
80-84	789	215 (27)	1.47 (1.15-1.89)	1.46 (1.14-1.86)
85-89	784	222 (28)	1.55 (1.20-2.01)	1.59 (1.25-2.03)
≥90	994	334 (34)	1.90 (1.53-2.36)	2.14 (1.70-2.69)
Sex				
Male	2051	451 (22)	1 [Reference]	1 [Reference]
Female	3185	671 (21)	0.90 (0.78-1.04)	0.69 (0.60-0.80)
Race/ethnicity				
White	3741	859 (23)	1 [Reference]	1 [Reference]
Black	909	164 (18)	0.75 (0.61-0.92)	0.77 (0.62-0.96)
Other[a]	586	99 (17)	0.67 (0.50-0.89)	0.60 (0.45-0.81)
ADL score				
0-13	1327	209 (16)	1 [Reference]	1 [Reference]
14-18	1320	221 (17)	1.05 (0.84-1.32)	0.98 (0.77-1.25)
19-20	1179	288 (24)	1.77 (1.41-2.23)	1.49 (1.18-1.88)
21-28	1410	404 (29)	2.15 (1.71-2.70)	1.64 (1.30-2.08)
Cognitive function				
Cognitively intact	2023	275 (14)	1 [Reference]	1 [Reference]
Impairment				
Mild	1179	202 (17)	1.28 (1.04-1.59)	1.11 (0.89-1.39)
Moderate	1547	469 (30)	2.61 (2.14-3.19)	2.09 (1.68-2.59)
Severe	463	165 (36)	3.36 (2.58-4.39)	2.79 (2.14-3.66)
Comorbidities				
Heart failure				
No	4035	870 (22)	1 [Reference]	1 [Reference]
Yes	1201	252 (21)	0.95 (0.78-1.15)	0.90 (0.74-1.10)
Coronary artery disease				
No	4009	841 (21)	1 [Reference]	1 [Reference]
Yes	1227	281 (23)	1.14 (0.97-1.33)	1.03 (0.86-1.23)
Asthma or COPD				
No	3870	850 (22)	1 [Reference]	1 [Reference]
Yes	1366	272 (20)	0.90 (0.77-1.06)	1.00 (0.84-1.17)
Chronic kidney disease				
No	3851	783 (20)	1 [Reference]	1 [Reference]
Yes	1385	339 (24)	1.29 (1.08-1.54)	1.33 (1.11-1.61)
Hypertension				
No	1120	247 (22)	1 [Reference]	1 [Reference]
Yes	4116	875 (21)	1.00 (0.84-1.19)	0.81 (0.69-0.96)
Type 2 diabetes				
No	3124	695 (22)	1 [Reference]	1 [Reference]
Yes	2112	427 (20)	0.87 (0.76-0.99)	1.21 (1.05-1.40)

Table 2. Associations Between Clinical Risk Factors and 30-Day All-Cause Mortality in Symptomatic Nursing Home Residents Who Tested Positive for SARS-CoV-2 (continued)

Risk factor	Patients with COVID-19, No.	Deaths, No. (%)	Odds ratio (95% CI)	
			Univariable	Multivariable
Symptoms				
Fever				
No	2602	472 (18)	1 [Reference]	1 [Reference]
Yes	2654	657 (25)	1.54 (1.33-1.78)	1.66 (1.41-1.96)
Shortness of breath				
No	4674	905 (19)	1 [Reference]	1 [Reference]
Yes	582	224 (38)	2.78 (2.29-3.38)	2.52 (2.00-3.16)
Tachycardia				
No	4356	886 (20)	1 [Reference]	1 [Reference]
Yes	900	243 (27)	1.96 (1.60, 2.41)	1.31 (1.04-1.64)
Hypoxia				
No	4277	798 (19)	1 [Reference]	1 [Reference]
Yes	979	331 (34)	2.15 (1.76-2.62)	2.05 (1.68-2.50)

Figure 3. Cumulative Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Mortality Rates



A, Age groups. B, Categories of physical functioning. C, Categories of cognitive functioning. Physical functioning was assessed with the activities of daily living (ADL) score, which ranges from 0 to 28 and describes a patient's range of impairment from substantial to very severe, with higher values indicating greater impairment. To facilitate interpretation of findings, scores were divided into 4 quartiles (ie, 0-14, 15-19, 20-21, and 22-28). Cognitive functioning was assessed with the Cognitive Function Scale (CFS), which is a hierarchical 4-level scale derived from a resident's Brief Interview for Mental Status (BIMS) assessment and/or Cognitive Performance Scale (CPS) and integrates their findings into a single score. Accordingly, a residents' cognitive function is assessed as severely impaired (ie, individuals who were not able to complete the BIMS by themselves or have a CPS score of 5 or 6), moderately impaired (ie, a BIMS score of ≤7 or a CPS score of 3-4), mildly impaired (ie, a BIMS score of 8-12 or a CPS score of ≤2), or cognitively intact (ie, individuals who were able to complete the BIMS and scored between 13 and 15).

