The Daily COVID-19 Literature Surveillance Summary

August 12, 2020























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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?		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)	of cross sectional studies with consistently applied reference	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)	of randomized trials or <i>n</i> -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)		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)		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.

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

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

^{*} 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

A group sponsored by the Canadian Institutes of Health Research discusses that moving forward, the World Health Organization's 2005 International Health Regulations should be utilized to advise international travel restrictions during the next phases of the 2020 COVID-19 pandemic and may act as an opportunity to reform the WHO's role and regain some lost credibility due to their management of the pandemic.

Epidemiology

- A comparison of outcomes among COVID-19 patients with (n=21) and without (n=236) chronic hepatitis B virus (HBV) infection found that a similar proportion of patients in both groups progressed to severe disease and exhibited at least one transaminase elevation, suggesting that chronic HBV infection does not appear to affect COVID-19 outcomes.
- A systematic review and meta-analysis including 5829 COVID-19 pediatric patients found that in general, nonspecific symptoms such as fever and cough were very common in these patients as were normal white blood cell counts. Additionally, among children younger than 1 year, there was a relatively high incidence of vomiting (33%) as well as critical illness (14%).

Understanding the Pathology

A genomic analysis using samples from 18 COVID-19 patients with no comorbidities (10 mild, 8 severe) found genome <u>deletions near the Spike S1 and S2 cleavage sites</u> in all of the mild cases and half of the severe cases. The authors propose that these deletions may result in free S1 protein which could compete with viral particles or act as a decoy to weaken the disease and modulate the virus's virulence.

Management

Seven critically ill patients diagnosed with COVID-19 underwent successful treatment consisting of early noninvasiveinvasive sequential ventilation, prone positioning, and pharmacotherapy consisting of antivirals, anti-inflammatory drugs, immune enhancing medications, and complication prophylaxis agents. All 7 patients were extubated following a median ICU stay of 12.9 days and discharged home, suggesting that this protocol may contribute to successful outcomes in critically ill patients with COVID-19.

Adjusting Practice During COVID-19

The Irish College of General Practitioners discuss a remote care model they developed to facilitate patient access to opioid agonist treatment in Ireland during the pandemic and enable continued care for this vulnerable population while mitigating exposure and transmission of the virus.

R&D: Diagnosis & Treatments

A case control study at Johns Hopkins evaluated the clinical validity of serum antibodies to SARS-CoV-2 in 11,066 patients by using IgG/IgA assays. 60 patients tested positive for COVID-19 and shortly after infection developed IgG that was sustained for up to 58 days. Furthermore, for every 2-fold increase in IgG, there was a 62% increase in the predicted odds of developing acute respiratory distress syndrome.

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CLIMATE

GLOBAL

THE INTERNATIONAL HEALTH REGULATIONS (2005) AND THE RE-ESTABLISHMENT OF INTERNATIONAL TRAVEL AMIDST THE COVID-19 **PANDEMIC**

von Tigerstrom BJ, Halabi SF, Wilson KR.. J Travel Med. 2020 Aug 4:taaa127. doi: 10.1093/jtm/taaa127. Online ahead of print. Level of Evidence: Other - Opinion

BLUF

An expert opinion conducted in Canada sponsored by the Canadian Institutes of Health Research discussed that moving forward, the World Health Organization's (WHO) 2005 International Health Regulations (IHR), further formal recommendations, and informal guiding measures should be utilized to advise international travel restrictions during the next phases of the 2020 COVID-19 pandemic. The authors suggest that this is an opportunity to reform the WHO's role as it has lost some credibility in the wake of failing to provide guidelines early in the pandemic and having guidelines widely ignored thereafter.

SUMMARY

Examples of suggested possible measures include:

- -Requiring guarantine for travelers returning to the country
- -Restricting travel to certain countries that are high risk or fall outside a travel bubble
- -Creating a harmonized, unified system between countries to share COVID information and create travel guidelines
- -Continuing to make recommendations on an ongoing basis
- -WHO issuing formal recommendations for traveling

ABSTRACT

As countries modify or lift travel restrictions implemented in response to the COVID-19 pandemic, some variation in approaches is to be expected, but harmonization is important to re-establishing international travel. Despite challenges, the International Health Regulations (2005) and WHO recommendations can provide a balance of consistency and flexibility.

DISPARITIES

GENDER DIFFERENCES IN THE BATTLE AGAINST COVID-19: IMPACT OF GENETICS, COMORBIDITIES, INFLAMMATION AND LIFESTYLE ON DIFFERENCES IN OUTCOMES

Stoian AP, Toth PP, Kempler P, Rizzo M.. Int J Clin Pract. 2020 Aug 8:e13666. doi: 10.1111/ijcp.13666. Online ahead of print. Level of Evidence: Other - Review / Literature Review

BLUF

Authors from Romania, USA, Italy, and Hungary present a literature review with consistent evidence of men having higher COVID-19 infection and mortality rates than women. They suggest that superior hygiene measures, low smoking rates, heightened protective immune responses due to X-linked genetic factors, and estrogen in women make them less vulnerable to severe infection than men, indicating male gender may have more negative prognosis in disease outcome.

SUMMARY

Gender differences in the severity of COVID-19 based on hygiene, lifestyle factors (i.e. smoking), immune responses based on genetics and hormones are discussed below.

- Gender: Disparity studies conducted in China highlight men having higher mortality rate than women (2.8% vs 1.7%), and case fatality rates were 1.7-2.6 times higher among men than women in Italy.
- Hygiene: Women tend to practice hygienic measures such as hand-washing more frequently than men, predisposing them to

lesser infection rates.

- Smoking/Comorbidities: More men have smoking habits (50% vs 9%) and are active smokers (35% vs 22%) than women. Obesity, diabetes, and cardiovascular diseases are generally higher in men and lead to more severe disease.
- Genetics: As the genes involved in immunity localize to X-chromosomes, and women have XX genetic makeup, they tend to mount heightened protective immune responses against infections than men.
- Hormones: It is postulated that estrogen activates immune cells (macrophages, dendritic cells, natural-killer cells) leading to immunity against infections. Testosterone, generally higher in men, produces more cytokines, leading to cytokine storm syndrome in COVID-19 supporting the evidence that men have more severe infection than women.

ABSTRACT

It has been over six months now since the entire globe was struck by the new Coronavirus Disease 2019 (COVID-19; aka severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]), which has affected 215 nations. The medical and scientific communities continue to search for and study potential treatments for COVID-19 as well as an effective vaccine. As of 21 June 2020, 11.4 million cases have been confirmed worldwide, with approximately 530,000 deaths. A large number of scientific papers have been produced, hundreds of thousands of patients have been hospitalized and studied, several treatments and vaccines are being tested in randomized clinical trials, social distancing regulations have been implemented, with most of the planet in partial or full lockdown, and we have yet to control this pandemic.

