The Daily COVID-19 Literature Surveillance Summary

June 25, 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

Climate

- A survey of 2,402 adults in the United States found that 79.5% of respondents supported government-issued stay-at-home orders and nonessential business closures and 77.3% reported they were self-isolating at home suggesting that attitudes broadly support COVID-19 public health interventions.
- A review describes how the consideration of many sexual and reproductive healthcare facilities as non-essential during the COVID-19 pandemic has led to decreased accessibility to vital family planning services worldwide, highlighting the recent and expected increase in cases of unsafe abortions and gender-based violence, especially in developing countries.

Epidemiology

- A review of 82 studies found that the most consistent hemocytometric findings in patients admitted for COVID-19 were lymphopenia and an increased neutrophil-lymphocyte ratio – and these findings often intensify with more serious cases.
- A study of data on 1353 COVID-19 positive children found the three most common symptoms in these children were fever (21.7%), cough (15.4%), and abnormal breathing (8.1%) with the most severe manifestations, such as intubation or myocarditis, occurring in less than 0.7% of patients, and 1.9% of patients required ICU care.

Transmission and Prevention

- A report by the Center for Disease Control and Prevention of the COVID-19 outbreak that ocurred on the USS Theodore Roosevelt showed that 60% of respondents exhibited evidence of exposure to SARS-CoV-2 via positive neutralizing antibody assay, ageusia and anosmia were the symptoms most associated with current or previous infection among crew members, and 212 (90.2%) of the 235 respondents that reported a previous positive COVID-19 test via RT-PCR tested positive for neutralizing antibodies.

Management

- Guidelines for managing COVID-19 patients includes:
  - Diagnosis, treatment, and prevention of venous thromboembolic disease
  - Donor and candidate selection for transplants
- Pediatric specialists warn about the potential detrimental effects the COVID-19 pandemic will have on children, given the unprecedented shift to aggressive therapies such as early intubation which are yet to be specifically proven in pediatric patients.

Adjusting Practice During COVID-19

- A retrospective study found that patients with diminished ovarian reserve who delayed in vitro fertilization treatment (to 90 -180 days from their first visit) had similar live birth rates transfer than those that did not suggesting that delaying IVF in these patients does not affect live birth rate. This data can facilitate decision-making concerning treatment delays and disruptions in this population during the COVID-19 pandemic.

R&D: Diagnosis and Treatments

- A meta-analysis of 22 studies assessing the diagnostic efficiency of anti-SARS-CoV-2 IgG and IgM tests found specificities of 99% in both tests and sentisivities of 85% and 74% for IgG and IgM respectively.
- Analysis of SARS-CoV-2 IgM and total antibody levels in 192 patients with severe or mild COVID-19 found no statistically significant differences between mild and severe COVID-19 cases within 6 days of disease onset; however, after day 6, severe cases exhibited higher IgM and a higher overall positivity rate for total antibody titers than that of mild cases. Further, 12/35 mild cases never exhibited IgM positivity and 5/35 remained negative for total antibody titers highlighting the possible limitations in antibody testing of patients with mild COVID-19

TABLE OF CONTENTS

CLIMATE

PUBLIC ATTITUDES, BEHAVIORS, AND BELIEFS RELATED TO COVID-19, STAY-AT-HOME ORDERS, NONESSENTIAL BUSINESS CLOSURES, AND PUBLIC HEALTH GUIDANCE - UNITED STATES, NEW YORK CITY, AND LOS ANGELES, MAY 5-12, 2020

32555138. Public Attitudes, Behaviors, and Beliefs Related to COVID-19, Stay-at-Home Orders, Nonessential Business Closures, and Public Health Guidance - United States, New York City, and Los Angeles, May 5-12, 2020
Level of Evidence: 1 - Local and current random sample surveys (or censuses)

BLUF

A group of international researchers conducted a panel survey of 2,402 adults (aged ≥ 18 years) in New York City (NYC), Los Angeles (LA), and broadly across the United States to analyze public attitudes, behaviors, and beliefs related to nationwide COVID-19 public health orders. They found that 79.5% of respondents in the US cohort supported government-issued stay-at-home orders and nonessential business closures (86.7% in NYC cohort and 81.5% in LA cohort) and 77.3% of the US cohort reported they were self-isolating at home (84.6% in NYC cohort and 83.0% in LA cohort, see Table 2). The authors suggest that attitudes broadly support COVID-19 public health interventions and emphasize continued assessment of public priorities to educate mitigation strategies, normalizing safe practices, and future planning if subsequent outbreak waves were to occur.

SUMMARY

They reported the following additional data from survey respondents:

- Out of approximately 90% of respondents who reported being in public, 74.1% always or often wore cloth face coverings (89.6% in NYC and 89.8% in LA)
- 16.8% knew someone who had positive test results for COVID-19 (42.0% in NYC and 10.8% in LA)
- 5.9% knew someone who had died from COVID-19 (23.1% in NYC and 7.3% in LA)
- 67.3% agreed that nonessential workers should stay home (76.6% in NY and 69.1% in LA)
- The majority of respondents agreed with public health guidelines, including recommendations for maintaining 6 feet of distance between persons (>87% in each area) and limiting gatherings to fewer than 10 persons (>82% in each area)
- 66.6% agreed that dining inside restaurants should not be allowed (81.5% in NYC and 71.8% in LA)
- Respondents who reported that they were essential workers (47.2% of employed respondents) were significantly less likely than were nonessential workers to report self-isolating (63.1% versus 80.6%) and more likely than were nonessential workers to report that they would feel safe if COVID-19 community mitigation strategies were lifted (37.7% versus 23.7%).

Limitations of this study include self-reported survey data and selection bias, possibly leading to limited generalizability.

ABSTRACT

SARS-CoV-2, the virus that causes coronavirus disease 2019 (COVID-19), is thought to be transmitted mainly by person-to-person contact (1). Implementation of nationwide public health orders to limit person-to-person interaction and of guidance on personal protective practices can slow transmission (2,3). Such strategies can include stay-at-home orders, business closures, prohibitions against mass gatherings, use of cloth face coverings, and maintenance of a physical distance between persons (2,3). To assess and understand public attitudes, behaviors, and beliefs related to this guidance and COVID-19, representative panel surveys were conducted among adults aged >=18 years in New York City (NYC) and Los Angeles, and broadly across the United States during May 5-12, 2020. Most respondents in the three cohorts supported stay-at-home orders and nonessential business closures* (United States, 79.5%; New York City, 86.7%; and Los Angeles, 81.5%), reported always or often wearing cloth face coverings in public areas (United States, 74.1%, New York City, 89.6%; and Los Angeles 89.8%), and believed that their state's restrictions were the right balance or not restrictive enough (United States, 84.3%; New York City, 89.7%; and Los Angeles, 79.7%). Periodic assessments of public attitudes, behaviors, and beliefs can guide evidence-based public health decision-making and related prevention messaging about mitigation strategies needed as the COVID-19 pandemic evolves.

HYGIENIC AND COSMETIC CARE HABITS IN POLISH WOMEN DURING COVID-19 PANDEMIC

Mościcka P, Chróst N, Terlikowski R, Przylipiak M, Wołosik K, Przylipiak A.. J Cosmet Dermatol. 2020 Jun 23. doi: 10.1111/jocd.13539. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

A prospective questionnaire-based study of 140 women conducted at the Medical University of Bialystok in Poland by a multidisciplinary group of researchers found that, compared to pre-pandemic baselines, respondents reported increased hand washing and showering after returning home, using local transportation, before cooking or eating, and after contact with animals ($p<0.01$ for all, Figure 1). Use of cosmetics had also changed, with reported increased use of hand creams but significantly decreased use of face and eye cosmetics, lipsticks, and nail varnishes during the pandemic compared to pre-pandemic norms, with 44% of respondents stating they will not return to previous habits after the pandemic (Figure 3). These data suggest that the instability of the current situation has altered ingrained habits of everyday people, and that customer behavior may be permanently shifted as a result of the COVID-19 pandemic.

ABSTRACT

BACKGROUND: COVID-19 pandemic influences a lot of aspects of human life. Particularly, hygienic habits are affected.
OBJECTIVES: Changes in washing and cosmetic standards during the pandemic toward the past are in the focus of our interest.
MATERIAL AND METHODS: The questionnaire study was conducted anonymously in 140 women. The examination concerned pre- and during-pandemic routine hygiene activities such as hands washing, hair washing, bathing, the use of disinfectants, and use of specific type of cosmetics.
RESULTS AND DISCUSSION: Compared were data before and during pandemic. Responders declared increased handwashing and taking shower after coming back home and after using local city transportation. We found also that increased use of disinfectants during COVID-19 pandemic. In contrary to that, number of people washing their hair decreased slightly. Work documents that profile of used cosmetics was changed; increasing hand cream use and decreasing in makeup cosmetics. Nearly, half of the respondents declare that they will maintain new habits also after the pandemic has ended.

FIGURES

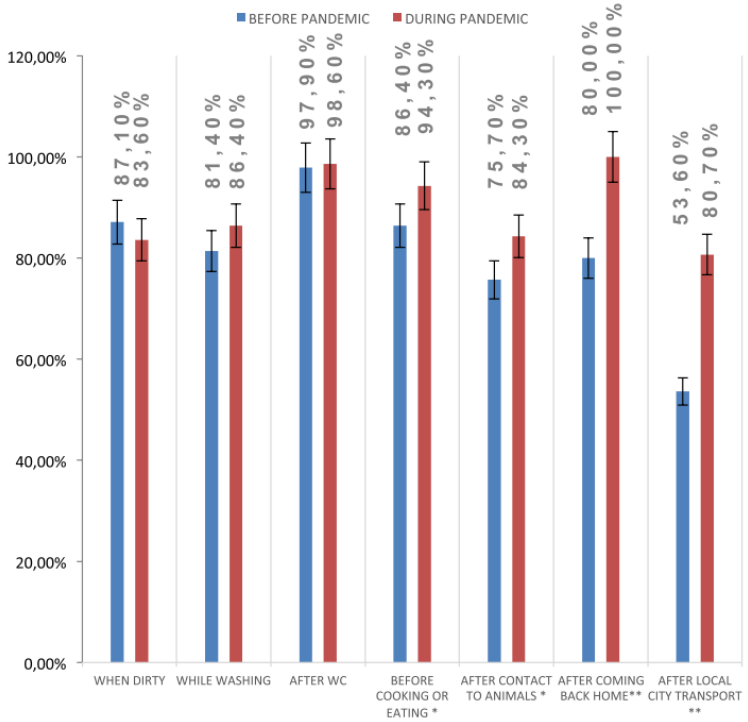

FIGURE 1: Frequency of handwashing before and during an epidemic. Statistic analysis was done comparing "before pandemic" versus "during pandemic." **P < .001; *P < .01

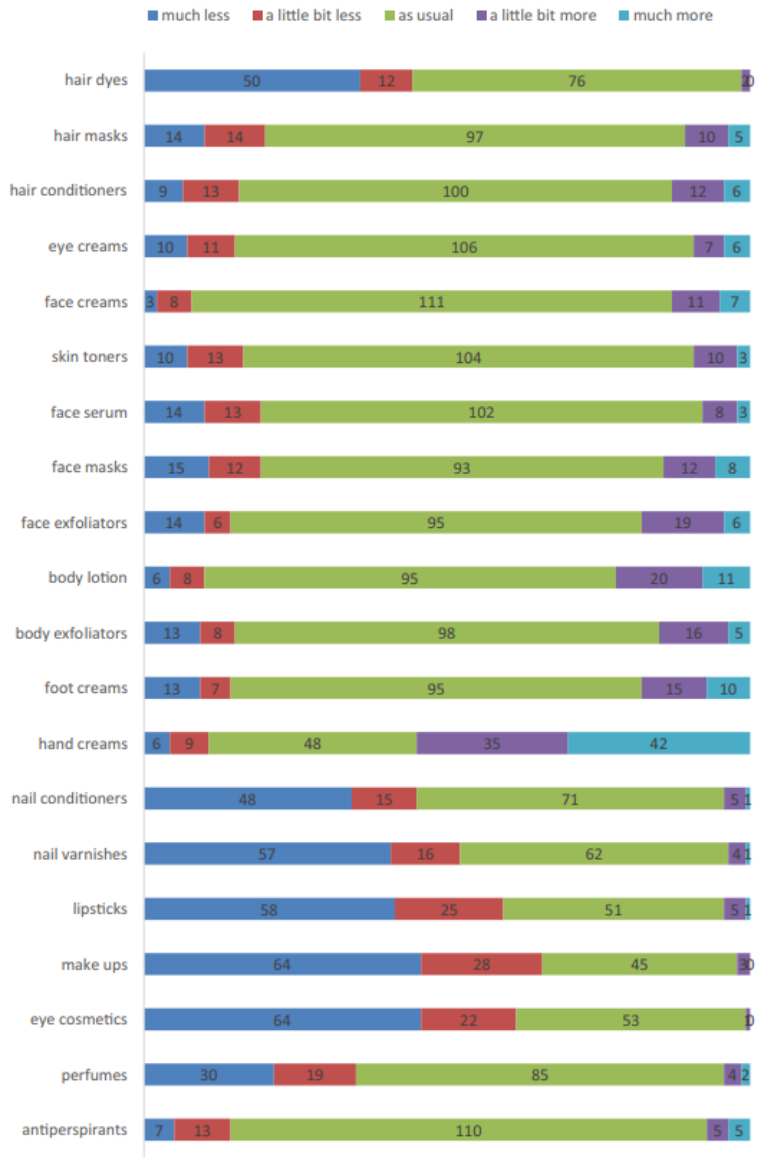

FIGURE 3: Change in the frequency of use of cosmetics during a pandemic compared to the state before

THREE MONTHS OF INFORMATIONAL TRENDS IN COVID-19 ACROSS NEW YORK CITY

Lieberman-Cribbin W, Alpert N, Gonzalez A, Schwartz RM, Taioli E.. J Public Health (Oxf). 2020 Jun 16:fdaa082. doi: 10.1093/pubmed/fdaa082. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

Researchers analyzed calls from New York City to 311, a nonemergency service and information phone line, and Google Trends data on "coronavirus" searches from 22 January to 22 April 2020. There were 50,845 COVID-19-related calls: 25,272 calls (49.7%) were placed to gather information on SARS-CoV-2 and COVID-19; 24,572 (48.3%) inquired about symptoms, testing, and disease prevention; and 951 (1.5%) regarded recent travel to China or the Middle East. Both COVID-19 related calls and internet searches for "coronavirus" increased prior to the number of COVID-19 cases in NYC (Figure 1), emphasizing the need for quick dissemination of accurate information for this and future public health crises.

ABSTRACT

In the midst of widespread community transmission of coronavirus disease 2019 (COVID-19) in New York, residents have sought information about COVID-19. We analyzed trends in New York State (NYS) and New York City (NYC) data to quantify

the extent of COVID-19-related queries. Data on the number of 311 calls in NYC, Google Trend data on the search term 'Coronavirus' and information about trends in COVID-19 cases in NYS and the USA were compiled from multiple sources. There were 1228 994 total calls to 311 between 22 January 2020 and 22 April 2020, with 50 845 calls specific to COVID-19 in the study period. The proportion of 311 calls related to COVID-19 increased over time, while the 'interest over time' of the search term 'Coronavirus' has exponentially increased since the end of February 2020. It is vital that public health officials provide clear and up-to-date information about protective measures and crucial communications to respond to information-seeking behavior across NYC.

FIGURES

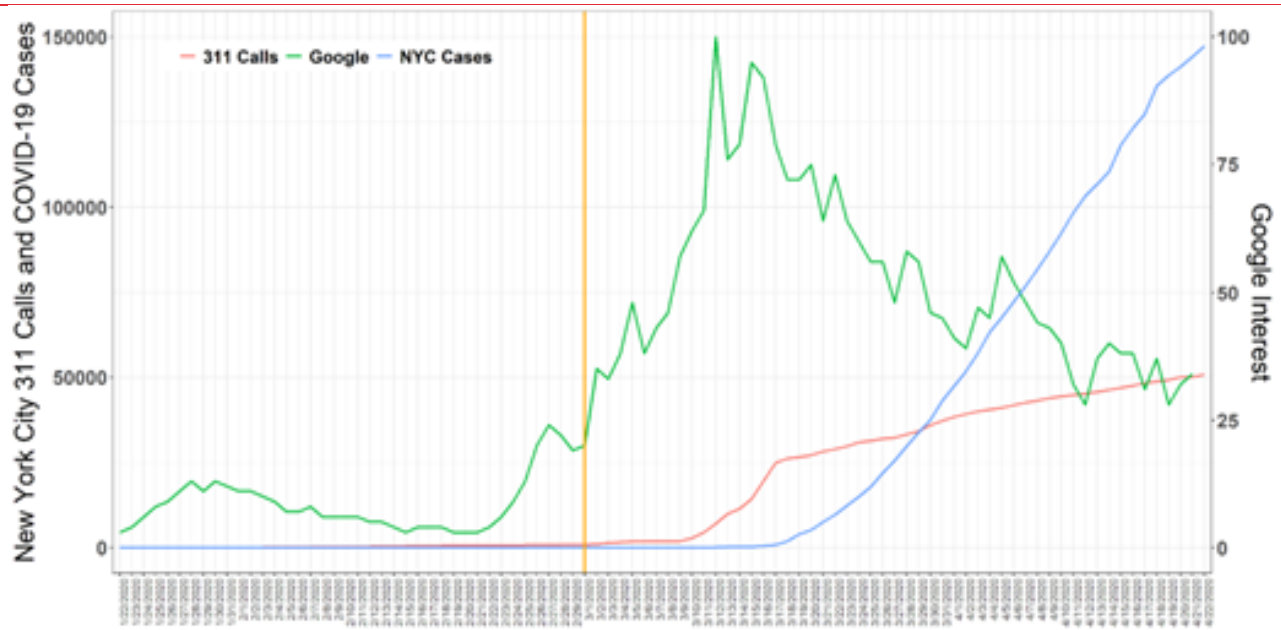

Figure 1: Cumulative frequency of 311 Calls (solid line) and cumulative confirmed cases in NYC (dotted), as well as the interest in 'Coronavirus' according to Google Trends (two-dash). The black vertical line represents when the first case was confirmed in NYS (1 March).