TROPISM OF SARS-COV-2, SARS-COV AND INFLUENZA VIRUS IN CANINE TISSUE EXPLANTS

Bui CHT, Yeung HW, Ho JCW, Leung CYH, Hui KPY, Perera RAPM, Webby RJ, Schultz-Cherry SL, Nicholls JM, Peiris JSM, Chan MCW.. J Infect Dis. 2021 Jan 4:jiab002. doi: 10.1093/infdis/jiab002. Online ahead of print.
Level of Evidence: 5 - Mechanism-based reasoning

BLUF

An ex-vivo study conducted at The University of Hong Kong of replication activity of various viruses, including SARS-CoV, SARS-CoV-2, and subtypes of influenza A and B on canine tissues found that the canine tissue was less susceptible to and had less replication of SARS-CoV and SARS-CoV-2 than the other viruses. However, the tissue did have high ACE2 receptor levels, suggesting the availability of these receptors in canines could allow for the reassortment and increased virulence of the virus, which should prompt researchers to continue closely studying canines as the COVID-19 pandemic continues.

ABSTRACT

BACKGROUND: Human spillovers of SARS-CoV-2 to dogs and the emergence of a highly contagious avian-origin H3N2 canine influenza virus have raised concerns towards the role of dogs in the spread of SARS-CoV-2 and their susceptibility to existing human and avian influenza viruses which might result in further reassortment. METHODS: We systematically studied the replication kinetics of SARS-CoV-2, SARS-CoV, influenza A viruses of H1, H3, H5, H7 and H9 subtypes and influenza B viruses of Yamagata-like and Victoria-like lineages in ex-vivo canine nasal cavity (NC), soft palate (SP), trachea (T) and lung (L) tissue explant cultures and examined ACE2 and sialic acid (SA) receptor distribution in these tissues. RESULTS: There was limited productive replication of SARS-CoV-2 in canine NC and SARS-CoV in canine NC, SP and L with unexpectedly high ACE2 levels in canine NC and SP. Meanwhile, the canine tissues were susceptible to a wide range of human and avian influenza viruses, which matched with the abundance of both human and avian SA receptors. CONCLUSIONS: Existence of suitable receptors and tropism for the same tissue foster virus adaptation and reassortment. Continuous surveillance in dog populations should be conducted given the plenty of chances for spillover during outbreaks.

COVID-19 GLOBAL PANDEMIC PLANNING: PERFORMANCE AND ELECTRET CHARGE OF N95 RESPIRATORS AFTER RECOMMENDED DECONTAMINATION METHODS

Grillet AM, Nemer MB, Storch S, Sanchez AL, Piekos ES, Leonard J, Hurwitz I, Perkins DJ.. Exp Biol Med (Maywood). 2020 Dec 16:1535370220976386. doi: 10.1177/1535370220976386. Online ahead of print.
Level of Evidence: 5 - Mechanism-based reasoning

BLUF

Scientists from the Sandia National Laboratories in Albuquerque, NM studied respirator performance (fit, filtration efficiency, pressure drop, relationship between surface charge of the electret layer, and elastic properties of the straps) after several decontamination methods on two surgical N95 respirators (3M™ 1860 and 1870+ Aura™) (Figure 1) and found that VHP, wet heat, bleach, and UV light did not change filtration efficiency, pressure drop, or quantitative fit. Isopropyl alcohol and soap solution both showed degradation of quantitative fit, filtration efficiency, and electrostatic charge of the filtration later but were not associated with changes in pressure drop, and extended use or reuse of the respirators may be more damaging than many decontamination processes, highlighting the necessity for adequate PPE for healthcare workers, or at least the utilization of non-degrading decontamination methods.

ABSTRACT

Shortages of N95 respirators for use by medical personnel have driven consideration of novel conservation strategies, including decontamination for reuse and extended use. Decontamination methods listed as promising by the Centers for Disease Control and Prevention (CDC) (vaporous hydrogen peroxide (VHP), wet heat, ultraviolet irradiation (UVI)) and several methods considered for low resource environments (bleach, isopropyl alcohol and detergent/soap) were studied for two commonly used surgical N95 respirators (3M 1860 and 1870+ Aura). Although N95 filtration performance depends on the electrostatically charged electret filtration layer, the impact of decontamination on this layer is largely unexplored. As such, respirator performance following decontamination was assessed based on the fit, filtration efficiency, and pressure drop, along with the relationship between (1) surface charge of the electret layer, and (2) elastic properties of the straps. Decontamination with VHP, wet heat, UVI, and bleach did not degrade fit and filtration performance or electret charge. Isopropyl alcohol and soap significantly degraded fit, filtration performance, and electret charge. Pressure drop across the respirators was unchanged. Modest degradation of N95 strap elasticity was observed in mechanical fatigue testing, a model for repeated donnings and doffings. CDC recommended decontamination methods including VHP, wet heat, and UV light did not degrade N95 respirator fit or filtration performance in these tests. Extended use of N95 respirators may degrade strap elasticity, but a loss of face seal integrity should be apparent during user seal checks. NIOSH recommends performing user seal checks after every donning to detect loss of appropriate fit. Decontamination methods which degrade electret charge such as alcohols or detergents should not be used on N95 respirators. The loss of N95 performance due to electret degradation would not be apparent to a respirator user or evident during a negative pressure user seal check.

