The Daily COVID-19 Literature Surveillance Summary

September 15, 2020

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COVID-19 Daily Literature Surveillance

COVID19LST

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

LEVEL OF EVIDENCE

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

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

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

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

How to cite the Levels of Evidence Table

OCEBM Levels of Evidence Working Group*. "The Oxford 2011 Levels of Evidence".

Oxford Centre for Evidence-Based Medicine. http://www.cebm.net/index.aspx?o=5653

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

EXECUTIVE SUMMARY

Epidemiology

- Random COVID-19 testing of 200 people in Chelsea, MA using the BioMedomics SARS-CoV-2 combined IgM/IgG LFA to determine seropositivity in a group of asymptomatic patients showed that 24.7% of seropositive participants were asymptomatic, suggesting that better safety precautions such as improved testing, isolation, contact-tracing, and distancing are needed as a high number of individuals can be carrying the virus asymptomatically.

- A systematic review of 97 studies exploring COVID-19 in 230,398 health care workers (HCW) showed COVID-19 prevalence of 11% by RT-PCR (95% CI: 7-15%) and 7% by antibody detection (95% CI: 4-11%) with serious complications seen in 5% (95% CI: 3-8%) and mortality in 0.5% (95% CI: 0.02-1.3%). Overall, those working in nursing or in a non-emergency setting were found to be at highest risk. Because 40% of HCW were asymptomatic at diagnosis, they suggest HCW simultaneously risk spreading and contracting COVID-19 and emphasize the need to screen HCW and implement standard procedures for the use of personal protective equipment.

Management

- A multidisciplinary coalition of Brazilian investigators conducted a multi-center, randomized open-label clinical trial (CoDEX) exploring the clinical impact of dexamethasone on COVID-19 patients in 41 ICUs in Brazil (n=299). Adult patients presenting with moderate to severe ARDS who received dexamethasone (n=151) spent fewer days on mechanical ventilation within a 28 day period compared to those receiving standard care (mean 6.6 days [95% CI: 5.0-8.2] vs 4.0 days [95% CI: 2.9-5.4], difference 2.26 days [p=0.04])). This adds to a growing body of research suggesting dexamethasone improves outcomes in moderate to severe COVID-19.

R&D: Diagnosis & Treatments

- Investigators affiliated with International Medical University, Malaysia and the University of Huddersfield, UK performed a systemic review and meta-analysis with a total of 8,121 hospitalized patients with COVID-19 showing significantly lower odds for mortality with metformin use in diabetic, COVID-19 cases (pooled analysis OR: 0.62) than cases without use of metformin. The authors hypothesize that this finding may be due to anti-inflammatory mechanisms of metformin dampening the cytokine storm in COVID-19. However, as this finding was only seen in patients with pre-existing diabetes, further research is needed to provide evidence of the morbidity and mortality benefit in repurposing metformin for COVID-19 patients without concomitant diabetes.

TABLE OF CONTENTS

CURRENT DATA GAPS IN MODELLING ESSENTIAL WORKER ABSENTEEISM DUE TO COVID-19

White Z, Schlegelmilch J, Ratner J, Saxena G, Wongsodirdjo K, Aguilar S, Kushner D, Matevosyan N, Ortega J, Paaso A, Bahramirad S.. Disaster Med Public Health Prep. 2020 Sep 10:1-4. doi: 10.1017/dmp.2020.353. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

Researchers affiliated with The National Center for Disaster Preparedness (NCPD), Columbia University in conjunction with the utility company Commonwealth Edison developed a research dashboard for following publications on predicting COVID-19-related workforce absenteeism (Figure 1). Although initial analysis shows some support for modeling absenteeism, there continues to be gaps in current data, suggesting a need for further research to improve data on transmission, time-to-recovery, household member contact, and mental health impact on returning to work in the setting of the COVID-19 pandemic.

FIGURES

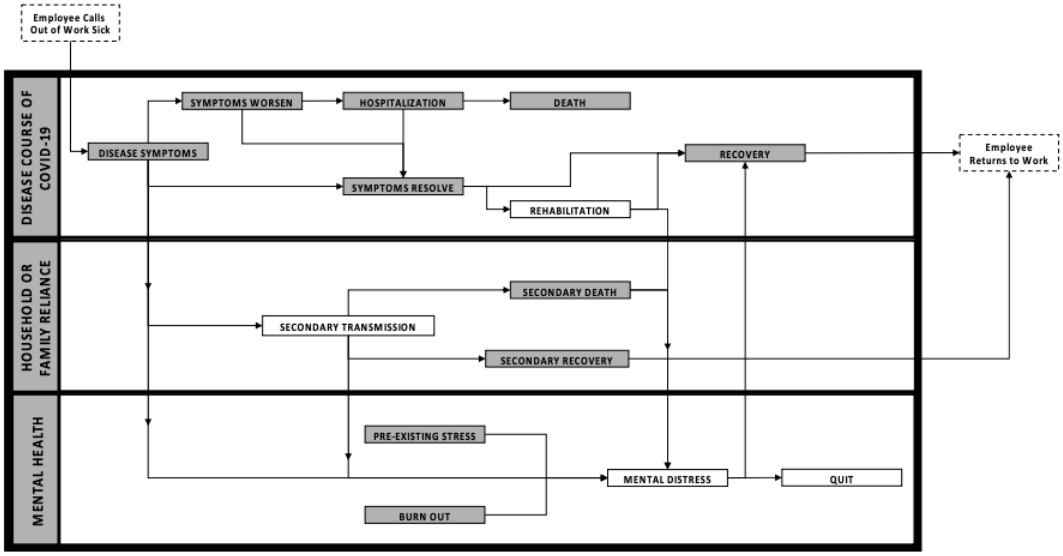


Figure 1: This swim lane diagram maps out the conceptual inner workings of employee absenteeism and shows how events may alter the timeline for the return to work. The shaded boxes indicate parameter values which have evidence to support the development of more robust absenteeism models. This diagram does not represent all events an individual may experience.

HIGH SEROPREVALENCE OF ANTI-SARS-COV-2 ANTIBODIES IN CHELSEA, MASSACHUSETTS

Naranbhai V, Chang CC, Beltran WFG, Miller TE, Astudillo MG, Villalba JA, Yang D, Gelfand J, Bernstein BE, Feldman J, Hauser BM, Caradonna TM, Alter G, Murali MR, Jasrasaria R, Quinlan J, Xerras DC, Betancourt JR, Louis DN, Schmidt AG, Lennerz J, Poznansky MC, Iafrate AJ.. J Infect Dis. 2020 Sep 9:jiaa579. doi: 10.1093/infdis/jiaa579. Online ahead of print.
Level of Evidence: 1 - Local and current random sample surveys (or censuses)

BLUF

A group of interdisciplinary researchers performed random COVID-19 testing of 200 people in Chelsea, MA between April 14-15, 2020 using the BioMedomics SARS-CoV-2 combined IgM/IgG LFA to determine seropositivity in a group of asymptomatic patients. Results showed that 24.7% of seropositive participants were asymptomatic (Summary), suggesting that better safety precautions such as improved testing, isolation, contact-tracing, and distancing are needed as a high number of individuals can be carrying the virus asymptomatically.

SUMMARY

Summary of findings:

•31.5% of participants were seropositive, either IgM and/or IgG
•24.7% of seropositive patients were asymptomatic the preceding 4 weeks (Figure 1)
•48.5% of participants endorsed COVID-19 like symptoms (cough, rhinitis, sore throat) the previous 4 weeks (Figure 1)
•Living with children was an independent risk factor of seropositivity; Odds Ratio (OR) 1.057 (95% Confidence interval (CI) 1.001-1.117; p=0.049) (Supplementary Table 1)

ABSTRACT

SARS-CoV-2 antibody testing allows quantitative determination of disease prevalence, especially important in high-risk communities. We performed anonymized convenience sampling of 200 currently asymptomatic residents of Chelsea, the epicenter of COVID-19 illness in Massachusetts by BioMedomics SARS-CoV-2 combined IgM-IgG point-of-care lateral flow immunoassay. The seroprevalence was 31.5% (17.5% IgM+IgG+, 9.0% IgM+IgG- and 5.0% IgM-IgG+). 50.5% of participants reported no symptoms in the preceding 4 weeks, of which 24.8% (25/101) were seropositive, and 60% of these were IgM+IgG-. These data are the highest seroprevalence rates observed to date and highlight the significant burden of asymptomatic infection.

