The Daily COVID-19 Literature Surveillance Summary

March 11, 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

Climate

- Is vaccine refusal leading to lack of access COVID-19 vaccination in people of color? A professor associated with Wellesley College and Harvard University in Massachusetts discusses the focus on COVID-19 vaccine refusal rather than lack of access to healthcare as factors in vaccination rates among communities of color despite lack of access being the larger problem. She states that attention needs to shift from stories of mistrust leading to vaccine denial towards harnessing social and political tools with long-term perspective and commitment to address the structural barriers that maintain racism and disparity. She recommends continuing to emphasize the safety and efficacy of the vaccine and deploying vaccinators to local churches and independent pharmacies to reach minority communities that may not have access to chain pharmacies or large healthcare centers.

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RACISM, DISEASE, AND VACCINE REFUSAL: PEOPLE OF COLOR ARE DYING FOR ACCESS TO COVID-19 VACCINES

Reverby SM.. PLoS Biol. 2021 Mar 8;19(3):e3001167. doi: 10.1371/journal.pbio.3001167. Online ahead of print.
Level of Evidence: 5 - Expert Opinion

BLUF

A professor associated with Wellesley College and Harvard University in Massachusetts discusses the focus on COVID-19 vaccine refusal rather than lack of access to healthcare as factors in vaccination rates among communities of color despite lack of access being the larger problem. She states that attention needs to shift from stories of mistrust leading to vaccine denial towards harnessing social and political tools with long-term perspective and commitment to address the structural barriers that maintain racism and disparity. She recommends continuing to emphasize the safety and efficacy of the vaccine and deploying vaccinators to local churches and independent pharmacies to reach minority communities that may not have access to chain pharmacies or large healthcare centers.

ABSTRACT

As the vaccines against COVID are slowly becoming available, we need to consider the paradox of why so many people of color are dying from the disease yet cannot get the vaccinations. Concerns focus on vaccine refusal but lack of access is the bigger problem.

PEDIATRICS

CHILDREN AND YOUNG ADULTS HOSPITALIZED FOR SEVERE COVID-19 EXHIBIT THROMBOTIC COAGULOPATHY

Mitchell WB, Davila J, Keenan J, Jackson J, Tal A, Morrone KA, Silver EJ, O'Brien S, Manwani D.. Pediatr Blood Cancer. 2021 Mar 4:e28975. doi: 10.1002/pbc.28975. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

Pediatricians and hematologists from Albert Einstein College of Medicine evaluated coagulopathies in a cohort of 27 children and young adults (2 months to 21 years old) hospitalized with COVID-19 between March 1 and May 31, 2020. They found 25 patients had D-dimer > 0.5 µg/mL on admission and 7 developed venous thromboembolism (VTE) (Table 1); however, D-dimer did not correlate with risk for VTE while patients increased respiratory support requirements had higher VTE risk (p 0.006) (Table 3). Due to their small cohort, authors suggest their conclusions are limited and recommend more research to guide future management regarding thrombo-prophylaxis in this age group.

ABSTRACT

We report the clinical and laboratory coagulation characteristics of 27 pediatric and young adult patients (2 months to 21 years) treated for symptomatic COVID-19 at a children's hospital in the Bronx, New York, between March 1 and May 31, 2020. D-Dimer was > 0.5 mug/mL (upper limit of normal) in 25 (93%) patients at admission; 11 (41%) developed peak D-dimer > 5 mug/mL during admission. Seven (26%) patients developed venous thromboembolism: three with deep vein thrombosis and four with pulmonary embolism. Requirement of increased ventilatory support was a risk factor for thrombosis (P = 0.006). Three of eight (38%) patients on prophylactic anticoagulation developed thrombosis; however, no patients developed VTE on low-molecular-weight heparin prophylaxis titrated to anti-Xa level. Manifestation of COVID-19 disease was severe or critical in 16 (59%) patients. Four (15%) patients died of COVID-19 complications: all had comorbidities. Elevated D-dimer and increased VTE rate were observed in this young cohort, particularly in those with severe respiratory complications, suggesting thrombotic coagulopathy. More data are needed to guide thromboprophylaxis in this age group.