FIGURES

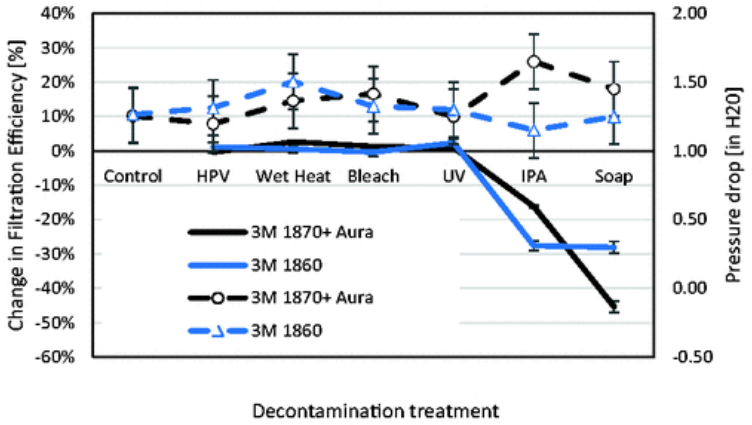


Figure 1. Change in filtration efficiency (solid line) and pressure drop (dashed line) as a function of decontamination treatment for 3M™ 1870+ Aura™ and 1860 respirators. Error bars of change in efficiency are the standard deviation. Error bars on the pressure drop are the measurement uncertainty reported by the pressure gauge manufacturer.

INCIDENCE AND SECONDARY TRANSMISSION OF SARS-COV-2 INFECTIONS IN SCHOOLS

Zimmerman KO, Akinboyo IC, Brookhart MA, Boutzoukas AE, McGann K, Smith MJ, Maradiaga Panayotti G, Armstrong SC, Bristow H, Parker D, Zadrozny S, Weber DJ, Benjamin DK Jr; ABC Science Collaborative.. Pediatrics. 2021 Jan 8:e2020048090. doi: 10.1542/peds.2020-048090. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

Pediatricians and child development experts from Duke University and University of North Carolina tracked secondary transmission of SARS-CoV-2 in 11 school districts in North Carolina with over 90,000 students and staff attending in-person in August 2020 after receiving training on SARS-CoV-2 prevention (Table 2). If secondary transmission were as common in schools as in the community, authors expected 800–900 cases of school-acquired SARS-CoV-2 between August 15 and October 23 (9 weeks), but only observed 32 (confirmed by contact tracing). Authors suggest school districts that implement robust SARS-CoV-2 prevention policies can reopen safely.

FIGURES

District	County Population	Staff 2019	Students 2019	Hispanic[1]	African American	Asian	White	Multiple Races[2]	Students in Person	Primary Infections
1	38,755	967	4971	11	4	1	78	5	3972	60
2	28,150	626	3087	12	<1	<1	82	4	2163	43
3	43,965	1073	6354	15	7	1	72	5	5068	69
4	223,842	3847	31116	15	22	2	54	7	19434	315
5	N/A[3]	727	4359	26	19	5	40	10	2835	24
6	184,023	3399	21829	14	14	3	63	6	16523	91
7	10,194	254	1109	11	35	<1	47	7	628	6
8	102,950	1733	12461	14	14	1	63	7	8815	69
9	N/A[3]	330	1727	21	8	1	64	6	1024	7
10	181,005	4228	25043	12	44	1	35	6	12700	83
11	38,236	1000	5361	26	3	<1	66	4	4284	6

[1]North Carolina reports ethnicity as a separate category within race.
[2]Races with <1% for all districts listed include Native American and Pacific Islander.
[3]Sites 5 and 9 are city districts and, therefore, county population cannot be estimated.

Table 2. Description of the 11 Districts within the ABC Science Collaborative

DIAGNOSIS OF SARS-COV-2 IN CHILDREN: ACCURACY OF NASOPHARYNGEAL SWAB COMPARED TO NASOPHARYNGEAL ASPIRATE

Di Pietro GM, Capecchi E, Luconi E, Lunghi G, Bosis S, Bertolozzi G, Cantoni B, Marano G, Boracchi P, Biganzoli E, Castaldi S, Marchisio P; Testing Pediatric Covid-19 (TPC-19).. Eur J Clin Microbiol Infect Dis. 2021 Jan 7. doi: 10.1007/s10096-020-04131-z. Online ahead of print.

Level of Evidence: 3 - Non-consecutive studies, or studies without consistently applied reference standards

BLUF

Members of the Testing Pediatric Covid-19 (TPC-19) research group based at the University of Milan evaluated the performance of nasopharyngeal swabs (NS) for detection of SARS-CoV-2 in 300 pediatric inpatients from March 13 to May 22, 2020. Using nasopharyngeal aspirates (NPA) as a reference, they found that NS had a specificity of 97.7% and a sensitivity of 58.1 (Table 1). Authors concluded NS has a low sensitivity, but high specificity in detecting SARS-CoV-2 in children compared to NPA, which are considered the gold standard for detection in children.

ABSTRACT

The tests currently used for the identification of SARS-CoV-2 include specimens taken from the upper and lower respiratory tract. Although recommendations from the World Health Organization prioritise the usage of a nasopharyngeal swab (NS), nasopharyngeal aspirates (NPA) are thought to be superior in identifying SARS-CoV-2 in children. To our knowledge, however, no paediatric study has been published on the subject. The aim of this study is to evaluate the diagnostic performances of NS referred to NPA for SARS-CoV-2 in children. We calculated the sensitivity and specificity of the NS referred to the NPA of the whole sample and considered both age and collection period as covariates in different analyses. We collected 300 paired samples. The NS had a specificity of 97.7% and a sensitivity of 58.1%. We found similar results for the group of subjects >= 6 years old, while for subjects < 6 years old, the sensitivity was 66.7% and the specificity 97.8%. Considering period as a covariate, the sensitivity and specificity for patients hospitalised in March (31 patients, 52 records) were 70.0% and 97.6%, while for patients involved in the follow-up (16 patients, 57 records), they were 57.2% and 89.7%. The NS has a low sensitivity in detecting SARS-CoV-2 in children when referred to the NPA, whereas its specificity is high. Our results suggest that in children under 6 years of age, NSs should be preferred whenever possible. Though statistically not significant, the sensitivity of the NS rises when performed before the NPA.