FIGURES

Figure 1

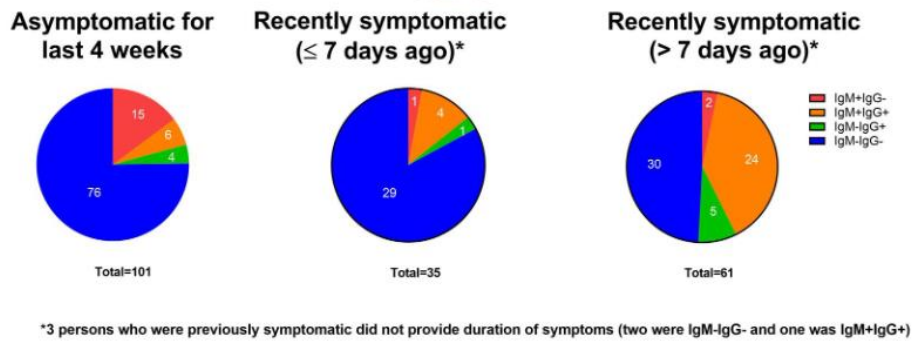


Figure 1: Anti SARS-CoV-2 IgM and IgG results according to presence of and recency of symptoms.

Supplementary Table 1

Risk factors for seropositivity from multivariate regression modelling including exposure variables with p<0.01 in univariate models

Risk factor	Multivariate	
	OR (95% CI)	p-value
Age (years)	1.000 (0.994-1.005)	0.896
Gender (n, % Female)	1.126 (0.985-1.288)	0.847
Cohabiting children	1.057 (1.001-1.117)	**0.0489**
Cohabiting adults	1.018 (0.981-1.057)	0.3488
Known COVID-19 contact (n, %)[§]	1.096 (0.935-1.285)	0.259
Any symptom in last 4 weeks	1.054 (0.914-1.215)	0.472
Thought they may have/ have had COVID-19 (n, %)[&]	1.049 (0.871-1.263)	0.618

ADULTS

PREVALENCE OF SUSPECTED COVID-19 INFECTION IN PATIENTS FROM ETHNIC MINORITY POPULATIONS: A CROSS-SECTIONAL STUDY IN PRIMARY CARE

Hull SA, Williams C, Ashworth M, Carvalho C, Boomla K.. Br J Gen Pract. 2020 Sep 7:bjgp20X712601. doi: 10.3399/bjgp20X712601. Online ahead of print.
Level of Evidence: 1 - Local and current random sample surveys (or censuses)

BLUF

A cross-sectional study of 1.2 million patients from 157 clinics in east London between January 1 and April 20, 2020 by health data experts found general practice (GP) records documented 8,985 suspected COVID-19 cases, which was triple the number of confirmed positive cases in the area (Figure 2), while south Asian and black individuals had increased odds of suspected infection compared to white individuals upon multivariate analysis (odds ratios [OR] 1.93 and 1.47 respectively; Tables 1,2). Authors indicate a need for further research on compounding factors (i.e. housing, occupation) impacting COVID-19 ethnic disparities, suggesting GP clinical records may be useful for identifying and monitoring potential COVID-19 cases.

ABSTRACT

BACKGROUND: The first wave of the London COVID-19 epidemic peaked in April 2020. Attention initially focused on severe presentations, intensive care capacity, and the timely supply of equipment. While general practice has seen a rapid uptake of technology to allow for virtual consultations, little is known about the pattern of suspected COVID-19 presentations in primary care. AIM: To quantify the prevalence and time course of clinically suspected COVID-19 presenting to general practices, to report the risk of suspected COVID-19 by ethnic group, and to identify whether differences by ethnicity can be explained by clinical data in the GP record. DESIGN AND SETTING: Cross-sectional study using anonymised data from the primary care records of approximately 1.2 million adults registered with 157 practices in four adjacent east London clinical commissioning groups. The study population includes 55% of people from ethnic minorities and is in the top decile of social deprivation in England. METHOD: Suspected COVID-19 cases were identified clinically and recorded using SNOMED codes. Explanatory variables included age, sex, self-reported ethnicity, and measures of social deprivation. Clinical factors included data on 16 long-term conditions, body mass index, and smoking status. RESULTS: GPs recorded 8985 suspected COVID-19 cases between 10 February and 30 April 2020.Univariate analysis showed a two-fold increase in the odds of suspected COVID-19 for South Asian and black adults compared with white adults. In a fully adjusted analysis that included clinical factors, South Asian patients had nearly twice the odds of suspected infection (odds ratio [OR] = 1.93, 95% confidence interval [CI] = 1.83 to 2.04). The OR for black patients was 1.47 (95% CI = 1.38 to 1.57). CONCLUSION: Using data from GP records, black and South Asian ethnicity remain as predictors of suspected COVID-19, with levels of risk similar to hospital admission reports. Further understanding of these differences requires social and occupational data.

FIGURES

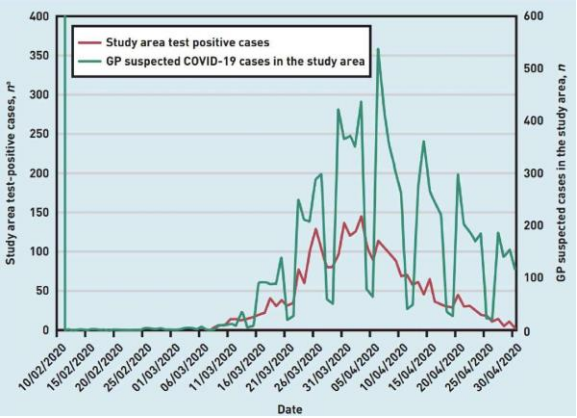


Figure 2. Test-positive COVID-19 cases across the study area compared with daily counts of GP-suspected COVID-19 cases from 10 February to 30 April 2020. *Data on study area test-positive cases from UK's Government Digital Service website. Results from these positive tests were not routinely returned to general practices.

Variable	GP-suspected COVID-19, *n* (%)	Without suspected COVID-19, *n* (%)	Univariate OR (95% CI)
Total	8985	1 248 152	—
CCG			
Tower Hamlets	2558 (28.5)	292 653 (23.4)	—
Newham	2732 (30.4)	377 171 (30.2)	—
City & Hackney	2674 (29.8)	351 060 (28.1)	—
Waltham Forest	1021 (11.4)	227 268 (18.2)	—
Age, years			
18–49	5134 (57.1)	926 886 (74.3)	ref
50–69	2723 (30.3)	235 616 (18.9)	2.18 (2.08 to 2.29)
≥70	1128 (12.6)	85 650 (6.9)	2.45(2.29 to 2.62)
Sex			
Male	3982 (44.3)	632 082 (50.6)	ref
Female	5003 (55.7)	616 070 (49.4)	1.28 (1.22 to 1.33)
Ethnicity			
White	2890 (32.2)	476 302 (38.2)	ref
South Asian	2859 (31.8)	259 464 (20.8)	1.98 (1.86 to 2.09)
Black	1642 (18.3)	153 240 (12.3)	1.88 (1.77 to 2.00)
Other	594 (6.6)	78 454 (6.3)	1.24 (1.13 to 1.35)
Not stated/missing	1000 (11.1)	280 692 (22.5)	0.64 (0.60 to 0.69)
National IMD 2015 quintiles			
1 least deprived	30 (0.3)	8964 (0.7)	ref
2	96 (1.1)	24 029 (1.9)	1.35 (0.88 to 2.06)
3	485 (5.4)	99 395 (8.0)	1.22 (0.83 to 1.79)
4	3557 (39.6)	541 773 (43.4)	1.53 (1.05 to 2.23)
5 most deprived	4807 (53.5)	560 245 (44.9)	1.88 (1.29 to 2.74)
Missing	10 (0.1)	13 746 (1.1)	0.21 (0.10 to 0.43)
BMI (kg/m²)			
Normal weight (18.5 to <25)	2528 (28.1)	431 279 (34.6)	ref
Underweight (<18.5)	200 (2.2)	39 067 (3.1)	0.85 (0.73 to 1.00)
Overweight (25 to <30)	2770 (30.8)	299 136 (24.0)	1.60 (1.52 to 1.69)
Obese (30 to <40)	2451 (27.3)	169 982 (13.6)	2.49 (2.35 to 2.63)
Morbidly obese (≥40)	483 (5.4)	23 717 (1.9)	3.48 (3.15 to 3.84)
Out of range/Unknown	553 (6.2)	284 971 (22.8)	0.33 (0.30 to 0.36)
QOF long-term conditions			
0	3740 (41.6)	881 460 (70.6)	ref
1	2461 (27.4)	226 961 (18.2)	2.41 (2.29 to 2.54)
2	1350 (15.0)	81 093 (6.5)	3.75 (3.52 to 3.99)
3	690 (7.7)	33 497 (2.7)	4.60 (4.25 to 5.02)
≥4	744 (8.3)	25 141 (2.0)	6.50 (6.00 to 7.05)
Current smoker	1047 (11.7)	217 396 (17.4)	0.60 (0.56 to 0.63)
Asthma	1512 (16.8)	111 641 (8.9)	1.92 (1.81 to 2.03)
Atrial fibrillation	248 (2.8)	10 299 (0.8)	3.16 (2.78 to 3.59)
Cancer	429 (4.8)	22 989 (1.8)	2.50 (2.26 to 2.75)
Coronary heart disease	504 (5.6)	23 114 (1.9)	2.98 (2.72 to 3.26)
Chronic kidney disease (stages 3–5)	716 (8.0)	32 203 (2.6)	3.11 (2.88 to 3.37)
COPD	331 (3.7)	14 467 (1.2)	2.92 (2.61 to 3.26)
Dementia	258 (2.9)	4442 (0.4)	7.37 (6.48 to 8.39)
Depression	1811 (20.2)	121 290 (9.7)	2.15 (2.04 to 2.27)
Diabetes	1696 (18.9)	79 445 (6.4)	3.31 (3.13 to 3.49)
Epilepsy	157 (1.7)	10 321 (0.8)	2.00 (1.70 to 2.34)
Heart failure	234 (2.6)	8039 (0.6)	3.75 (3.28 to 4.28)
Hypertension	2290 (25.5)	131 318 (10.5)	2.85 (2.71 to 2.99)
Learning disability	70 (0.8)	4660 (0.4)	1.89 (1.49 to 2.40)
Severe mental illness	250 (2.8)	17 322 (1.4)	1.88 (1.65 to 2.13)
Peripheral arterial disease	87 (1.0)	3608 (0.3)	3.00 (2.41 to 3.71)
Stroke and TIA	284 (3.2)	11 514 (0.9)	3.24 (2.87 to 3.65)