EPIDEMIOLOGY

SYMPTOMS AND CLINICAL PRESENTATION

ADULTS

LONGITUDINAL CHANGES OF LIVER FUNCTION AND HEPATITIS B REACTIVATION IN COVID-19 PATIENTS WITH PRE-EXISTING CHRONIC HBV **INFECTION**

Liu J, Wang T, Cai Q, Sun L, Huang D, Zhou G, He Q, Wang FS, Liu L, Chen J.. Hepatol Res. 2020 Aug 6. doi: 10.1111/hepr.13553. Online ahead of print. Level of Evidence: 3 - Local non-random sample

BLUF

Chinese hepatologists conducted a retrospective cohort study to compare outcomes of adult patients with (n=21) and without (n=236) chronic hepatitis B virus (HBV) infection who were hospitalized with COVID-19 at the Third People's Hospital of Shenzhen from January 1 to March 1, 2020. They found a similar proportion of patients in both groups who progressed to severe disease (30% vs. 31.4%, p=0.97; Figure 1) and had at least one transaminase elevation (Figure 2), while 3 patients had HBV reactivation (Figure 4). The authors suggest HBV infection does not appear to affect COVID-19 outcomes, but all COVID-19 patients should have close liver function monitoring.

ABSTRACT

AIM: With pandemic of COVID-19 currently and high endemic of chronic HBV infection worldwide, it is quite urgent to investigate liver function changes of COVID-19 patients with chronic HBV infection, and how SARS-CoV-2 infection in turn affects the course of chronic HBV infection. METHOD: We conducted a retrospective study based on 347 COVID-19 patients (21 vs. 326 with vs. without chronic HBV infection). With the PSM method, we yielded 20 and 51 matched patients for HBV group and non-HBV group, respectively. RESULTS: At the end of follow-up, all these 71 patients achieved SARS-CoV-2 clearance (p=0.1). During the follow-up, 30% vs. 31.4% in HBV group vs. non-HBV group progressed to severe COVID-19 (p=0.97). After PSM, the longitudinal changes of median values for liver biochemistries were no significant difference between two groups. In HBV group vs. non-HBV-group, 35% (7/20) vs. 37.25% (19/51) (p = 0.86) had abnormal ALT at least once during hospitalization, while 30% (6/20) vs. 31.37% (16/51) for abnormal AST (p = 0.91), 40% (8/20) vs. 37.25% (19/51) for abnormal GGT (p = 0.83), and 45% (9/20) vs. 39.22% (20/51) for abnormal TBIL (p = 0.91). Moreover, 3 patients in HBV group had hepatitis B reactivation. CONCLUSIONS: Liver dysfunction presented in COVID-19 patients with/without chronic HBV. Moreover, those COVID-19 patients coinfected with chronic HBV could had a risk of hepatitis B reactivation. It is necessary to monitor liver function of COVID-19 patients, as well as HBV DNA levels for those coinfected with HBV during the whole disease course.

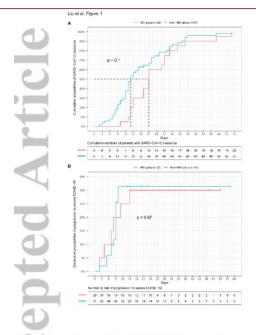


Figure 1. Cumulative probabilities of SARS-CoV-2 clearance and progression to severe status for COVID-19 patients with vs. without HBV: cumulative probabilities of SARS-CoV-2 clearance (A); cumulative probabilities of progression to severe COVID-19 (B).

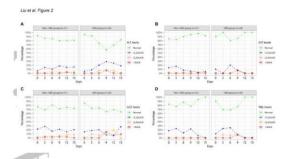


Figure 2. The proportion of patients with abnormal values of liver biochemistries (ALT, AST, GGT, TBIL) over time in HBV group vs. non-HBV group: ALT levels (A); AST levels (B); GGT levels (C); TBIL levels (D), ALT, admin aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; TBIL, total bilirubin.

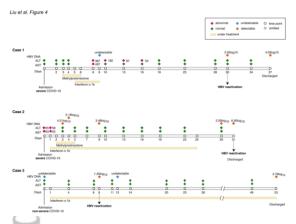


Figure 4. HBV DNA viral load and liver biochemistries, and treatment information of three hepatitis B reactivation cases. ALT, alanine aminotransferase; AST, aspartate aminotransferase.

PEDIATRICS

A SYSTEMATIC REVIEW AND META-ANALYSIS OF CHILDREN WITH **CORONAVIRUS DISEASE 2019 (COVID-19)**

Cui X, Zhao Z, Zhang T, Guo W, Guo W, Zheng J, Zhang J, Dong C, Na R, Zheng L, Li W, Liu Z, Ma J, Wang J, He S, Xu Y, Si P, Shen Y, Cai C., I Med Virol. 2020 Aug 6. doi: 10.1002/jmv.26398. Online ahead of print. Level of Evidence: 2 - Systematic review of surveys that allow matching to local circumstances

BLUF

Authors affiliated with the Children's Hospital of Tianjin and other institutions in China conducted a systematic review and meta-analysis (n=48) including a total of 5829 COVID-19 infected pediatric patients to report on clinical manifestations of COVID-19 in this population (Figure 4). Based on the findings (summarized below), the authors suggest that pediatric COVID-19 manifestations may differ from the typical COVID-19 symptoms seen in adults, calling for the development of special diagnostic and therapeutic criteria for pediatric patients.

SUMMARY

Several findings include, but are not limited to, the following:

- Nonspecific symptoms, such as fever (51%; 95% CI: 45 to 57%; I^2: 78.9%) and cough (41%; 95% CI: 35 to 47%; I^2:81.0%), were common presenting complaints among these pediatric COVID-19 patients.
- Normal white blood cell (69%; 95% CI: 64 to 75%; I^2: 58.5%) and rare lymphopenia (16%; 95% CI: 11 to 21%; I^2: 76.9%) were the typical laboratory findings among this population (Figure 5)
- Among the children younger than 1-year-old, there was a high incidence of vomiting (33%; 95% CI: 18 to 67%; I^2=0.0%) and critical illness (14%; 95% CI: 13 to 34%; I^2: 37.3%; Figure 3).