Table 1

Sensitivity, specificity and mismatch for positive and negative results of nasopharyngeal swab (NS) referred to nasopharyngeal aspirate (NPA) in children

	Positive NPA and negative NS % (95% CI)	Negative NPA and positive NS % (95% CI)	NS sensitivity % (95% CI)	NS specificity % (95% CI)
"All records"	41.9% (28.2–56.9%)	2.3% (1.1–5.1%)	58.1% (43.1–71.8%)	97.7% (94.9–98.9%)
"All records" ≥ 6 years old	45.2% (28.9–62.6%)	2.5% (0.8–7.5%)	54.8% (37.4–71.1%)	97.5% (92.5–99.2%)
"All records" < 6 years old	33.3% (13.1–62.4%)	2.2% (0.7–6.6%)	66.7% (37.6–86.9%)	97.8% (93.4–99.3%)
Hospitalised in March	30% (10–62.4%)	2.4% (0.3–14.7%)	70.0% (37.6–90.0%)	97.6% (85.3–99.7%)
Follow-up	42.9% (27.2–60.1%)	10.3% (3.5–26.7%)	57.2% (39.9–72.8%)	89.7% (73.3–96.5%)

NPA nasopharyngeal aspirate

NS nasopharyngeal swab

CI confidence interval

NASOPHARYNGEAL SWAB-INDUCED PAIN FOR SARS-COV-2 SCREENING: A RANDOMISED CONTROLLED TRIAL OF CONVENTIONAL AND SELF-SWABBING

Moisset X, Gautier N, Godet T, Parabère S, Pereira B, Meunier E, Gerbaud L, Lesens O, Henquell C, Beytout J, Clavelou P..
Eur J Pain. 2021 Jan 4. doi: 10.1002/ejp.1722. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

A randomized control trial was performed by an interdisciplinary group of researchers at Clermont-Ferrand Medical School to assess for the reported pain level of nasopharyngeal "self-swab" testing for COVID-19 compared to the conventional swabbing performed by a healthcare professional that is currently in practice. 190 medical students were randomized to either the self-swabbing group or the conventional swabbing group and self-reported their pain and discomfort on a 0-10 scale. The researchers found no statistically significant difference in reported pain levels between the two groups, and concluded that self-swabbing techniques could be a means by which society can circumvent the apprehension of pain that is associated with conventional swabbing techniques. This study is limited by the supporting evidence that it provides. In stating that apprehension to pain is maintaining a low level of attendance when it comes to COVID-19 testing, there is no cited evidence reported in the article to support their claim. Further investigation is necessary to first establish whether or not this is a significant hinderance in obtaining high levels of testing.

ABSTRACT

BACKGROUND: Massive screening campaigns for SARS-CoV-2 are currently carried out throughout the world, relying on reverse-transcriptase-polymerase chain reaction (RT-PCR) following nasopharyngeal swabbing performed by a healthcare professional. Yet, due to the apprehension of pain induced by nasopharyngeal probing, poor adhesion to those screening campaigns can be observed. To enhance voluntary participation and to avoid unnecessary exposition to SARS-CoV-2, self-swabbing could be proposed. To date, no data have been published concerning pain induced by conventional- or self-swabbing. Thus, the primary objective of the present study was to evaluate pain induced with the conventional swabbing method and compare it to self-swabbing. Secondary objectives focused on swabbing-induced discomfort and acceptability of the two methods. METHODS: The study was conducted in Clermont-Ferrand medical school (France). Overall, 190 students were randomised into 2 groups and experienced either self- or conventional-swabbing. Each subject had to rate pain, discomfort and acceptability of such swabbing on a 0-10 numeric rating scale. RESULTS: No significant difference was found between the two methods. Mean pain level was 2.5+-1.9, 28% rating pain as >=4/10. Discomfort was 4.8+-2.2, 66% indicating significant (>=4/10) discomfort. Higher pain and discomfort were associated with female sex. Acceptability was >=8/10 for 89.0% of the subjects and all would have accepted to undergo a new test with the same technique if necessary. CONCLUSION: Both conventional and self-swabbing induce low levels of pain for most young healthy volunteers whereas discomfort is very frequent. Nonetheless, both methods are indifferently well-accepted in medical students. Future studies among symptomatic subjects are awaited.

COVID-19 SCREENING TEST BY USING RANDOM OROPHARYNGEAL SALIVA

Rao M, Rashid FA, Sabri FSAH, Jamil NN, Seradja V, Abdullah NA, Ahmad H, Aren SL, Ali SAS, Ghazali M, Manaf AA, Talib H, Hashim R, Zain R, Thayan R, Amran F, Aris T, Ahmad N.. J Med Virol. 2021 Jan 4. doi: 10.1002/jmv.26773. Online ahead of print.
Level of Evidence: 4 - Case-control studies, or "poor or non-independent reference standard

BLUF

Infectious disease specialists from the Malaysian Ministry of Health screened 562 asymptomatic adults (Figure 1) for SARS-CoV-2 infection using nasopharyngeal and oropharyngeal (NP+OP)swabs and random oropharyngeal saliva samples for qRT-PCR. They found 11.6% (65/562) were SARS-CoV-2 positive by random saliva, NP+OP, or both. Saliva had better detection rates (detected 92.3% of cases vs 73.8%, $p<0.05$), sensitivity (95.0% vs 72.2%), and specificity (99.9% vs. 99.4%, $p<0.05$) compared to NP+OP swabs (Tables 1,2). Authors suggest saliva specimens can be used as a non-invasive, cost-effective method to detect asymptomatic SARS-CoV-2 for surveillance purposes.