BMI = body mass index. CCG = clinical commissioning group. COPD = chronic obstructive pulmonary disease. QOF = Quality and Outcomes Framework. IMD = Index of Multiple Deprivation. OR = odds ratio. TIA = transient ischaemic attack.

Table 1. Characteristics of those with and without GP-suspected COVID-19 codes from 10 February to 30 April 2020 (N = 1,257,137 patients aged ≥18 years from 157 practices)

Variable		Model 1 Demographic factors			Model 2 Demographic and clinical factors		
		OR[a]	95% CI	*P*-value	OR[a]	95% CI	*P*-value
Sex	Male	1.00	ref	ref	1.00	ref	ref
	Female	1.25	[1.20 to 1.31]	<0.001	1.17	[1.12 to 1.22]	<0.001
Age, years	18–49	1.00	ref	ref	1.00	ref	ref
	50–69	2.14	[2.03 to 2.24]	<0.001	1.30	[1.23 to 1.37]	<0.001
	≥69	2.57	[2.40 to 2.74]	<0.001	1.25	[1.16 to 1.35]	<0.001
Ethnicity	White	1.00	ref	ref	1.00	ref	ref
	South Asian	2.06	[1.94 to 2.18]	<0.001	1.93	[1.83 to 2.04]	<0.001
	Black	1.66	[1.56 to 1.77]	<0.001	1.47	[1.38 to 1.57]	<0.001
	Other	1.28	[1.17 to 1.40]	<0.001	1.41	[1.29 to 1.54]	<0.001
	Not stated/missing	0.68	[0.63 to 0.73]	<0.001	1.13	[1.05 to 1.22]	0.002
Internal IMD 2015 quintiles[b]	1 (least deprived)	1.00	ref	ref	1.00	ref	ref
	2	1.24	[1.14 to 1.33]	<0.001	1.18	[1.09 to 1.28]	<0.001
	3	1.23	[1.13 to 1.32]	<0.001	1.16	[1.07 to 1.25]	<0.001
	4	1.32	[1.22 to 1.43]	<0.001	1.21	[1.17 to 1.37]	<0.001
	5 (most deprived)	1.40	[1.29 to 1.51]	<0.001	1.26	[1.17 to 1.37]	<0.001
QOF long-term conditions	0	—	—	—	1.00	ref	ref
	1	—	—	—	1.77	[1.67 to 1.87]	<0.001
	2	—	—	—	2.28	[2.13 to 2.43]	<0.001
	3	—	—	—	2.60	[2.37 to 2.85]	<0.001
	≥4	—	—	—	3.67	[3.33 to 4.03]	<0.001
BMI (kg/m²)[c]	Normal weight (18.5 to <25)	—	—	—	1.00	ref	ref
	Underweight (<18.5)	—	—	—	0.84	[0.73 to 0.97]	0.02
	Overweight (25 to <30)	—	—	—	1.31	[1.24 to 1.38]	<0.001
	Obese (30 to <35)	—	—	—	1.73	[1.63 to 1.84]	<0.001
	Morbidly obese (≥40)	—	—	—	2.23	[2.01 to 2.47]	<0.001

Intraclass correlation coefficient for practice variation is 0.16 (95% CI = 0.13 to 0.20). [a]Adjusted for other variables in the table. [b]Unknown IMD quintiles not shown. [c]Unknown BMI not shown. BMI = body mass index; IMD = Index of Multiple Deprivation; OR = odds ratio; QOF = Quality and Outcomes Framework.

Table 2. Multivariate model for predictors of GP-suspected COVID-19 for adults aged ≥18 years (N = 1,257,137 patients contributing to the model)

COVID-19 IN HEALTHCARE WORKERS: A LIVING SYSTEMATIC REVIEW AND META-ANALYSIS OF PREVALENCE, RISK FACTORS, CLINICAL CHARACTERISTICS, AND OUTCOMES

Gómez-Ochoa SA, Franco OH, Rojas LZ, Raguindin PF, Roa-Díaz ZM, Wyssmann BM, Guevara SLR, Echeverría LE, Glisic M, Muka T.. Am J Epidemiol. 2020 Sep 1:kwaa191. doi: 10.1093/aje/kwaa191. Online ahead of print.
Level of Evidence: 2 - Systematic review of surveys that allow matching to local circumstances

BLUF

An international, multidisciplinary group of investigators conducted a systematic review of 97 studies exploring COVID-19 in 230,398 health care workers (HCW). Among HCW, analysis showed COVID-19 prevalence of 11% by RT-PCR (95% CI: 7-15%) and 7% by antibody detection (95% CI: 4-11%). Serious complications were seen in 5% (95% CI: 3-8%) and mortality in 0.5% (95% CI: 0.02-1.3%). Overall, those working in nursing or in a non-emergency setting were found to be at highest risk (Table 2). Because 40% of HCW were asymptomatic at diagnosis, they suggest HCW simultaneously risk spreading and contracting COVID-19 and emphasize the need to screen HCW and implement standard procedures for the use of personal protective equipment.

SUMMARY

Of note heterogeneity in this sample was significant. Per the authors: " ...the heterogeneity of the included studies represented a challenge when pooling the results; thus, we aimed to overcome this limitation by performing different sub-group analyses when estimating the prevalence." Of these multiple subgroups i^2 values ranged from 10-99% and the heterogeneity of the studied groups limits the conclusions that can be drawn from this data.

ABSTRACT

Health care workers (HCW) are at the frontline response to the new coronavirus disease 2019 (COVID-19), being at a higher risk of acquiring the disease, and subsequently, exposing patients and colleagues. Searches in eight bibliographic databases were performed to systematically review the evidence on the prevalence, risk factors, clinical characteristics, and prognosis of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection among HCW. Ninety-seven studies (All published in 2020), including 230,398 HCW, met the inclusion criteria. From the screened HCW using RT-PCR and the presence of antibodies, the estimated prevalence of SARS-CoV-2 infection was 11% (95%CI; 7%-15%) and 7% (95% CI; 4%-11%), respectively. The most frequently affected personnel were the nurses (48%. 95%CI; 41%-56%), while most of the COVID-19 positive medical personnel were working in hospitalization/non-emergency wards during the screening (43%, 95%CI;28%-59%). Anosmia, fever and myalgia were identified as the only symptoms associated with HCW SARS-CoV-2 positivity. Among RT-PCR positive HCW, 40% (95%CI;17%-65%) did not show symptoms at the time of diagnosis. Finally, 5% (95%CI;3%-8%) of the COVID-19 positive HCW developed severe clinical complications, and 0.5% (95% CI; 0.02%-1.3%) died. HCW suffer a significant burden from COVID-19, with HCW working in hospitalization/non-emergency wards and nurses being the most infected personnel.

Table 2. Areas in which COVID-19 positive health care workers were laboring during RT-PCR screenings

Area/Setting	Number of studies	Proportion, (%)	95% CI	I^2
Clinics/Wards	5	43	28% - 59%	91%
Operating Room	4	24	17% - 31%	60%
Others	4	29	13% - 48%	91%
Emergency Room	5	16	6% - 29%	91%
ICU	5	9	4% - 15%	68%

COVID-19: Coronavirus disease 2019; ICU: Intensive care unit.