GLOBAL

TOURISM AND COVID-19: IMPACTS AND IMPLICATIONS FOR ADVANCING AND RESETTING INDUSTRY AND RESEARCH

Sigala M.. J Bus Res. 2020 Sep;117:312-321. doi: 10.1016/j.jbusres.2020.06.015. Epub 2020 Jun 12.
Level of Evidence: Other - Expert Opinion

BLUF

An expert from the University of South Australia's Centre for Tourism & Leisure Management explores the effects that COVID-19 has had on the tourism industry and comments on the ways that this pandemic may serve as an opportunity for researchers to question pre-conceived notions about the anthropologic and economic nature of tourism. Ultimately, the author outlines necessary considerations for emerging research within the tourism field in the setting of COVID-19, arguing that future research must focus on the following issues:

- Employees' mental and physical health, engagement, and working conditions
- Overall tourism supply and demand by both academics and industry specialists
- Evolving tourism management, policies, and practices including designing and implementing crisis recovery and response strategies

Research in these areas will better inform policies to prevent further transmission of SARS-CoV-2 and promote more sustainable post-pandemic tourism models.

ABSTRACT

The paper aims to critically review past and emerging literature to help professionals and researchers alike to better understand, manage and valorize both the tourism impacts and transformational affordance of COVID-19. To achieve this, first, the paper discusses why and how the COVID-19 can be a transformational opportunity by discussing the circumstances and the questions raised by the pandemic. By doing this, the paper identifies the fundamental values, institutions and pre-assumptions that the tourism industry and academia should challenge and break through to advance and reset the research and practice frontiers. The paper continues by discussing the major impacts, behaviours and experiences that three major tourism stakeholders (namely tourism demand, supply and destination management organisations and policy makers) are experiencing during three COVID-19 stages (response, recovery and reset). This provides an overview of the type and scale of the COVID-19 tourism impacts and implications for tourism research.

DISPARITIES

HEAT-RELATED DEATHS - UNITED STATES, 2004-2018

32555133. Heat-Related Deaths - United States, 2004-2018
Level of Evidence: 3 - Local non-random sample

BLUF

A Morbidity and Mortality Weekly Report from the CDC analyzing heat-related deaths in the United States from 2004-2018. The total death count reported was 10,527; 70% were male, 39% were over the age of 65, and Indian American/Alaskan Natives had the highest mortality rate, followed by African Americans (0.6 and 0.3 per 100,000, respectively) (Tables 1 and 2). Although it is only briefly discussed, the most relevant recommendation related to COVID-19 is the suggestion that operational cooling centers may need to employ extra precautions during the current pandemic (e.g. social distancing with physical separation when possible if suspicion of infection is high).

ABSTRACT

Deaths attributable to natural heat exposure, although generally considered preventable (1), represent a continuing public health concern in the United States. During 2004-2018, an average of 702 heat-related deaths occurred in the United States annually. To study patterns in heat-related deaths by age group, sex, race/ethnicity, and level of urbanization, and to explore comorbid conditions associated with deaths resulting from heat exposure, CDC analyzed nationally comprehensive mortality data from the National Vital Statistics System (NVSS).* The rate of heat-related mortality tended to be higher among males, persons aged >=65 years, non-Hispanic American Indian/Alaska Natives, and persons living in noncore nonmetropolitan and large central metropolitan counties. Natural heat exposure was a contributing cause of deaths attributed to certain chronic medical conditions and other external causes. Preparedness and response initiatives directed toward extreme heat events, currently underway at local, state, and national levels, can contribute to reducing morbidity and mortality associated with natural heat exposure. Successful public health interventions to mitigate heat-related deaths include conducting outreach to vulnerable communities to increase awareness of heat-related symptoms and provide guidance for staying cool and hydrated, particularly for susceptible groups at risk such as young athletes and persons who are older or socially isolated (2). Improved coordination across various health care sectors could inform local activities to protect health during periods of high heat. For instance, jurisdictions can monitor weather conditions and syndromic surveillance data to guide timing of risk communication and other measures (e.g., developing and implementing heat response plans, facilitating communication and education activities) to prevent heat-related mortality in the United States. CDC also recommends that federal, state, local, and tribal jurisdictions open cooling centers or provide access to public locations with air conditioning for persons in need of a safe, cool, environment during hot weather conditions. In light of the coronavirus disease 2019 (COVID-19) pandemic, CDC updated its guidance on the use of cooling centers to provide best practices (e.g., potential changes to staffing procedures, separate areas for persons with symptoms of COVID-19, and physical distancing) to reduce the risk for introducing and transmitting SARS COV-2, the virus that causes COVID-19, into cooling centers. .

FIGURES

TABLE 1. Number and rate of heat-related deaths, by cause of death category,* age group, and sex — United States, 2004–2018†

Age group (yrs)	Cause of death category, no. (rate)§								
	Heat-related codes as the underlying cause			Heat-related codes as a contributing cause			All heat-related deaths		
	Total	Male	Female	Total	Male	Female	Total	Male	Female
<1	160 (0.3)	76 (0.2)	84 (0.3)	87 (0.1)	43 (0.1)	44 (0.2)	247 (0.4)	119 (0.4)	128 (0.4)
1–4	303 (0.1)	178 (0.1)	125 (0.1)	125 (0.1)	76 (0.1)	49 (0.0)	428 (0.2)	254 (0.2)	174 (0.1)
5–14	56 (0.0)	42 (0.0)	14 (—)¶	17 (—)¶	14 (—)¶	3 (—)¶	73 (0.0)	56 (0.0)	17 (—)¶
15–24	234 (0.0)	203 (0.1)	31 (0.0)	94 (0.0)	77 (0.0)	17 (—)¶	328 (0.0)	280 (0.1)	48 (0.0)
25–34	430 (0.1)	378 (0.1)	52 (0.0)	230 (0.0)	195 (0.1)	35 (0.0)	660 (0.1)	573 (0.2)	87 (0.0)
35–44	670 (0.1)	550 (0.2)	120 (0.0)	352 (0.1)	287 (0.1)	65 (0.0)	1,022 (0.2)	837 (0.3)	185 (0.1)
45–54	1,090 (0.2)	874 (0.3)	216 (0.1)	684 (0.1)	533 (0.2)	151 (0.0)	1,774 (0.3)	1,407 (0.4)	367 (0.1)
55–64	1,024 (0.2)	762 (0.3)	262 (0.1)	895 (0.2)	658 (0.2)	237 (0.1)	1,919 (0.3)	1,420 (0.5	499 (0.2)
65–74	862 (0.2)	562 (0.3)	300 (0.2)	774 (0.2)	534 (0.3)	240 (0.1)	1,636 (0.4)	1,096 (0.7)	540 (0.3)
75–84	778 (0.4)	441 (0.5)	337 (0.3)	657 (0.3)	382 (0.4)	275 (0.2)	1,435 (0.7)	823 (1.0)	612 (0.5)
≥85	562 (0.7)	251 (0.9)	311 (0.5)	386 (0.5)	173 (0.6)	213 (0.4)	948 (1.1)	424 (1.5)	524 (0.9)
Not stated**	51 (N/A)	46 (N/A)	5 (N/A)	6 (N/A)	6 (N/A)	0 (N/A)	57 (N/A)	52 (N/A)	5 (N/A)
All ages	**6,220 (0.1)**	**4,363 (0.2)**	**1,857 (0.1)**	**4,307 (0.1)**	**2,978 (0.1)**	**1,329 (0.1)**	**10,527 (0.2)**	**7,341 (0.3)**	**3,186 (0.1)**

Abbreviation: N/A = not applicable.

* Heat-related deaths are identified using International Classification of Diseases, Tenth Revision cause-of-death codes X30 (exposure to excessive natural heat), P81.0 (environmental hyperthermia of newborn), and T67 (effects of heat and light) listed as the underlying cause or as one of the contributing causes in death records. Records with code W92 (exposure to excessive heat of man-made origin) listed anywhere on the death certificate were excluded from this selection.

† Based on multiple-cause-of-death data from the National Center for Health Statistics (NCHS) Vital Statistics System (https://www.cdc.gov/nchs/nvss/deaths.htm) and NCHS Bridged-Race Population data (https://www.cdc.gov/nchs/nvss/bridged_race.htm). This information is available from https://wonder.cdc.gov.

§ Crude rate per 100,000 population.

¶ Rate estimates based on fewer than 20 deaths were deemed unreliable and not reported.

** Rate estimates were not calculated because a population denominator was unavailable.

TABLE 2. Number and rate of heat-related deaths,* by race/ethnicity and level of urbanization — United States, 2004–2018†

Characteristic	No. of deaths (rate)§
Race/Ethnicity¶	
Hispanic	1,349 (0.2)
American Indian/Alaska Native, non-Hispanic	241 (0.6)
Asian/Pacific Islander, non-Hispanic	194 (0.1)
Black, non-Hispanic	1,965 (0.3)
White, non-Hispanic	6,602 (0.2)
Not stated**	176 (N/A)
Level of urbanization††	
Large central metro	4,402 (0.3)
Large fringe metro	1,607 (0.1)
Medium metro	1,764 (0.2)
Small metro	990 (0.2)
Micropolitan	879 (0.2)
Noncore	885 (0.3)
Total	**10,527 (0.2)**

Abbreviation: N/A = not applicable.

* Heat-related deaths are identified using International Classification of Diseases, Tenth Revision cause-of-death codes X30 (exposure to excessive natural heat), P81.0 (environmental hyperthermia of newborn), and T67 (effects of heat and light) listed as the underlying cause or as one of the contributing causes in death records. Records with code W92 (exposure to excessive heat of man-made origin) listed anywhere on the death certificate were excluded from this selection.

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§ Crude rate per 100,000 population.

¶ American Indian/Alaska Native, Asian/Pacific Islander, black, and white decedents were non-Hispanic; Hispanic decedents could have been of any race.

** Rate estimates were not calculated because a population denominator was unavailable.

†† https://www.cdc.gov/nchs/data/series/sr_02/sr02_166.pdf.

COVID 19 ERA: A BEGINNING OF UPSURGE IN UNWANTED PREGNANCIES, UNMET NEED FOR CONTRACEPTION AND OTHER WOMEN RELATED ISSUES

Kumar N.. Eur J Contracept Reprod Health Care. 2020 Jun 22:1-3. doi: 10.1080/13625187.2020.1777398. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

A review conducted by All India Institute of Medical Sciences describes how the consideration of many sexual and reproductive healthcare facilities as non-essential during the COVID-19 pandemic has led to decreased accessibility to vital family planning services worldwide, highlighting the recent and expected increase in cases of unsafe abortions and gender-based violence, especially in developing countries. Ultimately, the authors argue that sexual and reproductive healthcare must be considered essential during lockdowns in order to address such disparities.

ABSTRACT

The Novel Coronavirus disease that started in Wuhan city of China in December 2019 has emerged as one of the fastest spreading pandemics all over the world affecting millions of people and causing millions of deaths worldwide. In an attempt to control its spread, countries have imposed local and national lockdowns, affecting many healthcare services, especially sexual and reproductive health services which are actually essential and lifesaving. In near future this will result in a large number of grave consequences including increased unmet need for modern contraceptives, unintended pregnancies, increased unsafe abortions, maternal and neonatal deaths and other harmful practices like female genital mutilation and child marriages in developing countries. The present short review focusses on such issues which will be dramatically increased depending on the duration of lockdowns and the time for which the sexual and reproductive health services will remain halted. It also reflects the need for considering reproductive health services as essential, allowing the people to avail these services without any fear and hence, saving many more lives which will be lost not due to coronavirus infection. Methodology: The data was searched from various governmental and non-governmental organisation sites including the World Health Organisation, United Nations, United Nations Population Fund, Guttmacher Institute and many PubMed indexed journals.

ADULTS

A SUMMARY OF THE DIAGNOSTIC AND PROGNOSTIC VALUE OF HEMOCYTOMETRY MARKERS IN COVID-19 PATIENTS

Khartabil TAT, Russcher HH, van der Ven AA, de Rijke YBY.. Crit Rev Clin Lab Sci. 2020 Jun 22:1-17. doi: 10.1080/10408363.2020.1774736. Online ahead of print.
Level of Evidence: 1 - Review / Literature Review

BLUF

A review of 82 papers mostly from China between the publication dates of December 2019 and 20 May 2020 found that the most consistent hemocytometric findings in patients admitted for COVID-19 were lymphopenia and an increased neutrophil-lymphocyte ratio – and these findings often intensify with more serious cases. The authors advise creating risk models, utilizing data mining or machine learning, to enable the prediction of survival rates based on results of hemocytometric tests. This may help clinicians diagnose and predict the severity of the disease in patients.

SUMMARY

A review of 82 papers from various databases including PubMed, MedRxiv, and Embase with publication dates between December 2019 and 20 May 2020 mostly from China but also from Japan, Taiwan, Singapore, Iran, Spain, and Italy found that the most consistent hemocytometric findings in patients admitted for COVID-19 were lymphopenia and an increased neutrophil-lymphocyte ratio – and these findings often intensify with more serious cases. The authors also found various patterns of basophils, eosinophils, platelets, and red blood cells in the setting of COVID-19 and suggest these parameters may be useful for diagnosis or prognosis, with or without other parameters. The authors advise creating risk models, utilizing data mining or machine learning, that will enable the prediction of survival rates based on results of hemocytometric tests. This may help clinicians diagnose and predict the severity of the disease in patients.

ABSTRACT

Many studies have reported hemocytometric changes in COVID-19 infection at admission and during the course of disease, but an overview is lacking. We provide a summary of the literature of hemocytometric changes and evaluate whether these changes may assist clinicians in diagnosing and predicting disease progression of COVID-19. Eighty-three out of 250 articles from December 2019 to 20 May 2020 were included from the databases, PubMed, Web of Science Core Collection, Embase, Cochrane and MedRxiv. Our review of the literature indicates that lymphopenia and an elevated neutrophil/lymphocyte ratio are the most consistent abnormal hemocytometric findings and that these alterations may augment in the course of time, especially in those with severe disease.

HERPES ZOSTER AND SEVERE ACUTE HERPETIC NEURALGIA AS A COMPLICATION OF COVID-19 INFECTION

Shors AR.. JAAD Case Rep. 2020 Jul;6(7):656-657. doi: 10.1016/j.jdcr.2020.05.012. Epub 2020 May 20.
Level of Evidence: 5 - Case report

BLUF

A physician practicing in Montana and Washington State describes a telemedicine case of a 49 year old woman with new onset herpes zoster facial rash (Figure 1 and 2) in a V2 dermatomal distribution in the setting of RT-PCR-confirmed COVID-19 that progressed to severe herpetic neuralgia despite treatment with valacyclovir. The author hypothesizes this is due to varicella reactivation secondary to lymphopenia or an inflammatory response in the dorsal root ganglion. Overall, this case adds to the growing findings of varicella-like skin manifestations in the setting of COVID-19 internationally.

SUMMARY

A physician practicing in Montana and Washington State describes a telemedicine case of a 49 year old woman with new onset herpes zoster facial rash (Figure 1 and 2) in a V2 dermatomal distribution after one week of general malaise, chills, and a headache. She began treatment with valacyclovir at that time. On follow up visit two days later, she had a positive RT-PCR test for COVID-19. After one week of valacyclovir, her rash persisted. After four weeks, she was diagnosed with severe acute herpetic neuralgia that was minimally responsive to gabapentin. The author hypothesizes this is due to varicella reactivation secondary to lymphopenia or SARS-CoV-2-induced inflammatory response in the dorsal root ganglion. Overall, this case adds to the growing findings of varicella-like skin manifestations in the setting of COVID-19 internationally, highlighting the potential for COVID-19 to present with dermatological symptoms.

FIGURES

Figure 1. V2 herpes zoster occurring on day 8 of coronavirus 2019 symptoms.

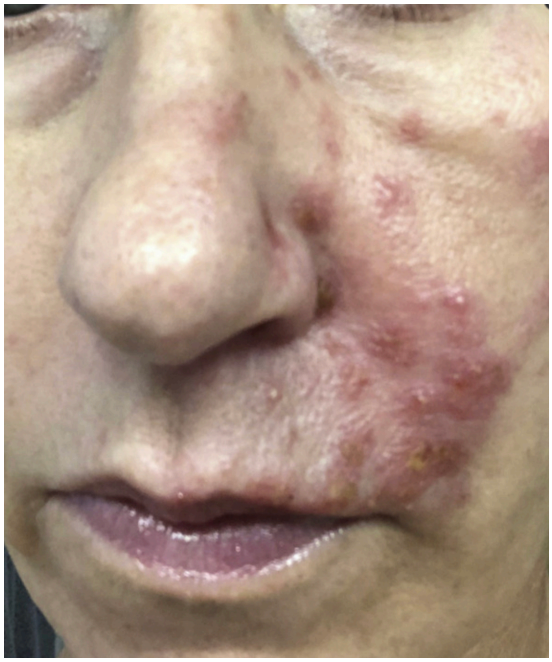


Figure 2. The eruption at 1 week despite prompt intervention with valacyclovir.

PEDIATRICS

COVID-19 MULTISYSTEM INFLAMMATORY SYNDROME IN THREE TEENAGERS WITH CONFIRMED SARS-COV-2 INFECTION

Ng KF, Kothari T, Bandi S, Bird PW, Goyal K, Zoha M, Rai V, Tang JW.. J Med Virol. 2020 Jun 22. doi: 10.1002/jmv.26206. Online ahead of print.
Level of Evidence: 4 - Case-series

BLUF

In this case series, physicians from the United Kingdom present three children diagnosed with Pediatric Multisystem Inflammatory Syndrome (PMIS) secondary to SARS-CoV-2. All three had lab findings of neutrophilia, lymphopenia, and elevated inflammatory markers with findings of myocarditis; all required ICU admission with respiratory support (two required inotropic support) (Figure 2); and all were ultimately discharged with eventual resolution of symptoms. This series contributes to growing evidence that PMIS can cause a severe but varied clinical course after SARS-CoV-2 infection.

ABSTRACT

Coronavirus Disease 2019 (COVID-19) is generally a relatively mild illness in children. An emerging disease entity coined as pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS) has been reported recently, but is very rare and only affects very small minority of children. Here we describe the clinical presentations and outcomes of three teenagers with serologically-confirmed SARS-CoV-2 infection admitted to pediatric intensive care unit for PIMS-TS. Although their initial presentations were very similar, their COVID-19-related disease varied in severity. This article is protected by copyright. All rights reserved.