ABSTRACT

BACKGROUND: An optimal clinical specimen for an accurate detection of SARS-CoV-2 by minimizing the usage of consumables and reduce hazard exposure to healthcare workers is a dire priority. The diagnostic performance of SARS-CoV-2 detection between healthcare worker-collected nasopharyngeal and oropharyngeal (NP+OP) swabs and patient performed self-collected random saliva was assessed. METHODS: Paired NP+OP swabs and random saliva were collected and processed within 48 hours of specimen collection from two cohort study which recruited 562 asymptomatic adult candidates. Real time reverse transcriptase polymerase chain reaction (qRT-PCR) targeting Open reading frame 1a (ORF1a) and nucleocapsid (N) genes was performed and the results were compared. RESULTS: Overall, 65 of 562 (28.1%) candidates tested positive for COVID-19 based on random saliva, NP+OP swabs or both testing techniques. The detection rate of SARS-CoV-2 was higher in random saliva compared to NP+OP testing (92.3%; 60/65 versus 73.8%; 48/65; $p<0.05$). The estimated sensitivity and specificity of random saliva were higher than NP+OP swabs (95.0;99.9 vs 72.2;99.4). The Ct-values of ORF1a and N genes were significantly lower in random saliva compared to NP+OP swabs specimens. CONCLUSIONS: Our findings demonstrate that random saliva is an alternative diagnostic specimen for detection of SARS-CoV-2. Self-collected random oropharyngeal saliva is a valuable specimen which provides accurate SARS-CoV-2 surveillance testing of a community.

FIGURES

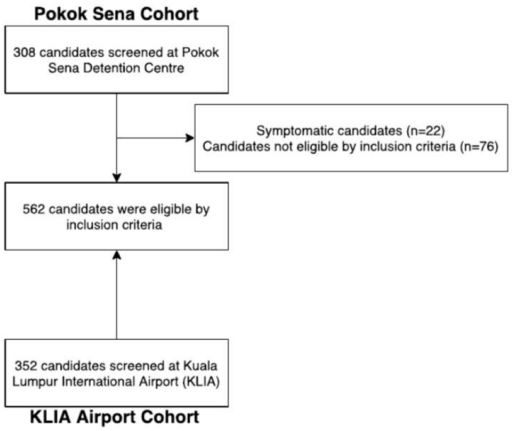


Figure 1: "Screened and eligible candidates for the study".

Characteristic	Results	*p*-value
Age (years), median (IQR)		
Overall, n=562	33 (25-42)	<0.05
COVID-19, n=65	31 (26-41)	
Non COVID-19, n=497	33 (29-42)	
Gender [male, n (%)]		
Overall	392 (69.8%)	<0.05
COVID-19	59 (15.1%)	
Non COVID-19	333 (84.9%)	

*Abbreviations: IQR, interquartile range

Table 1: "Characteristic of studied candidates".

Cohort study	Pokok Sena Detention Centre, (n=210)	Airport Travelers, (n=352)
Total Positive Case, (n)	59	6
Kappa Coefficient, κ (*p*)	0.75, (p<0.05)	0.66, (p<0.05)
Agreement, (%)	91.0	99.1

McNemar test, (*p*)	< 0.05	0.564
Prevalence by Bayesian LCM, (95% credible interval)	28.0(22.1-34.7)	1.2(0.4-2.9)
Nasopharygneal and Oropharyngeal swabs (NP+OP swabs) (95% credible interval):		
i) Sensitivity	72.2 (60.0-82.6)	
ii) Specificity	99.4 (98.2-100)	
iii) PPV	93.9 (82.6-99.7)	
iv) NPV	96.6 (94.6-98.0)	
Random saliva (95% credible interval):		
i) Sensitivity	95.0 (83.8-100)	
ii) Specificity	99.9 (98.9-100)	
iii) PPV	98.9 (91.0-100)	
iv) NPV	99.4 (97.8-100)	

Table 2: "Kappa coefficient (□), agreement (%), McNemar test, prevalence, sensitivities, and specificities estimated by assuming either NP+OP swabs or random saliva as a perfect gold standard".

DIFFERENT ASPECTS OF CONVALESCENT PLASMA THERAPY FOR COVID-19 TREATMENT; A CRITICAL REVIEW

Khadka S, Nisar S, Syed NI, Shrestha DB, Budhathoki P.. Immunopharmacol Immunotoxicol. 2020 Dec 27:1-7. doi: 10.1080/08923973.2020.1863983. Online ahead of print.
Level of Evidence: 5 - Mechanism-based reasoning

BLUF

Physicians and scientists from Nepal and Pakistan review the use of convalescent plasma (CP) therapy for the treatment of COVID-19 in an effort to increase the efficacy of current therapeutic protocol. After analyzing the risks and benefits associated with taking, purifying and treating patients with CP (Table 1), they concluded that CP therapy may act as an alternative option when no other treatment is available, or as a concurrent treatment during the height of the pandemic. They further note that the hesitancy involved with using CP therapy is due to the the availability from donors, the actual process of acquiring CP from donors, and the potential risk of thrombotic events.

