The Daily COVID-19 Literature Surveillance Summary

August 17, 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

- Faculty of Medicine from The Chinese University of Hong Kong, China found previously affected countries were more likely to incur lower COVID-19 incidence (p=0.021) than countries not exposed to SARS and/or MERS.

- Pediatricians at Boston Children's Hospital suggested several laboratory characteristics distinguish multisystem inflammatory syndrome from Kawasaki disease in children, including cytopenias, degree of hyperferritinemia, and pattern of cytokine production, making the diagnosis and subsequent treatment of these very similar presentations quicker.

Understanding the Pathology

- A Spanish letter to the editor outlines a proteomics analysis investigating the presence of coronaviruses and SARS-CoV-2 in domestic cat fleas. Based on the preliminary results, the authors recommend preventing against flea infestation in cats as a prophylactic measure against possible COVID-19 transmission from fleas to humans and an investigation of arthropods as intermediate hosts and vectors of COVID-19.

Management

- Prominent coagulation disorder is closely related to inflammatory response and could be as a prognostic indicator for ICU patients with COVID-19: Authors affiliated with Peking University found that coagulation dysfunction may be associated with multiple inflammatory markers, suggesting that coagulation tests (namely, PT, FDP, D-dimer, and antithrombin III) may be useful prognostic indicators for ICU patients with COVID-19.

R&D: Diagnosis & Treatments

- A case series found that 6 out of the 7 had a decrease in proinflammatory cytokines and inflammatory markers with clinical improvement in health/mortality compared to 17 control patients, suggesting that early anti-inflammatory therapy with infliximab may decrease cytokine storm related organ failure.

TABLE OF CONTENTS

CLIMATE

GLOBAL

INTERNET PUBLIC OPINION EVOLUTION IN THE COVID-19 EVENT AND COPING STRATEGIES

Zhong Z.. Disaster Med Public Health Prep. 2020 Aug 12:1-23. doi: 10.1017/dmp.2020.299. Online ahead of print.
Level of Evidence: 1 - Local and current random sample surveys (or censuses)

BLUF

This study analyzed 15,800 internet posts with the phrase "COVID-19 outbreak" from the BaiduPost Bar by Chinese netizens (avid users of the Internet) from January 1st, 2020 through April 10th, 2020, using algorithms to assess topic clustering and distribution. The results demonstrated:

1. An exponential increase in COVID-19 related posts after February 22nd, 2020, chronologically correlated with the number of confirmed cases (Figure 1).
2. The 5 most replied to posts (Table 1) and 8 most discussed topics (Table 2) encompassed topics related to multiple aspects of the pandemic, including source, prevention, treatment, call for attention, and encouragement to the medical staff and patients.

The authors suggest the results highlight the importance of information transmission through online modalities as a vital component of public opinion, attitudes, and willingness to comply with public health policies.

ABSTRACT

OBJECTIVE: In this study, we carried out a text analysis on the information disseminated and discussed among netizens on the Baidu Post Bar (the world's largest Chinese forum) during the COVID-19 epidemic, to create a policy basis for health administrative departments. METHODS: We used Python tools to search for the relevant data on the Baidu Post Bar. Next, a text analysis was performed on the posts' contents using a combination of LDA, sentiment analysis, and correlation analysis. RESULTS: According to the LDA analysis, the public was highly interested in topics such as COVID-19 prevention, infection symptoms, infection and coping measures, sources of transmission and treatments, community management, and work resumption. The majority of the public had negative emotional values, yet a portion of the public held positive emotional values. We also performed a correlation analysis of the influencing factors was established. CONCLUSION: Netizens' degree of concern shown in their posts was greatly associated with the spread of COVID-19. With the rise, diffusion, outbreak, and mitigation of COVID-19 in China, netizens have successively created a large number of posts, and the topics of discussion varied over time. Therefore, the media and the government have the responsibility to distribute positive information, to correctly guide the public's emotions to bring some sort of reassurance to the public.

FIGURES

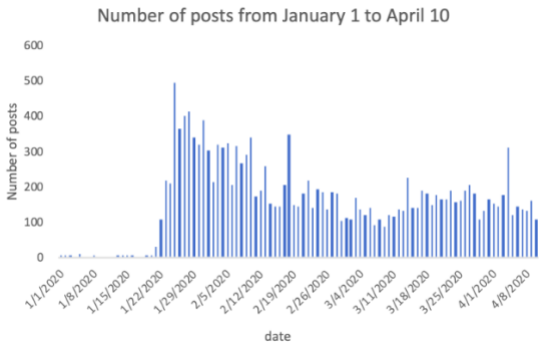


Figure 1. Number of posts published on a daily basis.

Table 1 The top 5 posts

Topic	Number of replies	Post time
Excuse me, can COVID-19 be prevented by a facemask respirator?	159	2020/1/23
I've always wanted to write a post to record the course of my illness	102	2020/3/3
Fight the coronavirus together	86	2020/1/28
How long do you think it will be before the vaccine is developed?	84	2020/1/25
Update on the latest news	83	2020/1/25

Table 1. The top 5 posts.

Table 2 Eight topics according to the Latent Dirichlet Allocation (English version)

	Topic	High frequency words
Topic 1	Prevention of COVID-19	virus,mask,reply,epidemic situation,coronavirus,Wuhan, pneumonia,Infected,hospital,U.S.A.,novel coronavirus,China,country, symptom,quarantine,case,feel,testing,Chinese medicine
Topic 2	Effect of TCM on COVID-19	virus,reply,Mask,epidemic situation,pneumonia,China, novel coronavirus,Infected,chinese medicine, patient,human body,hospital,Wuhan,U.S.A.,coronavirus,quarantine,case
Topic 3	The infection of COVID-19	virus,epidemic situation,mask,hospital,pneumonia,patient,China,Wuhan,reply,coronavirus, diagnosis,symptom,new type,infected,spread,novel coronavirus,case
Topic 4	Death of patients diagnosed with COVID-19	epidemic situation,virus,mask,reply,novel coronavirus,pneumonia,country,hospital,Wuhan,China,coronavirus,U.S.A.,infected,patient,situation,diagnosis,death
Topic 5	Comparison of the epidemic situation between China and the U.S.A.	epidemic situation,novel coronavirus,China, reply,mask,pneumonia,infected,Wuhan,quarantine,U.S.A.,symptom,hospital,coronavirus,human beings,diagnosis,healthy
Topic 6	Isolation policy, infection and death toll in China and the U.S.A	virus,reply,mask,novel coronavirus,epidemic situation,pneumonia, diagnosis,China,Infected,coronavirus,treatment,U.S.A,country,really,quarantine,doctor,death
Topic 7	Symptoms and origin of COVID-19	China,epidemic situation,infected,novel coronavirus,hospital, Wuhan,symptom,mask,coronavirus,pneumonia,quarantine,U.S.A,treatment,one kind,country,find,feel,human beings
Topic 8	China's help to other countries	virus,mask,reply,epidemic situation,infected,China,patient,pneumonia,novel coronavirus,Wuhan, U.S.A.,quarantine,coronavirus,hospital,expert,Italy,protect

Table 2. Eight topics according to the Latent Dirichlet Allocation (English version).

A MEDICALIZED HOTEL AS A PUBLIC HEALTH RESOURCE FOR THE CONTAINMENT OF COVID-19: MORE THAN A PLACE FOR QUARANTINING

Ramírez-Cervantes KL, Romero-Pardo V, Pérez-Tovar C, Martínez-Alés G, Quintana-Diaz M.. J Public Health (Oxf). 2020 Aug 10:fdaa129. doi: 10.1093/pubmed/fdaa129. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

This study describes the implementation of a medicalized hotel in Madrid, Spain, and specifically highlights the reasons for referral to the hotel, criteria for discharge from the hotel, patient characteristics, and hotel logistics (Figures 1 and 3). Most referrals were for patients who were immigrants to Spain and patients who lacked housing suitable for quarantining (Table 2). The authors urge public health agencies to adopt similar measures to offer housing to individuals who cannot access resources to safely quarantine.

ABSTRACT

BACKGROUND: To describe the implementation of a medicalized hotel in the community of Madrid as a public health resource for the containment of coronavirus disease (COVID-19) and to describe the characteristics of population benefitted. METHODS: A descriptive study of the implementation of the Via Castellana Medicalised Hotel (VCMH) was conducted. The average monthly household income, educational level and occupational social class of the subjects admitted were obtained through a survey conducted during their stay. RESULTS: There was no guidance for launching; however the hotel was coordinated by a tertiary referral hospital and attended the preventive medicine regulations and the decrees of legal regimes and authorization of health services in Madrid. Between 19 March and the 9 May 2020, 399 patients were admitted; 59% (235) were migrant; the main reason for referral (58%) was a lack of house conditions for quarantining, including overcrowding, which when compared with the migrant status a positive correlation was found. Some other reasons for referral were homelessness and eviction. Most of the survey participants had low monthly household income, educational level and social class. CONCLUSIONS: This medicalized hotel provided medical care and offered housing to a subgroup of vulnerable population who could not afford a safe quarantine.