ABSTRACT

OBJECTIVE: To provide a comprehensive and systematic analysis of demographic characteristics, clinical symptoms, laboratory findings and imaging features of coronavirus disease 2019 (COVID-19) in pediatric patients. METHODS: A metaanalysis was carried out to identify studies on COVID-19 from December 25, 2019 to April 30, 2020. RESULTS: A total of 48 studies with 5829 pediatric patients were included. Children at all ages were at risk for COVID-19. The main illness classification ranged as: 20% (95% CI: 14 to 26%, I2 =91.4%) asymptomatic, 33% (95% CI: 23 to 43%, I2 =95.6%) mild and 51% (95% CI: 42 to 61%, I2 = 93.4%) moderate. The typical clinical manifestations were fever 51% (95% CI: 45 to 57%, I2 =78.9%) and cough 41% (95% CI: 35 to 47%, I2 =81.0%). The common laboratory findings were normal white blood cell 69% (95% CI: 64 to 75%, I2 =58.5%), lymphopenia 16% (95% CI: 11 to 21%, I2 =76.9%) and elevated creatine-kinase MB (CK-MB) 37% (95% CI: 25 to 48%, I2 =59.0%). The frequent imaging features were normal images 41% (95% CI: 30 to 52%, I2 =93.4%) and ground-glass opacity 36% (95% CI: 25 to 47%, I2 =92.9%). Among children under 1-year old, critical cases account for 14% (95% CI: 13 to 34%, I2 = 37.3%) that should be of concern. In addition, vomiting occurred in 33% (95% CI: 18 to 67%, I2 = 0.0%) cases that may also need attention. CONCLUSIONS: Pediatric patients with COVID-19 may experience milder illness with atypical clinical manifestations and rare lymphopenia. High incidence of critical illness and vomiting symptoms reward attention in children under 1-year old. This article is protected by copyright. All rights reserved.

Fig. 5 Summary results of laboratory examination in children with COVID-19.

Laboratory outcomes	No. Reports (n)	No. Patients (n)		Prevalance% (96%CI)	(20) In	Egger's test
Normal white blood cell	39	698	-	-e- 69(64-75)	58.5	0.002
Leukocytosis	38	907	-	10(7-14)	63.1	0.002
Leukopenia	42	978		19(14-25)	80.9	0.000
Lymphopenia	39	795		16(11-21)	76.9	0.090
High PCT	29	709		36(21-61)	97.0	0.056
High CRP	32	651		19(13-26)	79.3	0.009
High LDH	24	301		29(29-39)	69.8	0.984
High ALT	32	686		11(7-16)	38.6	0.422
High AST	28	629	-	18(13-23)	48.6	0.978
High CK	17	109		9(1-17)	33.2	0.054
High CK-MB	23	228	-	37(25-48)	59.0	0.260
High D-dimer	24	194		11(8-14)	0.0	0.347
			0 29 40 60	80		

Fig. 4 Aggregated results of clinical presentation in children with COVID-19.

Clinical Systoms	No. Reports (n)	No. Patients (n)		Prevalance% (95%CI)	(%)	Egger's test
Fever	48	1494	-	- 51(45-57)	78.9	0.675
Cough	45	1435		41(35-47)	81.0	0.144
Sore throat	38	1040		16(7-25)	91.6	0.411
Tachycardia	35	950		12(3-21)	93.9	0.350
Rhinorrhea	36	990		14(8-19)	75.4	0.088
Nasal congestion	33	623		17(6-27)	87.2	0.167
Tachypnea	29	1034		9(4-14)	87.4	0.278
Diarrhea	42	1250	-	8(6-11)	47.0	0.004
Vomiting	42	1238	-	7(5-10)	50.4	0.016
Myalgia or fatigue	42	1253		12(7-17)	77.7	0.405
Hypoxemia	33	623		3(1-4)	0.0	0.007
Chest pain	34	673	-	3(0-5)	0.0	0.356
			0 20 40	60		

Disease Severity	No. Reports (n)	No. Patients (n)		Prevalance (95%CI)	(%)	Egger's test
Asymptomatic*	42	3287		20(14-26)	91.4	0.000
Mild ^b	42	3048		33(23-43)	95.6	0.379
Moderate ^c	40	3046		51(42-61)	93.4	0.217
Severe ^d	41	3775		7(4-11)	90.2	0.128
Critical*	42	3121	•	5(2-9)	87.5	0.008
Death	42	5684	•	0(0-0)	94.9	0.186
			0 20 40 60 80			

Fig. 3 Summary results of illness severity in children with COVID-19. The definition of illness severity was mentioned as follows: a. Without any clinical symptoms and signs. Chest imaging examination was normal, while the 2019-nCoV nucleic acid test is positive. b. The main manifestations were acute upper respiratory tract infection and some children may have only digestive symptoms. Physical examination shows no auscultatory abnormalities. c. With pneumonia, some cases may have no clinical symptoms and signs, but chest CT shows lung lesions, which are subclinical. d. The disease usually progresses in about 1 week, and dyspnea occurs, oxygen saturation is less than 92%. e. Children can quickly progress to acute respiratory distress syndrome. (ARDS) or respiratory failure, Multiple organ dysfunction can be life threatening.

UNDERSTANDING THE PATHOLOGY

CIRCULATING ENDOTHELIAL PROGENITORS ARE INCREASED IN COVID-19 PATIENTS AND CORRELATE WITH SARS-COV-2 RNA IN SEVERE CASES

Mancuso P, Gidaro A, Gregato G, Rayeane A, Cremonesi P, Quarna J, Caccia S, Gusso L, Rusconi S, Giacomelli A, Cogliati C, Bertolini F., J Thromb Haemost. 2020 Aug 6. doi: 10.1111/jth.15044. Online ahead of print. Level of Evidence: 3 - Non -randomized controlled cohort/follow-up study

BLUF

Authors used multiparametric flow cytometry to analyze the quantity of cluster of differentiation 146 positive (CD146+) circulating endothelial cells (CEC's) and circulating endothelial progenitors (CEP's) in 27 patients with active COVID-19; 9 individuals who had COVID-19, recovered, and tested negative at the time of the study; and 8 age- and gender-matched controls in April 2020. The findings suggest a potential for further investigation into the use of CEP's and CEC's as biomarkers of endothelial damage in COVID-19 patients.

SUMMARY

Specific findings included:

- 1. Patients with active COVID-19 had an increased level of viable CEP's compared to controls and patients who had recovered from COVID-19
- 2. Active COVID-19 patients had skewed viable/apoptotic CD146+ CEC's, with fewer apoptotic CD146+ CEC's in both mild and severe cases compared with controls
- 3. A positive correlation (R=0.8) was seen among copies of SARS-CoV-2 RNA in the cellular fraction and apoptotic CEP's per milliliter in severe COVID-19 patients
- 4. Several correlations between CEP's and CEC's and various hematologic cells and markers including lymphocytes, leukocytes, neutrophils, eosinophils, platelets, hemoglobin, interleukin-6, and others in severe (Figure 2), mild (Figure 3), and recovered COVID-19 patients.