TABLE 1 Baseline clinical characteristics and laboratory values

	Total ($n = 27$)
Gender, male/female *n* (%)	14/13 (52)
Age, *n* (%)	
< 1 year	3 (11)
1-6 years	4 (15)
7-12 years	8 (30)
13-21 years	12 (44)
Race, *n* (%)	
Black	3 (11)
White	1 (4)
Other	11 (41)
Not reported	12 (44)
Ethnicity *n*(%)	
Spanish/Hispanic/Latino	16 (59)
Not Spanish/Hispanic/Latino	9 (33)
Not reported	2 (7)
Comorbidity, *n* (%)	
BMI ≥ 95%	5 (19)
Sickle cell anemia	5 (19)
COVID-19 severity, *n* (%)	
Severe/critical illness	16 (59)
Deceased	4 (15)
Ventilatory support, *n* (%)	
Oxygen > 5 L NC	14 (52)
Intubated	9 (33)
Central venous line, *n* (%)	16 (59)
D-dimer	
> 5 μg/mL	11 (41)
< 5 μg/mL	11 (41)
Laboratory finding	Mean (SD, range)
WBC peak (k/μL)	20.6 (12.1, 2.8-55.9)
ANC peak (k/μL)	15.3 (10.0, 1.5-49.8)
ALC nadir (k/μL)	1.27 (1.1, 0.1-4.4)
AMC peak (k/μL)	2.0 (2.1, 0.2-11)
Hemoglobin nadir (g/dL)	9.4 (2.9, 5.5-17.3)
Platelets peak (k/μL)	416 (173, 183-789)
Platelets nadir (k/μL)	175 (173, 5-683)
Creatinine peak (mg/dL)	0.84 (1.1, 0.3-5.9)
D-dimer peak (μg/mL)	6.41 (4.69, 0.27-16.19)
PT peak (seconds)	17.8 (6.0, 13.8-43.3)
aPTT peak (seconds)	65.6 (46.9, 29.3-200)
Fibrinogen peak (mg/dL)	642 (328, 227-1800)

Abbreviations: NC, nasal cannula; SCD, sickle cell disease.

TABLE 3. Venous thromboembolism risk factors, all patients (*n* = 27)

Variable		Thrombosis *N* (%)	OR	95% CI	*P*
Gender	Male	5 (36)	3.06	0.47-19.66	0.385
	Female	2 (15)			
BMI	≥ 95%	1 (20)	0.667	0.061-7.23	1.0
	< 95%	6 (27)			
CVL	Yes	5 (31)	2.045	0.318-13.19	0.446
	No	2 (18)			
Ventilatory support	> 5 L by NC	7 (50)	NA	NA	**0.006**
	≤ 5 L by NC	0			
D-dimer	≥ 5 µg/mL	5 (45)	3.75	0.54-26.04	0.361
	< 5 µg/mL	2 (18)			

CVL, central venous line; NC, nasal cannula; OR, odds ratio. Bold font indicates statistical significance.

UNDERSTANDING THE PATHOLOGY

VASCULAR DAMAGE MAY MIMIC RETINITIS AND OPTIC NEURITIS IN COVID-19

Finsterer J, Scorza FA, Scorza CA, Fiorini AC.. Curr Eye Res. 2021 Mar 4. doi: 10.1080/02713683.2021.1896743. Online ahead of print.
Level of Evidence: 5 - Opinion

BLUF

Neurologists and a speech therapist challenge a case report by Liu et al reporting the first case of retinitis and optic neuritis due to SARS-CoV-2 infection. They argue the original authors did not sufficiently exclude other diagnoses such as vascular pathology, underlying cardiac or neurologic disease, and anti-COVID-19 drug side effects.