FIGURES

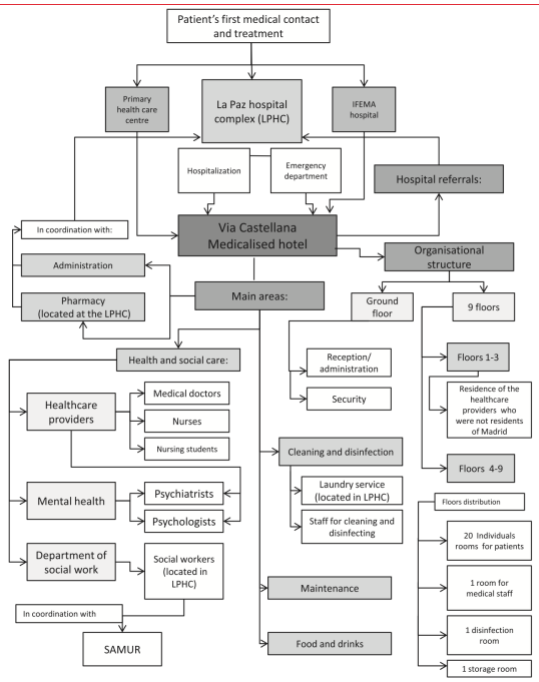


Figure 1. Hotel logistics. The performance of the VCMH involved: 29 nursing students; 21 medical doctors (including 2 psychiatrists); 20 nurses; 7 hospital administrators; 4 hospital wardens; 3 information technologists; 3 maintenance workers; and 2 volunteers (1 chiropodist and 1 priest).

Nationality**	Lack of house conditions for quarantining**		Total	Pearson
	NO (%)	SI (%)		
Spanish				
YES	87 (21%)	74 (19%)	399[1]	19.4 (P = 0.00)*
NO	72 (18%)	155 (39%)		

*Obtained by χ^2 test.
**Extracted from electronic clinical register.
[1]Proportions estimated over the whole sample including missing data (2.2%).

Table 2. Sociodemographic variables in patients admitted to the Hotel. Migrant status and lack of house conditions for quarantining (including house overcrowding).

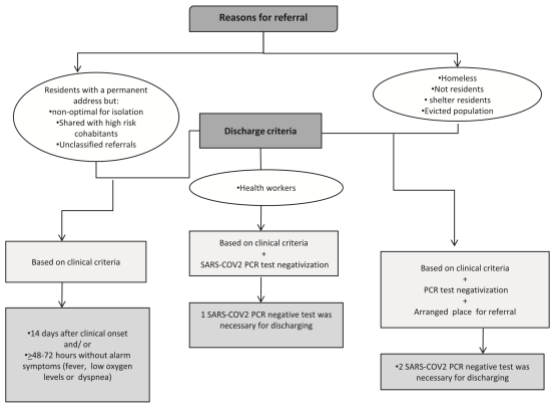


Figure 3. Reasons for referral and discharge criteria.

EPIDEMIOLOGY

THE POTENTIAL IMPACT OF PREVIOUS EXPOSURE TO SARS OR MERS ON CONTROL OF THE COVID-19 PANDEMIC

Huang J, Teoh JY, Wong SH, Wong MCS.. Eur J Epidemiol. 2020 Aug 10. doi: 10.1007/s10654-020-00674-9. Online ahead of print.

Level of Evidence: 3 - Local non-random sample

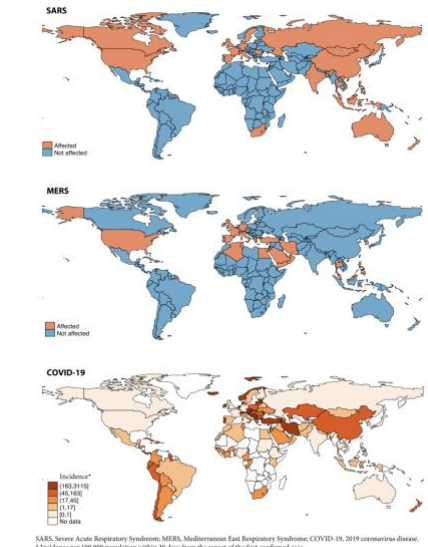
BLUF

Faculty of Medicine from The Chinese University of Hong Kong, China collected 30-day COVID-19 incidence rates (COVID-19 cases per 100,000 population within 30 days of the first reported case) in 94 countries, including those previously affected by the 2003 SARS epidemic and/or 2012 MERS epidemic (Figure 1) and found previously affected countries were more likely to incur lower COVID-19 incidence (p=0.021) than countries not exposed to SARS and/or MERS, while countries labeled as “full democracy” (based on Democracy Index) suffered greater COVID-19 incidences (p=0.011; Table 1). Authors suggest prior epidemic exposure and Democracy Index are associated with COVID-19 response performance, but further prospective studies are needed to examine this association in greater detail.

ABSTRACT

The Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2) is believed to share similar characteristics with SARS in 2003 and Mediterranean East Respiratory Syndrome (MERS) in 2012. We hypothesized that countries with previous exposure to SARS and MERS were significantly more likely to have fewer cases and deaths from coronavirus disease 2019 (COVID-19). We retrieved the incidence of COVID-19 per 100,000 population within 30 days since the first confirmed case was reported from the 2019 Novel COVID-19 data repository by the Johns Hopkins Centre for Systems Science and Engineering for 94 countries. The association between previous exposure to SARS and/or MERS and the 30-day COVID-19 incidence rate was examined by multivariable linear regression analysis, whilst controlling for potential confounders including the INFORM COVID-19 Risk Index, Testing Policies, Democracy Index, Scientific Citation Index, Gross Domestic Product (GDP), Human Development Index (HDI) and the population density of each country. We found that countries with previous exposure to SARS and/or MERS epidemics were significantly more likely to have lower incidence of COVID-19 (beta coefficient - 225.6, 95% C.I. - 415.8,- 35.4, p = 0.021). However, countries being classified as having "full democracy" using Democracy Index had higher incidence of COVID-19 (reference: authoritarian regime; beta coefficient 425.0, 95% C.I. 98.0, 752.0, p = 0.011). This implies that previous exposure to global epidemics and Democracy Index for a country are associated its performance in response to COVID-19. We recommend future studies should evaluate the impact of various pandemic control strategies at individual, community, and policy levels on mitigation of the disease.

FIGURES



SARS, Severe Acute Respiratory Syndrome; MERS, Mediterranean East Respiratory Syndrome; COVID-19, 2019 coronavirus disease.
* Incidence per 100,000 population within 30 days from the report of the first confirmed case.

Fig. 1 Spatial distribution of countries affected by Severe Acute Respiratory Syndrome (SARS), Mediterranean East Respiratory Syndrome (MERS), and 2019 coronavirus disease (COVID-19)

Table 1 The association between exposure to SARS and/or MERS and the incidence of COVID-19 per 100,000 population within 30 days from the report of the first confirmed case

Epidemics*		Number of countries affected
SARS		29
MERS		27
COVID-19 (as of 05 June, 2020)		216
Potential factors associated with incidence	β coefficients (95% C.I.)	p value
Never exposure to SARS and/or MERS	Reference	
Exposure to SARS and/or MERS	−225.6 (−415.8,−35.4)	0.021
Inform COVID-19 risk index	66.9 (−56.6, 190.3)	0.285
Testing policies	114.8 (−42.4, 272.0)	0.150
Democracy index		
Authoritarian regime	Reference	
Hybrid regime	−24.0 (−314.8, 266.9)	0.870
Flawed democracy	−43.2 (−295.8, 209.4)	0.735
Full democracy	425.0 (98.0, 752.0)	0.011
Scientific citation index	0.04 (−5.14, 5.23)	0.987
GDP per capita	−28.5 (−103.9, 46.9)	0.454
HDI	1236.8 (−66.1, 2539.7)	0.063
Population density	−20.0 (−122.0, 82.0)	0.698

*References from: WHO. Summary of probably SARS cases with onset of illness from 1 November 2002 to 31 July 2003. Available at: https://www.who.int/csr/sars/country/table2004_04_21/en/. Accessed on 05 June, 2020; WHO. Middle East respiratory syndrome coronavirus (MERS-CoV). Available at: https://www.who.int/emergencies/mers-cov/en/. Accessed on 05 June, 2020; Updated figures from the WHO. Available at: https://www.who.int/emergencies/diseases/novel-coronavirus-2019, Accessed on 05 June, 2020

SYMPTOMS AND CLINICAL PRESENTATION

PEDIATRICS

DISTINCT CLINICAL AND IMMUNOLOGICAL FEATURES OF SARS-COV-2-INDUCED MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN

Lee PY, Day-Lewis M, Henderson LA, Friedman K, Lo J, Roberts JE, Lo MS, Platt CD, Chou J, Hoyt KJ, Baker AL, Banzon T, Chang MH, Cohen E, de Ferranti S, Dionne A, Habiballah S, Halyabar O, Hausmann JS, Hazen M, Janssen E, Meidan E, Nelson RW, Nguyen AA, Sundel RP, Dedeoglu F, Nigrovic PA, Newburger JW, Son MBF.. J Clin Invest. 2020 Jul 23:141113. doi: 10.1172/JCI141113. Online ahead of print.
Level of Evidence: 4 - Case-series, case-control, or historically controlled studies

BLUF

This retrospective study analyzed 28 cases of multisystem inflammatory syndrome in children (MIS-C) at Boston Children's Hospital from March 17 to June 6, 2020 to clinically differentiate MIS-C verses Kawasaki disease (KD) and macrophage activation syndrome (MAS). The results suggested several laboratory characteristics (Table 2) to narrow the specificity of disease, including cytopenias, degree of hyperferritinemia, and pattern of cytokine production, making the diagnosis and subsequent treatment of these very similar presentations quicker.