ABSTRACT

BACKGROUND: During the course of Covid-19, the disease caused by the new Coronavirus SARS-CoV-2, thrombotic phenomena and/or diffuse vascular damage are frequent, and viral elements have been observed within endothelial cells. OBJECTIVES: CD146+ circulating endothelial cells (CD146+ CECs) and their progenitors (CEPs) are increased in cardiovascular, thrombotic, infectious and cancer diseases. The present study was designed to investigate their kinetics in Covid-19 patients. METHOD: We used a validated flow cytometry procedure to enumerate viable and apoptotic CD146+ CECs and CEPs in Covid-19 patients during the course of the disease and in patients who recovered. RESULT: Viable CEPs/mL were significantly increased in Covid-19 patients compared to healthy controls. This increase was observed in patients with mild symptoms and not further augmented in patients with severe symptoms. In patients who recovered, CEPs decreased, but were in a range still significantly higher than normal controls. Regarding mature CD146+ CECs, in Covid-19 patients their absolute number was similar to those observed in healthy controls, but the viable/apoptotic CD146+ CEC ratio was significantly different. Both mild and severe Covid-19 patients had significantly less apoptotic CD146+ CECs compared to healthy controls. Patients who recovered had significantly less CD146+ CECs/mL when compared to controls as well as to mild and severe Covid-19 patients. A positive correlation was found between the copies of SARS-CoV-2 RNA in the cellular fraction and apoptotic CEPs/mL in severe Covid-19 patients. CONCLUSIONS: CD146+ CECs and CEPs might be investigated as candidate biomarkers of endothelial damage in Covid-19 patients.

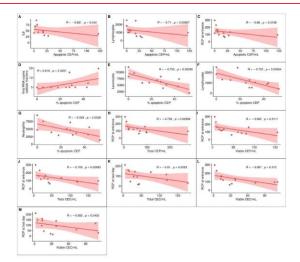


Figure 2. Significant correlations among CEP and CD146+ CEC categories and hematological parameters in severe COVID-19 patients.

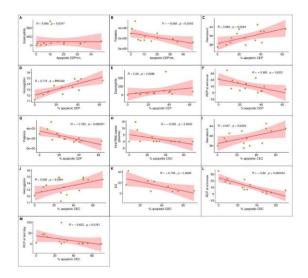


Figure 3. Significant correlations among CEP and CD146+ CEC categories and hematological parameters in mild COVID-19 patients.

NATURALLY OCCURRING SARS-COV-2 GENE DELETIONS CLOSE TO THE SPIKE S1/S2 CLEAVAGE SITE IN THE VIRAL QUASISPECIES OF COVID19 PATIENTS

Andres C, Garcia-Cehic D, Gregori J, Piñana M, Rodriguez-Frias F, Guerrero-Murillo M, Esperalba J, Rando A, Goterris L, Codina MG, Quer S, Martín MC, Campins M, Ferrer R, Almirante B, Esteban JI, Pumarola T, Antón A, Quer J. Emerg Microbes Infect. 2020 Aug 5:1-48. doi: 10.1080/22221751.2020.1806735. Online ahead of print. Level of Evidence: 3 - Mechanism-based reasoning

BLUF

A genomic analysis conducted in Spain using samples from 18 COVID-19 patients with no comorbidities (10 mild, 8 severe) found genome deletions near the Spike (S) S1 and S2 cleavage sites. These deletions resulted in free S1 (detects and binds ACE2 receptor) and absent S2 (fixes S-proteins to the viral membrane surface) among all 10 mild cases and half the severe cases. This free S1 may compete with viral particles or act as a decoy to weaken the disease/immune response (Figure 3), suggesting this genetic change may decrease virulence while maintaining high transmissibility, which could potentially provide a target for vaccination and antiviral treatment.

ABSTRACT

The SARS-CoV-2 spike (S) protein, the viral mediator for binding and entry into the host cell, has sparked great interest as a target for vaccine development and treatments with neutralizing antibodies. Initial data suggest that the virus has low mutation rates, but its large genome could facilitate recombination, insertions, and deletions, as has been described in other coronaviruses. Here, we deep-sequenced the complete SARS-CoV-2 S gene from 18 patients (10 with mild and 8 with severe COVID-19), and found that the virus accumulates deletions upstream and very close to the S1/S2 cleavage site (PRRAR/S), generating a frameshift with appearance of a stop codon. These deletions were found in a small percentage of the viral quasispecies (2.2%) in samples from all the mild and only half the severe COVID-19 patients. Our results suggest that the virus may generate free S1 protein released to the circulation. We suggest that natural selection has favored a "Don't burn down the house" strategy, in which free S1 protein may compete with viral particles for the ACE2 receptor, thus reducing the severity of the infection and tissue damage without losing transmission capability.

FIGURES

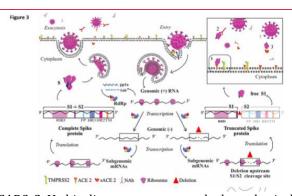


Figure 3. Based on the life cycle of SARS-CoV, this diagram represents the hypothesis derived from our results. Entry of the virus in the host cell is shown at the top right of the diagram. At the transcription step, two scenarios are depicted: to the left, the viral particle resulting from normal S protein, and to the right the viral particle resulting from truncated S. In normal conditions, once the nucleoprotein is freed into the cytoplasm ss+RNA is translated into the non-structural proteins required for transcription, ss+RNA is transcribed into ss-RNA and later into genomic ss+RNA which is encapsidated (left side of the figure). Once the complete viral particle has been formed, it is secreted from the cell by exocytosis. The right side of the figure depicts the situation when a deletion occurs in the S gene during transcription of the complete genome and before subgenomic mRNAs are generated to produce the structural proteins. Translation of a deleted subgenomic spike mRNA would lead to a truncated S protein composed of the S1 domain without S2, which could be shed outside the cell as free S1. The box depicts possible destinations of free S1, which could bind to 1) the ACE2 cell receptor, 2) S1-specific neutralizing antibodies, or 3) free ACE2 receptor. The red triangle indicates the deletion in genomic RNA. Abbreviations: ACE2, angiotensin converting enzyme 2; mRNA, messenger RNA; NAb; neutralizing antibodies; pp1a, polyprotein 1a; RdRp, RNA-dependent RNA polymerase; S, spike; S1, subunit S1 at the N-terminal domain of the S protein, which includes receptor binding domain (RBD); S2, subunit S2 located at the C-terminal domain of S protein, which includes fusion peptide (FP), heptad repeat (HR) domain 1 and 2, and the transmembrane domain (TM); ss, single stranded; ss+RNA, single-stranded positive sense RNA; TMPRS22, human serine protease TMPRSS2

NEUROPATHOLOGIC FEATURES OF FOUR AUTOPSIED COVID-19 PATIENTS

Kantonen J, Mahzabin S, Mäyränpää MI, Tynninen O, Paetau A, Andersson N, Sajantila A, Vapalahti O, Carpén O, Kekäläinen E, Kantele A, Myllykangas L.. Brain Pathol. 2020 Aug 6. doi: 10.1111/bpa.12889. Online ahead of print. Level of Evidence: 4 - Case-series

BLUF

Researchers at the Helsinki University Hospital performed autopsies between April 14 and May 18, 2020 to describe the neuropathological findings in four COVID-19 positive patients and found the following (Table 1):

- 3 of the 4 cases showed only mild hypoxia-related neuropathological changes.
- 1 case (patient with a medical history of obesity, DM2, and Parkinson's Disease) showed extensive perivascular hemorrhages and some foci of white matter lesions.
- All CNS samples were negative for SARS-CoV-2.
- No signs of meningitis or encephalitis in all cases.