ABSTRACT

The novel coronavirus disease (COVID-19) has been declared a pandemic by the World Health Organization (WHO) and is ominously threatening the survival of humankind on the whole planet. With a quick spread of the outbreak from its origin, Wuhan, China, to almost all over the world, it has affected more than seven million people to date, hence it has devastated every part of the infrastructural skeleton of governance. Continuously escalating disease burden and lack of proven therapeutic approaches are mounting challenges to health scientists and ultimately to healthcare providers. Although recent studies have shown benefits in decreasing the severity and duration of the illness and there are more benefits compared to risks, plasma therapy cannot be considered as a standard of care until the ongoing trials are completed and they establish definite evidence on its therapeutic efficacy and safety. Though a beneficial aspect may be there, acquiring donors and adequate availability of plasma is equally challenging, and its associated untoward effects related to biological therapeutic agents. The rational practice of CP therapy guided by risk-benefit judgment from aspects of donor and recipient can be a therapeutic option in such a global health crisis.

FIGURES

Table 1. Studies showing effects of convalescent plasma therapy in COVID-19 cases.

S.N.	Studies, year, location	Dosage of convalescent plasma	Study population	Concomitant therapy	Outcome	Side effects
1.	Li et al. [20], 2020, Randomized controlled trial, China	4-13 ml/kg 10 ml for the first 15 min followed by 100 ml/h with close monitoring.	T: 52 C: 51 Both groups received standard treatment Median age 70 years 60 M, 43 F	Antiviral medications, antibacterial medications, steroids, human immunoglobulin, Chinese herbal medicines, and other medication	• Primary outcome was time to clinical improvement within 28 days , defined as patient discharged alive or reduction of 2 points on a 6-point disease severity scale (ranging from 1 [discharge] to 6 [death] • Clinical improvement occurred within 28 days in 51.9% of the convalescent plasma group vs 43.1% in the control group (difference, 8.8% [95% CI, −10.4% to 28.0%]; hazard ratio [HR], 1.40 [95% CI, 0.79-2.49]; $p = .26$) • In severe disease, the primary outcome occurred in 91.3% (21/23) of the convalescent plasma group vs 68.2% (15/22) of the control group (HR, 2.15 [95% CI, 1.07–4.32]; $p = .03$) • In life-threatening disease, the primary outcome occurred in 20.7% (6/29) of the convalescent plasma group vs 24.1% (7/29) of the control group (HR, 0.88 [95% CI, 0.30–2.63]; $p = .83$) (P for interaction = .17). • There was no significant difference in 28 day mortality (15.7% vs 24.0%; OR, 0.59 [95% CI, 0.22–1.59]; $p = .30$) or time from randomization to discharge (51.0% vs 36.0% discharged by day 28; HR, 1.61 [95% CI, 0.88-2.95]; $p = .12$). • Negative conversion rate of viral PCR at 72 hours in 87.2% of the convalescent plasma group vs 37.5% of the control group (OR, 11.39 [95% CI, 3.91–33.18]; $p < .001$)	Two cases of adverse effects. First patient developed non-severe febrile non-hemolytic transfusion reaction. Second patient developed severe-transfusion associated dyspnea.
2.	Joyner et al. [30], 2020, Multi-center open label, Expanded Access Program, USA	At least one unit 200 ml with options to add additional dosage if justified	35332 52.3 % ICU patients 27.5% receiving mechanical ventilation	Azithromycin, remdesivir, steroid, chloroquine, hydroxychloroquine	• The seven-day mortality rate • Transfusion within 3 days = 8.7% [95% CI 8.3%–9.2%] • Transfused 4 or more days after diagnosis = 11.9% [11.4%–12.2%] • 7 day mortality • Recipient of high IgG Plasma: −8.9% (6.8%, 11.7%) • Recipients of medium IgG plasma: −11.6% (10.3%, 13.1%) • Recipients of low IgG plasma: −13.7% (11.1%, 16.8%) ($p = .048$) • The unadjusted dose-response relationship with IgG was observed in 30-day mortality ($p = .021$). • The pooled relative risk of mortality among patients transfused with high antibody level plasma units was 0.65 [0.47–0.92] 86 for 7-D and 0.77 [0.63–0.94] for 30-D compared to low antibody level plasma units	Not Documented
3.	Salazar [31], 2020, Prospective case series, USA	300 ml of CP therapy	25 14 F, 11 M 12 patients mechanically ventilated 52% developed ARDS at the time of admission	Antiviral in most patients, steroids, hydroxychloroquine, azithromycin, and remdesevir (2 patients)	• Day 7 post transfusion Based on 6 point the WHO ordinal scale 9 patients had improvement, 13 patients were static and 3 patients deteriorated) 7 patients were discharged • Day 14 post transfusion 19 patients improved, three were unchanged, and 3 deteriorated	One patient developed morbilliform rash in 24 h
4.	Joyner et al. [19], 2020, Clinical trial, USA	200 – 500 ml of Convalescent plasma	5000 (3153 M, 1824 F, 23 Other) 3316 admitted to ICU and 4051 patients were severe and life threatening	Not mentioned	• Seven day mortality rate was 14.9 %	Incidence of side effects was < 1% Mortality rate (0.3%) 7 patients developed TACO, 3 patients developed severe allergic reaction and a total of 11 patients developed TRALI
5.	Shen et al. [14], 2020 , Case series, China	2 doses of 400 ml in the same day	5 (3 M, 2 F) Age range: 36–73 years All patients mechanically ventilated with severe ARDS	Antivirals, methylprednisolone and interferon	• Normal temperature within 3 days in 4 patients • Increase in PaO_2/FiO_2 within 12 days (range,172–276 before and 284–366 after) • Neutralizing antibody titers increased (range 40–60 before and 80–320 on 7th day) • Resolution of ARDS ($n = 4$) at 12th day, mechanical ventilation weaning ($n = 3$) in 2 weeks • Discharge 32–35 days after CP therapy	No

(*continued*)

Table 1. Studies showing effects of convalescent plasma therapy in COVID-19 cases.