SUMMARY

The analysis and evaluation of the 28 cases of MIS-C consisted of:

- Demographic and clinical characteristics (Table 1)
- Laboratory and imagining results (Table 2)
- Treatment responses (Table 3)
- Comparison between MIS-C verses historic cohorts of KD (Figure 1) and MAS (Figure 2)

The results revealed distinguishing characteristics of cytopenias to differentiate MIS-C from KD, and the degree of hyperferritinemia and pattern of cytokine production to differentiate from MAS. The authors also observed a noticeable overrepresentation of MIS-C in minority groups, reflecting the disproportionate burden of illness during this pandemic among minority groups. They also observed an overlapping of preexisting conditions that are also seen in adults with COVID-19 infections including obesity, asthma and heart disease.

ABSTRACT

BACKGROUND: Pediatric SARS-CoV-2 infection can be complicated by a dangerous hyperinflammatory condition termed multisystem inflammatory syndrome in children (MIS-C). The clinical and immunologic spectrum of MIS-C and its relationship to other inflammatory conditions of childhood have not been studied in detail. METHODS: We retrospectively studied confirmed cases of MIS-C at our institution from March to June 2020. The clinical characteristics, laboratory studies and treatment response were collected. Data were compared with historic cohorts of Kawasaki disease (KD) and macrophage

activation syndrome (MAS). RESULTS: Twenty-eight patients fulfilled the case definition of MIS-C. Median age at presentation was 9 years (range 1 month to 17 years); 50% of patients had pre-existing conditions. All patients had laboratory confirmation of SARS-CoV-2 infection. Seventeen patients (61%) required intensive care, including 7 patients (25%) requiring inotrope support. Seven patients (25%) met criteria for complete or incomplete KD and coronary abnormalities were found in 6 cases. Lymphopenia, thrombocytopenia, and elevation in inflammatory markers, D-dimer, B-type natriuretic peptide, IL-6 and IL-10 levels were common but not ubiquitous. Cytopenias distinguished MIS-C from KD and the degree of hyperferritinemia and pattern of cytokine production differed between MIS-C and MAS. Immunomodulatory therapy given to MIS-C patients included IVIG (71%), corticosteroids (61%) and anakinra (18%). Clinical and laboratory improvement were observed in all cases, including 6 cases that did not require immunomodulatory therapy. No mortality was recorded in this cohort. CONCLUSION: MIS-C encompasses a broad phenotypic spectrum with clinical and laboratory features distinct from Kawasaki disease and macrophage activation syndrome. FUNDING: This work was supported by the National Institute of Health / National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) K08-AR074562 (PYL), K08-AR AR073339 (LAH), R01-AR065538, R01-AR073201 and P30-AR070253 (PAN); National Institute of Allergy and Infectious Diseases 5T32AI007512-34 (JL, JR, TB, AAN and RWN); Rheumatology Research Foundation Investigator Awards (PYL and LAH) and Medical Education Award (JSH); Boston Children's Hospital Faculty Career Development Awards (PYL and LAH), the McCance Family Foundation (JWN), and the Samara Jan Turkel Center (JC, RPS, MBS).

FIGURES

Table 1. Demographic and clinical characteristics of MIS-C patients [A]

Number of patients	28	**Details of hospitalization**	
CDC case definition	100%	Intensive care unit	61%
WHO case definition	93%	Inotropes	25%
Demographics		Supplemental oxygen	43%
Age, median (range)	9.0 y (0.1-17)	Non-invasive ventilation	25%
Female (%)	43%	Invasive ventilation [B]	4%
White (%)	36%	**Clinical manifestations**	
Black or African American (%)	18%	Fever	100%
Hispanic or Latino (%)	43%	Conjunctivitis	57%
Pre-existing condition	50%	Gastrointestinal symptoms	54%
Duration of symptoms at admission	5 d (1-10)	Hypotension / shock	54%
Reported contact with COVID-19	29%	Skin rash	36%
SARS-CoV-2 testing	100%	Mucositis	25%
SARS-CoV-2 serology +	95% (18/19)	Extremity swelling / erythema	21%
Nasopharyngeal swab PCR +	61% (17/28)	Acute kidney injury	21%

Table 2. Radiographic and laboratory finding in MIS-C patients [A]

Echocardiography		**Hematologic parameters**	
Ejection fraction <55%	39% (11/28)	ALC < 2 x 10^3/mL	75% (21/28)
Dilated coronary vessel [B]	7% (2/28)	Platelets < 200 x 10^3/mL	64% (18/28)
Coronary aneurysm [C]	14% (4/28)	WBC > 10 x 10^3/mL	39% (11/28)
Chest X-ray		Hemoglobin < 11 g/dL	32% (9/28)
Focal consolidation / opacity	38% (10/26)	WBC < 5 x 10^3/mL	25% (7/28)
Prominent vasculature	15% (4/26)	ANC < 2 x 10^3/mL	18% (5/28)
Enlarged cardiac silhouette	8% (3/26)	**Coagulation parameters**	
Pleural effusion	12% (2/26)	D-dimer > 0.5 mg/mL	96% (26/27)
Peribronchiel thickening	12% (2/26)	Fibrinogen > 400 mg/dL	71% (15/21)
Cardiac biomarkers		PT > 14.6 seconds	62% (16/26)
BNP > 100 pg/mL	52% (12/23)	PTT > 37 seconds	38% (10/26)
Troponin > 0.09 ng/mL	27% (6/22)	**Organ function parameters**	
Inflammatory markers		LDH > 250 U/L	74% (14/19)
Procalcitonin ≥ 0.1 ng/mL	96% (24/25)	AST > 50 U/L	46% (13/28)
CRP > 0.5 mg/dL	93% (26/28)	ALT > 40 U/L	32% (9/28)
Ferritin > 200 ng/mL	86% (24/28)	BUN > 18 mg/dL	25% (7/28)
ESR > 30 mm/h	63% (15/24)	Creatinine > 0.8 mg/dL	21% (6/28)

Table 3. Treatment approaches and outcome in MIS-C patients

	Total (n = 28)	ICU (n = 17)	Non-ICU (n = 11)
Duration of hospitalization (days, median)	8.0	9.5	4.0
Discharge from hospital (%)	100%	-	-
Death	0%	-	-
Immunomodulatory therapy [A], n (%)			
None	6 (21%)	3 (18%)	3 (27%)
IVIG only	4 (14%)	0 (0%)	4 (36%)
Methylprednisolone only	1 (4%)	1 (6%)	0 (0%)
Anakinra only	1 (4%)	0 (0%)	1 (9%)
IVIG + Methylprednisolone	12 (43%)	9 (53%)	3 (27%)
IVIG + Methylprednisolone + Anakinra	4 (14%)	4 (24%)	0 (0%)
Anti-microbial therapy, n (%)			
Remdesivir	7 (25%)	6 (35%)	1 (9%)
Antibiotics	15 (54%)	12 (71%)	3 (27%)
Anticoagulation therapy [B], n (%)			
None	4 (14%)	2 (12%)	2 (18%)
Aspirin	19 (68%)	13 (76%)	6 (55%)
Enoxaparin	18 (64%)	13 (76%)	5 (45%)