FIGURES

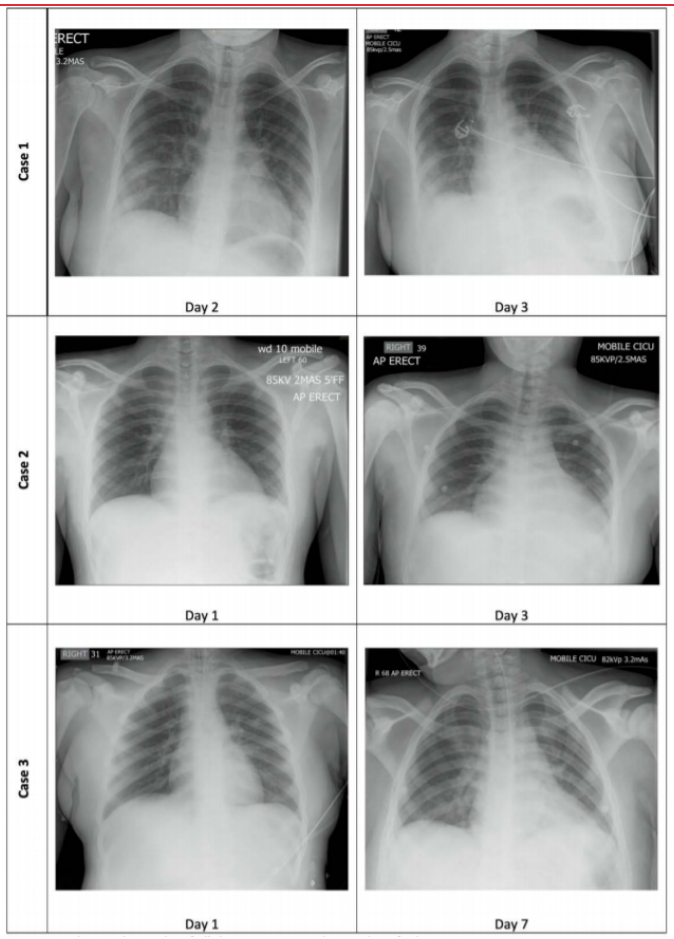


Figure 2. Chest radiographs of all three patients according to day of admission

SPECTRUM OF COVID-19 IN CHILDREN

Ranabothu S, Onteddu S, Nalleballe K, Dandu V, Veerapaneni K, Veerapandiyan A.. Acta Paediatr. 2020 Jun 15. doi: 10.1111/apa.15412. Online ahead of print.
Level of Evidence: 4 - Case-series

BLUF

A study of data obtained from TriNetX, a global EMR aggregation collaborative, on 1353 COVID-19 positive children was conducted by a group of researchers from Arkansas Children's Hospital and the University of Arkansas in order to characterize the spectrum of clinical findings in this patient group. The three most common symptoms in these children were fever (21.7%), cough (15.4%), and abnormal breathing (8.1%). The most severe manifestations, such as intubation or myocarditis, occurred in less than 0.7% of patients, and 1.9% of patients required ICU care (Table 1). This data sheds light on clinical expectations for children with COVID-19 and provides more information by which treatment, control of transmission, and allocation of healthcare allocation may occur.

ABSTRACT

The prevalence of coronavirus disease 2019 (COVID-19) is lower in children compared to adults. Children contribute to 1-5% of all COVID-19 cases (1) . A recent study from China reported that 171(12.3%) of 1391 children with suspected disease had confirmed COVID-19 infection (2) . As of May 15, 2020, there are 33,241 children with COVID-19 in the United States (3) . The most common symptoms in children with confirmed and suspected COVID-19 include fever and cough followed by diarrhea, and abdominal pain.

FIGURES

Charecteristics	N=1353 (100%)
Age distribution- no. (%)	
<1 yr	155(11.4%)
1 to 5 yr	284 (21%)
6 to 10 yr	205(15.2%)
11 to 18 yr	709(52.4%)
Sex - no. (%)	
Female	659(49%)
Male	694(51%)
Race- no. (%)	
White	455(34%)
Black or African American	223(16%)
Asian	29(2%)
Unknown Race	646(48%)
Ethnicity- no. (%)	
Not Hispanic or Latino	297(22%)
Unknown	789(58%)
Hispanic or Latino	267(20%)
Hospital Admission- no. (%)	
Inpatient/Observation	260(19.2%)
Intensive Care Unit (ICU)	26(1.9%)
Symptoms - no. (%)	
Fever	293(21.7%)
Cough	209(15.4%)

Abnormal Breathing	109(8.1%)
Sore throat	58(4.3%)
Abdominal/pelvic pain	56(4.1%)
Headache	54(4.0%)
Nausea/Vomiting	45(3.3%)
Diarrhea	42(3.1%)
Concerning food/fluid intake	36(2.7%)
Rash and other skin eruptions	36(2.7%)
Malaise/Fatigue	33(2.4%)
Loss of smell/taste	28(2.1%)
Myalgias	22(1.6%)
Emotional disturbances	19(1.4%)
Nasal congestion	15(1.1%)
Convulsions	≤10 (≤0.7%)
Dizziness	≤10 (≤0.7%)
Non specific symptoms of Infanc	≤10 (≤6.5% of Infants)
Organ System Involvement- no. (%)	
Respiratory sytem	400(29.6%)
Acute upper respiratory infecti	150(11.1%)
Intubation	≤10 (≤0.7%)
Endocrine/Nutritional/Metabolic	116(8.6%)
Disorders of Blood & Immune sy:	103(7.6%)
Circulatory system	87(6.4%)
Myocarditis	≤10 (≤0.7%)
Digestive system	83(6.1%)
Musculo-skeletal/Connective Tiss	82(6.1%)
Kawasaki Disease	16(1.2%)
Toxic shock syndrome	0 (0%)
Mental/Behavioral Disorders	65(4.8%)
Anxiety Disorders	19(1.4%)
Mood Disorders	22(1.6%)
Nervous system	62(4.6%)
Sleep Disorders	16(1.2%)
Stroke	≤10 (≤0.7%)
GBS	0 (0%)
Skin and Subcutaneous Tissue	49(3.6%)
Vasculitis limited to skin	0 (0%)
Genito-urinary system	47(3.5%)
Acute kidney Injury	12(0.9%)
Dialysis	≤10 (≤0.7%)
Mortality	≤10 (≤0.7%)

Table 1: Presentations of children in COVID-19

CLINICAL ANALYSIS OF 25 COVID-19 INFECTIONS IN CHILDREN

Bai K, Liu W, Liu C, Fu Y, Hu J, Qin Y, Zhang Q, Chen H, Xu F, Li C.. Pediatr Infect Dis J. 2020 Jul;39(7):e100-e103. doi: 10.1097/INF.0000000000002740.

Level of Evidence: 4 - Case-series

BLUF

A case series in Chongqing, China describes the clinical course of 25 pediatric COVID-19 cases between January 19 and March 12, 2020. They report the children in this study had less severe prognosis (Table 1), different immunologic laboratory values (Tables 2 and 3), and different radiographic findings compared to COVID-19 positive adults. Of note, however, this article did not report COVID-19 positive adult data. All patients received combination treatment; interferon [Group A (n=7)], interferon plus Ribavirin [Group B (n=6)], and interferon plus Lapinavair or Ritonavir [Group C (n=12)]. They found no significant difference in nucleic acid studies (p = 0.394) or length of hospital stay (p=0.522) in the different treatment groups. All the children recovered and, in children with symptoms, these lasted an average of 13 days (range: 8.0-25.0 days). Resolution of positive RNA testing was seen in 15.20 ± 6.55 days. The authors believe the lower pediatric morbidity and mortality rates in this group may be associated with higher immunity to SARS-CoV-2 from frequent respiratory viruses infections compared to adults with advanced inflammatory responses.

ABSTRACT

BACKGROUND: To describe the characteristics of clinical manifestations of children with 2019 novel coronavirus (2019-nCoV) infection in Chongqing.
METHODS: All 25 children with laboratory-confirmed 2019-nCoV infection by real-time reverse transcription-PCR (RNA-PCR) were admitted from the 4 designated treatment hospitals of 2019-nCoV in Chongqing from January 19 to March 12, 2020. Clinical data and epidemiologic history of these patients were retrospectively collected and analyzed.
RESULTS: The diagnosis was confirmed through RNA-PCR testing. Among the 25 cases, 14 were males and 11 were females. The median age was 11.0 (6.3-14.5) years (range 0.6-17.0 years). All children were related to a family cluster outbreak, and 7 children (28%) with a travel or residence history in Hubei Province. These patients could be categorized into different clinical types, including 8 (32%) asymptomatic, 4 (16%) very mild cases and 13 (52%) common cases. No severe or critical cases were identified. The most common symptoms were cough (13 cases, 52%) and fever (6 cases, 24%). The duration time of clinical symptoms was 13.0 (8.0-25.0) days. In the 25 cases, on admission, 21 cases (84%) had normal white blood cell counts, while only 2 cases (8%) more than 10 x 10/L and 2 cases (8%) less than 4 x 10/L, respectively; 22 cases(88%) had normal CD4+ T lymphocyte counts, while in the remaining 3 cases(8%) this increased mildly; 23 cases had normal CD8+ T lymphocyte counts, while in the remaining 2 cases (8%) CD8+ T lymphocyte counts were mildly increased as well. All Lymphocyte counts were normal. There were no statistical differences of lab results between the groups of asymptomatic cases, mild cases and common cases. There were only 13 cases with abnormal CT imaging, most of which were located in the subpleural area of the bottom of the lung. All patients were treated with interferon, 6 cases combined with Ribavirin, and 12 cases combined with lopinavir or ritonavir. The days from onset to RNA turning negative was 15.20 +- 6.54 days. There was no significant difference of RNA turning negative between the groups of interferon, interferon plus ribavirin and interferon plus lopinavir or ritonavir treatment. All the cases recovered and were discharged from hospital.
CONCLUSIONS: The morbidity of 2019-nCoV infection in children is lower than in adults and the clinical manifestations and inflammatory biomarkers in children are nonspecific and milder than that in adults. RNA-PCR test is still the most reliable diagnostic method, especially for asymptomatic patients.

FIGURES

TABLE 1. Baseline Characteristics

	n	Percentage (%)
Age, median, years	11.0 (6.3, 14.5)	
Sex		
Male	14/25	56
Female	11/25	44
CCP	25/25	100
Signs and symptoms		
Asymptomatic	8/25	32
Fever	6/25	24
Cough	13/25	52
Sore throat	3/25	12
Running nose	3/25	12
Nasal obstruction	3/25	12
Diarrhea	1/25	4
Weakness	1/25	4
Clinical classification		
Asymptomatic	8/25	32
Mild cases	4/25	16
Common cases	13/25	52
Symptom duration (d)	13.0(8.0–25.0)	
RTNT (d)	15.20±6.54	
Hospital stays (d)	15.24±6.55	

The signs and symptoms were recorded all over the course of the disease including before and during hospitalization.

CCP indicates close contact with 2019-CoV patients; DS, duration of symptoms; RTNT, the time from onset to nucleic acid turning negative.

Table 1. Baseline Characteristics

TABLE 2. Laboratory Findings

	n	Percentage (%)
White blood cell count, $\times 10^9$/L		
<4	2	8
4–10	21	84
>10	2	8
Lymphocyte count, $\times 10^9$/L		
Normal	25	100
hsCRP (1–11 mg/L)		
1–11	22	88
>11	3	12
IL-6 (0–5.4 pg/mL)		
Normal	10/15	66.7
Increased	5/15	33.3
CD4+T lymphocyte count (610–1446)		
Normal	22	88
Increased	3	12
CD8+T lymphocyte count (282–749)		
Normal	23	92
Increased	2	8

hsCRP indicates high-sensitivity C-reactive protein.

Table 2. Laboratory Findings

TABLE 3. Laboratory Data Comparisons According to Illness Severity

	Asymptomatic cases (n = 8)	Mild cases (n = 4)	Common cases (n = 13)	*P*
WBC ($\times 10^9$/L)	6.36 (5.13–8.75)	7.22 (5.67–12.80)	6.08 (4.33–6.79)	0.429
Lymphocyte count ($\times 10^9$/L) (n = 15)	2.37 ± 1.01 (n = 4)	3.90 ± 2.42 (n = 5)	2.73 ± 1.00 (n = 6)	0.174
CRP (mg/L)	0.09 (0.03–1.09)	1.76 (0.42–2.27)	2.10 (0.33–13.18)	0.058
CD4+ T cell count	714.00 (626.50–885.75)	800.50 (639.00–1541.00)	617.00 (428.00–1118.50)	0.600
CD8+ T cell count	601.50 (428.25–908.00)	661.50 (470.00–1261.00)	610.00 (468.50–836.00)	0.837

Table 2. Laboratory Findings

EOSINOPHIL RESPONSE AGAINST CLASSICAL AND EMERGING RESPIRATORY VIRUSES: COVID-19

Rodrigo-Muñoz JM, Sastre B, Cañas JA, Gil-Martínez M, Redondo N, Del Pozo V.. J Investig Allergol Clin Immunol. 2020 Jun 16:0. doi: 10.18176/jiaci.0624. Online ahead of print.
Level of Evidence: 3 - Review / Literature Review

BLUF

In this literature review, immunology experts in Spain describe eosinophils as versatile immune cells that are involved in the response against helminths, fungi, bacteria, and also viruses, including the respiratory syncytial virus, human rhinovirus, influenza virus, human parainfluenza virus, SARS-CoV-1, and SARS-CoV-2 (Figure 1). The authors specifically:

1. Highlight that eosinophil infiltration of lung tissue was a common problem in animal studies trialing SARS-CoV-1 vaccines
2. Discuss conflicting evidence on whether or not the eosinopenia seen in COVID-19 correlates with disease severity and poor outcomes
3. Call for additional research with a larger sample size to clarify the role of eosinophils in SARS-CoV-2 infection.

ABSTRACT

Eosinophils were discovered more than 140 years ago. This polymorphonuclear leukocyte has a very active metabolism, containing numerous intracellular secretory granules that allow it exerts multiple functions in both health and disease status. Classically, eosinophils have been considered as important immune cells in the pathogenesis of inflammatory processes such as parasitic helminth infections and allergic or pulmonary diseases like asthma, being always associated to a type 2 immune response; furthermore, in the last years, it has been linked to immune response conferring host protection against fungi, bacteria, and viruses, recognizing them through several molecules such as toll-like receptors (TLRs) or retinoic acid-inducible gene 1 (RIG-1)-like receptor (RLR). The immune protection is exerted through multiple mechanisms and properties of these cells. They contain numerous cytoplasmatic granules that release cationic proteins, cytokines, chemokines and other molecules that contribute to their functions. In addition to their competence as effectors cells, its capabilities like antigen-presenting cell allow them to act in multiple situations promoting diverse aspects of the immune response. This review summarizes diverse aspects of eosinophil biology and mainly, it goes over the mechanisms and roles carried out by eosinophils in host defence against virus infections and vaccines response, focusing the attention in respiratory viruses like the new coronavirus, SARS-CoV-2.

FIGURES

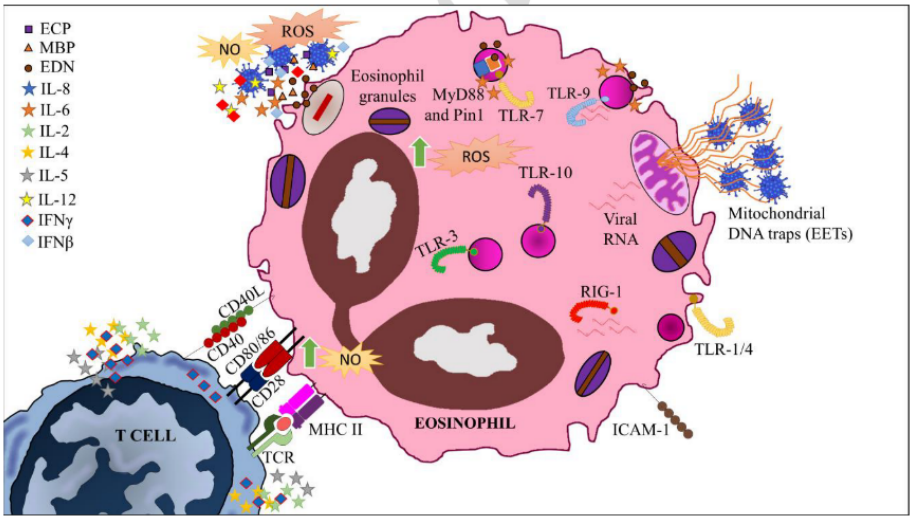


Figure 1. The eosinophilic response against viral infection comprises the following mechanisms: recognition of viral molecules (RNA) by the Toll Like Receptors (TLRs) 3, 7 and 9, through Myeloid differentiation primary response 88 (MyD88) and the prolyl isomerase Pin1 eliciting the expression of Interleukin (IL)-6 and granule proteins; antigen presentation to T cells trough Major Histocompatibility Complex (MHC)-II and molecular co-stimulation by CD80/86 and CD40L causing T cell activation and

secretion of eosinophil chemoattractants as IL-4 and IL-5; and finally secretion of antiviral molecules including eosinophil granule proteins like eosinophil derived neurotoxin (EDN), Eosinophil Cationic Protein (ECP) or Mayor Basic Protein (MBP) and Reactive Oxygen Species (ROS) and Nitric Oxide (NO), alongside interleukins with both antiviral and immune enhancing properties like IL-2, IL-8, IL-12 and Interferon (IFN)γ/β. Eosinophils are also able to secrete mitochondrial DNA traps, that are Eosinophil Extracellular Traps (EETs) with the ability to catch and destroy virus.

UNDERESTIMATION OF COVID-19 CASES IN JAPAN: AN ANALYSIS OF RT-PCR TESTING FOR COVID-19 AMONG 47 PREFECTURES IN JAPAN

Sawano T, Kotera Y, Ozaki A, Murayama A, Tanimoto T, Sah R, Wang J.. QJM. 2020 Jun 23:hcaa209. doi: 10.1093/qjmed/hcaa209. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

A cross sectional study conducted by researchers in Japan from January 15 - April 6, 2020 investigated Japan's policy of limiting RT-PCR tests. Results show that although the median number of RT-PCR tests was low (e.g., testing per 100,000 people in Japan was as low as 38.6), the number of positive cases was high (Figure 1), suggesting a likely higher rate of infection in untested individuals. Authors note that densely populated areas have higher rates of infection, and that prefectures with more liberal testing policies were better able to stymie the spread of COVID-19.