Table 1. Continued.

S.N.	Studies, year, location	Dosage of convalescent plasma	Study population	Concomitant therapy	Outcome	Side effects
6.	Zeng et al. [32], 2020, Retrospective observational study, China	200–600 ml Median:- 300 ml	21 16 M, 5 F T: 6 C: 15 All patients admitted in ICU 5 patients in treatment and 13 patients in control group mechanically ventilated	Antibiotics, antiviral, immunoglobulin and steroid	• 100 % SARS CoV-2 Clearance in treatment group • One patient discharged from both group • 5 mortality in treatment group and 14 in control group	None
7.	Chen et al. [33], 2020, Case series, China	200 – 1200 ml Majority 200 ml	16 5 F, 11 M Age 30 – 90 years 5 Severely ill 11 Critically ill 10 patients had persistently positive viral NAA test results	Supportive treatment, antiviral treatment, antibacterial treatment, traditional Chinese medicine treatment, and respiratory circulation support treatment	• Eight patients (8/10) became negative from 2 to 8 days after transfusion. • Severe patients showed a shorter time for NAA test turning negative after transfusion (mean rank 2.17 vs 5·90, $p = .036$). • Two critically ill patients transfused plasma with lower antibody level remained a positive result of NAA test. • CRP level demonstrated a decline 1 day after convalescent plasma treatment, compared with the baseline ($p = .017$)	No adverse effects
8.	Duan et al. [15], 2020, Prospective single-arm intervention, China	2 doses of 200 ml in 4 hr	10 (6 M, 4 F) Mechanical ventilation in 3 patients, Nasal cannula high flow in 3 patients and Low flow in 2 patients	Antivirals and supportive care, antibacterial/antifungal agent, glucocorticoids	• Improvement in clinical symptoms in first 3 days • Weaning of mechanical ventilation after 2 days of transfusion • Resolution of CT abnormalities in 7 days Improvement in pulmonary function and normal lab tests	One patient developed temporary red facial spot
9.	Ye et al. [17], 2020, Case series, China	200 ml in 1 dose in 3 patients, 600 ml in 3 doses in 2 patients and 400 ml in 1 dose in one patient	(3 M, 3 F) 3 patients required oxygen support	Levofloxacin and arbidol	• Improvement in clinical symptoms • Discharge and resolution of consolidation in 4 patients • Patients were discharged 4–10 days after transfusion	None
10.	Rasheed et al. [34], 2020, Cohort study, Iraq	Not mentioned	49 $T = 21$ $C = 28$ 75% M, 25 % F Target Population Critically-ill patients at their early stages of admission to RCU before developing full-blown ARDS or respiratory and/or multiple organ failure	Not mentioned	• Reduced duration of infection in about 4 days • Decreased death rate, 1/21 in treatment versus 8/28 in control group. • Decreased death rate from 28% in control group compared to only 4.8% in treatment group. • All of the patients received convalescent plasma showed high levels of SARS-CoV-2 IgG and IgM at day 3 after plasma transfusion. • Plasma from donors with high levels of SARS-CoV-2 IgG and donors with positive SRAS-CoV-2 IgM showed better therapeutic results than other donors.	One patient developed mild skin redness and itching.

Abbreviations: ARDS: Acute respiratory distress syndrome; C: Control; CRP: C – Reactive protein; CI: Confidence interval; CT: Computed tomography; F: Female; FiO2: Fraction of inspired oxygen; HR: Hazard ratio; ICU: Intensive care unit; M: Male NAAT: Nucleic acid amplification test; Pa02: Partial pressure of oxygen; PCR: Polymerase chain reaction; RCU: Respiratory care unit; SARS: Severe acute respiratory syndrome; T: Treatment; TACO: Transfusion associated circulatory overload; TRALI: Transfusion related acute lung injury; USA: United States of America; Vs: Versus.

Table 1. Continued. Studies showing effects of convalescent plasma therapy in COVID-19 cases.

PUBLIC CONCERN ABOUT VIOLENCE, FIREARMS, AND THE COVID-19 PANDEMIC IN CALIFORNIA

Kravitz-Wirtz N, Aubel A, Schleimer J, Pallin R, Wintemute G.. JAMA Netw Open. 2021 Jan 4;4(1):e2033484. doi: 10.1001/jamanetworkopen.2020.33484.
Level of Evidence: 1 - Local and current random sample surveys (or censuses)

BLUF

A survey conducted on 2870 adults living in California during July 14 - July 27, 2020 by researchers at University of California - Davis School of Medicine found that fear of personal safety due to violence of others was heightened during the pandemic compared to pre-pandemic concerns (Table 1). 110,000 individuals purchased a firearm during the pandemic, 47,000 of which were new owners, suggesting that violence-related harm is crucial particularly during the pandemic, and short-term crisis interventions may become key in reducing impulsive violence.