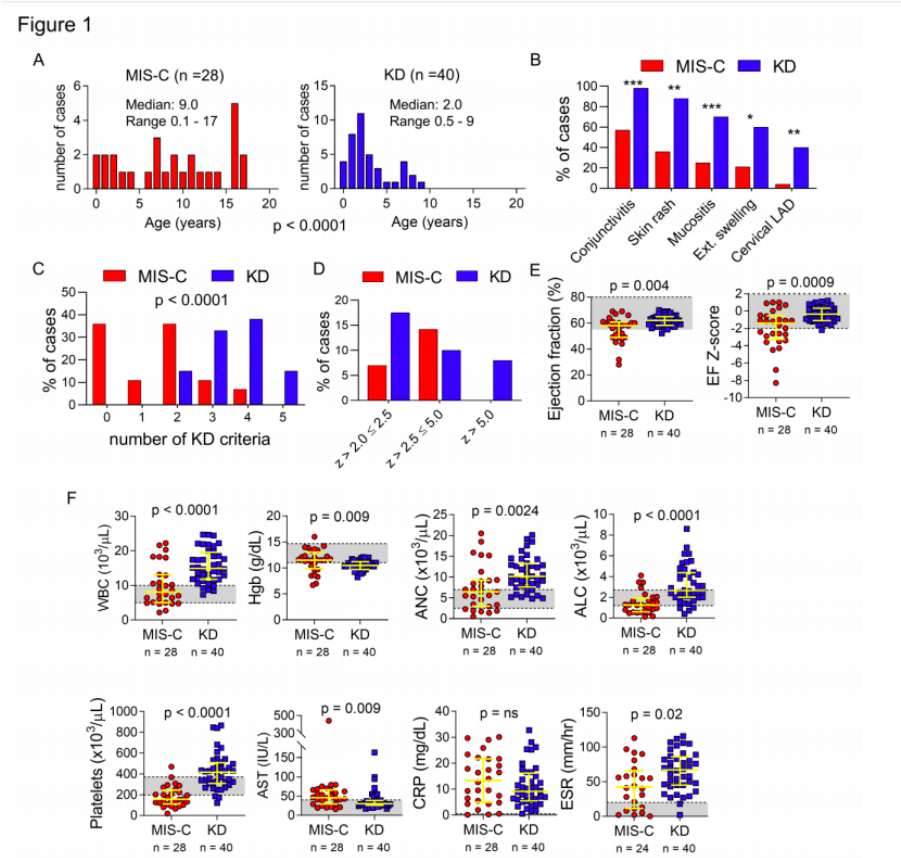


Figure 1: Comparison of clinical features and laboratory parameters in patients with MIS-C (n = 28) versus KD (n = 40). A) Histogram display of age range of MIS-C and KD patients. Comparisons of B) prevalence of individual KD features (* $p < 0.01$; ** $p < 0.001$; *** $p < 0.0001$, Fisher's exact test), C) the number of KD diagnostic feature ($p < 0.0001$, Chi-square test), D) prevalence of coronary abnormalities ($p > 0.05$, Chi-square test), and E) ejection fraction as an index of left ventricular function (by percentage and by z score) in MIS-C and KD groups. F) Comparison of key laboratory parameters including white blood cell count (WBC), hemoglobin, absolute neutrophil count (ANC), absolute lymphocyte count (ALC), platelet count, aspartate transaminase (AST), erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Median with interquartile range and p value by Mann-Whitney U test are displayed for each plot. Gray shades indicate the normal range for laboratory parameters.

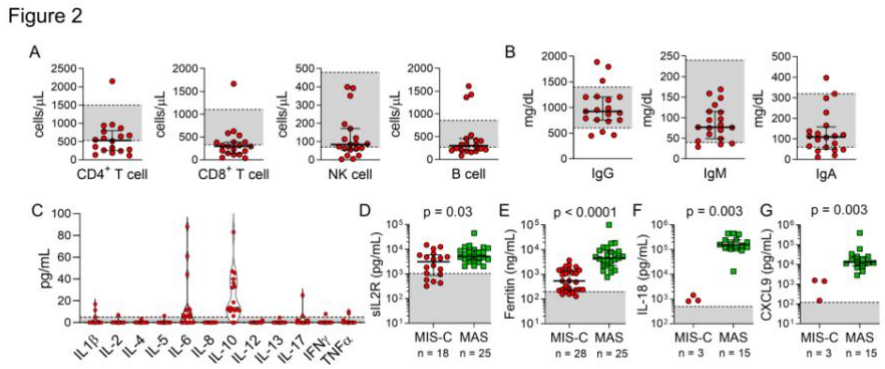


Figure 2: Immunologic profile of MIS-C patients and comparison with MAS. A) Quantitation of lymphocyte populations, B) baseline immunoglobulin levels, C) serum cytokine levels in MIS-C patients (n = 15 to 22 for each panel). D-G) Comparison of D) soluble IL2 receptor levels, E) ferritin, F) IL-18 and G) CXCL9 levels in MIS-C with a cohort of patients with MAS associated with sJIA or infection. Median with interquartile range and p value by Mann-Whitney U are displayed for each plot. Gray shades indicate the normal range for laboratory parameters.

ASSOCIATION BETWEEN MARKERS OF IMMUNE RESPONSE AT HOSPITAL ADMISSION AND COVID-19 DISEASE SEVERITY AND MORTALITY: A META-ANALYSIS AND META-REGRESSION

Khinda J, Janjua NZ, Cheng S, van den Heuvel ER, Bhatti P, Darvishian M.. J Med Virol. 2020 Aug 10. doi: 10.1002/jmv.26411. Online ahead of print.
Level of Evidence: 1 - Systematic review of cross sectional studies with consistently applied reference standard and blinding

BLUF

A systematic review and meta analysis conducted by researchers in Canada of 64 case series (Figure 1) published between December 1, 2019 and May 1, 2020 found significant differences in laboratory values between patients with severe and non-severe COVID-19, and fatal and non-fatal COVID-19 (details summarized below). The results suggest that overactive inflammation, blunted adaptive immunity, and intravascular coagulation are associated with increased severity and mortality of COVID-19.

SUMMARY

Meta-analysis of laboratory results and disease severity found:
- weighted mean difference (WMD) of white blood cells (WBC) was 1.23x10^9 (0.85,1.60) cells/L.
- WMD of absolute neutrophil count (ANC) was 1.49x10^9 (0.96, 2.01) cells/L.
- WMD of absolute lymphocyte count (ALC) was -0.30x10^9 (-0.37,-0.24) cells/L.
- WMD of platelet count (PLT) was -16.69x10^9 (-35.35, 1.96) cells/L.
- WMD of ferritin was 423.13 (281.41, 582.85) ng/mL.
- IL-6 and IL-10 showed significant associations with disease severity.
- WMD of lactate dehydrogenase (LDH) was 120.31 (93.50, 147.12) U/L.
- WMD of creatine kinase (CK) was 45.33 (18.60, 72.07) U/L
- WMD of high sensitivity troponin I (hsTropI) was 11.07 (3.64, 18.50) pg/mL.

Meta-analysis of laboratory results and disease mortality found:
- WMD of WBC was 3.49x10^9 (2.71, 4.27) cells/L.
- WMD of ANC was 3.82x10^9 (2.76, 4.87) cells/L.
- WMD of PLT was -43.41x10^9 (-54.55, -32.27) cells/L.
- WMD of ALC was -0.34x10^9 (-0.45, -0.23) cells/L.
- WMD of ferritin was 814.14 (551.58, 1076.81) ng/mL.
- C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), IL-6, IL-10, and procalcitonin (PCT) were positively associated with mortality.
- WMD of D-dimer was 5.74 (3.91, 7.58) mg/L.
- WMD of LDH was 232.41 (178.31, 286.52) U/L.
- WMD of CK was 97.18 (60.01, 134.25) U/L.
- WMD of hsTropI was 90.47 (47.79, 133.14) pg/mL.

ABSTRACT

To determine the utility of admission laboratory markers in the assessment and prognostication of COVID-19, a systematic review and meta-analysis was conducted on the association between admission laboratory values in hospitalized COVID-19 patients and subsequent disease severity and mortality. Searches were conducted in MEDLINE, Pubmed, Embase, and the WHO Global Research Database from Dec 1, 2019 to May 1, 2020 for relevant articles. A random effects meta-analysis was used to calculate the weighted mean difference (WMD) and 95% confidence interval (95% CI) for each of 27 laboratory markers. The impact of age and sex on WMDs was estimated using meta-regression techniques for 11 markers. In total, 64 studies met inclusion criteria. The most marked WMDs were for neutrophils (ANC) at 3.82x109 /L (2.76, 4.87), lymphocytes (ALC) at -0.34x109 /L (-0.45, -0.23), interleukin-6 (IL-6) at 32.59pg/mL (23.99, 41.19), ferritin at 814.14ng/mL (551.48, 1076.81), C-reactive protein (CRP) at 66.11mg/L (52.16, 80.06), Ddimer at 5.74mg/L (3.91, 7.58), LDH at 232.41U/L (178.31, 286.52), and high sensitivity troponin I at 90.47pg/mL (47.79, 133.14) when comparing fatal to non-fatal cases. Similar trends were observed comparing severe to non-severe groups. There were no statistically significant associations between age or sex and WMD for any of the markers included in the meta-regression. The results highlight that hyperinflammation, blunted adaptive immune response, and intravascular coagulation play key roles in the pathogenesis of COVID-19. Markers of these

processes are good candidates to identify patients for early intervention and, importantly, are likely reliable regardless of age or sex in adult patients.

FIGURES

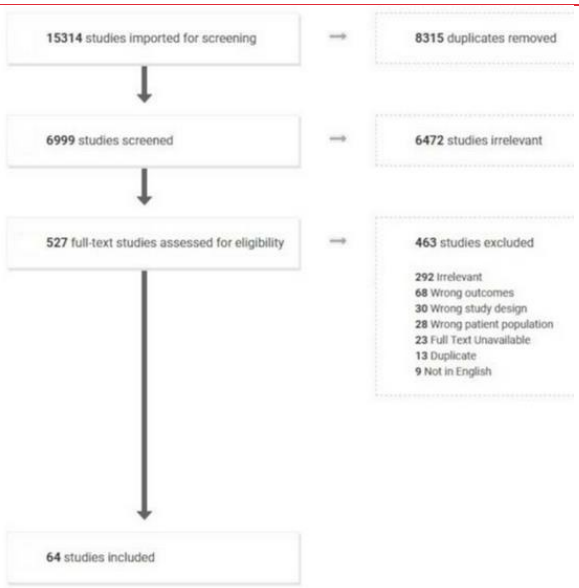


Figure 1. PRISMA flow diagram outlining study selection.