ABSTRACT

BACKGROUND: Under the unique Japanese policy to restrict reverse transcriptase-polymerase chain reaction (RT-PCR) testing against severe acute respiratory syndrome coronavirus 2, a nationwide number of its confirmed cases and mortality remains to be low. Yet the information is lacking on geographical differences of these measures and their associated factors.
AIM: Evaluation of prefecture-based geographical differences and associated predictors for the incidence and number of RT-PCR tests for COVID-19. DESIGN: Cross-sectional study using regression and correlation analysis.
METHODS: We retrieved domestic laboratory-confirmed cases, deaths, and the number of RT-PCR testing for COVID-19 from January 15 to April 6, 2020 in 47 prefectures in Japan, using publicly-available data by the Ministry of Health, Labour and Welfare. We did descriptive analyses of these three measures and identified significant predictors for the incidence and RT-PCR testing through multiple regression analyses and correlates with the number of deaths through correlation analysis.
RESULTS: The median prefectural-level incidence and number of RT-PCR testing per 100,000 population were 1.14 and 38.6, respectively. Multiple regression analyses revealed that significant predictors for the incidence were prefectural-level population ($p < 0.001$) and the number of RT-PCR testing ($p = 0.03$); and those for RT-PCR testing were the incidence ($p = 0.025$), available beds ($p = 0.045$) and cluster infections ($p = 0.034$).
CONCLUSION: Considering bidirectional association between the incidence and RT-PCR testing, there may have been an underdiagnosed population for the infection. The restraint policy for RT-PCR testing should be revisited to meet the increasing demand under the COVID-19 epidemic.

FIGURES

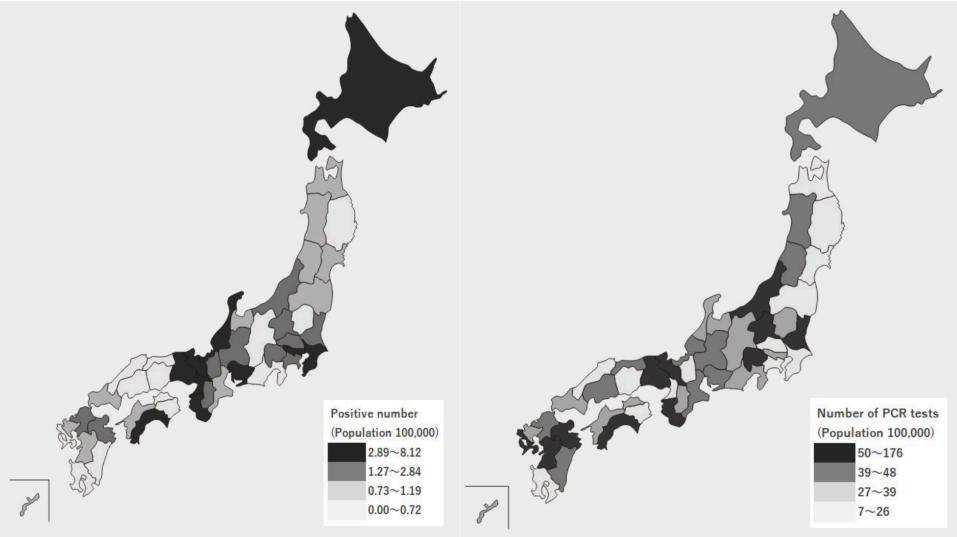


Figure 1

Figure 1. Number of COVID-19 patients and RT-PCR testing per 100,000 population in each prefecture

PERSISTENCE OF SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2 IN AEROSOL SUSPENSIONS

Fears AC, Klimstra WB, Duprex P, Hartman A, Weaver SC, Plante KS, Mirchandani D, Plante JA, Aguilar PV, Fernández D, Nalca A, Totura A, Dyer D, Kearney B, Lackemeyer M, Bohannon JK, Johnson R, Garry RF, Reed DS, Roy CJ.. Emerg Infect Dis. 2020 Jun 22;26(9). doi: 10.3201/eid2609.201806. Online ahead of print.
Level of Evidence: Other - Mechanism-based reasoning

BLUF

A study based out of 4 aerobiology laboratories measured the concentration of aerosolized viral particles of SARS-CoV-2, SARS-CoV, and MERS-CoV at less than 1 minute in controlled chambers to compare with the original nebulizer concentration and found that SARS-CoV2 was most efficient at aerosolizing (Figure 1). They also measured aerosol samples in tanks at different time points (10 min, 30 min, 2 h, 4 h, and 16 h) and found the presence of SARS-CoV-2 at all points with limited decay, such that the experiment failed to find the viral half-life (Figure 2). The authors concluded that although the study is limited as it was performed under laboratory conditions, the findings support maintained infectivity and virion stability of SARS-CoV-2 for at least 16 hours in respirable-sized aerosols.

ABSTRACT

We aerosolized severe acute respiratory syndrome coronavirus 2 and determined that its dynamic aerosol efficiency surpassed those of severe acute respiratory syndrome coronavirus and Middle East respiratory syndrome. Although we performed experiment only once across several laboratories, our findings suggest retained infectivity and virion integrity for up to 16 hours in respirable-sized aerosols.

FIGURES

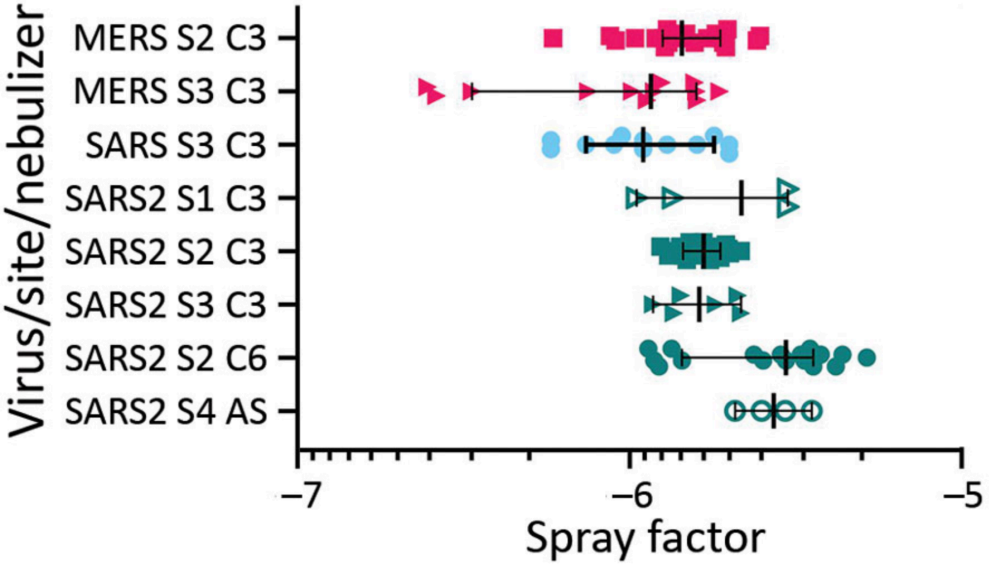


Figure 1. Aerosol efficiency of MERS-CoV, SARS-CoV and SARS-CoV-2 at different sites. Graph shows the spray factor (i.e., ratio of nebulizer concentration to aerosol concentration) for MERS-CoV (red), SARS-CoV (blue), and SARS-CoV2 (green). Aerosols were performed at 4 sites and with different nebulizers. AS, Aerogen Solo nebulizer; C3, Collison 3-jet nebulizer; C6, Collison 6-jet nebulizer; MERS-Cov, Middle East respiratory syndrome coronavirus; S1, Tulane University, New Orleans, LA, USA; S2, National Institutes of Health Integrated Research Facility, Fort Detrick, MD, USA; S3, US Army Medical Institute for Infectious Diseases, Fort Detrick, MD, USA; S4, University of Pittsburgh, Pittsburgh, PA, USA; SARS-CoV, severe acute respiratory syndrome coronavirus; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

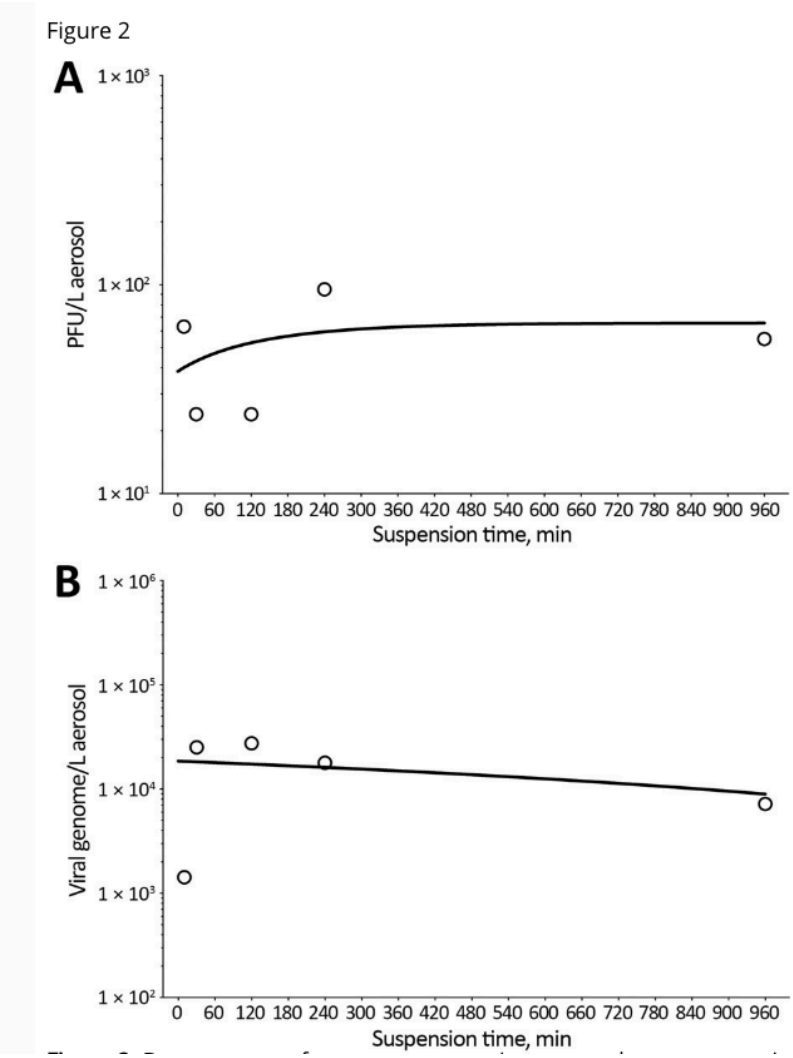


Figure 2. Decay curves of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in aerosol suspension. A) Aerosol concentration of infectious SARS-CoV-2 as measured by plaque assay found in impinger samples collected at 5 time points of increased aging in aerosol suspension. B) Corresponding aerosol concentration of SARS-CoV-2 in time-matched impinger samples as a function of viral genome copies as measured by reverse transcription quantitative PCR. Both time point virus estimates were graphed, and nonlinear least-squares regression analysis single-order decay with no outlier detection was performed, resulting in a poor curve fit by either method of viral quantitation resulting from number and lack of iterative samples in this analysis.

PREVENTION IN THE COMMUNITY

SARS-COV-2 INFECTIONS AND SEROLOGIC RESPONSES FROM A SAMPLE OF U.S. NAVY SERVICE MEMBERS - USS THEODORE ROOSEVELT, APRIL 2020

Payne DC, Smith-Jeffcoat SE, Nowak G, Chukwuma U, Geibe JR, Hawkins RJ, Johnson JA, Thornburg NJ, Schiffer J, Weiner Z, Bankamp B, Bowen MD, MacNeil A, Patel MR, Deussing E; CDC COVID-19 Surge Laboratory Group, Gillingham BL.. MMWR Morb Mortal Wkly Rep. 2020 Jun 12;69(23):714-721. doi: 10.15585/mmwr.mm6923e4.
Level of Evidence: 3 - Local non-random sample

BLUF

This report by the Centers for Disease Control and Prevention (CDC) and the US Navy examines a COVID-19 outbreak that occurred on the USS Theodore Roosevelt between January and March 2020 utilizing questionnaires completed by 382 crew members, of whom 267 provided a nasopharyngeal swab sample, providing valuable information regarding how the virus

spread in this closed, compact environment. This study highlights the benefits of social distancing measures and suggests that immunity after exposure to SARS-CoV-2 is common. Results revealed that:

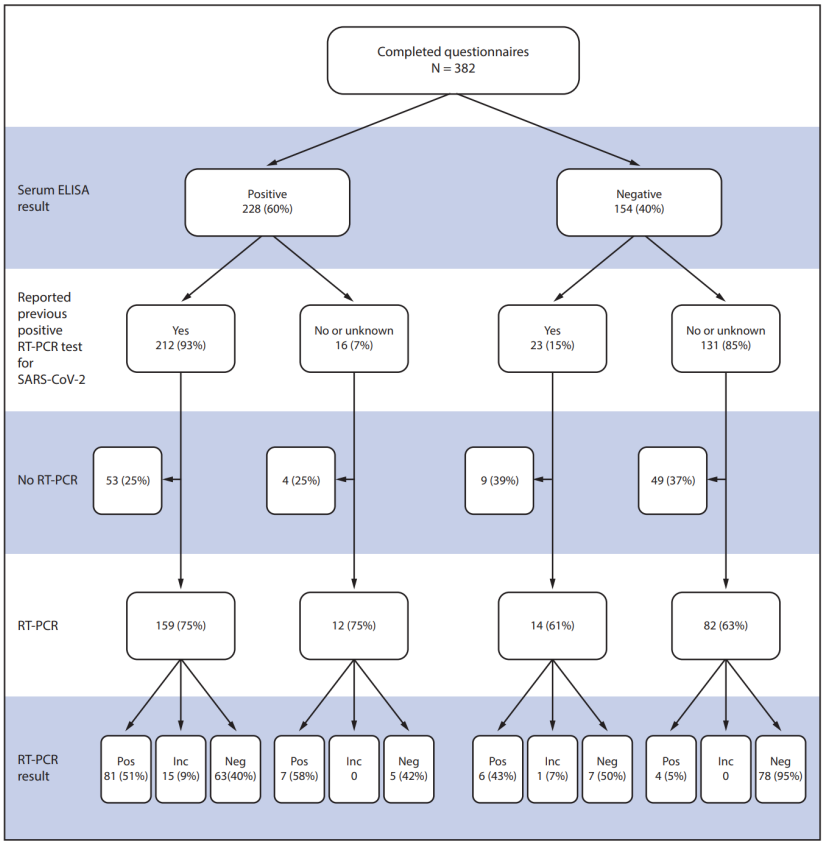
- 60% of respondents exhibited evidence of previous exposure to SARS-CoV-2 via positive ELISA assay for neutralizing antibodies (Figure 1)
- Ageusia and anosmia were the symptoms most associated with current or previous infection among crew members that reported symptoms (Figure 2, Table 1)
- 212 (90.2%) of the 235 respondents that reported a previous positive COVID-19 test via RT-PCR tested positive for neutralizing antibodies via ELISA
- Crew members that self-reported following measures such as mask-wearing, avoiding common areas, and social distancing had lower odds of infection

ABSTRACT

Compared with the volume of data on coronavirus disease 2019 (COVID-19) outbreaks among older adults, relatively few data are available concerning COVID-19 in younger, healthy persons in the United States (1,2). In late March 2020, the aircraft carrier USS Theodore Roosevelt arrived at port in Guam after numerous U.S. service members onboard developed COVID-19. In April, the U.S. Navy and CDC investigated this outbreak, and the demographic, epidemiologic, and laboratory findings among a convenience sample of 382 service members serving aboard the aircraft carrier are reported in this study. The outbreak was characterized by widespread transmission with relatively mild symptoms and asymptomatic infection among this sample of mostly young, healthy adults with close, congregate exposures. Service members who reported taking preventive measures had a lower infection rate than did those who did not report taking these measures (e.g., wearing a face covering, 55.8% versus 80.8%; avoiding common areas, 53.8% versus 67.5%; and observing social distancing, 54.7% versus 70.0%, respectively). The presence of neutralizing antibodies, which represent antibodies that inhibit SARS-CoV-2, among the majority (59.2%) of those with antibody responses is a promising indicator of at least short-term immunity. This report improves the understanding of COVID-19 in the U.S. military and among young adults in congregate settings and reinforces the importance of preventive measures to lower risk for infection in similar environments.

FIGURES

FIGURE 1. Laboratory results among a convenience sample of U.S. service members who provided serum specimens* (N = 382) and nasopharyngeal swabs (N = 267) for SARS-CoV-2 testing — USS Theodore Roosevelt, April 2020



Abbreviations: Ab = antibody; ELISA = enzyme-linked immunosorbent assay; Inc = inconclusive; Neg = negative; Pos = positive; RT-PCR = real-time reverse transcription–polymerase chain reaction.
* Of those with positive serum ELISA tests, 59% demonstrated positive microneutralization tests.