The researchers acknowledge there is a limited amount of evidence and suggest additional studies are warranted to better understand COVID-19 effects on neurological processes.

ABSTRACT

Published descriptions of the neuropathological features of COVID-19 patients have been controversial, ranging from only modest or no pathology to severe hypoxic and hemorrhagic phenotypes, thrombotic complications, acute disseminated encephalomyelitis-like changes, and encephalitis and meningitis. Here we describe the neuropathological findings of four COVID-19-positive patients autopsied at the Helsinki University Hospital during the spring of 2020. While three of the patients (age range 63-90) exhibited merely mild to moderate hypoxia-associated changes, one 38-year-old subject with obesity, diabetes (type 2), Parkinson's disease, and a very severe clinical course was found to have severe ischemic injury, abundant microhemorrhages and enlarged perivascular spaces most pronounced in the white matter and deep gray matter. The pattern of ischemic changes suggested a defect in microcirculation. In addition, a few small perivascular white matter lesions, with macrophages engulfing myelin, were found. No signs of encephalitis or meningitis were detected in any of the patients. When conducting RT-PCR and immunohistochemical analyses of brain tissue we could not demonstrate in any of the patients marked injury or presence of SARS-CoV2 in the olfactory epithelium, olfactory bulbs, or brain areas responsible for respiratory control. In conclusion, our small autopsy series demonstrates various hypoxia-associated neuropathological features in COVID-19 patients, but no evidence of neurotropism or meningitis/encephalitis.

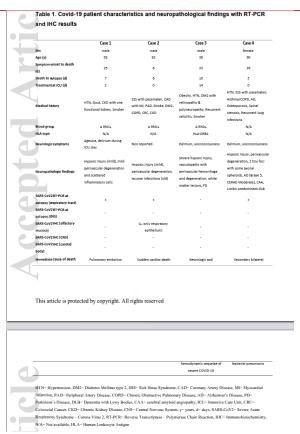


Table 1: Covid-19 patient characteristics and neuropathological findings with RT-PCR and IHC results

TRANSMISSION & PREVENTION

EXPLORING THE GROWTH OF COVID-19 CASES USING EXPONENTIAL MODELLING ACROSS 42 COUNTRIES AND PREDICTING SIGNS OF EARLY CONTAINMENT USING MACHINE LEARNING

Kasilingam D, Prabhakaran SPS, Dinesh Kumar R, Rajagopal V, Santhosh Kumar T, Soundararaj A.. Transbound Emerg Dis. 2020 Aug 4. doi: 10.1111/tbed.13764. Online ahead of print.

Level of Evidence: Other - Modeling

BLUF

A modeling study by researchers in India used data of COVID-19 cases in 42 countries (n=448,989; 84.78% of worldwide infections) through 26 March 2020 and found an association between early containment and healthcare infrastructure (beds per 1000 population) as well as lockdown policies via exponential growth model (Figures 2,3) and machine learning model with logistic regression (76.2%-92.9% prediction accuracy, Table 3). Authors suggest these results can be used by government officials to take action on developing proper infrastructure (healthcare facilities in particular) and lockdown measures for early SARS-CoV-2 containment.

ABSTRACT

COVID-19 pandemic disease spread by the SARS-COV-2 single-strand structure RNA virus, belongs to the 7th generation of the coronavirus family. Following an unusual replication mechanism, it's extreme ease of transmissivity has put many counties under lockdown. With uncertainty of developing a cure/vaccine for the infection in the near future, the onus currently lies on healthcare infrastructure, policies, government activities, and behaviour of the people to contain the virus. This research uses exponential growth modelling studies to understand the spreading patterns of the COVID-19 virus and identifies countries that have shown early signs of containment until 26th March 2020. Predictive supervised machine learning models are built using infrastructure, environment, policies, and infection-related independent variables to predict early containment. COVID-19 infection data across 42 countries are used. Logistic regression results show a positive significant relationship between healthcare infrastructure and lockdown policies, and signs of early containment. Machine learning models based on logistic regression, decision tree, random forest, and support vector machines are developed and show accuracies between 76.2% to 92.9% to predict early signs of infection containment. Other policies and the decisions taken by countries to contain the infection are also discussed.

Independent Variable	Regression	Wald				
	Coefficient					
Doctors Per 1000 Population	0.215	0.209				
Beds Per 1000 Population	0.241**	2.773				
Average Temperature	0.052	0.766				
Average Humidity	-0.004	0.040				
Days Since Official Lockdown	-0.098	0.757				
Percentage of Lockdown Days	9.998***	3.410				
Total Cases Per Million Population	0.000	0.025				
Deaths Per Million Population	-0.026	0.799				
Days Since First Contact	0.001	0.001				
Percentage of Serious Cases of	-1.151	0.005				
Infected						
*** p <0.001, ** p<0.01, * p<0.05						
Accuracy – 78.6%						
Dependent Variable – Early containment						

Table 3. Logistic Regression Results.

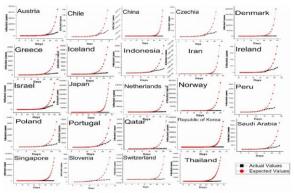


Figure 2. Countries Showing Initial Level of Containment of COVID-19.

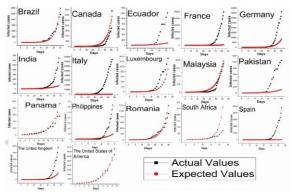


Figure 3. Countries Not Showing Initial Level of Containment of COVID-19.

MANAGEMENT

ACUTE CARE

THE UNCERTAIN ROLE OF CORTICOSTEROIDS IN THE TREATMENT OF COVID-

Ellsworth GB, Glesby MJ, Gulick RM.. JAMA Intern Med. 2020 Aug 3. doi: 10.1001/jamainternmed.2020.2444. Online ahead of

Level of Evidence: Other - Expert Opinion

BLUF

Authors affiliated with Weill Cornell Medicine highlight concerns regarding the efficacy of corticosteroid treatment in COVID-19 patients based on several studies where no improvement in mortality was found and potential harms were identified. Furthermore, in cohort studies reporting decreased mortality, survivor selection bias may have impacted the accuracy of the results. The authors caution against the use of corticosteroids in patients unless presenting with co-morbidities specified in the World Health Organization's guidelines for COVID-19 treatment such as chronic obstructive pulmonary disease exacerbation or septic shock.