IN ANIMAL MODELS

CORONAVIRUS IN CAT FLEA: FINDINGS AND QUESTIONS REGARDING COVID-19

Villar M, Fernández de Mera IG, Artigas-Jerónimo S, Contreras M, Gortázar C, de la Fuente J.. Parasit Vectors. 2020 Aug 10;13(1):409. doi: 10.1186/s13071-020-04292-y.
Level of Evidence: Other - Mechanism-based reasoning

BLUF

This letter to the editor, written by experts from Spain, outlines a proteomics analysis investigating the presence of coronaviruses and SARS-CoV-2 in domestic cat fleas (Figure 1). Based on the preliminary results, the authors recommend preventing against flea infestation in cats as a prophylactic measure against possible COVID-19 transmission from fleas to humans. The authors call for future studies to investigate COVID-19 transmission via intermediate animal hosts and arthropod vectors.

SUMMARY

The results and limitations of this study are summarized below:
- Real-time RT-PCR analysis of coronavirus ORF1b showed positive results in laboratory-reared unfed fleas as well as fleas obtained from a feral cat.
- All three SARS-CoV-2 specific RT-PCRs were negative, suggesting that the coronavirus found in the fleas was not SARS-CoV-2 (Table 1).
- The authors believe SARS-CoV-2 was not found in the fleas possibly because only two feral cats were included in this study and the remaining samples from laboratory-reared cat flea were processed in 2016.
- To further explore the possibility of coronavirus infection and replication in fleas, angiotensin-converting enzyme (ACE) receptor was identified in the exoproteome of fleas with high sequence homology to a fruit fly ACE (Figure 3). The authors highlight that these findings suggest a possibility of interaction between SARS-CoV and cat flea ACE.

ABSTRACT

The coronavirus disease 19 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has affected millions of people worldwide. Recent evidence raised the question about the possibility that cats may be a domestic host for SARS-CoV-2 with unknown implications in disease dissemination. Based on the fact that the domestic cat

flea, Ctenocephalides felis, are abundant ectoparasites infesting humans, companion animals and wildlife and that coronavirus-like agents have been identified in the ectoparasite tick vector, Ixodes uriae of seabirds, herein we considered the presence of coronaviruses in general and SARS-CoV-2 in particular in C. felis. We identified coronavirus-derived and cell receptor angiotensin-converting enzyme RNA/proteins in C. felis. Although current evidence suggests that pets are probably dead-end-hosts with small risk of transmission to humans, our results suggested that cat flea may act as biological and/or mechanical vectors of SARS-CoV. Although preliminary, these results indicate a possibility of ectoparasites acting as reservoirs and vectors of SARS-CoV and related beta-coronavirus although with little disease risk due to systemic transmission route, low viremia, virus attenuation or other unknown factors. These results support the need to further study the role of animal SARS-CoV-2 hosts and their ectoparasite vectors in COVID-19 disease spread.

FIGURES

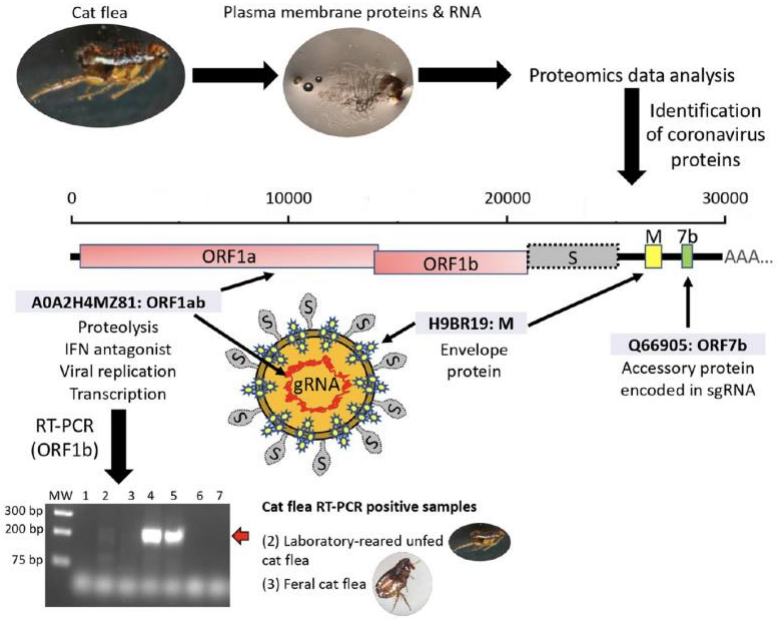


Fig. 1 Experimental design and identification of coronavirus-derived RNA and proteins in cat flea. Representative images of a laboratory-reared domestic cat flea and tissues used for extraction of RNA and plasma membrane proteins for RT-PCR and proteomics analysis. Schematic representation of the coronavirus genome organization and virion structure based on SARS-CoV-2. Coronavirus proteins identified by proteomics analysis included ORF1a, ORF1b, protein M and protein 7b. Genomic RNA (gRNA) serves as mRNA for ORF1a and ORF1b. Other major subgenomic RNAs (sgRNAs) are produced to encode for envelope (e.g. protein M) and accessory (e.g. protein 7b) proteins in addition to the gRNA. Real-time RT-PCR targeting ORF1b identified in coronavirus-derived RNA in laboratory-reared unfed cat flea (sample 2) and feral cat flea (sample 3). MW, molecular weight O'GeneRuler 1 kb Plus DNA Ladder (Thermo Fisher Scientific); sample 1, laboratory-reared unfed cat flea, samples 4 and 5, positive controls; samples 6 and 7, nuclease-free water negative controls.

RT-PCR target	Primers: 5'–3' sequences (amplicon size)	Results (flea sample: Ct)
Coronavirus generic group ORF1b	11-FW: TGATGATGSNGTTGTNTGYTAYAA 13-RV: GCATWGTRTGYTGNGARCARAATTC (179 bp)	Fed: na Unfed: 35.24 Feral cat 1: 36.16 Feral cat 2: na
SARS-CoV-2, RdRp-IP2	nCoV_IP2-12669Fw: ATGAGCTTAGTCCTGTTG nCoV_IP2-12759Rv: CTCCCTTTGTTGTGTTGT nCoV_IP2-12696b: AGATGTCTTGTGCTGCCGGTA [5']Flex [3']BHQ-1 (108 bp)	Fed: na Unfed: na Feral cat 1: na Feral cat 2: na
SARS-CoV-2, RdRp-IP4	nCoV_IP4-14059Fw: GGTAACTGGTATGATTTCG nCoV_IP4-14146Rv: CTGGTCAAGGTTAATATAGG nCoV_IP4-14084: TCATACAAACCACGCCAGG [5']Fam [3']BHQ-1 (107 bp)	Fed: na Unfed: na Feral cat 1: na Feral cat 2: na
SARS-CoV-2, E-gene	E_Sarbeco_F1: ACAGGTACGTTAATAGTTAATAGCGT E_Sarbeco_R2: ATATTGCAGCAGTACGCACACA E_Sarbeco_P1: ACACTAGCCATCCTTACTGCGCTTCG [5']Fam [3']BHQ-1 (125 bp)	Fed: na Unfed: na Feral cat 1: na Feral cat 2: na

Table 1. RT-PCR targets, oligonucleotide primers, and results.

Notes: RNA samples were extracted using the AllPrep DNA/RNA/Protein Mini Kit (Qiagen, Valencia, CA, USA) from midguts dissected from laboratory-reared unfed and fed cat fleas and from the pools of fleas collected from feral cats. A SYBR green One-Step real-time RT-PCR assay (BioRad, Hercules, CA, USA) targeting the ORF1b was used for generic detection of coronaviruses. Three SARS-CoV-2-specific RT-PCRs targeting the envelop protein E-coding gene and two targets (IP2 and IP4) of RNA-dependent RNA polymerase gene (RdRp) were conducted using the SuperScript III Platinum One-Step qRT-PCR kit (Thermo Fisher Scientific). The protocols used for RT-PCR are included in the WHO guidelines (https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/laboratory-guidance). The positive controls included a positive sample loaned from the University Hospital of Ciudad Real, Spain and an in vitro

transcribed RNA derived from the strain BetaCoV_Wuhan_WIV04_2019 (EPI_ISL_402124) loaned by the Pasteur Institute, Paris, France. Real-time RT-PCR was carried out using the CFX96 Touch Real-Time PCR Detection System Thermal Cycler (BioRad, Hercules, CA, USA). Flea samples: Fed and Unfed, laboratory-reared cat flea; Feral cat, pool of feral cat fleas
Abbreviations: na, not amplified; Ct, cycle threshold