UNDERSTANDING THE PATHOLOGY

SEROCONVERSION AGAINST SARS-COV-2 OCCURRED AFTER THE RECOVERY IN PATIENTS WITH COVID-19

Yamamoto S, Saito M, Nagai E, Toriuchi K, Nagai H, Yotsuyanagi H, Nakagama Y, Kido Y, Adachi E.. J Med Virol. 2020 Sep 8. doi: 10.1002/jmv.26495. Online ahead of print.
Level of Evidence: 4 - Case-series, case-control, or historically controlled studies

BLUF

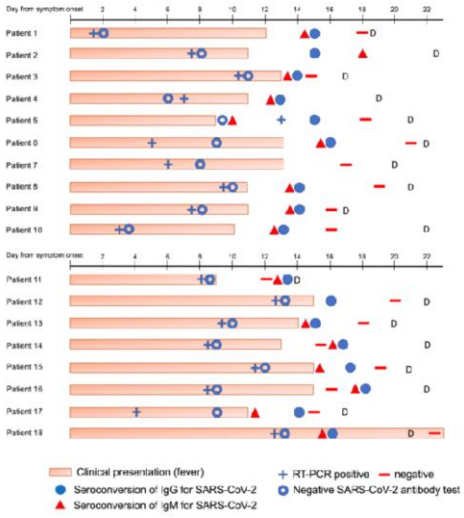
A retrospective study of patients with confirmed mild-moderate COVID-19 (n=18) and their serological statuses (Figure 1) at IMSUT Hospital, Tokyo, Japan from March 1 - May 15, 2020 found that 89% (16/18) had IgG seroconversion after becoming afebrile (median: 15 days from onset, range: 10-22 days), in addition to 83% (15/18) exhibiting IgM seroconversion (median: 14.5 days from onset, range: 9-22 days) after becoming afebrile. These results suggest seroconversion may indicate clinical recovery from COVID-19 (convalescence phase) in non-critical patients, and that these individuals may begin to discontinue isolation precautions.

ABSTRACT

Little is known about the protective immunity for coronavirus disease 2019 (COVID-19) while the demand for COVID-19 serology tests is increasing. This article is protected by copyright. All rights reserved.

FIGURES

Figure 1. Comparison of clinical features and dynamics of serological status in COVID-19 patients



DETECTION OF SARS-COV-2 RNA IN BLOOD OF PATIENTS WITH COVID-19: WHAT DOES IT MEAN?

Jacobs JL, Mellors JW.. Clin Infect Dis. 2020 Sep 8:ciaa1316. doi: 10.1093/cid/ciaa1316. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

Researchers in Infectious Diseases from the University of Pittsburgh School of Medicine comment that the quantity of SARS-CoV-2 RNA in COVID-19 patients is a strong indicator of prognosis; they reference Veyer et al. (2020)'s study findings that the level of plasma viral RNA as detected using PCR correlates with the severity of COVID-19. Authors propose that therapies that prevent or reduce viremia may improve outcome for COVID-19 patients.

THE EMERGING SARS-COV-2 PAPAIN-LIKE PROTEASE: ITS RELATIONSHIP WITH RECENT CORONAVIRUS EPIDEMICS

Kandeel M, Kitade Y, Fayez M, Venugopala KN, Ibrahim A.. J Med Virol. 2020 Sep 9. doi: 10.1002/jmv.26497. Online ahead of print.
Level of Evidence: Other - Mechanism-based reasoning

BLUF

Veterinary researchers based in Saudi Arabia and Egypt used molecular modeling tools to compare papain-like protease (PLpro), an enzyme involved in polyprotein processing, among SARS-CoV-2, SARS-CoV, and MERS-CoV. SARS-CoV-2 was far more similar to SARS-CoV than MERS-CoV in regards to PLpro sequencing, PLpro structure alignment, and deubiquitination activity. These findings suggest SARS-CoV-2 is more phylogenetically related to SARS-CoV than MERS-CoV, which contributes to the current understanding of the viral pathogenicity, modulation of immunity, and viral processing.

ABSTRACT

BACKGROUND: The papain-like protease (PLpro) is an important enzyme for coronavirus polyprotein processing, as well as for virus-host immune suppression. Previous studies reveal that a molecular analysis of PLpro indicates the catalytic activity of viral PLpro and its interactions with ubiquitin. METHODS: By using sequence comparisons, molecular models and protein-protein interaction maps, PLpro was compared in the three recorded fatal CoV epidemics, which involved SARS-CoV-2, SARS-CoV and MERS-CoV. RESULTS: The pairwise sequence comparison of SARS-CoV-2 PLpro indicated similarity percentages of 82.59% and 30.06% with SARS-CoV PLpro and MERS-CoV PLpro , respectively. In comparison with SARS-CoV PLpro , in SARS-CoV-2, the PLpro had a conserved catalytic triad of C111, H278 and D293, with a slightly lower number of polar interface residues and of hydrogen bonds, a higher number of buried interface sizes and a lower number of residues that interact with ubiquitin and PLpro . These features might contribute to a similar or slightly lower level of deubiquitinating activity in SARS-CoV-2 PLpro . It was, however, a much higher level compared to MERS-CoV, which contained amino acid mutations and a low number of polar interfaces. CONCLUSION: SARS-CoV-2 PLpro and SARS-CoV PLpro showed almost the same catalytic site profiles, interface area compositions and polarities, suggesting a general similarity in deubiquitination activity. Compared with MERS-CoV, SARS-CoV-2 had a higher potential for binding interactions with ubiquitin. These estimated parameters contribute to the knowledge gap in understanding how the new virus interacts with the immune system. This article is protected by copyright. All rights reserved.

TRANSMISSION & PREVENTION

DEVELOPMENTS IN TRANSMISSION & PREVENTION

TRAINED INNATE IMMUNITY, EPIGENETICS, AND COVID-19

Mantovani A, Netea MG.. N Engl J Med. 2020 Sep 10;383(11):1078-1080. doi: 10.1056/NEJMcibr2011679.
Level of Evidence: Other - Expert Opinion

BLUF

An expert opinion piece discusses how the innate immune system can be trained/epigenetically remodeled via exposure of myeloid progenitor cells to microbial products such as the BCG vaccine (Figure 1) by involving various regulatory mechanisms including chromatin conformational changes, noncoding RNA transcription, DNA methylation, exposure of enhancers, and promoters of host-defense genes. The authors note that because the BCG vaccine has displayed an ability to train the innate immune system, several trials (two of which are being conducted by one of the authors of this paper) are currently investigating if it possesses the ability to prevent or lessen the effects of COVID-19.

FIGURES

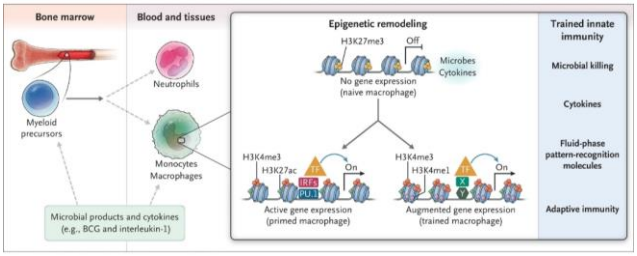


Figure 1: Cellular and Molecular mechanisms underlying Trained Innate Immunity.

PREVENTION IN THE COMMUNITY

COVID-19 PREVALENCE AMONG PEOPLE EXPERIENCING HOMELESSNESS AND HOMELESSNESS SERVICE STAFF DURING EARLY COMMUNITY TRANSMISSION IN ATLANTA, GEORGIA, APRIL-MAY 2020

Yoon JC, Montgomery MP, Buff AM, Boyd AT, Jamison C, Hernandez A, Schmit K, Shah S, Ajoku S, Holland DP, Prieto J, Smith S, Swancutt MA, Turner K, Andrews T, Flowers K, Wells A, Marchman C, Laney E, Bixler D, Cavanaugh S, Flowers N, Gaffga N, Ko JY, Paulin HN, Weng MK, Mosites E, Morris SB.. Clin Infect Dis. 2020 Sep 8:ciaa1340. doi: 10.1093/cid/ciaa1340. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

Investigators affiliated with Emory University School of Medicine and the CDC, in conjunction with 24 homeless shelters and 9 unsheltered outreach events, administered facility-wide SARS-CoV-2 testing for 2,326 people experiencing homelessness (PEH; 72% living sheltered, 27.3% unsheltered) and 549 homelessness service staff in Atlanta, Georgia from April 7 to May 6, 2020. Results revealed positive SARS-CoV-2 in 2.1% of PEH living in shelters, 0.5% of PEH living without shelter, and 1.3% of the service staff, leading to 1.6% total of participants testing positive (46/2,857; Table 1). These results are relatively low compared with other PEH in large, urban settings, suggesting an early view into the guidance and best practices for congregate and high-risk settings to prevent COVID-19 transmission.