EMERGENCY MEDICINE

A 46-YEAR-OLD WOMAN WHO PRESENTED WITH DIABETIC KETOACIDOSIS AND COVID-19 PNEUMONIA WITH MULTIPLE PULMONARY THROMBOEMBOLI: A CASE REPORT

Haider MB, Abbas F, Hafeez W.. Am J Case Rep. 2020 Jul 20;21:e925794. doi: 10.12659/AJCR.925794. Level of Evidence: Other - Case Report

BLUF

This case report of a 46 year old woman from Detroit, MI discusses a co-presentation with diabetic ketoacidosis (DKA) and COVID-19. The patient was started on DKA management therapy, hydroxychloroquine, and subcutaneous heparin for venous thromboembolism (VTE)prophylaxis. However, elevated D-Dimer on day 4 prompted a pulmonary CT scan, which revealed multiple small emboli within the lobar arteries and lung lobes as well as an enlarged spleen (Figure 2). The patient then received enoxaparin sodium (1mg/kg q 12 hours) for the remainder of her admission and was discharged with a 3-month course of Apixaban. The authors conclude that low-molecular-weight heparin prophylaxis may be insufficient to in preventing COVID-19-related VTE and suggest prophylactic half- or full-doses of anticoagulants.

ABSTRACT

BACKGROUND Coronavirus disease 2019 (COVID-19) occurs because of a novel enveloped ribonucleic acid coronavirus called severe acute respiratory distress syndrome coronavirus-2 (SARS-CoV-2). One of the major reported complications of COVID-19 includes both arterial and venous thromboembolism (VTE). Here we describe a case of COVID-19 provoked pulmonary embolism in a young patient already receiving prophylactic treatment for VTE. CASE REPORT A 46-year-old female with past medical history of diabetes mellites, hypertension, and asthma presented in the emergency department (ED) with dyspnea requiring 6 liters per minute of oxygen on presentation. Her main complaints were cough and vomiting. In the ED, hypoxemia worsened, and she ultimately required endotracheal intubation. Labs were suggestive of diabetic ketoacidosis (DKA) and showed increase in all inflammatory markers and absolute lymphocytopenia. Chest X-ray showed bilateral diffuse patchy airspace opacities. Standard DKA management was started. She was also started on ceftriaxone, azithromycin, hydroxychloroquine, and subcutaneous heparin (5000 U every 8 h) for VTE prophylaxis. SARS-Cov2 reverse transcriptionpolymerase chain reaction returned positive. Ceftriaxone and azithromycin were discontinued the very next day because of low suspicion of bacterial infection while hydroxychloroquine was completed for 5 days. On the third day of admission, the patient self-extubated and was immediately placed on nonrebreather with sp02 in low 90s. On the fourth day of admission, Ddimer came back 4.74 mg/L, which was elevated from a prior value, so computed tomography angiography of the lungs was done, which disclosed multiple emboli in the lungs. She was started on therapeutic doses of enoxaparin sodium, which was continued through her admission. She was switched to Apixaban on discharge. CONCLUSIONS The finding of the case

suggested that low-molecular-weight heparin prophylaxis may not be sufficient to prevent VTE in COVID-19 pneumonia. Some of these patients may benefit from receiving prophylactic half doses or full doses of anticoagulants.

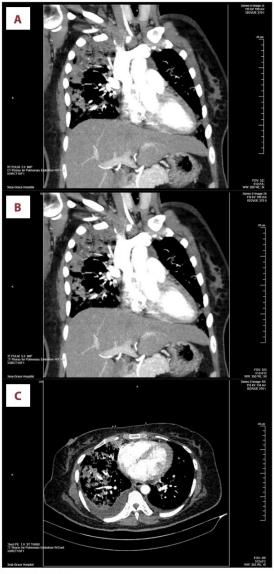


Figure 2. (A-C) Computed tomography angiography demonstrating multiple emboli involving segmental and subsegmental pulmonary arteries in the left lower and upper lobes and the left lower lobe lobar artery and subsegmental emboli in the right upper lobe. No large central emboli.

CRITICAL CARE

SUCCESSFUL MANAGEMENT OF SEVEN CASES OF CRITICAL COVID-19 WITH EARLY NONINVASIVE-INVASIVE SEQUENTIAL VENTILATION ALGORITHM AND BUNDLE PHARMACOTHERAPY

Peng M, Liu X, Li J, Ren D, Liu Y, Meng X, Lyu Y, Chen R, Yu B, Zhong W.. Front Med. 2020 Aug 6. doi: 10.1007/s11684-020-0796-3. Online ahead of print.

Level of Evidence: 4 - Case-series, case-control studies, or historically controlled studies

BLUF

Seven critically ill patients diagnosed with COVID-19 (Figure 3) and admitted to the intensive care unit (ICU) at the Third Affiliated Hospital of Shenzen University in China underwent successful treatment consisting of early noninvasive-invasive sequential ventilation (Figure 4), prone positioning, and pharmacotherapy (antivirals, anti-inflammatory drugs, immune enhancing medications, and complication prophylaxis agents). All 7 patients were extubated following a median ICU stay of 12.9 days and discharged home, suggesting that this protocol may contribute to successful outcomes in critically ill patients with COVID-19.

ABSTRACT

We report the clinical and laboratory findings and successful management of seven patients with critical coronavirus disease 2019 (COVID-19) requiring mechanical ventilation (MV). The patients were diagnosed based on epidemiological history, clinical manifestations, and nucleic acid testing. Upon diagnosis with COVID-19 of critical severity, the patients were admitted to the intensive care unit, where they received early noninvasive-invasive sequential ventilation, early prone positioning, and bundle pharmacotherapy regimen, which consists of antiviral, anti-inflammation, immune-enhancing, and complicationprophylaxis medicines. The patients presented fever (n = 7, 100%), dry cough (n = 3, 42.9%), weakness (n = 2, 28.6%), chest tightness (n = 1, 14.3%), and/or muscle pain (n = 1, 14.3%). All patients had normal or lower than normal white blood cell count/lymphocyte count, and chest computed tomography scans showed bilateral patchy shadows or ground glass opacity in the lungs. Nucleic acid testing confirmed COVID-19 in all seven patients. The median MV duration and intensive care unit stay were 9.9 days (interquartile range, 6.5-14.6 days; range, 5-17 days) and 12.9 days (interquartile range, 9.7-17.6 days; range, 7-19 days), respectively. All seven patients were extubated, weaned off MV, transferred to the common ward, and discharged as of the writing of this report. Thus, we concluded that good outcomes for patients with critical COVID-19 can be achieved with early noninvasive-invasive sequential ventilation and bundle pharmacotherapy.