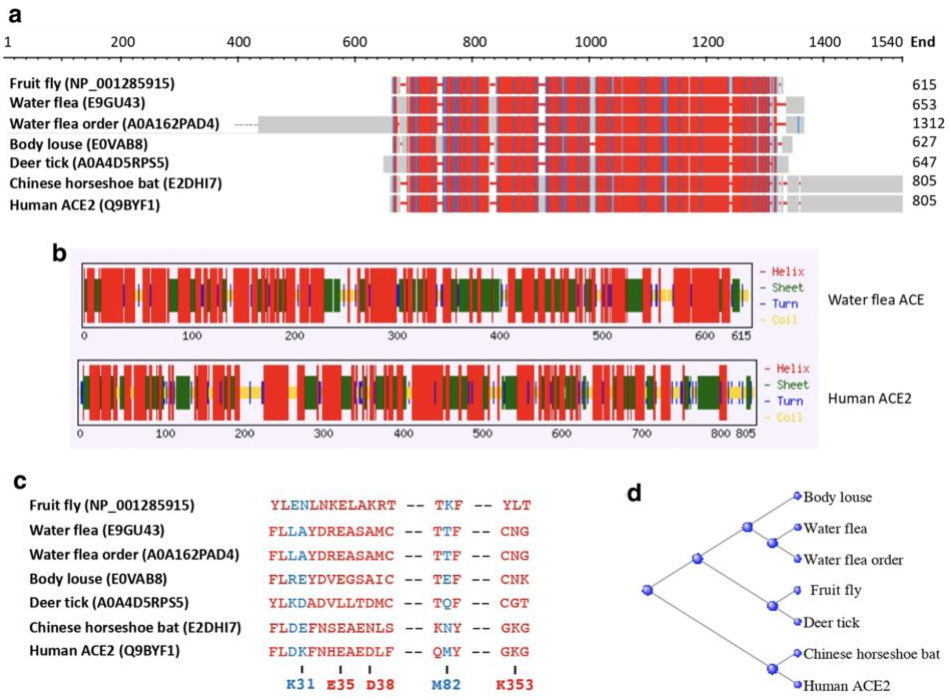


Figure 3. Evolutionary conservation of SARS-CoV receptor ACE protein. a Amino acid sequence alignment (Blast E-value = 0.003, max cluster distance = 0.4) was performed with COBALT (https ://www.ncbi.nlm.nih.gov/tools /cobal t/cobal t.cgi?LINK_LOC=Blast HomeL ink) using protein sequences for ACE in fruit fly (Drosophila melanogaster; Uniprot ID: NP_001285915), water flea (Daphnia pulex; E9GU43), water flea order (D. pulex; A0A162PAD4), body louse (Pediculus humanus corporis; E0VAB8), deer tick (Ixodes scapularis; A0A4D5RPS5), Chinese horseshoe bat (Rhinolophus sinicus; E2DHI7) and human ACE2 (Homo sapiens; Q9BYF1). Conserved regions are highlighted in red. b Prediction of fruit fly ACE and human ACE2 proteins secondary structure using CFSSP: Chou & Fasman Secondary Structure Prediction Server (http://www.bioge m.org/tool/chou-fasma n/index .php). c Amino acids K31, E35, D38, M82 and K353 identified as involved in the interface between SARS-CoV and human ACE2. d Slanted cladogram of ACE protein sequences using the Neighbor joining algorithm (max seq difference = 0.85, distance = Grishin protein) at NCBI tree viewer (https://www.ncbi.nlm.nih.gov/tools /treeviewer/)

ASSOCIATION OF FRAILTY WITH MORTALITY IN OLDER INPATIENTS WITH COVID-19: A COHORT STUDY

Aw D, Woodrow L, Ogliari G, Harwood R.. Age Ageing. 2020 Aug 10:afaa184. doi: 10.1093/ageing/afaa184. Online ahead of print.

Level of Evidence: 3 - Cohort study or control arm of randomized trial

BLUF

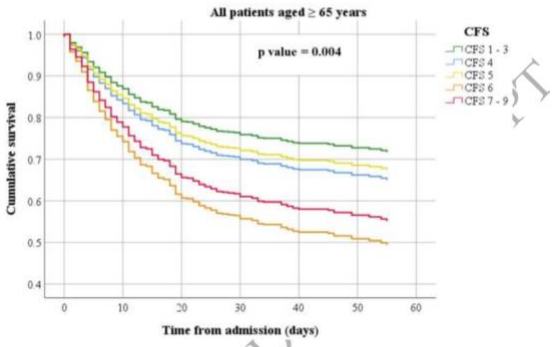
Authors affiliated with Nottingham University Hospitals NHS Trust conducted a cohort study examining the relationship between frailty and all-cause mortality in elderly COVID-19 patients (65+; n=677) admitted between March 1 to April 30th, 2020. The researchers found that elderly patients classified as moderately frail (Clinical Frailty Scale (CFS) score of 6) or severely frail/very severely frail/terminally ill (CFS 7-9) had a statistically significant increase in all-cause mortality risk (2.13-fold, p=0.001 and 1.79-fold, p=0.016) compared to the fittest elderly patients (CFS scores 1-3; Figure 1). The researchers propose that their findings could help manage family expectations for patient prognosis.

ABSTRACT

BACKGROUND: COVID-19 has disproportionately affected older people. OBJECTIVE: to investigate whether frailty is associated with all-cause mortality in older hospital inpatients, with COVID-19. DESIGN: cohort study. SETTING: secondary care acute hospital. PARTICIPANTS: six hundred and seventy-seven consecutive inpatients aged 65 years and over. METHODS: Cox proportional hazards models were used to examine the association of frailty with mortality. Frailty was assessed at baseline, according to the Clinical Frailty Scale (CFS), where higher categories indicate worse frailty. Analyses were adjusted for age, sex, deprivation, ethnicity, previous admissions and acute illness severity. RESULTS: six hundred and sixty-four patients were classified according to CFS. Two hundred and seventy-one died, during a mean follow-up of 34.3 days. Worse frailty at baseline was associated with increased mortality risk, even after full adjustment (p = 0.004). Patients with CFS 4 and CFS 5 had non-significant increased mortality risks, compared to those with CFS 1-3. Patients with CFS 6 had a 2.13-fold (95% CI 1.34-3.38) and those with CFS 7-9 had a 1.79-fold (95% CI 1.12-2.88) increased mortality risk, compared to those with CFS 1-3 (p = 0.001 and 0.016, respectively). Older age, male sex and acute illness severity were also associated with increased mortality risk. CONCLUSIONS: frailty is associated with all-cause mortality risk in older inpatients with COVID-19.

FIGURES

Figure 1. All-cause mortality by frailty in patients aged 65 years and older



This Figure presents the survival curves for 664 patients aged 65 years and older with known Clinical Frailty Scale (CFS) category. The p value is for the association between CFS category and all-cause mortality, after full adjustment for age, sex, ethnicity, IMD quintile, NEWS-2 score on admission and previous admissions in 2019 (Cox regression). Number of patients in each CFS category: CFS 1-3, n = 97; CFS 4, n = 96; CFS 5, n = 101; CFS 6, n = 203; CFS 7 – 9, n = 166. Number of patients who died during follow-up in each CFS category: CFS 1-3, n = 26; CFS 4, n = 30; CFS 5, n = 31; CFS 6, n = 102; CFS 7 – 9, n = 81. One patient with CFS4, who died during follow-up, was excluded from the analysis for missing NEWS 2 score on admission. Abbreviation: CFS: Clinical Frailty Scale, IMD: Index of Multiple deprivation, NEWS-2 score: National Early Warning score.

Figure 1. All-cause mortality by frailty in patients aged 65 years and older. This Figure presents the survival curves for 664 patients aged 65 years and older with known
Clinical Frailty Scale (CFS) category. The p value is for the association between CFS category and all-cause mortality, after full adjustment for age, sex, ethnicity, IMD quintile, NEWS-2 score on admission and previous admissions in 2019 (Cox regression). Number of patients in each CFS category: CFS 1-3, n = 97; CFS 4, n = 96; CFS 5, n = 101; CFS 6, n = 203; CFS 7 – 9, n= 166. Number of patients who died during follow-up in each CFS category: CFS 1-3, n = 26;CFS 4, n = 30; CFS 5, n = 31; CFS 6, n = 102; CFS 7 – 9, n = 81. One patient with CFS4, who died during follow-up, was excluded from the analysis for missing NEWS 2 score on admission. Abbreviation: CFS: Clinical Frailty Scale, IMD: Index of Multiple deprivation, NEWS-2 score: National Early Warning score.

FUNCTIONAL AND COGNITIVE OUTCOMES AFTER COVID-19 DELIRIUM

Mcloughlin BC, Miles A, Webb TE, Knopp P, Eyres C, Fabbri A, Humphries F, Davis D.. Eur Geriatr Med. 2020 Jul 14. doi: 10.1007/s41999-020-00353-8. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

This point prevalence study at the University of College London found that 31 out of 71 COVID-19 patients had delirium, of which only 12 were identified by healthcare staff. At 4-week follow-up, mean cognitive scores were similar in patients with and without delirium, and physical function had worsened significantly in those with delirium (p = 0.01) (Figure 2). Delirium was not associated with increased mortality despite the death of 20 patients at follow-up. The authors conclude that COVID-19-related delirium is associated with poor functional outcomes and requires increased vigilance both in-hospital and at follow-up care for increased detection and management.