SUMMARY

The purpose of this study and faculty-wide SARS-CoV-2 testing for PEH and homelessness service staff was to:
1."Determine SARS-CoV-2 prevalence among clients living sheltered and unsheltered and homelessness service staff through viral testing.
2. Describe the clinical status of PEH and staff at the time of testing.

3. Evaluate the sensitivity and specificity of symptom screening for COVID-19 detection.
4. Review shelter infection prevention and control (IPC) policies and provide recommendations to mitigate SARS-CoV-2 transmission."

ABSTRACT

BACKGROUND: In response to reported COVID-19 outbreaks among people experiencing homelessness (PEH) in other U.S. cities, we conducted multiple, proactive, facility-wide testing events for PEH living sheltered and unsheltered and homelessness service staff in Atlanta, Georgia. We describe SARS-CoV-2 prevalence and associated symptoms and review shelter infection prevention and control (IPC) policies. METHODS: PEH and staff were tested for SARS-CoV-2 by reverse transcription polymerase chain reaction (RT-PCR) during April 7-May 6, 2020. A subset of PEH and staff was screened for symptoms. Shelter assessments were conducted concurrently at a convenience sample of shelters using a standardized questionnaire. RESULTS: Overall, 2,875 individuals at 24 shelters and nine unsheltered outreach events underwent SARS-CoV-2 testing and 2,860 (99.5%) had conclusive test results. SARS-CoV-2 prevalence was 2.1% (36/1,684) among PEH living sheltered, 0.5% (3/628) among PEH living unsheltered, and 1.3% (7/548) among staff. Reporting fever, cough, or shortness of breath in the last week during symptom screening was 14% sensitive and 89% specific for identifying COVID-19 cases compared with RT-PCR. Prevalence by shelter ranged 0%-27.6%. Repeat testing 3-4 weeks later at four shelters documented decreased SARS-CoV-2 prevalence (0%-3.9%). Nine of 24 shelters completed shelter assessments and implemented IPC measures as part of the COVID-19 response. CONCLUSIONS: PEH living in shelters experienced higher SARS-CoV-2 prevalence compared with PEH living unsheltered. Facility-wide testing in congregate settings allowed for identification and isolation of COVID-19 cases and is an important strategy to interrupt SARS-CoV-2 transmission.

FIGURES

	Total	Sheltered Clients	Unsheltered Clients	Homelessness Service Staff
	N=2,875	n=1,690	n=636	n=549
	n (%)	n (%)	n (%)	n (%)
SARS-CoV-2 Prevalence (missing=15)	46 (1.6)	36 (2.1)[a]	3 (0.5)[a]	7 (1.3)[a]
Characteristic				
Age				
Mean age, years	46.6	44.1	51.2	49.1
Median age, years	50.7	48.5	54.3	51.5
<18 years	134 (4.7)	130 (7.7)	3 (0.5)	0 (0.0)
18–34	534 (18.6)	364 (21.5)	79 (12.4)	92 (16.8)
35–49	701 (24.4)	386 (22.8)	154 (24.2)	161 (29.3)
50–64	1,306 (45.4)	722 (42.7)	334 (52.5)	250 (45.5)
≥65	200 (7.0)	88 (5.2)	66 (10.4)	46 (8.4)
Sex (missing=2)				
Male	1,967 (68.5)	1,123 (66.5)	541 (85.1)	303 (55.2)
Female	834 (29.0)	503 (29.8)	89 (14.0)	242 (44.1)
Other	72 (2.5)	62 (3.7)	6 (0.9)	4 (0.7)
Race and Ethnicity (missing=36)				
Black, non-Hispanic	2,169 (76.4)	1,299 (78.3)	497 (78.6)	373 (68.2)
White, non-Hispanic	466 (16.4)	250 (15.1)	67 (10.6)	149 (27.2)
Hispanic	101 (3.6)	51 (3.1)	37 (5.9)	13 (2.4)
Other[b]	103 (3.6)	60 (3.6)	31 (4.9)	12 (2.2)

[a]chi-square test P=0.01

[b]Includes American Indian/Alaskan Native, Asian, Native Hawaiian/Pacific Islander, and other. Not reported individually due to small size.

Table 1. SARS-CoV-2 prevalence and demographic characteristics of 2,875 sheltered and unsheltered clients and homelessness service staff tested in Atlanta, Georgia, United States, April–May 2020

CRITICAL CARE

EFFECT OF DEXAMETHASONE ON DAYS ALIVE AND VENTILATOR-FREE IN PATIENTS WITH MODERATE OR SEVERE ACUTE RESPIRATORY DISTRESS SYNDROME AND COVID-19: THE CODEX RANDOMIZED CLINICAL TRIAL

Tomazini BM, Maia IS, Cavalcanti AB, Berwanger O, Rosa RG, Veiga VC, Avezum A, Lopes RD, Bueno FR, Silva MVAO, Baldassare FP, Costa ELV, Moura RAB, Honorato MO, Costa AN, Damiani LP, Lisboa T, Kawano-Dourado L, Zampieri FG, Olivato GB, Righy C, Amendola CP, Roepke RML, Freitas DHM, Forte DN, Freitas FGR, Fernandes CCF, Melro LMG, Junior GFS, Morais DC, Zung S, Machado FR, Azevedo LCP; COALITION COVID-19 Brazil III Investigators.. JAMA. 2020 Sep 2. doi: 10.1001/jama.2020.17021. Online ahead of print.
Level of Evidence: 2 - Randomized trial or observational study with dramatic effect

BLUF

A multidisciplinary coalition of Brazilian investigators conducted a multi-center, randomized open-label clinical trial (CoDEX) exploring the clinical impact of dexamethasone on COVID-19 patients in 41 ICUs in Brazil (n=299) between April 17 and June 23, 2020. Adult patients presenting with moderate to severe ARDS who received dexamethasone (n=151) spent fewer days on mechanical ventilation within a 28 day period compared to those receiving standard care (mean 6.6 days [95% CI: 5.0-8.2] vs 4.0 days [95% CI: 2.9-5.4], difference 2.26 days [p=0.04]) (Figure 2, Table 2)). This adds to a growing body of research suggesting dexamethasone improves outcomes in moderate to severe COVID-19.

SUMMARY

These authors compared multiple outcomes between a control group receiving standard care (n=148) and standard care plus 10 to 20 mg of dexamethasone IV daily over the course of 5 days or until ICU discharge (n=151). They found an increase in ventilator free days for adult patients presenting with moderate to severe ARDS on mechanical ventilators and diagnosed or highly likelihood of COVID-19 (n=299) in the experimental group (mean 6.6 days, 95% CI, 5.0-8.2) compared to standard care alone (4.0 days, 95% CI, 2.9-5.4). This difference of 2.26 ventilator-free days during the 28 day follow up period was statistically significant (p=0.04)(Figure 2). There was no significant differences in all-cause mortality, incidence of secondary infections, insulin requirement for glucose control, and serious adverse events (Table 2), suggesting that secondary benefits were less prevalent than length of time spent on mechanical ventilators.

ABSTRACT

Importance: Acute respiratory distress syndrome (ARDS) due to coronavirus disease 2019 (COVID-19) is associated with substantial mortality and use of health care resources. Dexamethasone use might attenuate lung injury in these patients. Objective: To determine whether intravenous dexamethasone increases the number of ventilator-free days among patients with COVID-19-associated ARDS. Design, Setting, and Participants: Multicenter, randomized, open-label, clinical trial conducted in 41 intensive care units (ICUs) in Brazil. Patients with COVID-19 and moderate to severe ARDS, according to the Berlin definition, were enrolled from April 17 to June 23, 2020. Final follow-up was completed on July 21, 2020. The trial was stopped early following publication of a related study before reaching the planned sample size of 350 patients. Interventions: Twenty mg of dexamethasone intravenously daily for 5 days, 10 mg of dexamethasone daily for 5 days or until ICU discharge, plus standard care (n =151) or standard care alone (n = 148). Main Outcomes and Measures: The primary outcome was ventilator-free days during the first 28 days, defined as being alive and free from mechanical ventilation. Secondary outcomes were all-cause mortality at 28 days, clinical status of patients at day 15 using a 6-point ordinal scale (ranging from 1, not hospitalized to 6, death), ICU-free days during the first 28 days, mechanical ventilation duration at 28 days, and Sequential Organ Failure Assessment (SOFA) scores (range, 0-24, with higher scores indicating greater organ dysfunction) at 48 hours, 72 hours, and 7 days. Results: A total of 299 patients (mean [SD] age, 61 [14] years; 37% women) were enrolled and all completed follow-up. Patients randomized to the dexamethasone group had a mean 6.6 ventilator-free days (95% CI, 5.0-8.2) during the first 28 days vs 4.0 ventilator-free days (95% CI, 2.9-5.4) in the standard care group (difference, 2.26; 95% CI, 0.2-4.38; P = .04). At 7 days, patients in the dexamethasone group had a mean SOFA score of 6.1 (95% CI, 5.5-6.7) vs 7.5 (95% CI, 6.9-8.1) in the standard care group (difference, -1.16; 95% CI, -1.94 to -0.38; P = .004). There was no significant difference in