DEVELOPMENTS IN TRANSMISSION & PREVENTION

LARGE SCALE SCREENING FOR SARS-COV-2 AMONG HEALTHCARE WORKERS: PREVALENCE AND RISK FACTORS FOR ASYMPTOMATIC/PAUCI-SYMPTOMATIC CARRIERS, WITH EMPHASIS ON PPE USE

Rajme-López S, González-Lara MF, Ortiz-Brizuela E, Román-Montes CM, Santiago-Cruz J, Mendoza-Rojas MÁ, Méndez-Ramos S, Tamez-Torres KM, Pérez-García E, Martínez-Guerra BA, Cervantes-Villar LE, Ramos-Cervantes P, Ibarra-González V, Kershenobich-Stalnikowitz D, Sifuentes-Osornio J, Ruíz-Palacios GM, Ponce-de-León A.. Infect Control Hosp Epidemiol. 2021 Feb 24:1-17. doi: 10.1017/ice.2021.68. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

A cross-sectional study conducted at a COVID-19 center in Mexico City by researchers at the Instituto Nacional de Ciencias Medicas y Nutrition in Salvador Zubiran involved 2000 healthcare workers and hospital staff who were screened for COVID-19 infection, 933 asymptomatic and 1067 paucisymptomatic, and found 5.5% prevalence of positive SARS-CoV-2 PCR tests (See Figure 1), 21.9% of which were asymptomatic cases. Nursing staff caring directly for COVID-19 patients were more likely to have PCR-positive tests (See Table 2), however there was no difference between surgical or N95 masks nor goggles or face shields in any of the study's population. Given the prevalent asymptomatic transmission of SARS-CoV-2, especially among healthcare workers, these findings suggest the benefit of screening asymptomatic employees to isolate workers earlier with positive PCR test to prevent transmission.

ABSTRACT

HCWs not fulfilling COVID-19 case definition underwent SARS-CoV-2 screening. Risk of exposure, PPE adherence and symptoms were assessed. Two thousand HCWs were screened: 5.5% were PCR+. There were no differences in PPE use between PCR+ and PCR- HCWs (adherence >90%). Nursing and kitchen staff were independently associated with PCR+.

FIGURES

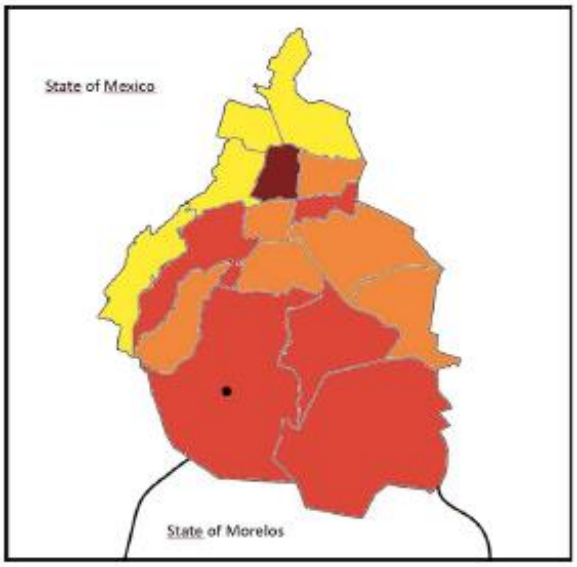

Figure 1. Distribution of cases based on current personal address
Mexico City is divided into 16 counties. Percentage of PCR positivity among HCWs from our study is marked on the map as follows: dark red >10%, red >5-10%, orange 1-5%, yellow <1%. Two hundred healtchare workers lived outside Mexico City. Sate of Mexico PCR positivity percentage was 8.3% and State of Morelos 6.3%. This distribution is consistent with Mexico´s City community transmission hot spots during the months of May through mid July26.
*Black dot indicates location of our Institution