FIGURE 2. Odds ratios and 95% confidence intervals of previous or current SARS-CoV-2 infection, by individual symptoms among service members reporting at least one symptom (n = 284) — USS Theodore Roosevelt, April 2020

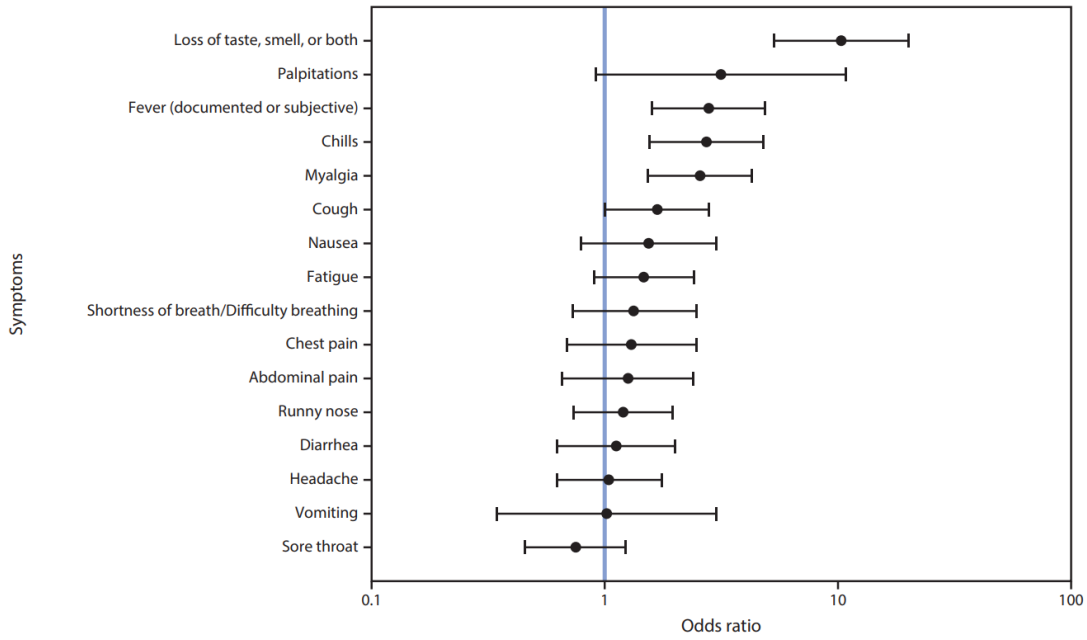


TABLE. Comparison of U.S. Navy service members with and without previous or current SARS-CoV-2 infection (N = 382) — USS Theodore Roosevelt, April 2020

Characteristic	No. (%)		
	Current or previous SARS-CoV-2 infection* (N = 238)	No evidence of SARS-CoV-2 infection (N = 144)	Infection versus no infection OR (95% CI)†
RT-PCR and antibody results			
RT-PCR positive and ELISA positive	88 (37.0)	0	**N/A**
RT-PCR negative and ELISA positive	83 (34.9)	0	N/A
RT-PCR positive and ELISA negative	10 (4.2)	0	N/A
RT-PCR not done and ELISA positive	57 (23.9)	0	N/A
RT-PCR negative or not done and ELISA negative	0	144 (100)	N/A
Sex			
Male	190 (65.7)	99 (34.3)	1.80 (1.12–2.89)§
Female	48 (51.6)	45 (48.4)	Referent
Age group (yrs)			
18–24	77 (68.1)	36 (31.9)	Referent
25–29	50 (64.1)	28 (35.9)	0.84 (0.45–1.54)
30–39	87 (58.8)	61 (41.2)	0.67 (0.40–1.11)
40–59	24 (55.8)	19 (44.2)	0.59 (0.29–1.21)
Race/Ethnicity¶			
AI/AN or NH/PI	9 (60.0)	6 (40.0)	0.86 (0.29–2.49)
Asian	13 (61.9)	8 (38.1)	0.93 (0.37–2.33)
Black	25 (61.0)	16 (39.0)	0.89 (0.45–1.77)
Hispanic/Latino	47 (61.8)	29 (38.2)	0.92 (0.54–1.58)
Other/Unknown	2 (33.3)	4 (66.7)	0.29 (0.05–1.59)
White	142 (63.7)	81 (36.3)	Referent
History of asthma, hypertension, diabetes, or immunosuppression	15 (53.6)	13 (46.4)	0.68 (0.31, 1.47)
Reported ≥1 symptom			
Yes	194 (81.5)	90 (62.5)	2.65 (1.65–4.23)§
No	44 (18.5)	54 (37.5)	Referent
Symptoms (among those reporting ≥1 symptom)			
Symptoms (CSTE criteria)**			
Category A	97 (50.0)	36 (40.0)	3.50 (1.90–6.45)§
Category B	67 (34.5)	15 (16.7)	5.81 (2.78–12.11)§
Other symptom(s)	30 (15.5)	39 (43.3)	Referent
Individual symptoms			
Loss of taste, smell, or both	119 (61.3)	12 (13.3)	10.31 (5.26–20.21)§
Palpitations	19 (9.8)	3 (3.3)	3.15 (0.91–10.93)
Fever (documented or subjective)	89 (45.9)	21 (23.3)	2.79 (1.58–4.90)§
Chills	85 (43.8)	20 (22.2)	2.73 (1.54–4.84)§
Myalgia	109 (56.2)	30 (33.3)	2.56 (1.52–4.32)§
Cough	86 (44.3)	29 (32.2)	1.68 (0.99–2.83)
Nausea	40 (20.6)	13 (14.4)	1.54 (0.78–3.05)
Fatigue	107 (55.2)	41 (45.6)	1.47 (0.89–2.43)
Shortness of breath/difficulty breathing	46 (23.7)	17 (18.9)	1.33 (0.72–2.49)
Chest pain	40 (20.6)	15 (16.7)	1.30 (0.68–2.50)
Abdominal pain	39 (20.1)	15 (16.7)	1.26 (0.65–2.42)
Runny nose	108 (55.7)	46 (51.1)	1.20 (0.73–1.98)
Diarrhea	47 (24.2)	20 (22.2)	1.12 (0.62–2.03)
Headache	129 (66.5)	59 (65.6)	1.04 (0.62–1.77)
Vomiting	11 (5.7)	5 (5.6)	1.02 (0.34–3.03)
Sore throat	81 (41.8)	44 (48.9)	0.75 (0.45–1.24)
Sought medical care for symptoms	115 (59.3)	35 (38.9)	2.29 (1.37–3.82)§
Hospitalized	2 (1.0)	0	N/A
Number of symptoms			
1–3	51 (26.3)	49 (54.4)	Referent
4–5	37 (19.1)	13 (14.4)	2.74 (1.30–5.75)§
6–8	50 (25.8)	16 (17.8)	3.00 (1.51–5.96)§
>8	56 (28.9)	12 (13.3)	4.48 (2.15–9.37)§
Still symptomatic at time of survey (n = 275)			
Yes	65 (34.0)	24 (28.6)	1.29 (0.74–2.26)
No	126 (66.0)	60 (71.4)	Referent
Duration >1 week (n = 186)	70 (55.6)	29 (48.3)	1.34 (0.72–2.47)
Reported prevention behaviors			
Increased hand washing	218 (62.1)	133 (37.9)	0.90 (0.42–1.94)
Hand sanitizer use	219 (61.5)	137 (38.5)	0.59 (0.24–1.44)
Avoiding common areas	78 (53.8)	67 (46.2)	0.56 (0.37–0.86)§
Face covering use	158 (55.8)	125 (44.2)	0.30 (0.17–0.52)§
Increased workspace cleaning	195 (63.5)	112 (36.5)	1.30 (0.78–2.16)
Increased berthing cleaning	156 (61.9)	96 (38.1)	0.95 (0.61–1.47)
Increased distance from others	105 (54.7)	87 (45.3)	0.52 (0.34–0.79)§

Abbreviations: AI/AN = American Indian or Alaska Native; CI = confidence interval; CSTE = Council of State and Territorial Epidemiologists; ELISA = enzyme-linked immunosorbent assay; N/A = not applicable; NH/PI = Native Hawaiian or other Pacific Islander; OR = odds ratio; RT-PCR = real-time reverse transcription–polymerase chain reaction.

* Current or previous SARS-CoV-2 infection is defined as a positive RT-PCR test result or a reactive antibody result determined by testing performed at CDC laboratories on specimens collected during April 20–24, 2020.

† Odds ratios are unadjusted.

§ P-values <0.05 were considered statistically significant.

¶ White, black, Asian, AIAN/NHPI, and Other persons were non-Hispanic/Latino. Hispanic/Latino persons might be of any race.

** Category A = ≥1 of cough or shortness of breath/difficulty breathing. Category B = no cough or shortness of breath, but ≥2 of fever, chills, muscle pain, headache, sore throat, no taste or smell disorder.

MANAGEMENT

PROPOSAL OF THE FRENCH SOCIETY OF VASCULAR MEDICINE FOR THE PREVENTION, DIAGNOSIS AND TREATMENT OF VENOUS THROMBOEMBOLIC DISEASE IN OUTPATIENTS WITH COVID-19

Khider L, Soudet S, Laneelle D, Boge G, Bura-Rivière A, Constans J, Dadon M, Desmurs-Clavel H, Diard A, Elias A, Emmerich J, Galanaud JP, Giordana P, Gracia S, Hamade A, Jurus C, Le Hello C, Long A, Michon-Pasturel U, Mirault T, Miserey G, Perez-Martin A, Pernod G, Quere I, Sprynger M, Stephan D, Wahl D, Zuily S, Mahe G, Sevestre MA; French Society of Vascular Medicine (SFMV).. J Med Vasc. 2020 Jul;45(4):210-213. doi: 10.1016/j.jdmv.2020.04.008. Epub 2020 Apr 27.
Level of Evidence: Other - Guidelines and Recommendations

BLUF

In this expert opinion article, physicians from the French Society of Vascular Medicine offer recommendations on the diagnosis, treatment, and prevention of venous thromboembolic (VTE) disease in patients with COVID-19. Relying on existing evidence and guidelines for VTE prophylaxis among hospitalized patients without COVID-19, the authors propose that outpatient COVID-19 patients with reduced mobility and at least one other risk factor for VTE should receive thromboprophylaxis for 7-14 days. They acknowledge their recommendations are based on limited evidence and will likely change as more is learned about COVID-19.

SUMMARY

- Venous thromboembolic (VTE) disease is one manifestation of COVID-19 and is associated with severe morbidity and mortality.
- Authors recommend 7-14 days of VTE prophylaxis with anticoagulation for outpatient management of COVID-19 for patients with a significant reduction in mobility and any one of the following risk factors: BMI > 30 kg/m2, age > 70 years, active cancer, history of VTE, major surgery in last 3 months.
- Authors offer recommendations for appropriate PPE and disinfection in non-suspected, suspected, and confirmed cases of COVID-19.
- The authors recommend against broad screening for VTE (e.g. with d-dimer or Doppler ultrasound) in ambulatory COVID-19 patients without clinical signs of VTE. They argue that these techniques have low sensitivity and increase risk of exposure for healthcare workers.
- VTE treatment recommendations include preference for teleconsulations when possible and anticoagulation for at least 3 months (unless contraindications are present).

MEDICAL SUBSPECIALTIES

CARDIOLOGY

SPONTANEOUS CORONARY ARTERY DISSECTION IN A PATIENT WITH COVID-19

32553344. Spontaneous Coronary Artery Dissection in a Patient With COVID-19
Level of Evidence: Other - Case Report

BLUF

A case study from France reports a 55-year-old COVID-19 positive male who developed chest pain 48 hours after admission to the hospital with inverted T waves and elevated troponin I levels (355 ng/l and 570 ng/l 3 hours later). A coronary angiogram revealed a spontaneous right coronary artery dissection, possibly due to intraplaque hemorrhage caused by systemic inflammation associated with COVID-19 (Figure 1). Per the authors, at the time of this report, this is the first case of a patient with COVID-19 experiencing a spontaneous coronary artery dissection. Additional details provided below.

SUMMARY

A 55-year-old male with a history of peripheral artery disease presented with cough and febrile dyspnea with a positive RT-PCR test and chest CT revealed bilateral "crazy paving." 48 hours after admission, the patient developed chest pain and 12-lead ECG revealed inverted T waves on inferior leads with elevated Troponin I levels (355 ng/l, increased to 570 ng/l three hours later). Transthoracic echocardiography showed LVEF 60% without abnormal wall motion and mild mitral regurgitation with no diastolic dysfunction. A coronary angiogram showed a chronically occluded posterior descending artery and a spontaneous dissection of the right coronary artery with intimal rupture that was confirmed on optical coherence tomography (Figure 1). The patient was treated conservatively with aspirin, statins, and beta-blockers. The authors suggest the viral infection may have elicited a systemic inflammatory response that caused an intraplaque hemorrhage leading to the right coronary artery dissection in this patient.

FIGURES

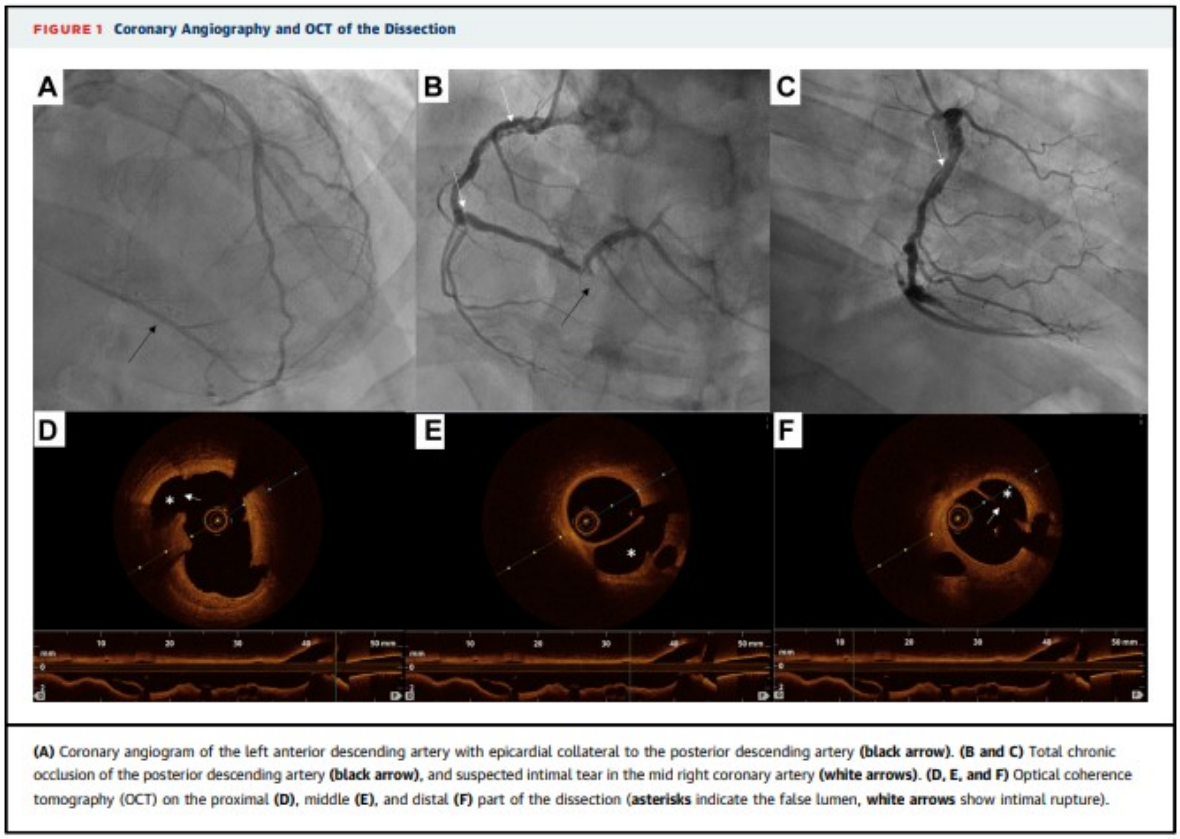


Figure 1. Coronary Angiography and OCT of the Dissection (A) Coronary angiogram of the left anterior descending artery with epicardial collateral to the posterior descending artery (black arrow). (B and C) Total chronic occlusion of the posterior descending artery (black arrow), and suspected intimal tear in the mid right coronary artery (white arrows). (D, E, and F) Optical coherence tomography (OCT) on the proximal (D), middle (E), and distal (F) part of the dissection (asterisks indicate the false lumen, white arrows show intimal rupture).

SURGICAL SUBSPECIALTIES

TRANSPLANT SURGERY

DONOR AND TRANSPLANT CANDIDATE SELECTION FOR SOLID ORGAN TRANSPLANTATION DURING THE COVID-19 PANDEMIC

Galvan NTN, Moreno NF, Garza JE, Bourgeois S, Hemmersbach-Miller M, Murthy B, Timmins K, O'Mahony CA, Anton J, Civitello A, Garcha P, Loor G, Liao K, Shaffi A, Vierling J, Stribling R, Rana A, Goss JA.. Am J Transplant. 2020 Jun 10. doi: 10.1111/ajt.16138. Online ahead of print.

Level of Evidence: Other - Guidelines and Recommendations

BLUF

Transplant surgeons in Texas developed protocols to address the continuing demand for life-saving transplants during the COVID-19 pandemic for both inpatient and outpatient settings (Figures 1 and 2, respectively) which they implemented from March 24th - May 11th 2020 (Table 5). Authors admit they potentially have developed an overly sensitive algorithm that may preclude certain candidates from life-saving therapy but their main goal was to avoid SARS-CoV-2 transmission in immunocompromised transplant recipients and hope that their work will advance discussion for future solid organ transplant protocols during the pandemic.

SUMMARY

Donors undergo two levels of screening:

1. Donor Exposure Assessment based on common COVID-19 screening assessments (e.g., travel history, known contact exposure).
2. Donor Clinical Risk Assessment, which evaluates for COVID-19 symptoms (e.g., lower respiratory tract infection, fever, anosmia), RT-PCR testing, non-contrast Chest CT, and bronchoscopy with lower respiratory tract sampling in lung donors.

The authors break down these two levels of screening into a 4 tiered system with Category 0 having a low risk and Categories 1-3 being moderate to high risk donors.

ABSTRACT

SARS-CoV-2, a novel coronavirus responsible for a worldwide pandemic has forced drastic changes in medical practice in an alarmingly short period of time. Caregivers must modify their strategies as well as optimize the utilization of resources to ensure public and patient safety. For organ transplantation, in particular, the loss of life-saving organs for transplantation could lead to increased waitlist mortality. The priority is to select uninfected donors to transplant uninfected recipients while maintaining safety for healthcare systems in the backdrop of a virulent pandemic. We do not yet have a standard approach to evaluating donors and recipients with possible SARS-CoV-2 infection. Our current communication shares a protocol for donor and transplant recipient selection during the COVID-19 pandemic to continue life-saving solid organ transplantation for heart, lung, liver and kidney recipients. The initial results using this protocol are presented here and meant to encourage dialogue between providers, offering ideas to improve safety in solid organ transplantation with limited health care resources. This protocol was created utilizing the guidelines of various organizations and from the clinical experience of the authors and will continue to evolve as more is understood about SARS-CoV-2 and how it affects organ donors and transplant recipients.