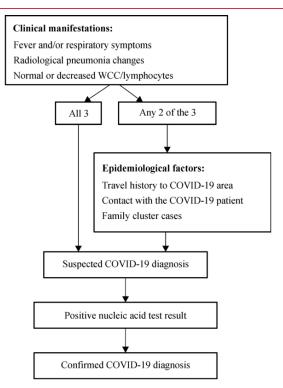


Figure 3. COVID-19 diagnoses algorithm

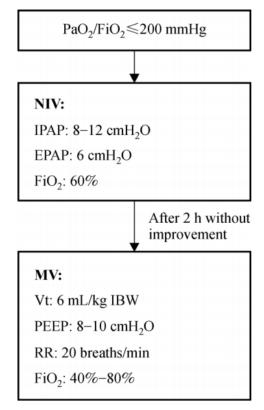


Figure 4. Sequential noninvasive-invasive ventilation process. Vt, tidal volume; PEEP, positive end-expiratory pressure; RR, respiratory rate; IBW, ideal body weight.

ADJUSTING PRACTICE DURING COVID-19

PSYCHIATRY

A NATIONAL MODEL OF REMOTE CARE FOR ASSESSING AND PROVIDING OPIOID AGONIST TREATMENT DURING THE COVID-19 PANDEMIC: A REPORT

Crowley D, Delargy I.. Harm Reduct J. 2020 Jul 17;17(1):49. doi: 10.1186/s12954-020-00394-z. Level of Evidence: Other - Guidelines and Recommendations

BLUF

This article discusses a model developed by the Irish College of General Practitioners and the National Health Service Executive Office for Social Inclusion for remote care for patients to gain access to opioid agonist treatment (OAT) in Ireland during the COVID-19 pandemic allowing for continued care to this vulnerable population while attempting to mitigate exposure and transmission of disease. This remote model consists of the follow steps:

- Initial assessment via telephone of the patient.
- If the patient does not have COVID-19 symptoms, they proceed with a local point of care (POC) drug screen.
- Video consultation with prescriber.
- Begin methadone treatment and titrations followed by telephone/video reviews.
- Continued monitoring by telephone/video for intoxication, withdrawal, and psychological symptoms.
- Weekly virtual case reviews between senior nurses and specialist prescribers.

ABSTRACT

BACKGROUND: Health services globally are struggling to manage the impact of COVID-19. The existing global disease burden related to opioid use is significant. Particularly challenging groups include older drug users who are more vulnerable to the effects of COVID-19. Increasing access to safe and effective opioid agonist treatment (OAT) and other harm reduction services during this pandemic is critical to reduce risk. In response to COVID-19, healthcare is increasingly being delivered by telephone and video consultation, and this report describes the development of a national model of remote care to eliminate waiting lists and increase access to OAT in Ireland. PURPOSE AND FINDINGS: The purpose of this initiative is to provide easy access to OAT by developing a model of remote assessment and ongoing care and eliminate existing national waiting lists. The Irish College of General Practitioners in conjunction with the National Health Service Executive office for Social Inclusion agreed a set of protocols to enable a system of remote consultation but still delivering OAT locally to people who use drugs. This model was targeted at OAT services with existing waiting lists due to a shortage of specialist medical staff. The model involves an initial telephone assessment with COVID-risk triage, a single-patient visit to local services to provide a point of care drug screen and complete necessary documentation and remote video assessment and ongoing management by a GP addiction specialist. A secure national electronic health link system allows for the safe and timely delivery of scripts to a designated local community pharmacy. CONCLUSION: The development of a remote model of healthcare delivery allows for the reduction in transmission risks associated with COVID-19, increases access to OAT, reduces waiting times and minimises barriers to services. An evaluation of this model is ongoing and will be reported once completed. Fast adaptation of OAT delivery is critical to ensure access to and continuity of service delivery and minimise risk to our staff, patients and community. Innovative models of remote healthcare delivery adapted during the COVID-19 crisis may inform and have important benefits to our health system into the future.

R&D: DIAGNOSIS & TREATMENTS

DEVELOPMENTS IN DIAGNOSTICS

CLINICAL VALIDITY OF SERUM ANTIBODIES TO SARS-COV-2: A CASE-CONTROL **STUDY**

Caturegli G, Materi J, Howard BM, Caturegli P.. Ann Intern Med. 2020 Jul 6. doi: 10.7326/M20-2889. Online ahead of print. Level of Evidence: 4 - Case-series, case-control, or historically controlled studies

BLUF

This case control study at Johns Hopkins Hospital Baltimore, Maryland evaluated the clinical validity of serum antibodies to SARS-CoV-2 in 11,066 patients by using IgG/IgA assays (Figures 1, 2, 3). 60 patients tested positive for COVID-19 and shortly after infection developed IgG that was sustained for up to 58 days. Furthermore, for every 2 fold increase in IgG, there was a 62% increase in the predicted odds of developing acute respiratory distress syndrome (p < 0.001). Sensitivity and specificity of the SARS-CoV-2 IgG assay were 0.976 (95% CI: 0.928 to 0.995) and 0.988 respectively (95% CI: 0.974 to 0.995). The authors suggest that SARS-CoV-2 antibodies may provide diagnostic information and insight into disease severity.

ABSTRACT

BACKGROUND: The clinical utility of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antibodies remains undefined. OBJECTIVE: To determine the clinical validity and utility of SARS-CoV-2 antibodies. DESIGN: Case-control study. SETTING: First month of testing for coronavirus disease 2019 (COVID-19) by using a nucleic acid amplification test (NAAT) on nasopharyngeal swabs at the Johns Hopkins Hospital, Baltimore, Maryland (11 066 persons). PARTICIPANTS: Of the 11 066 tested persons, 115 (1%) were hospitalized adults investigated for COVID-19. Clinical record review was performed to classify them into a COVID-19 case group (n = 60) or a non-COVID-19 control group (n = 55). The laboratory control groups comprised 513 persons not tested by NAAT: 160 healthy laboratory employees, 101 persons positive for IgG antibodies against Epstein-Barr virus capsid antigen, 215 positive for thyroperoxidase antibody, and 37 positive for rheumatoid factor. MEASUREMENTS: Serum IgG and IgA antibodies against SARS-CoV-2 spike protein were detected by using enzyme-linked immunosorbent assay. RESULTS: Sensitivity and specificity of the SARS-CoV-2 IgG assay were 0.976 (95% CI, 0.928 to 0.995) and 0.988 (CI, 0.974 to 0.995), respectively, when performed 14 days or later after symptom onset, but sensitivity decreased at earlier time points. Immunoglobulin G developed rapidly and was sustained at high levels throughout follow-up (up to 58 days). Antibodies to SARS-CoV-2 predicted the odds of developing acute respiratory distress syndrome, which increased by 62% (CI, 48% to 81%; P < 0.001) for every 2-fold increase in IgG. Of 11 066 NAAT-tested patients, 457 were repeatedly NAAT-negative, and serum samples were obtained for 18 such patients: 6 COVID-19 case patients and 12 non-COVID-19 control patients. Antibodies were present in 5 of 6 case patients and none of the 12 control patients (P = 0.001). LIMITATIONS: The study was retrospective and performed at a single-center; the sample was small; follow-up was limited; and selection bias may have occurred. CONCLUSION: Antibodies to SARS-CoV-2 demonstrate infection when measured at least 14 days after symptom onset, associate with clinical severity, and provide valuable diagnostic support in patients who test negative by NAAT but remain clinically suspicious for COVID-19. PRIMARY FUNDING SOURCE: Clinical Immunology Laboratory, Department of Pathology, Johns Hopkins Hospital.