SUMMARY

Data for the survey used in this study was collected through the 2020 California Safety and Well-being Survey.

ABSTRACT

Importance: Violence is a significant public health problem that has become entwined with the coronavirus disease 2019 (COVID-19) pandemic. Objective: To describe individuals' concerns regarding violence in the context of the pandemic, experiences of pandemic-related unfair treatment, prevalence of and reasons for firearm acquisition, and changes in firearm storage practices due to the pandemic. Design, Setting, and Participants: This survey study used data from the 2020 California Safety and Well-being Survey, a probability-based internet survey of California adults conducted from July 14 to 27, 2020. Respondents came from the Ipsos KnowledgePanel, an online research panel with members selected using address-based sampling methods. Responses were weighted to be representative of the adult population of California. Main Outcomes and Measures: Topics included worry about violence for oneself before and during the pandemic; concern about violence for someone else due to a pandemic-related loss; experiences of unfair treatment attributed to the pandemic; firearm and ammunition acquisition due to the pandemic; and changes in firearm storage practices due to the pandemic. Results: Of 5018 invited panel members, 2870 completed the survey (completion rate, 57%). Among respondents (52.3% [95% CI, 49.5%-55.0%] women; mean [SD] age, 47.9 [16.9] years; 41.9% [95% CI, 39.3%-44.6%] White individuals), self-reported worry about violence for oneself was significantly higher during the pandemic for all violence types except mass shootings, ranging from a 2.8 percentage point increase for robbery (from 65.5% [95% CI, 62.8%-68.0%] to 68.2% [95% CI, 65.6%-70.7%]; P = .008) to a 5.6 percentage point increase for stray bullet shootings (from 44.5% [95% CI, 41.7%-47.3%] to 50.0% [47.3%-52.8%]; P < .001). The percentage of respondents concerned that someone they know might intentionally harm themselves was 13.1% (95% CI, 11.5%-15.3%). Of those, 7.5% (95% CI, 4.5%-12.2%) said it was because the other person had experienced a pandemic-related loss. An estimated 110 000 individuals (2.4% [95% CI, 1.1%-5.0%] of firearm owners in the state) acquired a firearm due to the pandemic, including 47 000 new owners (43.0% [95% CI, 14.8%-76.6%] of those who had acquired a firearm). Of owners who stored at least 1 firearm in the least secure way, 6.7% (95% CI, 2.7%-15.6%) said they had adopted this unsecure storage practice in response to the pandemic. Conclusions and Relevance: In this analysis of findings from the 2020 California Safety and Well-being Survey, the COVID-19 pandemic was associated with increases in self-reported worry about violence for oneself and others, increased firearm acquisition, and changes in firearm storage practices. Given the impulsive nature of many types of violence, short-term crisis interventions may be critical for reducing violence-related harm.

Violence	Respondents, % (95% CI)				Difference among those not worried, percentage points	*P* value	Difference among those somewhat or very worried, percentage points	*P* value
	Before the pandemic		During the pandemic					
	Not worried	Somewhat or very worried	Not worried	Somewhat or very worried				
Type								
Homicide	54.7 (51.9-57.5)	44.0 (41.2-46.9)	51.2 (48.4-54.0)	47.6 (44.8-50.4)	-3.5	.001	3.6	.001
Suicide	74.6 (71.9-77.1)	24.5 (22.0-27.2)	71.0 (68.3-73.7)	27.7 (25.1-30.5)	-3.5	.001	3.2	.002
Mass shooting	39.1 (36.5-41.7)	59.9 (57.3-62.6)	43.2 (40.5-46.0)	55.3 (52.6-58.1)	4.2	<.001	-4.6	<.001
Assault	39.9 (37.3-42.6)	59.1 (56.4-61.8)	36.5 (33.9-39.2)	62.4 (59.7-65.1)	-3.4	.001	3.3	.002
Robbery	33.5 (31.0-36.2)	65.5 (62.8-68.0)	30.8 (28.4-33.4)	68.2 (65.6-70.7)	-2.7	.008	2.8	.008
Police violence	53.7 (50.8-56.5)	45.3 (42.5-48.1)	48.1 (45.4-50.9)	50.6 (47.8-53.4)	-5.5	<.001	5.4	<.001
Unintentional shooting	56.2 (53.3-59.0)	42.7 (39.9-45.5)	51.0 (48.2-53.8)	48.0 (45.3-50.9)	-5.2	<.001	5.4	<.001
Stray bullet shooting	54.7 (51.9-57.5)	44.5 (41.7-47.3)	48.8 (46.0-51.6)	50.0 (47.3-52.8)	-5.9	<.001	5.6	<.001
Location								
Home	70.6 (67.9-73.1)	27.9 (25.4-30.5)	69.4 (66.7-72.0)	29.1 (26.5-31.7)	-1.2	.29	1.2	.29
Neighborhood	50.0 (47.3-52.8)	48.8 (46.0-51.6)	46.5 (43.7-49.2)	52.2 (49.4-55.0)	-3.6	.002	3.4	.003
Somewhere else	27.2 (24.8-29.7)	71.3 (68.8-73.7)	26.7 (24.3-29.1)	71.7 (69.2-74.1)	-0.1	.65	0.0	.71

Table 1. Prevalence of Worry About Violence, Before and During the Coronavirus Disease 2019 Pandemic, by Violence Type and Location Among 2870 Respondents to the 2020 California Safety and Well-being Survey

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