the prespecified secondary outcomes of all-cause mortality at 28 days, ICU-free days during the first 28 days, mechanical ventilation duration at 28 days, or the 6-point ordinal scale at 15 days. Thirty-three patients (21.9%) in the dexamethasone group vs 43 (29.1%) in the standard care group experienced secondary infections, 47 (31.1%) vs 42 (28.3%) needed insulin for glucose control, and 5 (3.3%) vs 9 (6.1%) experienced other serious adverse events. Conclusions and Relevance: Among patients with COVID-19 and moderate or severe ARDS, use of intravenous dexamethasone plus standard care compared with standard care alone resulted in a statistically significant increase in the number of ventilator-free days (days alive and free of mechanical ventilation) over 28 days. Trial Registration: ClinicalTrials.gov Identifier: NCT04327401.

FIGURES

Table 2. Study Outcomes

Outcomes	Mean (95% CI)		Effect statistic	Between-group effect			
				Adjusted[a]		Unadjusted	
	Dexamethasone (n = 151)	Standard care (n = 148)		Estimate (95% CI)	*P* value	Estimate (95% CI)	*P* value
Primary outcome							
Days alive and ventilator free at 28 d							
Mean (95% CI)	6.6 (5.0 to 8.2)	4.0 (2.9 to 5.4)	MD	2.26 (0.2 to 4.38)[b]	.04	2.55 (0.46 to 4.6)	.02
Median (IQR)	0 (0 to 17)	0 (0 to 3)					
Secondary outcomes							
6-Point ordinal scale at day 15, median (IQR)[c]	5 (3 to 6)	5 (5 to 6)	OR	0.66 (0.43 to 1.03)	.07	0.62 (0.41 to 0.94)	.03
28-Day results							
All-cause mortality No. (%)	85 (56.3)	91 (61.5)	HR	0.97 (0.72 to 1.31)	.85	0.86 (0.64 to 1.15)	.31
ICU free, d	2.1 (1.0 to 4.5)	2.0 (0.8 to 4.2)	MD	0.28 (−0.49 to 1.02)	.50	0.14 (−0.92 to 1.27)	.78
MV duration, d	12.5 (11.2 to 13.8)	13.9 (12.7 to 15.1)	MD	−1.54 (−3.24 to 0.12)	.11	−1.46 (−3.10 to 0.57)	.18
SOFA score[d]							
48 h	8.1 (7.6 to 8.6)	8.4 (7.8 to 8.9)	MD	−0.11 (−0.86 to 0.63)	.76	−0.24 (−1 to 0.51)	.53
No. of patients	151	147					
72 h	7.7 (7.2 to 8.3)	8.3 (7.8 to 8.9)	MD	−0.38 (−1.13 to 0.37)	.32	−0.6 (−1.37 to 0.16)	.12
No. of patients	145	144					
7 d	6.1 (5.5 to 6.7)	7.5 (6.9 to 8.1)	MD	−1.16 (−1.94 to −0.38)	.004	−1.38 (−2.21 to −0.55)	.001
No. of patients	127	120					

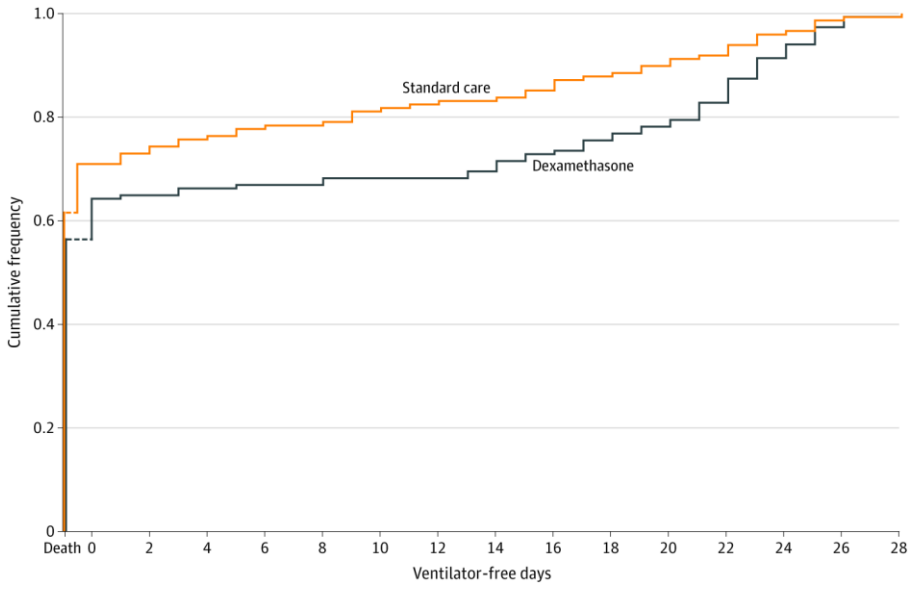
Abbreviations: ICU, intensive care unit; HR, hazard ratio; IQR interquartile range, MD, mean difference; MV, mechanical ventilation; OR, odds ratio; SOFA, Sequential Organ Failure Assessment.

[a] All models are adjusted for age and baseline at Pao_2:FIo_2 ratio with random intercept by site.

[b] Average marginal effect from generalized additive model with 0-inflated beta-binomial distribution adjusted for age and baseline Pao_2:FIo_2 ratio with random intercept by site. For the primary model coefficients see eTable 5 in Supplement 2.

[c] See the Methods section for the definitions of the 6-point ordinal scale. The distribution of values among the categories in the dexamethasone and control groups was 6 (35.8% vs 43.9%), 5 (31.8% vs 36.5%), 4 (4.6% vs 2.7%), 3 (16.6% vs 11.5%), 2 (0% vs 0%), and 1 (11.3% vs 5.4%).

[d] Measured in 6 organ systems (cardiovascular, hematologic, gastrointestinal, renal, pulmonary and neurologic), with each organ scored from 0 to 4, resulting in an aggregated score that ranges from 0 to 24, with higher scores indicating greater dysfunction. An initial SOFA score up to 9 predicts a mortality risk of less than 33%. An unchanged or increasing score in the first 48 hours predicts a mortality rate of 60% when the initial score is 8 to 11. Missing values on individual SOFA components were imputed as normal (eMethods in Supplement 2).



CARDIOLOGY

SURFACE ELECTROCARDIOGRAPHIC CHARACTERISTICS IN CORONAVIRUS DISEASE 2019: REPOLARIZATION ABNORMALITIES ASSOCIATED WITH CARDIAC INVOLVEMENT

Chen L, Feng Y, Tang J, Hu W, Zhao P, Guo X, Huang N, Gu Y, Hu L, Duru F, Xiong C, Chen M.. ESC Heart Fail. 2020 Sep 8. doi: 10.1002/ehf2.12991. Online ahead of print.
Level of Evidence: 4 - Case-series or case-control studies, or poor quality prognostic cohort study

BLUF

A retrospective observational study conducted at Jinyintan Hospital, Wuhan involving 63 hospitalized COVID-19 patients (23 with cardiac injury, 40 without) from Jan 1 - Feb 27, 2020 found that increased volume of abnormal T waves and prolonged QTc are independent predictors of cardiac injury, in addition to T wave changes independently predicting mortality after adjusting for age (Table 3; hazard ratio 3.57). The authors suggest these abnormalities in cardiac function in COVID-19 patients are indicative of poorer clinical outcome (Figure 1).

SUMMARY

This study involved hospitalized COVID-19 patients who have undergone biomarker analysis (high-sensitivity troponin I [hs-TnI], myohemoglobin, and creatinine kinase-myocardial band) and 12 lead ECG.