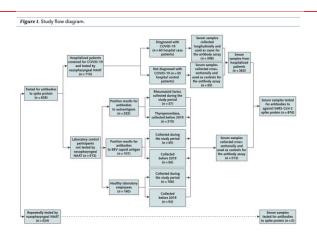


Figure 1. The study included 628 participants tested for serum antibodies against spike protein. The study also included clinical record review of all 558 patients with repeated nucleic acid amplification testing of nasopharyngeal swabs (34 were tested for antibodies, whereas 524 were not). COVID19 = coronavirus disease 2019; EBV = Epstein-Barr virus; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

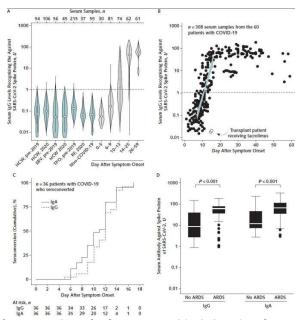


Figure 2. Biological characteristics of serum IgG antibodies against SARS-CoV-2 spike protein in the COVID-19 case group and the laboratory control groups.

A. Violin plot showing the distribution of IgG levels, indicating median and interquartile range. The horizontal dashed line represents the manufacturer cutoff (1.1 units). B. Overall relationship between IgG levels and day post symptom onset. The white circles represent a hypogammaglobulinemic patient receiving immunosuppressive therapy due to kidney transplant. C. Kaplan-Meier survival function of IgG and IgA seroconversion. D. Serum IgG and IgA antibody levels, stratified by the presence or absence of ARDS. ARDS = acute respiratory distress syndrome; COVID-19 = coronavirus disease 2019; EBV = Epstein-Barr virus; HCW = health care worker; RF = rheumatoid factor; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; TPO = thyroperoxidase.

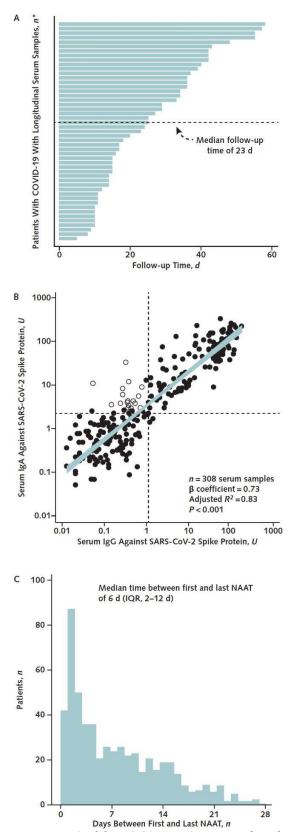


Figure 3. Top. Distribution of follow-up time in 49 of the 60 COVID-19 patients for whom longitudinal serum samples were available. Middle. Linear relationship between serum IgG and IgA levels. Open circles indicate patients who exclusively converted IgA but not IgG before day 12 post symptom onset. Bottom. Distribution of time between first and last NAAT in 558 patients tested repeatedly. COVID-19 = coronavirus disease 2019; IQR = interquartile range; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

MENTAL HEALTH & RESILIENCE NEEDS

COVID-19'S IMPACT ON HEALTHCARE WORKFORCE

UNDERSTANDING THE TRAUMATIC EXPERIENCES OF HEALTHCARE WORKERS RESPONDING TO THE COVID-19 PANDEMIC

Shigemura J, Ursano RJ, Kurosawa M, Morganstein JC, Benedek DM. Nurs Health Sci. 2020 Aug 6. doi: 10.1111/nhs.12766. Online ahead of print.

Level of Evidence: Other - Expert Opinion

BLUF

Authors from Tokyo, Japan and Bethesda, MD summarize the global impact of COVID-19 on healthcare workers since December 2019, such as the increased risk of infection, exposure to bereaving families, work demand and burden, and the dual-experience of being a hero while also facing public stigmatization and discrimination. The authors urge healthcare leaders to directly support, motivate, and educate the community and frontline workers about the pandemic's effect on mental health to mitigate potential consequences, including posttraumatic stress disorder (PTSD), complicated grief reactions, and suicide.

IMPACT ON PUBLIC MENTAL HEALTH

TECHNOLOGY AS A COPING TOOL DURING THE COVID-19 PANDEMIC: IMPLICATIONS AND RECOMMENDATIONS

Garfin DR.. Stress Health. 2020 Aug 6. doi: 10.1002/smi.2975. Online ahead of print. Level of Evidence: Other - Expert Opinion

BLUF

An expert opinion from University of California Irvine describes the use of technology as a potential tool for individuals to positively cope with the trauma acquired indirectly or directly during the COVID-19 pandemic and the new future that will ensue. The author cites previous research on telehealth and mobile apps used in the workplace, education, and chronic disease to suggest that online platforms may provide individuals with social support opportunities (such as virtual "happy hours" with friends), schedule flexibility, and better access to telehealth mental services that clinicians could effectively leverage to help patients deal with pandemic related stress.

ABSTRACT

The COVID-19 outbreak has caused unprecedented social disruption. This collective trauma has resulted in school closures, shuttered businesses, rising unemployment, and a spike in emotional distress from the pandemic and related secondary stressors. In this time of crisis, and due to sweeping stay-at-home orders across the United States and internationally, billions of individuals are engaging in work and school from home. This has resulted in an increasing reliance on technology to accomplish these tasks. Moreover, there has been a substantial rise in the use of technology as a way to stay connected to loved ones, for entertainment, for telehealth services, and to engage in at-home-fitness. This commentary reviews literature that discusses the potential harm of increased technology use as well as its benefits. If mindfully leveraged, technology can be harnessed to promote increased social connectedness, work productivity, and leisure time. Mental health services may be more widely distributed through telehealth and related services, improving access and reducing health disparities. Recommendations about how technology can promote effective coping and improve physical and mental health during and after the COVID-19 pandemic are discussed. This article is protected by copyright. All rights reserved.

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