FIGURES

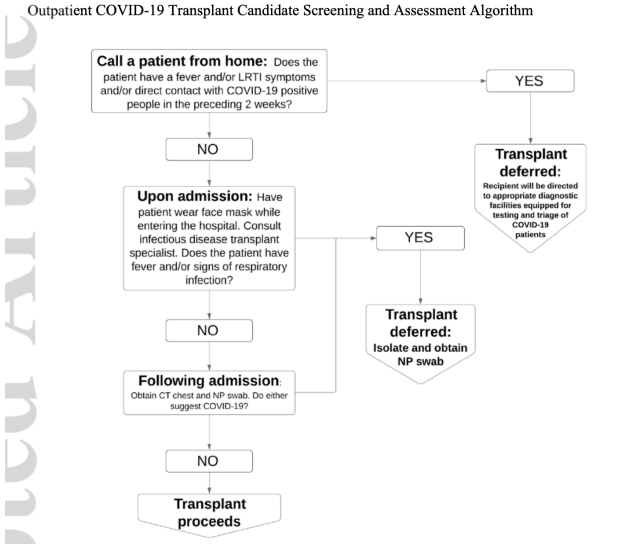


Figure 1. Outpatient COVID-19 Transplant Transplant candidate Screening and Assessment Algorithm.

Algorithm used for screening outpatient transplant transplant candidates for heart, lung, liver, and kidney transplants during the COVID-19 pandemic.

NP= nasopharyngeal, CT= computed tomography, COVID-19= Coronavirus Disease 2019

Heart	Decision		Exposure Category	Clinical Risk Category	Risk Category	Comment
7 primary offers	Transplanted	Donor	0	0	Low	Of note, one candidate received a heart/lung, and one candidate received a heart/kidney.
		Candidate	✓	✓		
1 primary offer	Not Transplanted	Donor	0	3	High	Donor was found to have an indeterminate SARS-CoV-2 RT-PCR.
		Candidate	✓	✓		
2 primary offers	Not Transplanted	Donor	0	0	Low	One transplant candidate was found to have a positive telephone screen (malaise and cough). The other transplant candidate had profound dyspnea on exam and a CT Chest suggestive of COVID-19. Both candidates tested negative for SARS-CoV-2.
		Candidate	×	×		
Lung						
3 primary offers	Transplanted	Donor	0	0	Low	
		Candidate	✓	✓		
Kidney						
2 primary offers	Transplanted	Donor	0	0	Low	
		Candidate	✓	✓		

Liver						
15 primary offers	Transplanted	Donor	0	0-1	Low	One donor was febrile, but clinical risk score was low and therefore transplant proceeded.
		Candidate	✓	✓		
1 primary offer	Not Transplanted	Donor	3	1	Moderate	Donor had symptoms of respiratory distress and known exposure to COVID-19 positive people.
		Candidate	✓	✓		
1 primary offer	Not Transplanted	Donor	0	0	Low	Candidate was found to have CT Chest imaging with ground glass opacities concerning for infectious etiology. Transplant was deferred per protocol, and repeated RT-PCRs were negative. The candidate later proceeded to transplant with a different donor organ.
		Candidate	✓	×		

Inpatient COVID-19 Transplant Candidate Assessment and Screening Algorithm

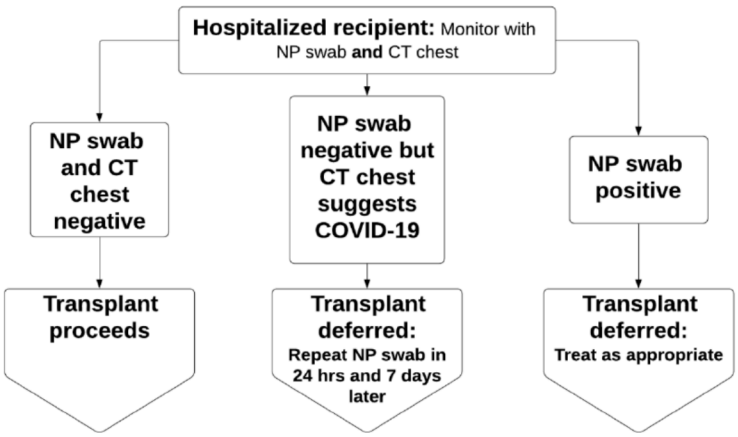


Figure 2. Inpatient COVID-19 Transplant Candidate Assessment and Screening Algorithm. Algorithm used for screening inpatient transplant candidates for heart, lung, liver and kidney transplants during the COVID-19 pandemic. Our institution uses the Cepheid Xpert Xpress SARS-CoV-2 assay.

NP= nasopharyngeal, CT= computed tomography, COVID-19= Coronavirus Disease 2019

OBGYN

SUCCESSFUL ANESTHETIC MANAGEMENT IN CESAREAN SECTION FOR PREGNANT WOMAN WITH COVID-19

Bani Hani DA, Alsharaydeh I, Bataineh AM, Al Athamneh M, Qamileh I, Al-Baik A, Al Shalakhti MH, Al-Ebbini MA, Aleshawi AJ.. Am J Case Rep. 2020 Jun 12;21:e925512. doi: 10.12659/AJCR.925512.
Level of Evidence: Other - Case Report

BLUF

Experts in Irbid, Jordan present a case report of a 29-year-old G2P1 woman at 37+4 weeks of gestation with COVID-19 successfully receiving a cesarean section (CS) without complication. The authors report that the female baby tested negative for COVID-19 and no cross-infection was reported among medical staff. This report provides further evidence that CS among COVID-19 patients can be carried out without complication if special precautions are taken.

SUMMARY

The authors suggest that special precautions should be considered when performing a cesarean section (CS) on pregnant women with COVID-19. Some of the authors' recommendations are summarized below:

- Mild cases of COVID-19: continuous fetal heart rate monitoring and maintaining oxygen saturation of >95% are needed.
- More severe cases of COVID-19: ICU teams should be involved.
- It is recommended not to use Betamethasone.
- Delivery in preterm pregnancy among mothers with mild COVID-19 illness should be delayed until the mother's infection is negative.
- If the pregnancy is past 32 weeks and delivery would improve the mother's condition, delivery is advised.
- The use of neuraxial blockade technique during delivery under CS or via vaginal route is recommended.

- Spinal anesthesia is recommended over general anesthesia.
- Sedative drugs should be avoided.

ABSTRACT

BACKGROUND The current COVID-19 pandemic highlights the importance of the mindful use of financial and human resources. Preventing infections and preserving resources and manpower are crucial in healthcare. It is important to ensure the ability of surgeons and specialized interventionalists to function through the pandemic. Until now, no justified protocol has been reported for the anesthetic management in cesarean section (CS).
CASE REPORT A 29-year-old pregnant woman, G2P1 at 37+4 weeks of gestation, was referred to our center on March 28, 2020, after she had tested positive for COVID-19. She was stable and the CS was planned after she reached term. Through spinal anesthesia, CS was conducted. The anesthesia team was protected with full personal protection equipment. The operation was carried out smoothly without complication. A female neonate was delivered and was tested to be negative for COVID-19. No medical staff cross-infection was reported. CONCLUSIONS Special precautions should be considered when pregnant women are undergoing CS. Spinal anesthesia is preferred over general anesthesia.

PEDIATRICS

PROTECTING CHILDREN FROM IATROGENIC HARM DURING COVID19 PANDEMIC

Camporesi A, Díaz-Rubio F, Carroll CL, González-Dambrauskas S.. J Paediatr Child Health. 2020 Jun 22. doi: 10.1111/jpc.14989. Online ahead of print.

Level of Evidence: Other - Expert Opinion

BLUF

In this viewpoint, published in the Journal of Pediatrics and Child Health, the authors warn about the potential detrimental effects the COVID-19 pandemic will have on children, both medically and non-medically (Figure 1), given the unprecedented shift to aggressive therapies and lack of evidence-based medicine when treating COVID-19 patients. Such therapies, including early intubation over more non-invasive breathing support, may be beneficial in adult COVID-19 cases, however they are yet to be proven in the pediatric population and should not be blindly mimicked without additional evidence.

ABSTRACT

Critical care management of patients with COVID-19 has been influenced by a mixture of public, media and societal pressure, as well as clinical and anecdotal observations from many prominent researchers and key opinion leaders. These factors may have affected the principles of evidence-based medicine and encouraged the widespread use of non-tested pharmacological and aggressive respiratory support therapies, even in intensive care units (ICUs). The COVID-19 pandemic has predominantly affected adult populations, while children appear to be relatively spared of severe disease. Notwithstanding, paediatric intensive care (PICU) clinicians may already have been influenced by changes in practices of adult ICUs, and these changes may pose unintended consequences to the vulnerable population in the PICU. In this article, we analyse several potential iatrogenic causes of the detrimental effects of the current pandemic to children and highlight the risks underlying a sudden change of clinical practice.

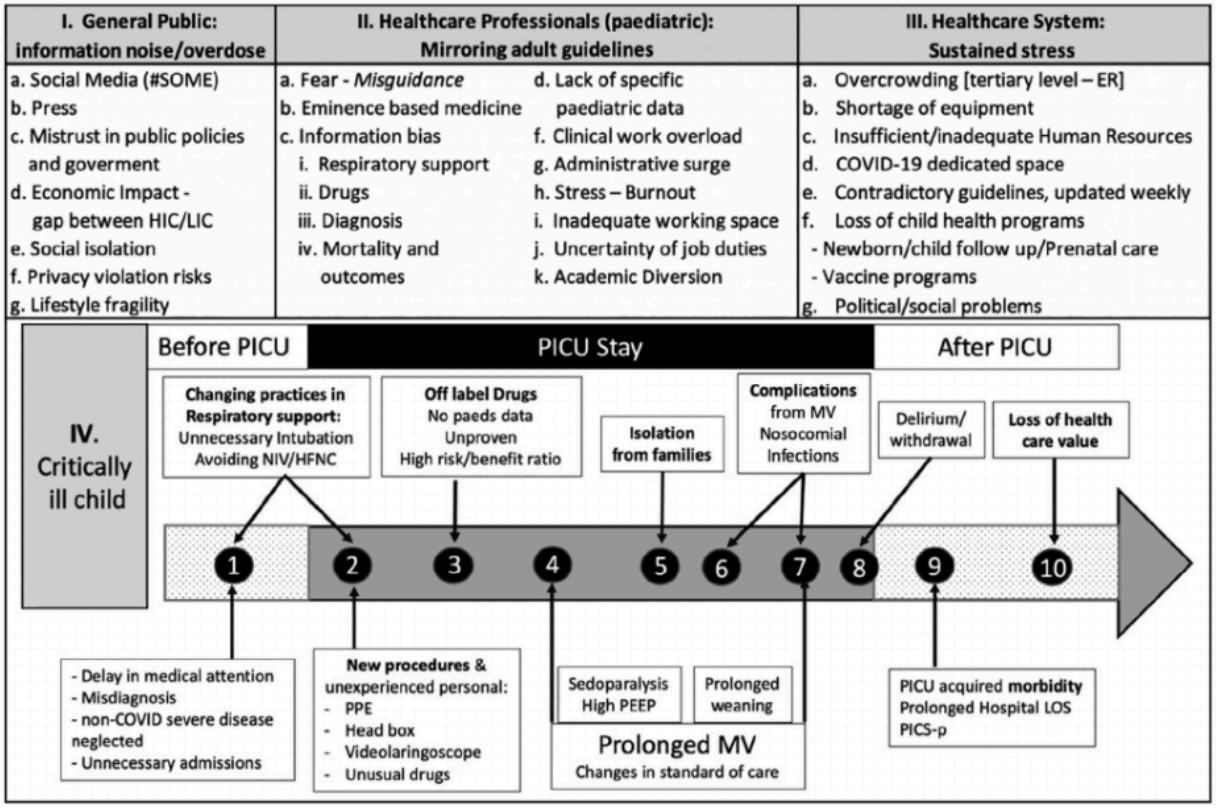


Fig. 1 Key factors that may affect optimal care of critically ill children. The figure specifically shows the multi-level involvement: general public information overload (Box I), paediatric health-care professionals' uncertainty (Box II) and sustained stress of health-care system (Box III). In addition, we added a detailed timeline of critically ill children with crucial steps and issues that can affect their clinical course (Box IV). (ER, emergency room; HFNC, high-flow nasal cannula; HIC, high-income countries; LIC, low-income countries; LOS, length of stay; MV, mechanical ventilation; NIV, non-invasive ventilation; PICS-p, post-intensive care syndrome in paediatrics; PICU, paediatric intensive care unit; PEEP, positive end expiratory pressure; PPE, personal protective equipment).

DELAY IN IVF TREATMENT UP TO 180 DAYS DOES NOT AFFECT PREGNANCY OUTCOMES IN WOMEN WITH DIMINISHED OVARIAN RESERVE

Romanski PA, Bortoletto P, Rosenwaks Z, Schattman GL.. Hum Reprod. 2020 Jun 16:deaa137. doi: 10.1093/humrep/deaa137. Online ahead of print.
Level of Evidence: 3 - Cohort study or control arm of randomized trial

BLUF

A retrospective cohort study in New York conducted between January 1, 2012 and December 31, 2018 by Weill Cornell Medical College of patients with diminished ovarian reserves (anti-Müllerian hormone (AMH) less than 1.1 ng/ml) found that those who underwent immediate in vitro fertilization (IVF) treatment (defined as initiating their first IVF cycle within 90 days of first visit) compared to those with delayed treatment (defined as initiating their first IVF cycle between 91 and 180 days) had similar live birth rates after embryo transfer (23.9% versus 25.6%; OR 1.08, 95% CI 0.85–1.38; Table 2). Similar findings were noted for patients with an AMH less than 0.5 ng/ml (immediate treatment: 18.8% versus delayed: 19.1%; OR 0.99, 95% CI 0.65–1.51; Table 3) as well as among patients greater than 40 years old with AMH less than 1.1 ng/ml (immediate treatment: 12.3% versus delayed: 14.7%; OR 1.21, 95% CI 0.77–1.91, Table 4). These findings suggest that delaying IVF treatment for up to 180 days in patients with decreased ovarian reserve does not affect live birth rate; this can facilitate decision-making concerning treatment delays and disruptions in this population during the COVID-19 pandemic.

ABSTRACT

STUDY QUESTION: Will a delay in initiating IVF treatment affect pregnancy outcomes in infertile women with diminished ovarian reserve?
SUMMARY ANSWER: A delay in IVF treatment up to 180 days does not affect the live birth rate for women with diminished ovarian reserve when compared to women who initiate IVF treatment within 90 days of presentation.
WHAT IS KNOWN ALREADY: In clinical practice, treatment delays can occur due to medical, logistical or financial reasons. Over a period of years, a gradual decline in ovarian reserve occurs which can result in declining outcomes in response to IVF treatment over time. There is disagreement among reproductive endocrinologists about whether delaying IVF treatment for a few months can negatively affect patient outcomes.
STUDY DESIGN, SIZE, DURATION: A retrospective cohort study of infertile patients in an academic hospital setting with diminished ovarian reserve who started an IVF cycle within 180 days of their initial consultation and underwent an oocyte retrieval with planned fresh embryo transfer between 1 January 2012 and 31 December 2018.
PARTICIPANTS/MATERIALS, SETTING, METHODS: Diminished ovarian reserve was defined as an anti-Mullerian hormone (AMH) <1.1 ng/ml. In total, 1790 patients met inclusion criteria (1115 immediate and 675 delayed treatment). Each patient had one included cycle and no subsequent data from additional frozen embryo transfer cycles were included. Since all cycle outcomes evaluated were from fresh embryo transfers, no genetically tested embryos were included. Patients were grouped by whether their cycle started 1-90 days after presentation (immediate) or 91-180 days (delayed). The primary outcome was live birth (>=24 weeks of gestation). A subgroup analysis of more severe forms of diminished ovarian reserve was performed to evaluate outcomes for patients with an AMH <0.5 and for patients >40 years old with an AMH <1.1 ng/ml (Bologna criteria for diminished ovarian reserve). Logistic regression analysis, adjusted a priori for patient age, was used to estimate the odds ratio (OR) with a 95% CI. All pregnancy outcomes were additionally adjusted for the number of embryos transferred.
MAIN RESULTS AND THE ROLE OF CHANCE: The mean +- SD number of days from presentation to IVF start was 50.5 +- 21.9 (immediate) and 128.8 +- 25.9 (delayed). After embryo transfer, the live birth rate was similar between groups (immediate: 23.9%; delayed: 25.6%; OR 1.08, 95% CI 0.85-1.38). Additionally, a similar live birth rate was observed in a subgroup analysis of patients with an AMH <0.5 ng/ml (immediate: 18.8%; delayed: 19.1%; OR 0.99, 95% CI 0.65-1.51) and in patients >40 years old with an AMH <1.1 ng/ml (immediate: 12.3%; delayed: 14.7%; OR 1.21, 95% CI 0.77-1.91).
LIMITATIONS, REASONS FOR CAUTION: There is the potential for selection bias with regard to the patients who started their IVF cycle within 90 days compared to 91-180 days after initial consultation. In addition, we did not include patients who were seen for initial evaluation but did not progress to IVF treatment with oocyte retrieval; therefore, our results should only be applied to patients with diminished ovarian reserve who complete an IVF cycle. Finally, since we excluded patients who started their IVF cycle greater than 180 days from their first visit, it is not known how such a delay in treatment affects pregnancy outcomes in IVF cycles.

WIDER IMPLICATIONS OF THE FINDINGS: A delay in initiating IVF treatment in patients with diminished ovarian reserve up to 180 days from the initial visit does not affect pregnancy outcomes. This observation remains true for patients who are in the high-risk categories for poor response to ovarian stimulation. Providers and patients should be reassured that when a short-term treatment delay is deemed necessary for medical, logistic or financial reasons, treatment outcomes will not be affected. STUDY FUNDING/COMPETING INTEREST(S): No financial support, funding or services were obtained for this study. The authors do not report any potential conflicts of interest. TRIAL REGISTRATION NUMBER: Not applicable.

FIGURES

Table II The association between time to treatment and IVF treatment outcomes.