The authors found the following:

- Patients with cardiac injury tended to be older, with co-morbidities, significantly elevated biomarkers, aspartate transaminases, D-dimer, ferritin, and lactate dehydrogenase.
- A higher mortality rate was reported in patients with cardiac injury (12/23 [52.2%], p=0.001).
- COVID-19 patients with cardiac injury showed abnormal ECG findings (Table 3) such as increased quantity of abnormal T wave leads (p<0.001), severe T wave alterations (p=0.002), and prolonged QTc intervals (p=0.006).
- Logistic regression analysis identified increased abnormal T waves (OR, 2.36, p=0.002) and QTc prolongations (OR 1.31, p=0.027) as independently predicting cardiac injury.
- Spearman tests validated a positive correlation between the number of T-wave changes, QTc interval prolongation, and Cardiac Troponin-I levels (hs-cTnI) with r=0.66, p<0.0001.
- Cox regression model highlighted T wave changes as an independent predictor of mortality when adjusted for age (HR 3.57, P=0.008) (Figures 1, 2)
- In patients with complete recovery of cardiac injury, some individuals exhibited recovery of T wave changes to baseline (Figure 2).

ABSTRACT

AIMS: The coronavirus disease 2019 (COVID-19) has spread rapidly around the globe, causing significant morbidity and mortality. This study aims to describe electrocardiographic (ECG) characteristics of COVID-19 patients and to identify ECG parameters that are associated with cardiac involvement. METHODS AND RESULTS: The study included patients who were hospitalized with COVID-19 diagnosis and had cardiac biomarker assessments and simultaneous 12-lead surface ECGs. Sixty-three hospitalized patients (median 53 [inter-quartile range, 43-65] years, 76.2% male) were enrolled, including patients with (n = 23) and without (n = 40) cardiac injury. Patients with cardiac injury were older, had more pre-existing co-morbidities, and had higher mortality than those without cardiac injury. They also had prolonged QTc intervals and more T wave changes. Logistic regression model identified that the number of abnormal T waves (odds ratio (OR), 2.36 [95% confidence interval (CI), 1.38-4.04], P = 0.002) and QTc interval (OR, 1.31 [95% CI, 1.03-1.66], P = 0.027) were independent indicators for cardiac injury. The combination model of these two parameters along with age could well discriminate cardiac injury (area the under curve 0.881, P < 0.001) by receiver operating characteristic analysis. Cox regression model identified that the presence of T wave changes was an independent predictor of mortality (hazard ratio, 3.57 [1.40, 9.11], P = 0.008) after adjustment for age. CONCLUSIONS: In COVID-19 patients, presence of cardiac injury at admission is associated with poor clinical outcomes.

Repolarization abnormalities on surface ECG such as abnormal T waves and prolonged QTc intervals are more common in patients with cardiac involvement and can help in further risk stratification.

FIGURES

Characteristics	Total (n = 63)	Without cardiac injury (n = 40)	With cardiac injury (n = 23)	P value
Heart rate, b.p.m.	80 (71, 89)	77 (68, 86.5)	85 (77, 101)	0.018
PR interval, ms	150 (139, 165)	155 (139, 164)	147 (139, 166)	0.597
QRS duration, ms	92 (86, 99)	92 (87, 100)	89 (84, 95)	0.155
QT interval, ms	372 (354, 402)	373 (355, 403)	369 (354, 402)	0.911
QTc, ms	432.5 (413, 452)	428 (407.5, 439.5)	452 (423, 479)	0.006
Sinus tachycardia	11 (17.5)	4 (10.0)	7 (30.4)	0.041
Branch bundle block	5 (7.9)	4 (10)	1 (4.3)	0.644
ST segment changes	5 (7.9)	3 (7.5)	2 (8.7)	1.000
Q wave	5 (7.9)	1 (2.5)	4 (17.4)	0.037
Abnormal T waves (≥1 lead)	29 (48.3)	11 (28.9)	18 (81.8)	<0.001
Severity of abnormal T wave[a]				0.002
Prominent T wave	9 (15)	4 (10.5)	5 (22.7)	
Mild TWI	10 (16.7)	4 (10.5)	6 (27.3)	
Isoelectric T wave	10 (16.7)	3 (7.9)	7 (31.8)	
Normal	31 (51.7)	27 (71.1)	4 (18.2)	
No. of abnormal T waves	0 (0, 2)	0 (0, 1)	2 (1, 2)	<0.001

[a]Abnormal T wave was defined as T wave inversion (TWI), isoelectric, or biphasic T wave.

Table 3: Electrocardiographic characteristics of patients with coronavirus disease 2019.

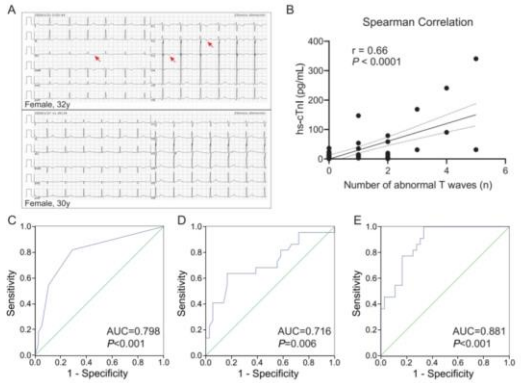


Figure 1: T wave changes associated with cardiac injury among patients with coronavirus disease 2019 (COVID-19). (A) Representative electrocardiogram (ECG) from patients with (upper panel, female, 70 years old, QTc 459 ms) and without (lower panel, 30 years, QTc 423 ms) cardiac injury. (B) Spearman correlation analysis between number of abnormal T waves and serum high-sensitivity troponin I (hs-TnI) concentrations. Receiver operating characteristic (ROC) curve in discriminating cardiac injury by number of abnormal T waves (C), QTc interval (D), and combined model of age, number of abnormal T waves and QTc interval with a sensitivity of 77.3% and specificity of 83.3% (E).

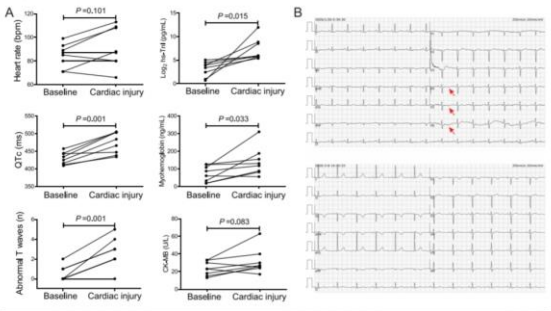


Figure 2: Dynamic changes of electrocardiogram (ECG). (A) The ECG parameters and cardiac biomarker alterations from baseline to the time of cardiac injury (compared by paired Student's t-test). (B) Representative ECG from one patient (male, 65 years old) during cardiac injury (upper panel) and recovery state (lower panel).

PREDICTING HEALTH CARE WORKERS' TOLERANCE OF PERSONAL PROTECTIVE EQUIPMENT: AN OBSERVATIONAL SIMULATION STUDY

Martín-Rodríguez F, Sanz-García A, López-Izquierdo R, Delgado Benito JF, Martín-Conty JL, Castro Villamor MA, Ortega GJ.. Clin Simul Nurs. 2020 Oct;47:65-72. doi: 10.1016/j.ecns.2020.07.005. Epub 2020 Sep 2.
Level of Evidence: Other - Modeling

BLUF

Investigators affiliated with Valladolid University and Hospital de la Princesa in Spain created a risk model for predicting health care workers' tolerance of wearing PPE (C category, 4B/5B/6B type) based on a 30-minute simulation study of 96 volunteers between April 3rd and 28th, 2017 (Table 1). In the simulation study, 48/96 of the participants developed fatigue 20 minutes after simulation completion. The developed model revealed that shorter females with low muscle mass, low bone mass, and moderate/high physical activity were more tolerant to metabolic fatigue when compared to people of different sex, build, or activity level (Table 2, Figure 3). The authors suggest that these findings and risk model may help emergency team members understand the limits of PPE-associated fatigue amongst healthcare workers and, thus, assist in decisions on staffing for critical situations.

ABSTRACT

Background: More recently, due to the coronavirus disease 2019 pandemic, health care workers have to deal with clinical situations wearing personal protective equipment (PPE); however, there is a question of whether everybody will tolerate PPE equally. The main objective of this study was to develop a risk model to predict whether health care workers will tolerate wearing PPE, C category, 4B/5B/6B type, during a 30-minute simulation. Methods: A nonexperimental simulation study was conducted at the Advanced Simulation Center, Faculty of Medicine, Valladolid University (Spain) from April 3rd to 28th, 2017. Health care students and professionals were equipped with PPE and performed a 30-minute simulation. Anthropometric, physiological, and analytical variables and anxiety levels were measured before and after simulation. A scoring model was constructed. Results: Ninety-six volunteers participated in the study. Half the sample presented metabolic fatigue in the 20 minutes after finishing the simulation. The predictive model included female sex, height, muscle and bone mass, and moderate level of physical activity. The validity of the main model using all the variables presented an area under the curve of 0.86 (95% confidence interval: 0.786-0.935), and the validity of the model had an area under the curve of 0.725 (95% confidence interval: 0.559-0.89). Conclusions: Decision-making in biohazard incidents is a challenge for emergency team leaders. Knowledge of health care workers' physiological tolerance of PPE could improve their performance.