ABSTRACT

PURPOSE: To ascertain delirium prevalence and outcomes in COVID-19. METHODS: We conducted a point-prevalence study in a cohort of COVID-19 inpatients at University College Hospital. Delirium was defined by DSM-IV criteria. The primary outcome was all-cause mortality at 4 weeks; secondary outcomes were physical and cognitive function. RESULTS: In 71 patients (mean age 61, 75% men), 31 (42%) had delirium, of which only 12 (39%) had been recognised by the clinical team. At 4 weeks, 20 (28%) had died, 26 (36%) were interviewed by telephone and 21 (30%) remained as inpatients. Physical function was substantially worse in people after delirium - 50 out of 166 points (95% CI - 83 to - 17, p = 0.01). Mean cognitive scores at follow-up were similar and delirium was not associated with mortality in this sample. CONCLUSIONS: Our findings indicate that delirium is common, yet under-recognised. Delirium is associated with functional impairments in the medium term.

FIGURES

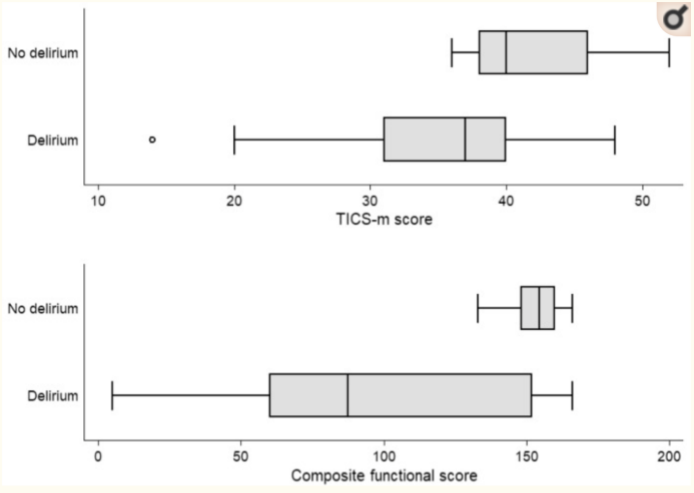


Fig. 2

Cognitive and functional outcomes 4 weeks after delirium ascertainment. TICS-m: modified Telephone Interview for Cognitive Status; Composite functional score formed from Barthel plus Nottingham Extended Activities of Daily Living scale

PROMINENT COAGULATION DISORDER IS CLOSELY RELATED TO INFLAMMATORY RESPONSE AND COULD BE AS A PROGNOSTIC INDICATOR FOR ICU PATIENTS WITH COVID-19

Liu Y, Gao W, Guo W, Guo Y, Shi M, Dong G, Ge Q, Zhu J, Lu J.. J Thromb Thrombolysis. 2020 Aug 6. doi: 10.1007/s11239-020-02174-9. Online ahead of print.
Level of Evidence: 4 - Case-series or case-control studies, or poor quality prognostic cohort study

BLUF

This retrospective study by authors affiliated with Peking University on 147 COVID-19 patients from 3 ICUs in Wuhan, China found that the prothrombin Time (PT), Fibrin/fibrinogen degradation products (FDP), and D-dimer were positively correlated with neutrophil levels, several inflammation markers (cytokines, ferritin, C-reactive protein, etc), LDH, and total bilirubin (Table 2). They also found that increased PT, FDP, and D-dimer were associated with higher in-hospital mortality rates (p less than 0.001; Figure 1, 2) and increased Acute Physiology and Chronic Health Evaluation II (APACHE II), Sepsis-related Organ Failure Assessment (SOFA), and quick SOFA (qSOFA) scores. Based on these findings, coagulation dysfunction may be associated with multiple inflammatory markers, suggesting that coagulation tests (namely, PT, FDP, D-dimer, and antithrombin III) may be useful prognostic indicators for ICU patients with COVID-19.

ABSTRACT

The new outbreak of Coronavirus Disease 2019 (COVID-19) has emerged as a serious global public health concern. A more in-depth study of blood coagulation abnormality is needed. We retrospectively analyzed 147 consecutive patients with COVID-19 who were admitted to three ICUs in Wuhan from February 9th, 2020 to March 20th, 2020. The baseline coagulation and other characteristics were studied. Our results showed that the prolonged PT, FDP, DD were positively correlated with the levels of neutrophils, ferritin, LDH, total bilirubin, multi-inflammation cytokines, and negatively correlated with the lymphocytes level ($p < 0.01$). The level of ATIII was significantly negatively correlated with the levels of neutrophils, ferritin, LDH, total bilirubin, IL2R, IL6 and IL8 ($p < 0.05$). The patients in the ARDS group had a more prominent abnormality in PT, FDP, DD and ATIII, while the patients in the AKI group had more prolonged PT, more severe FDP and DD level, more inferior ATIII and Fib level than those in the non-AKI group ($p < 0.01$). The value of PT, DD and FDP were positively correlated with the classical APACHE II, SOFA and qSOFA scores, while the ATIII was negatively correlated with them ($p < 0.001$). The high levels of PT, FDP and DD were correlated with in-hospital mortality ($p < 0.001$). In conclusion, blood coagulation disorder was prominent in ICU patients with COVID-19 and was correlated with multi-inflammation factors. The abnormality of blood coagulation parameters could be an adverse prognostic indicator for ICU patients with COVID-19.

FIGURES

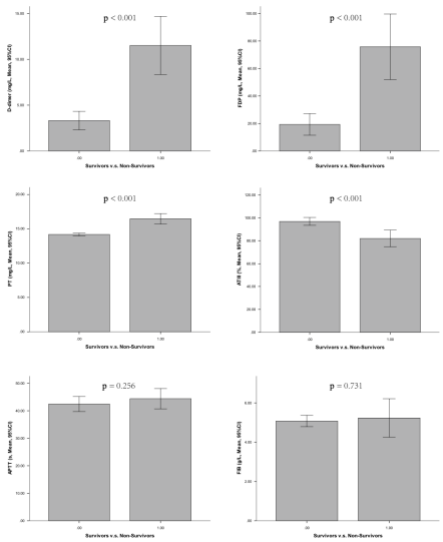


Figure 1. The blood coagulation dysfunction in survivors v.s. non-survivors. PT prothrombin time, APTT activated partial thromboplastin time, Fib fibrinogen, DD dimer, FDP fibrin/fibrinogen degradation products, AT antithrombin.

Table 2 Results of multivariate linear regression analysis for PT

Coefficients	Unstandardized β	SE	Standardized β	t	p
IL2R	0.000	0.000	0.187	1.699	0.092
IL6	− 0.001	0.000	− 0.307	− 2.365	0.020
IL8	0.003	0.001	0.307	2.703	0.008
IL10	0.001	0.006	0.008	0.082	0.935
CRP	0.001	0.002	0.051	0.553	0.581
PCT	0.003	0.011	0.022	0.286	0.776
LDH	0.002	0.001	0.374	3.338	0.001
Ferritin	− 4.24E−5	0.000	− 0.081	− 0.856	0.394
Tbil	0.019	0.013	0.125	1.478	0.142
Neu	0.071	0.031	0.229	2.288	0.024
Lyc	− 0.385	0.254	− 0.115	− 1.515	0.133

PT prothrombin time, *IL* Interleukin, *CPR* C reactive protein, *PCT* procalcitonin, *LDH* lactate dehydrogenase, *Neu* neutrophil, *Lyc* lymphocyte

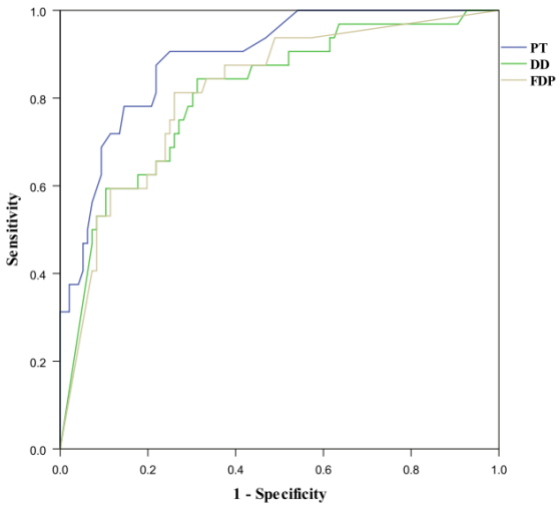


Figure 2. ROC curve for the coagulation parameter in predicting in-hospital mortality. PT prothrombin time, DD dimer, FDP fibrin/fibrinogen degradation products

R&D: DIAGNOSIS & TREATMENTS

INFLIXIMAB AGAINST SEVERE COVID-19-INDUCED CYTOKINE STORM SYNDROME WITH ORGAN FAILURE-A CAUTIONARY CASE SERIES

Stallmach A, Kortgen A, Gonnert F, Coldewey SM, Reuken P, Bauer M.. Crit Care. 2020 Jul 17;24(1):444. doi: 10.1186/s13054-020-03158-0.
Level of Evidence: 4 - Case-series, case-control studies, or historically controlled studies

BLUF

A case series by authors in internal medicine, anesthesiology and intensive care, and sepsis control and care examined 7 COVID-19 patients treated with infliximab found that 6 out of the 7 had a decrease in proinflammatory cytokines and inflammatory markers with clinical improvement in health/mortality (Figure 1) compared to 17 control patients, suggesting that early anti-inflammatory therapy may decrease cytokine storm related organ failure.