Outcome	Immediate treatment (1–90 days), $n = 1115$	Delayed treatment (91–180 days), $n = 675$
No transfer*	133 (11.9%)	69 (10.2%)
	1.00	0.84
	(Ref)	(0.62, 1.15)
Pregnancy rate among all IVF cycles	385 (34.5%)	264 (39.1%)
	1.00	1.23
	(Ref)	(0.99, 1.51)
Live birth rate among all IVF cycles[a]	235 (21.1%)	155 (23.0%)
	1.00	1.11
	(Ref)	(0.88, 1.42)
If embryo transfer	($n = 982$)	($n = 606$)
Pregnancy rate after embryo transfer	385 (39.2%)	264 (43.6%)
	1.00	1.20
	(Ref)	(0.97, 1.48)
Live birth rate after embryo transfer[a]	235 (23.9%)	155 (25.6%)
	1.00	1.08
	(Ref)	(0.85, 1.38)
If clinically pregnant[b]	($n = 385$)	($n = 264$)
SAB[c]	66 (17.1%)	43 (16.3%)
	1.00	0.96
	(Ref)	(0.62, 1.48)
Live birth[a]	235 (61.0%)	155 (58.7%)
	1.00	0.91
	(Ref)	(0.65, 1.26)

Data are *n* (%) with OR (95% CI). Logistic regression models adjusted *a priori* for age and number of embryos transferred to estimate the OR of pregnancy outcomes.

*Adjusted for age only. The reason for no transfer was due to unplanned upfront cryopreservation in six patients in the immediate treatment group and in six patients in the delayed treatment group. The reason for no transfer in all other patients was due to a lack of oocytes, sperm or embryo development.

[a]Live birth was defined as delivery at ≥24 weeks of gestational age.

[b]Clinical pregnancy was defined as the visualization of at least one gestational sac on ultrasound.

[c]Spontaneous abortion (SAB) was defined as a failed pregnancy after the observation of at least one gestational sac on ultrasound.

Table III The association between time to treatment and IVF treatment outcomes in patients with AMH <0.5 ng/ml.

Outcome	Immediate treatment (1–90 days), *n* = 506	Delayed treatment (91–180 days), *n* = 279
No transfer*	76 (15.0%)	38 (13.6%)
	1.00	0.90
	(Ref)	(0.59, 1.37)
Pregnancy rate among all IVF cycles	154 (30.4%)	86 (30.8%)
	1.00	1.01
	(Ref)	(0.72, 1.41)
Live birth rate among all IVF cycles[a]	81 (16.0%)	46 (16.5%)
	1.00	1.02
	(Ref)	(0.67, 1.54)
If embryo transfer	(*n* = 430)	(*n* = 241)
Pregnancy rate after embryo transfer	154 (35.8%)	86 (35.7%)
	1.00	0.99
	(Ref)	(0.70, 1.39)
Live birth rate after embryo transfer[a]	81 (18.8%)	46 (19.1%)
	1.00	0.99
	(Ref)	(0.65, 1.51)
If clinically pregnant[b]	(*n* = 154)	(*n* = 86)
SAB[c]	35 (22.7%)	18 (20.9%)
	1.00	0.97
	(Ref)	(0.50, 1.89)
Live birth[a]	81 (52.6%)	46 (53.5%)
	1.00	0.99
	(Ref)	(0.57, 1.72)

Data are *n* (%) with OR (95% CI). Logistic regression models adjusted *a priori* for age and number of embryos transferred to estimate the OR of pregnancy outcomes.
*Adjusted for age only.
[a]Live birth was defined as delivery at ≥24 weeks of gestational age.
[b]Clinical pregnancy was defined as the visualization of at least one gestational sac on ultrasound.
[c]SAB was defined as a failed pregnancy after the observation of at least one gestational sac on ultrasound.

Table IV The association between time to treatment and IVF treatment outcomes in patients >40 years old.

Outcome	Immediate treatment (1–90 days), *n* = 524	Delayed treatment (91–180 days), *n* = 305
No transfer*	60 (11.5%)	39 (12.8%)
	1.00	1.18
	(Ref)	(0.76, 1.83)
Pregnancy rate among all IVF cycles	135 (25.8%)	85 (27.9%)
	1.00	1.11
	(Ref)	(0.79, 1.55)
Live birth rate among all IVF cycles[a]	57 (10.9%)	39 (12.8%)
	1.00	1.19
	(Ref)	(0.76, 1.87)
If embryo transfer	(*n* = 464)	(*n* = 266)
Pregnancy rate after embryo transfer	135 (29.1%)	85 (32.0%)
	1.00	1.13
	(Ref)	(0.81, 1.59)
Live birth rate after embryo transfer[a]	57 (12.3%)	39 (14.7%)
	1.00	1.21
	(Ref)	(0.77, 1.91)
If clinically pregnant[b]	(*n* = 135)	(*n* = 85)
SAB[c]	43 (31.9%)	16 (18.8%)
	1.00	0.51
	(Ref)	(0.26, 0.98)
Live birth[a]	57 (42.2%)	39 (45.9%)
	1.00	1.10
	(Ref)	(0.63, 1.93)

Data are *n* (%) with OR (95% CI). Logistic regression models adjusted *a priori* for age and number of embryos transferred to estimate the OR of pregnancy outcomes.
*Adjusted for age only.
[a]Live birth was defined as delivery at ≥24 weeks of gestational age.
[b]Clinical pregnancy was defined as the visualization of at least one gestational sac on ultrasound.
[c]SAB was defined as a failed pregnancy after the observation of at least one gestational sac on ultrasound.

CASE REPORT: USE OF LENZILUMAB AND TOCILIZUMAB FOR THE TREATMENT OF CORONAVIRUS DISEASE 2019

Melody M, Nelson J, Hastings J, Propst J, Smerina M, Mendez J, Guru P.. Immunotherapy. 2020 Jun 17. doi: 10.2217/imt-2020-0136. Online ahead of print.
Level of Evidence: Other - Case Report

BLUF

Physicians from the Mayo Clinic present the case of a 68-year-old male patient with RT-PCR confirmed COVID-19 pneumonia. Initial treatment with lenzilumab and hydroxychloroquine was followed by deteriorating status, but after treatment with tocilizumab the patient showed marked clinical improvement and eventually recovered, leading the authors to call for increased research on the use of tocilizumab instead of lenzilumab in the treatment of COVID-19.

SUMMARY

Physicians from the Mayo Clinic present the case of a 68-year-old male patient who presented with a four-day history of productive cough, dyspnea, and fever. He was diagnosed with COVID-19 pneumonia via RT-PCR of nasopharyngeal swab sample. Upon admission the patient was treated with lenzilumab and hydroxychloroquine, however after three days the patient's clinical symptoms worsened and laboratory findings revealed a cytokine surge. The patient was then administered a single 680 mg dose of tocilizumab intravenously, after which there was a marked clinical improvement in his condition and subsequent recovery (Table 1, Figure 1, Figure 2). The authors recommend further exploration into the use of tocilizumab instead of lenzilumab in the treatment of COVID-19.

ABSTRACT

Background: Coronavirus disease 2019 (COVID-19) is a novel disease associated with a cytokine-mediated, severe, acute respiratory syndrome. Tocilizumab and lenzilumab are recombinant monoclonal antibodies against IL-6 and granulocyte macrophage colony-stimulating factor, respectively, and have been proposed as a potential treatment for acute, hypoxic respiratory failure associated with COVID-19. Results & methodology: We present the case of a 68-year-old man with COVID-19 who was initially treated with hydroxychloroquine and lenzilumab, but continued to develop hypoxemia, requiring an increase in respiratory support with an associated rise in serum inflammatory markers. He was subsequently treated with tocilizumab with marked clinical improvement and a decrease in acute phase reactants within 48 h. Discussion & conclusion: This case demonstrates the effective use of tocilizumab in the treatment of COVID-19 and suggests the superiority of tocilizumab over lenzilumab in the management of this cytokine-mediated syndrome.

FIGURES

	Day 4 presentation & lenzilumab dosing	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10 tocilizumab dosing	Day 11	Day 12	Day 13	Day 14
WBC	4.0	4.0	5.5	5.0	6.5	5.7	6.1	5.0	4.0	4.6	4.6
ANC	3.10	–	4.51	3.62	4.85	4.80	4.42	3.11	2.21	–	–
CRP (mg/l)	44.9	61.2	83.9	82.8	86.5	152.0	175.8	174.7	145.7	63.6	–
LDH (U/l)	282	–	267	272	267	388	226	234	233	206	–
Ferritin (mcg/l)	519	–	611	–	736	–	745	–	842	–	–
Procalcitonin (ng/ml)	0.08	–	–	0.11	–	–	–	–	0.13	0.10	–
IL-6 (pg/ml)	27.1	34.2	30.8	30.9	95.4	–	57.6	363	–	–	125
FiO_2 (%)	100	100	100	80	60	60	100	50	40	40	40
O_2 (l/min)	3	2.5	4	50	50	50	60	50	30	30	30

ANC: Absolute neutrophil count; CRP: C-reactive protein; FIO_2: Fraction of inspired oxygen; LDH: Lactate dehydrogenase; O_2: Oxygen; WBC: White blood cell count.

Table 1. Acute phase reactants and O2 requirements over course of hospitalization.

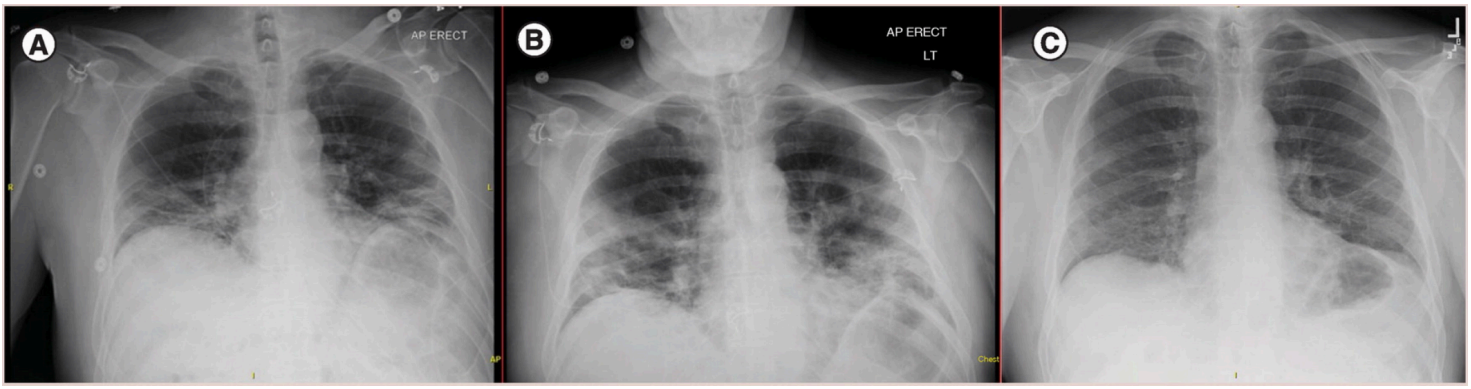


Figure 1. Radiographic images illustrating progression of COVID-19 related pneumonia.

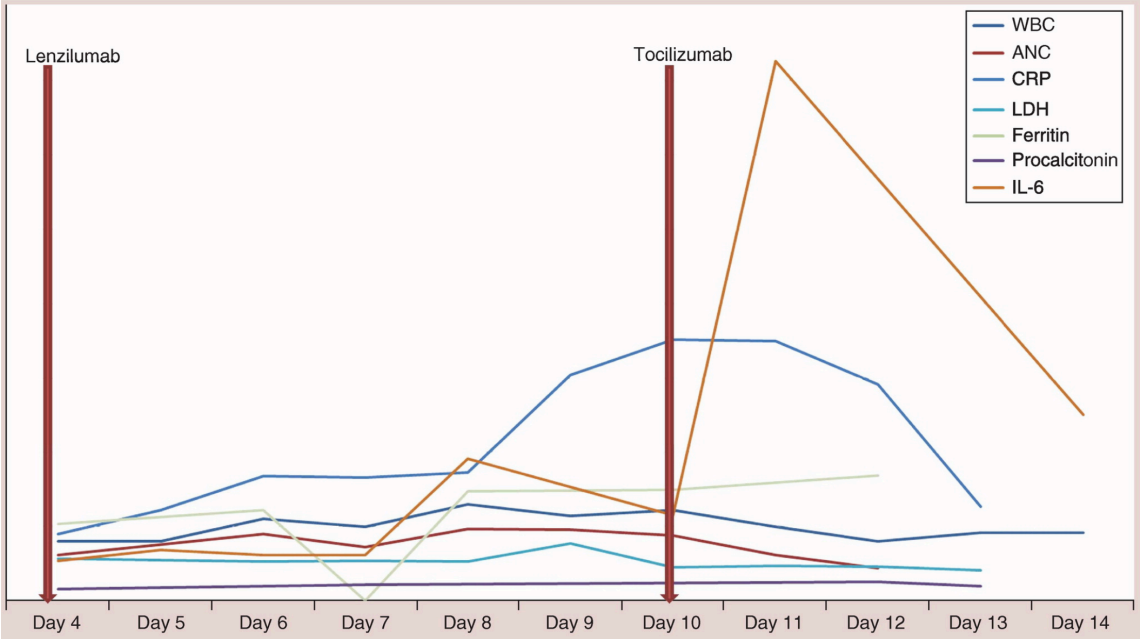


Figure 1. Radiographic images illustrating progression of COVID-19 related pneumonia.

CURRENT DIAGNOSTICS

DIAGNOSTIC EFFICACY OF ANTI-SARS-COV-2 IGG/IGM TEST FOR COVID-19: A META-ANALYSIS

Zhang ZL, Hou YL, Li DT, Li FZ.. J Med Virol. 2020 Jun 22. doi: 10.1002/jmv.26211. Online ahead of print.
Level of Evidence: 3 - Non-consecutive studies, or studies without consistently applied reference standards

BLUF

Authors from China conducted a meta-analysis of 22 studies involving a total of 3,767 individuals (2,282 patients with and 1,485 patients without SARS-CoV-2) in order to assess the diagnostic efficiency of the anti-SARS-CoV-2 IgG/IgM test. The respective pooled sensitivity, specificity, and area under the curve for each anti-SARS-CoV-2 test were the following:

1) IgG: 0.85, 0.99, and 0.99 at a 95% confidence interval (CI), and
2) IgM: 0.74, 0.99, and 0.95 at a 95% (CI) (figure 2).

Quality was assessed by the QUADAS-2 tool with a heterogeneity of I^2>50%. Although the diagnostic performance of IgG is slightly stronger than IgM, findings suggests that both tests are most promising in diagnosing patients that have shown symptoms for at least 5 days, and are less promising in diagnosing patients during the window period.

ABSTRACT

The serological testing of anti-SARS-CoV-2 IgG and/or IgM is widely used in the diagnosis of COVID-19. However, its diagnostic efficacy remains unclear. In this study, we searched diagnostic studies from Web of Science, PubMed, Embase, CNKI, Wanfang databases to calculate the pooled diagnostic accuracy measures using bivariate random-effects model meta-analysis. As a result, 22 from a total of 1613 articles, including 2,282 patients with SARS-CoV-2 and 1,485 healthy persons or patients without SARS-CoV-2, were selected for a meta-analysis. Pooled sensitivity, specificity, and area under curve (AUC) of summary receiver operator curve (SROC) were: (i) 0.85 (95% CI: 0.79- 0.90), 0.99 (95% CI: 0.98- 1.00), and 0.99 (95% CI: 0.97- 0.99) for anti-SARS-CoV-2 IgG; (ii) 0.74 (95% CI: 0.65- 0.81), 0.99 (95% CI: 0.97- 1.00), and 0.95 (95% CI: 0.93- 0.97) for IgM. A subgroup analysis among detection methods indicated the sensitivity of IgG and IgM using ELISA were slightly lower than those using gold immunochromatography assay (GICA) and chemiluminescence immunoassay (CLIA) (p > .05) These results showed that the detection of anti-SARS-CoV-2 IgG and IgM had high diagnostic efficiency to assist the diagnosis of SARS-CoV-2 infection. And, GICA might be used as the preferred method for its accuracy and simplicity. This article is protected by copyright. All rights reserved.

FIGURES

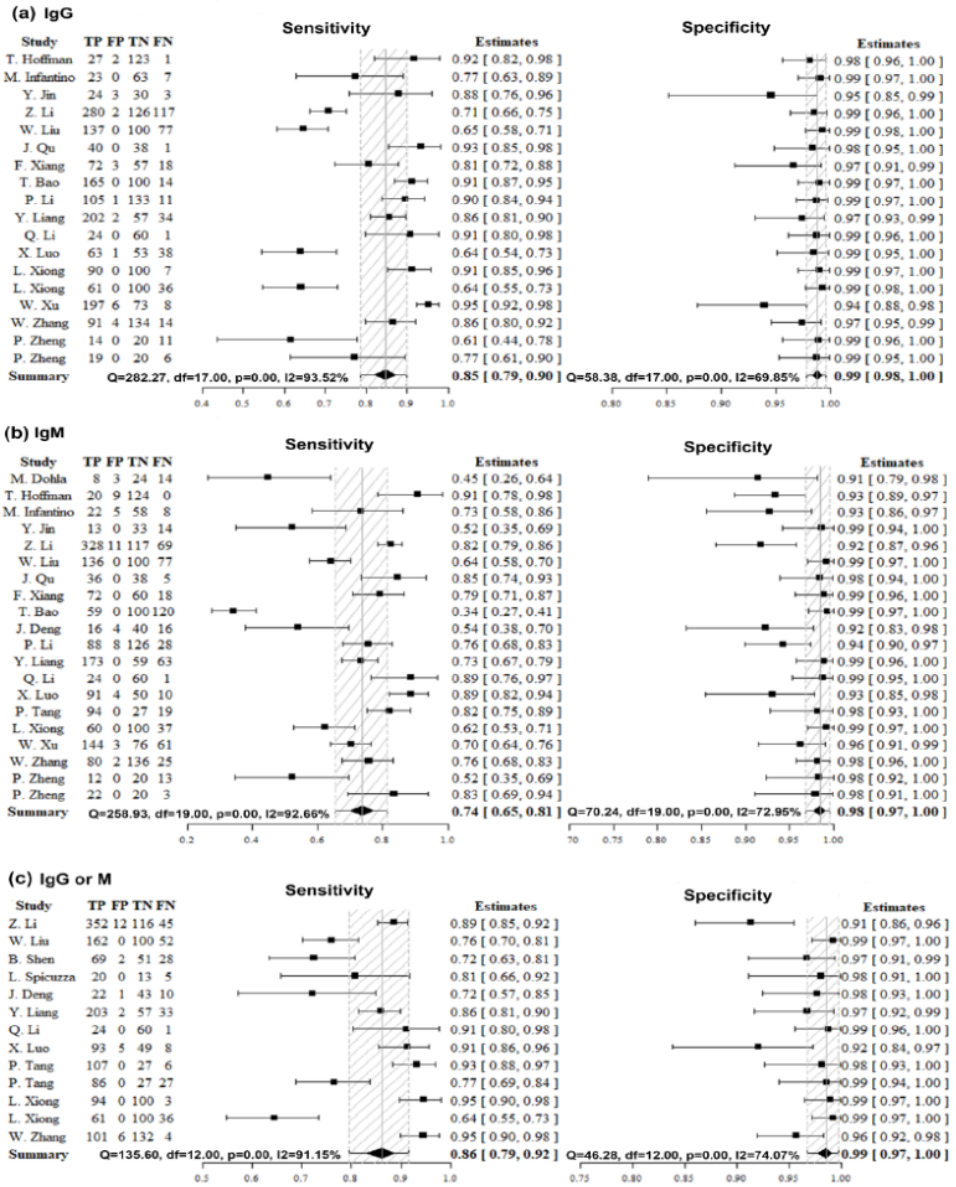


Figure 2. Forest plots of the pooled sensitivity and specificity for anti-SARS-CoV-2 IgG, IgM, and IgG or IgM in diagnosis of Covid-19. (a) IgG, (b) IgM, (c) IgG or IgM. Only the first author of each study is given. Sensitivity and specificity were given with confidence intervals (CI).