FIGURES

Table 1 Characteristics of the Study Population

Variable*	Total (N = 96)	No Fatigue (n = 48)	Fatigue (n = 48)	Odds Ratio (95% CI)	*p*-value
Age (years)	26 (22–41)	28 (23–40)	24 (22–41)	0.99 (0.95–1.03)	0.773
Sex					
Male	40 (41.7)	14 (29.2)	26 (54.2)		
Female	56 (58.3)	34 (70.8)	22 (45.8)	0.34 (0.15–0.80)	**0.014**
Worker/student					
Students	49 (51.0)	23 (47.9)	26 (54.2)		
Workers	47 (49.0)	25 (52.1)	22 (45.8)	0.78 (0.34–1.73)	0.540
Training in biological risk					
None	43 (44.8)	23 (47.9)	20 (41.7)		
Basic	20 (20.8)	8 (16.7)	12 (25.0)	0.92 (0.37–2.29)	0.864
Advanced	33 (34.3)	17 (35.4)	16 (33.3)	1.59 (0.51–4.91)	0.417
Anthropometric study					
Height (cm)	168 (162–173)	165 (161–172)	170 (164–178)	1.05 (1.00–1.10)	**0.037**
Weight (kg)	68 (58–79)	65 (57–74)	69 (61–81)	1.02 (0.99–1.05)	0.059
Fat (%)	21.7 (16.3–27.7)	22.2 (17.9–27.7)	20.7 (15.2–27.8)	0.98 (0.94–1.03)	0.656
Muscle mass (%)	47.0 (42.1–60.8)	44.9 (41.2–59.8)	52.6 (42.9–62.0)	1.04 (1.00–1.08)	**0.039**
Bone mass (%)	2.5 (2.3–3.2)	2.4 (2.2–3.1)	2.7 (2.3–3.2)	2.18 (1.00–4.74)	**0.048**
Total water (%)	57.3 (53.3–61.1)	57.0 (53.4–60.7)	57.3 (53.2–61.6)	0.99 (0.93–1.06)	0.967
BMI (kg/m^2)	23.9 (21.4–26.7)	23.2 (20.9–26.1)	23.9 (21.9–27.0)	1.05 (0.95–1.17)	0.260
IPAQ					
Low	49 (51.0)	16 (33.3)	33 (68.8)		
Moderate	30 (31.3)	18 (37.5)	12 (25.0)	9.62 (2.41–38.35)	**0.001**
High	17 (17.7)	14 (29.2)	3 (6.3)	3.11 (0.73–13.19)	0.124
BAI (points)	4 (2–7)	3 (2–7)	4 (2–8)	1.01 (0.91–1.11)	0.823
Basal vital signs					
Heart rate (bpm)	68 (62–75)	66 (60–71)	70 (64–76)	1.01 (0.97–1.06)	0.460
SBP (mmHg)	130 (120–138)	129 (121–136)	132 (119–139)	1.01 (0.98–1.04)	0.334
DBP (mmHg)	80 (73–87)	79 (73–86)	84 (74–90)	1.04 (0.99–1.08)	0.060
RR (bpm)	17 (15–18)	17 (15–18)	17 (15–18)	1.03 (0.80–1.33)	0.797
Temperature (°C)	36.7 (36.1–37.1)	36.7 (36.2–37.0)	36.7 (36.4–37.1)	1.20 (0.55–2.62)	0.635
HB (mg/dL)	13.7 (12.6–14.8)	13.5 (12.6–14.6)	14.2 (12.6–15.0)	1.15 (0.87–1.51)	0.319
Perfusion index (%)	2.0 (1.1–4.8)	1.9 (1.1–4.9)	2.2 (1.1–4.7)	1.01 (0.88–1.16)	0.849
Saturation (%)	98 (97–99)	98 (97–100)	98 (97–99)	1.09 (0.82–1.44)	0.524
CG (mg/dL)	106 (97–116)	107 (96–114)	106 (97–120)	1.01 (0.98–1.03)	0.361
CL (mmol/L)	2.1 (1.4–2.9)	2.0 (1.5–2.5)	2.2 (1.3–3.3)	1.18 (0.89–1.57)	0.236
Final vital signs					
Heart rate (bpm)	91 (83–101)	88 (81–94)	97 (85–108)	1.06 (1.02–1.11)	**0.001**
CL (mmol/L)	3.2 (2.3–4.5)	2.6 (1.7–3.1)	4.5 (3.4–5.3)	4.19 (2.30–7.64)	**<0.001**

*Values expressed as the total number (fraction) and medians (25 percentile–75 percentile) as appropriate. Statistical significance values are given in bold.
Note. CI = confidence interval; BMI = body mass index; IPAQ = International Physical Activity Questionnaire; BAI = Beck Anxiety Inventory; SBP = systolic blood pressure; DBP = diastolic blood pressure; RR = respiratory rate; HB = hemoglobin; CG = capillary glycemia; CL = capillary lactate.

Table 2 Variables in the Scoring Model

Variable	Estimate	Scale Value	Std. Error	Z Value	Odds Ratio (95% CI)	*p*-value
Sex						
Female	−2.02	−2	0.92	−2.18	0.13 (0.01−0.71)	0.029
IPAQ						
High	3.2	3	1.12	2.85	24.5 (3.43−309.5)	0.004

Note. Std = standard; CI = confidence interval; IPAQ = International Physical Activity Questionnaire.

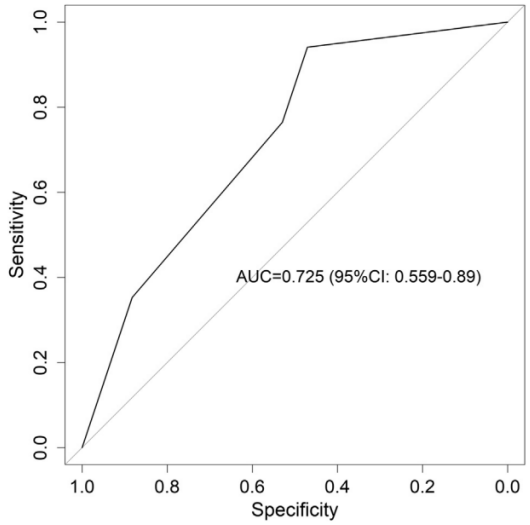


Figure 3 Receiver operating characteristic (ROC) by fatigue for the scoring model. The bold line shows the value of the ROC curve. The values in the graph represent the area under the curve (AUC) and its 95% confidence interval.

MORTALITY OF COVID-19 WITH PREADMISSION METFORMIN USE IN PATIENTS WITH DIABETES: A META-ANALYSIS

Kow CS, Hasan SS.. J Med Virol. 2020 Sep 9. doi: 10.1002/jmv.26498. Online ahead of print.
Level of Evidence: 2 - Systematic review of non-randomized trials

BLUF

Investigators affiliated with International Medical University, Malaysia and the University of Huddersfield, UK performed a systemic review and meta-analysis including 5 studies published before August 8, 2020 with a total of 8,121 hospitalized patients with COVID-19. Their analysis showed significantly lower odds for mortality with metformin use in diabetic, COVID-19 cases (Figure 1; pooled analysis OR: 0.62) than cases without use of metformin. The authors hypothesize that this finding may be due to anti-inflammatory mechanisms of metformin dampening the cytokine storm in COVID-19. However, as this finding was only seen in patients with pre-existing diabetes, further research is needed to provide evidence of the morbidity and mortality benefit in repurposing metformin for COVID-19 patients without concomitant diabetes.

ABSTRACT

The novel coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is currently the biggest threat to the public health and an enormous challenge to the healthcare systems across the world. This article is protected by copyright. All rights reserved.

FIGURES

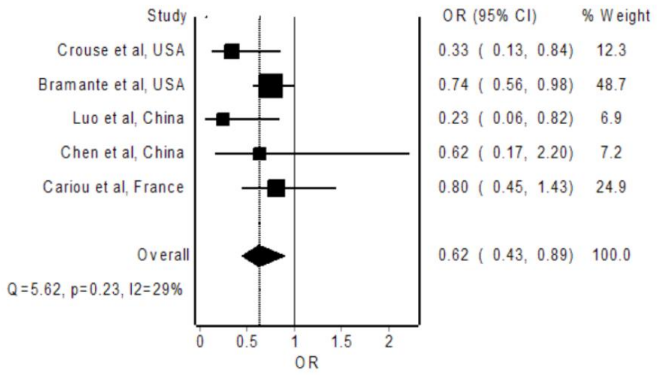


Figure 1: Pooled risk of mortality in hospitalized COVID-19 patients with diabetes with or without pre-admission metformin. (Heterogeneity: I2=29%; p = 0.23).

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