	Univariate		Multivariate	
	OR (CI 95%)	p	OR (CI 95%)	p
Comorbidity				
Overweight/obesity	1.39 (0.92-2.1)	0.12		
Hypertension	0.43 (0.10-1.76)	0.24		
Diabetes mellitus	1.26 (0.30-5.39)	0.75		
Ischemic heart disease	4.28 (0.48-38.7)	0.20		
Chronic lung disease (asthma, COPD, ILD)	1.22 (0.37-4.00)	0.33		
Current smoker	0.75 (0.43-1.31)	0.31		
Type of work				
Medical	0.69 (0.43-1.10)	0.12		
Nursing	1.79 (1.21-2.65)	0.004	1.66 (1.01-2.73)	0.04
Administrative	0.96 (0.56-1.65)	0.88		
Paramedical	0.42 (0.17-1.04)	0.06		
Cleaning	1.18 (0.62-2.25)	0.51		
Kitchen	2.18 (1.02-4.66)	0.045		
Workplace				
COVID-19 critical areas	1.19 (0.80-1.79)	0.39	1.06 (0.50-2.24)	0.88
COVID-19 general ward	1.44 (0.95-2.19)	0.09	1.48 (0.79-2.77)	0.22
Administrative building/office	0.72 (0.37-1.40)	0.33		
Non-COVID-19 outpatient visits	0.52 (0.24-1.13)	0.10	0.75 (0.32-1.74)	0.49
Laboratory	0.63 (0.27-1.47)	0.29		
Radiology	0.31 0.04-2.25)	0.25		
Hospital staff triage	0.75 (0.18-3.14)	0.70		
Staff kitchen	2.86 (1.18-6.92)	0.02	3.95 (1.53-10.2)	0.005
Radio-oncology unit	1.84 (0.55-6.17)	0.32		
Other	0.63 (0.23-1.72)	0.36		
Exposure to a COVID-19 case	1.75 (1.14-2.69)	0.01		
Face masking at workplace	1.52 (0.85-2.76)	0.16		
Directly taking care of COVID-19 patients	1.41 (0.96-2.17)	0.08	0.98 (0.50-1.92)	0.94
In charge of aerosol-generating procedures	1.45 (0.98-2.14)	0.06	1.15 (0.61-2.19)	0.65
Contact with the environment of COVID-19 patients	1.48 (0.99-2.2)	0.05		

Table 2. Univariate and multivariate analysis of characteristics associated with being PCR+

A CONSEQUENTIALIST ARGUMENT FOR CONSIDERING AGE IN TRIAGE DECISIONS DURING THE CORONAVIRUS PANDEMIC

Altman MC.. Bioethics. 2021 Mar 8. doi: 10.1111/bioe.12864. Online ahead of print.
Level of Evidence: 5 - Opinion

BLUF

A philosopher from the Central Washington University reviewed the current age-based triage algorithms for COVID-19 patients in the setting of limited life-saving resources. The author argues current standards should not only use age as a tie-breaker in cases where Sequential Organ Failure Assessment (SOFA) prognosis are similar, but that age should be considered in the primary triage algorithm as all patients should have equal opportunity to experience life-stages.

ABSTRACT

Most ethics guidelines for distributing scarce medical resources during the coronavirus pandemic seek to save the most lives and the most life-years. A patient's prognosis is determined using a SOFA or MSOFA score to measure likelihood of survival to discharge, as well as a consideration of relevant comorbidities and their effects on likelihood of survival up to one or five years. Although some guidelines use age as a tiebreaker when two patients' prognoses are identical, others refuse to consider age for fear of discriminating against the elderly. In this paper, I argue that age is directly relevant for maximizing health benefits, so current ethics guidelines are wrongly excluding or deemphasizing life-stage in their triage algorithms. Research on COVID-19 has shown that age is a risk factor in adverse outcomes, independent of comorbidities. And limiting a consideration of life-years to only one or five years past discharge does not maximize health benefits. Therefore, based on their own stated values, triage algorithms for coronavirus patients ought to include life-stage as a primary consideration, along with the SOFA score and comorbidities, rather than excluding it or using it merely as a tiebreaker. This is not discriminatory because patients ought to have equal opportunity to experience life-stages. The equitable enforcement of that right justifies unequal treatment based on age in cases when there is a scarcity of life-saving resources. A consideration of life-stage would thus allow healthcare workers to responsibly steward public resources in order to maximize lives and life-years saved.

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