ANTIBODY PROFILES IN MILD AND SEVERE CASES OF COVID-19

Liu ZL, Liu Y, Wan LG, Xiang TX, Le AP, Liu P, Peiris M, Poon LLM, Zhang W.. Clin Chem. 2020 Jun 10:hvaa137. doi: 10.1093/clinchem/hvaa137. Online ahead of print.
Level of Evidence: 3 - Non -randomized controlled cohort/follow-up study

BLUF

In this retrospective cohort study, authors affiliated with Nanchang University in China analyzed the IgM or total antibody levels specific to the SARS-CoV-2 spike protein receptor binding domain (RBD) with two commercially available chemiluminescence immunoassays in 192 patients with severe or mild COVID-19 and in 144 control serum samples. The authors found that there was no statistically significant difference between mild and severe COVID-19 cases within 6 days of disease onset (P>0.05); however, after day 6, severe cases had higher IgM (P=0.013, days 7-12) and a higher overall positivity rate for total antibody titers (P<0.00001) than that of mild cases (Figure 1). Further, of 35 mild cases with multiple serial samples (N >= 3), 12/35 were negative for all IgM assays performed and 5/35 were negative for total antibody titers. These findings highlight the possible limitations in antibody testing of patients with mild COVID-19, suggesting a need to further characterize the immune response in this population to elucidate methods on immunological surveillance and the potential for re-infection.

FIGURES

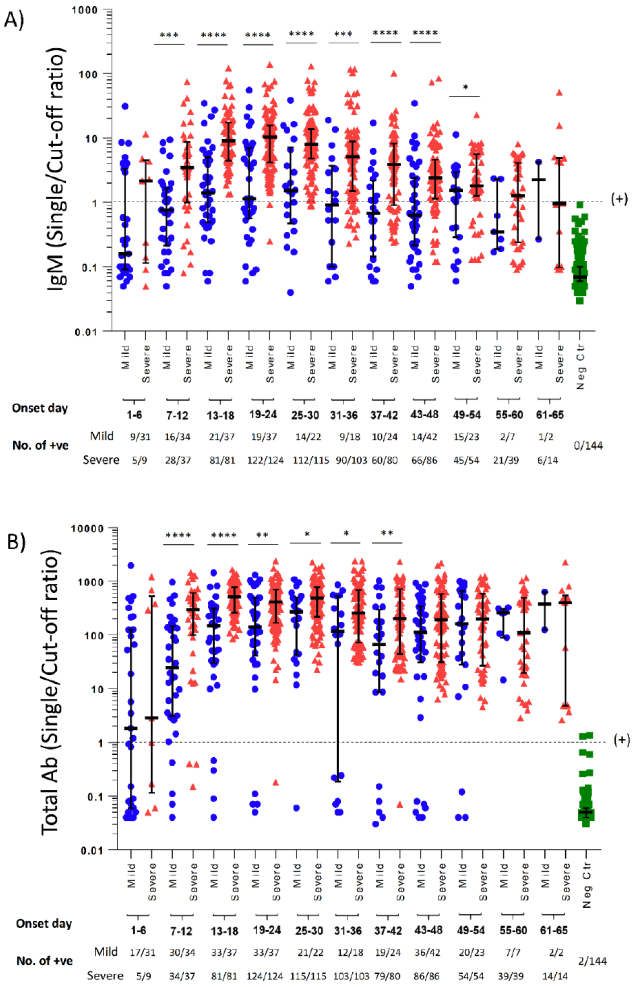


Figure 1. Antibody profiles of all COVID-19 patients. The levels of IgM (panel A) and total Ab (panel B) specific for the SARS-CoV-2 spike protein receptor binding domain (RBD) from patients at different periods after disease onset are shown (where day 1: the first day symptoms begin). The cut off value of positivity for each assay is indicated by a dotted line. The numbers of tested cases in severe and mild groups are indicated. Control serum samples (green; N=144) were collected from individuals who were not known to have COVID-19-like symptoms, but none of these donors were screened for SARS-CoV-2 by RT-PCR. Mann-Whitney test: ****P less than 0.0001, ***P less than 0.001, **P less than 0.01; *P less than 0.05.

DEVELOPMENT OF A LATERAL FLOW IMMUNOASSAY STRIP FOR RAPID DETECTION OF IGG ANTIBODY AGAINST SARS-COV-2 VIRUS

Wen T, Huang C, Shi FJ, Zeng XY, Lu T, Ding SN, Jiao YJ.. Analyst. 2020 Jun 22. doi: 10.1039/d0an00629g. Online ahead of print.

Level of Evidence: 5 - Mechanism-based reasoning

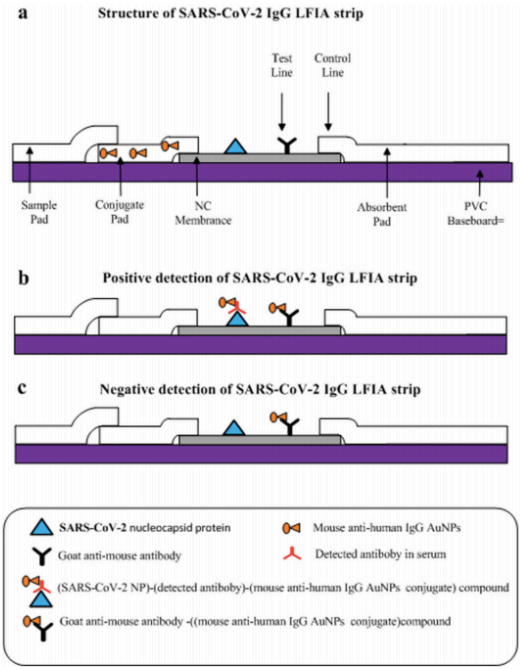
BLUF

Chinese researchers discuss the development of solid-phase lateral flow immunoassay strips (LFIAs) to detect IgG antibody against SARS-CoV-2 as a diagnostic tool for current and previous exposure (see Scheme 1 for mechanism). A total of 85 samples were collected, 55 from known COVID-19 patients and 30 controls. Analysis revealed a sensitivity of 69.1% (Table 1). The researchers believe LFIAs may be effective for preliminary testing but further improvements on signal amplification and quantification systems warrant further study.

ABSTRACT

The ongoing worldwide SARS-CoV-2 epidemic clearly has a tremendous influence on public health. Molecular detection based on oral swabs was used for confirmation of SARS-CoV-2 infection. However, high false negative rates were reported. We describe here the development of a point-of-care (POC) serological assay for the detection of IgG antibody against SARS-CoV-2. The principle of a lateral flow immunoassay strip (LFIAs) consists of fixing SARS-CoV-2 nucleocapsid protein to the surface of the strip and coupling anti-human IgG with colloidal gold nanoparticles (Au NPs). A series of parameters of this method were optimized, including the concentration of coating antigen, BSA blocking concentration and pH value for conjugation. The entire detection process took 15-20 min with a volume of 80 muL of the analyte solution containing 10 muL of serum and 70 muL sample diluent. The performance of the established assay was evaluated using serum samples of the clinically diagnosed cases of Coronavirus Disease 2019 (COVID-19). Our results indicated that the LFIAs for SARS-CoV-2 had satisfactory stability and reproducibility. As a result, our fast and easy LFIAs could provide a preliminary test result for physicians to make the correct diagnosis of SARS-CoV-2 infections along with alternative testing methods and clinical findings, as well as seroprevalence determination, especially in low-resource countries.

FIGURES



Scheme 1 Structure of the LFIA strip and mechanism of positive and negative detection.

Scheme 1. Structure of the LFIA strip and mechanism of positive and negative detection.

CHEMICAL-INFORMATICS APPROACH TO COVID-19 DRUG DISCOVERY: MONTE CARLO BASED QSAR, VIRTUAL SCREENING AND MOLECULAR DOCKING STUDY OF SOME IN-HOUSE MOLECULES AS PAPAIN-LIKE PROTEASE (PLPRO) INHIBITORS

Amin SA, Ghosh K, Gayen S, Jha T.. J Biomol Struct Dyn. 2020 Jun 22:1-10. doi: 10.1080/07391102.2020.1780946. Online ahead of print.
Level of Evidence: Other - Modeling

BLUF

In this study, Indian pharmacologic researchers sought to identify molecules with inhibitory action against papain-like protease (PLpro), an enzyme essential to SARS-CoV-2 replication. After applying several computational models, including Monte Carlo based Quantitative structure-activity relationship (QSAR); virtual screening; absorption, distribution, metabolism, and excretion (ADME) criteria (Figure 4); and lastly a molecular docking study (Figure 5), they were able to identify 13 in-house molecules with likely inhibitory action. The authors posit that these are potential therapeutic drugs for COVID-19, although they also acknowledge that extensive in vitro and in vivo studies are required to confirm their models and to explore efficacy.

ABSTRACT

World Health Organization characterized novel coronavirus disease (COVID-19), caused by severe acute respiratory syndrome (SARS) coronavirus-2 (SARS-CoV-2) as world pandemic. This infection has been spreading alarmingly by causing huge social and economic disruption. In order to response quickly, the inhibitors already designed against different targets of previous human coronavirus infections will be a great starting point for anti-SARS-CoV-2 inhibitors. In this study, our approach integrates different ligand based drug design strategies of some in-house chemicals. The study design was composed of some major aspects: (a) classification QSAR based data mining of diverse SARS-CoV papain-like protease (PLpro) inhibitors, (b) QSAR based virtual screening (VS) to identify in-house molecules that could be effective against putative target SARS-CoV PLpro and (c) finally validation of hits through receptor-ligand interaction analysis. This approach could be used to aid in the process of COVID-19 drug discovery. It will introduce key concepts, set the stage for QSAR based screening of active molecules against putative SARS-CoV-2 PLpro enzyme. Moreover, the QSAR models reported here would be of further use to screen large database. This study will assume that the reader is approaching the field of QSAR and molecular docking based drug discovery against SARS-CoV-2 PLpro with little prior knowledge.Communicated by Ramaswamy H. Sarma.

FIGURES

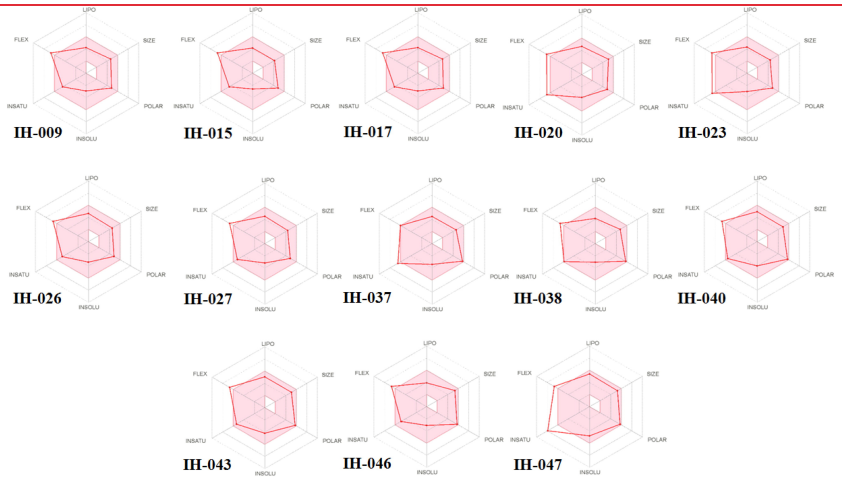


Figure 4. Radar plot of the in-house compounds after calculating ADME data by SwissADME server (http://www.swissadme.ch/) suggesting the drug-likeness [the pink area represents the optimal range of each properties. LIPO = Lipophilicity (between -0.7 and +5.0), SIZE = Molecular weight (between 150 and 500 g/mol), POLAR = Polarity (between 20 and 130Å 2), INSOLU = Solubility (not higher than 6), INSATU = Saturation (fraction of carbons in the sp3 hybridization not less than 0.25), FLEX = Flexibility (no more than 9 rotatable bonds).

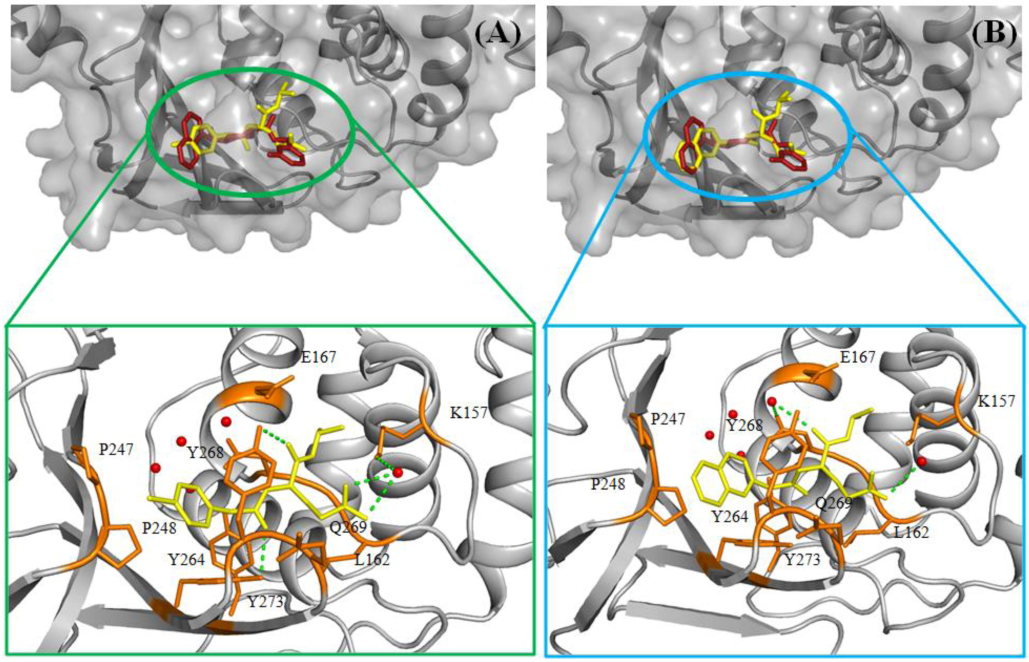


Figure 5. The docking modes of two prototype in-house [virtual screen] hits (A) IH-009 and (B) IH-027 in the catalytic site amino acid residues of SARS-CoV-2 PLpro (proetin, grey cartoon; active site amino acids, orange stick; in-bound ligand, red stick; in-house molecules, yellow stick; water molecule, red ball; hydrogen bond interactions, light green dashed lines).

MENTAL HEALTH & RESILIENCE NEEDS

DID THE GENERAL POPULATION IN GERMANY DRINK MORE ALCOHOL DURING THE COVID-19 PANDEMIC LOCKDOWN?

32556079. Did the General Population in Germany Drink More Alcohol during the COVID-19 Pandemic Lockdown?
Level of Evidence: 3 - Local non-random sample

BLUF

In this letter to the editor, German addiction medicine experts discuss an increase in alcohol consumption during the lockdown and report on an anonymous online survey of the German general population (n=2102). Of participants, 8.2% reported no alcohol use while 34.7% reported increased alcohol consumption since the beginning of lockdown. Use increased in respondents with less education and higher perceived stress (of note, no statistical analysis was reported). The authors raise concerns that increased alcohol use could lead to a higher incidence of alcohol use disorder and recommend healthcare providers prepare to support this vulnerable population.

COVID-19'S IMPACT ON HEALTHCARE WORKFORCE

MENTAL HEALTH OF HEALTH-CARE WORKERS IN THE COVID-19 ERA

Greenberg N.. Nat Rev Nephrol. 2020 Jun 19. doi: 10.1038/s41581-020-0314-5. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

This expert opinion from The Health Protection Research Unit, King's College London explores factors that increase healthcare workers' (HCWs) risk of developing mental health problems (PTSD, depression, anxiety, substance abuse, and suicidal ideations) while working in the COVID-19 pandemic. Contributing factors include long hours as well as traumatic and stressful events some HCWs endure. The author proposes six key elements to safeguard mental health in these professionals (see below).

SUMMARY

The recommendations for protecting the mental health of healthcare workers involves the following 6 key elements:

1. Be attentive and acknowledge HCWs and provide available resources that attend to their needs.
2. Follow-up on HCWs who have not returned to work following a traumatic experience and check on their mental-wellbeing.
3. HCWs should undergo "return to normal work interviews" by the supervisor prior to returning back to work.
4. Maintain transparency within the work environment to increase communications between HCWs, especially for BAME (Black, Asian, and minority ethnicity) individuals.
5. Actively monitor and proactively inquire about HCWs' mental health through an "online self-check tool" and offering tailored advice such as self-help information or ways to access professional care.
6. Managers should help HCWs share their experiences without blaming themselves or others as this may reduce the risk of developing psychological harm.

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