FIGURES

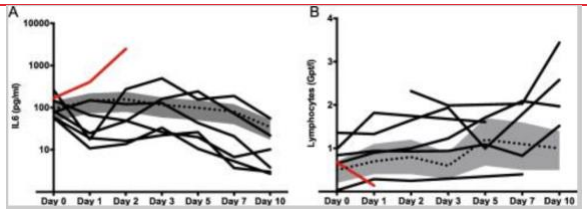


Figure 1: Impact of TNF neutralization by infliximab on the course of IL-6 (a) and lymphocytes (b) in severe COVID-19. Gray bar and dotted lines indicate Q1 and Q3 and median of 15 contemporary control patients, respectively. Solid lines indicate the individual course of seven patients treated with infliximab. Red: course of the non-survivor receiving infliximab

DEVELOPMENTS IN DIAGNOSTICS

PANDEMIC PRINTING: A NOVEL 3D-PRINTED SWAB FOR DETECTING SARS-COV-2

Williams E, Bond K, Isles N, Chong B, Johnson D, Druce J, Hoang T, Ballard SA, Hall V, Muhi S, Buising KL, Lim S, Strugnell D, Catton M, Irving LB, Howden BP, Bert E, Williamson DA.. Med J Aust. 2020 Aug 9. doi: 10.5694/mja2.50726. Online ahead of print.
Level of Evidence: 3 - Non -randomized controlled cohort/follow-up study

BLUF

Researchers from Melbourne, Australia designed a three-dimensional (3D) printed nasal swab (Box 1) for collection of samples for SARS-CoV-2 testing, which showed no differences in the detection of SARS-CoV-2 when compared to two existing types of nasal swabs used in Australia (Copan ESwab and Kang Jian swab) (Table 1, Figure 1). Fifty-two participants were tested using the 3D-printed swab and Copan ESwab, of which 67% preferred the 3D printed swab over Copan ESwab and 15% had no preference. The authors propose 3D printing to be an effective and scalable method to ensure availability of testing supplies in light of recent shortages with mass testing in many countries.

ABSTRACT

OBJECTIVES: To design and evaluate 3D-printed nasal swabs for collection of samples for SARS-CoV-2 testing. DESIGN: An iterative design process was employed. Laboratory evaluation included in vitro assessment of mock nasopharyngeal samples spiked with two different concentrations of gamma-irradiated SARS-CoV-2. A prospective clinical study compared SARS-CoV-2 and human cellular material recovery by 3D-printed swabs and standard nasopharyngeal swabs. SETTING, PARTICIPANTS: Royal Melbourne Hospital, May 2020. Participants in the clinical evaluation were 50 hospital staff members attending a COVID-19 screening clinic and two inpatients with laboratory-confirmed COVID-19. INTERVENTION: In the clinical evaluation, a flocked nasopharyngeal swab sample was collected with the Copan ESwab and a mid-nasal sample from the other nostril was collected with the 3D-printed swab. RESULTS: In the laboratory evaluation, qualitative agreement with regard to SARS-

CoV-2 detection in mock samples collected with 3D-printed swabs and two standard swabs was complete. In the clinical evaluation, qualitative agreement with regard to RNase P detection (a surrogate measure of adequate collection of human cellular material) in samples collected from 50 hospital staff members with standard and 3D-printed swabs was complete. Qualitative agreement with regard to SARS-CoV-2 detection in three pairs of 3D-printed mid-nasal and standard swab samples from two inpatients with laboratory-confirmed SARS-CoV-2 was also complete. CONCLUSIONS: Using 3D-printed swabs to collect nasal samples for SARS-CoV-2 testing is feasible, acceptable to patients and health carers, and convenient.

FIGURES

Box 1. Design G 3D-printed swab. A. Side profile. B. Flexibility of upper part of the swab shaft. C. Breakpoint of swab. D. Microscope image of swab head

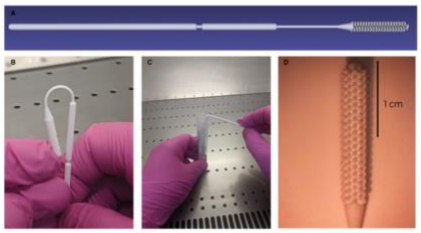
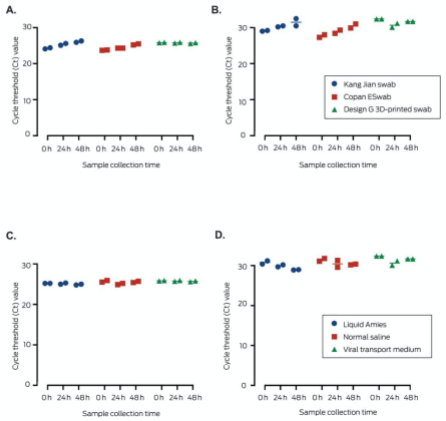


Table 1. ***In vitro*** **validation study: SARS-CoV-2 E gene cycle threshold values for mock nasopharyngeal samples, by swab types and transport medium (two samples for each combination)**

SARS-CoV-2 level	Swab	Medium	Storage temperature	E gene cycle threshold value		
				Day 0	Day 1	Day 2
16 PFU equivalents/mL	Kang Jian	Viral transport medium	4°C	29.0 29.2	30.5 30.2	32.5 30.5
16 PFU equivalents/mL	Copan ESwab	Liquid Amies	4°C	28.0 27.3	29.3 28.4	31.0 29.9
16 PFU equivalents/mL	Design G 3D-printed swab	Liquid Amies	4°C	30.4 31.2	30.2 29.7	28.9 29.0
16 PFU equivalents/mL	Design G 3D-printed swab	Viral transport medium	4°C	32.4 32.4	31.2 30.1	31.7 32.0
16 PFU equivalents/mL	Design G 3D-printed swab	Normal saline	4°C	31.8 31.1	29.6 31.3	30.2 30.4
160 PFU equivalents/mL	Kang Jian	Viral transport medium	4°C	24.4 24.1	25.6 25.1	26.3 25.9
160 PFU equivalents/mL	Copan ESwab	Liquid Amies	4°C	23.7 23.8	24.3 24.3	25.2 25.5
160 PFU equivalents/mL	Design G 3D-printed swab	Liquid Amies	4°C	25.2 25.2	25.0 25.3	25.0 24.8
160 PFU equivalents/mL	Design G 3D-printed swab	Viral transport medium	4°C	25.8 25.9	25.7 25.9	25.6 25.8
160 PFU equivalents/mL	Design G 3D-printed swab	Normal saline	4°C	25.5 25.9	24.9 25.2	25.4 25.7

PFU = plaque-forming units.

Figure 1. Cycle threshold (Ct) values for detecting the SARS-CoV-2 E gene. By swab type: A. Viral concentration, 160 plaque-forming unit (PFU) equivalents/mL; B. Viral concentration, 16 PFU equivalents/mL. Design G 3D-printed swab, by transport medium: C. Viral concentration, 160 PFU equivalents/mL; D. Viral concentration, 16 PFU equivalents/mL



DEFINING COVID-19 AS A DISASTER HELPS GUIDE PUBLIC MENTAL HEALTH POLICY

Alkhayyat A, Pankhania K.. Disaster Med Public Health Prep. 2020 Aug 12:1-4. doi: 10.1017/dmp.2020.301. Online ahead of print.

Level of Evidence: Other - Expert Opinion

BLUF

Authors affiliated with the University of Manchester suggest classifying mental health effects of COVID-19 as a mental health disaster. They discuss the challenges of addressing this disaster, including the lack of prior response templates and difficulties in implementing mental health aid globally via telemedicine, and note that disaster mental health frameworks may help to guide the approach to interventions during this time. Additionally, the authors state that more research should be done investigating efficient ways to confront a mental health disaster as well as how intervention, or lack thereof, impacts the percentage of mental health disorders during catastrophic events.

ABSTRACT

The coronavirus-2019 (COVID-19) pandemic continues to be a devastating chapter in history. The consequences of the pandemic unfold daily and they extend beyond physical health. Current research suggests that it is a public mental health crisis. With regards to the physical effects of COVID-19, policy makers have drawn from past experiences, such as the acute respiratory syndrome (SARS) outbreak of 2003, to craft unique responses. A similar approach must be taken to address the mental health effects of the pandemic. Because COVID-19 can fit the definitions of a mental health disaster, it can be addressed using the principles of disaster mental health management. This letter to the editor presents arguments for defining COVID-19 as a mental health disaster, the challenges facing policy makers in addressing it as such, and calls upon researchers to fill this gap in the literature.

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