The Daily COVID-19 Literature Surveillance Summary

July 3, 2020

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COVID-19 Daily Literature Surveillance

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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 medical ethicist discusses unique ethical dilemmas that the COVID-19 pandemic has presented including individual rights vs public good, data collection, resource rationing, and vaccine trials.

Epidemiology:
- Age demographics and travel histories of confirmed COVID-19 cases: Authors from the Hong Kong University of Science and Technology found that the largest incidence of positive cases occurred in the 15-24 age group (41%). Furthermore, (61%) had traveled to countries with known outbreak or been exposed to other infected travelers. These findings emphasize risk of transmission among younger, less symptomatic individuals and reveal the importance of travel restrictions/precautions during the pandemic.
- A retrospective cohort study from China (n=104) analyzed predictors of severe COVID-19 disease based on initial presentation. They found that older age (>63 years [odds ratio, OR=41.0; 95% CI: 2.8, 592.4]), decreased lymphocyte count ($\leq 1.02 \times 10^9$/L [OR=6.1; 95% CI: 1.5, 25.2]), and elevated serum CRP (≥ 65.08 mg/L [OR= 8.9; 95% CI = 1.0, 74.2]) are key early predictors of severe disease.
- Neurological effects of COVID-19: Nature Reviews Neurology highlights the significant evidence of CNS damage in COVID-19, noting the wide range of symptomatology and still undetermined mechanism injury.
- Cytokine release syndrome (CRS) in COVID-19: Data from 11 patients with acute respiratory distress syndrome (ARDS) in Guangzhou, China indicated that 8/11 patients developed CRS with characteristics including a continuous fever, end-organ dysfunction, and coagulopathy. A substantial increase of interleukin 6 (IL-6) suggests it may act as a prognostic factor for CRS development in COVID-19 patients with severe pneumonia.

Understanding the Pathology:
- Analysis of immune marker expression profiles of 24 patients in Germany found an association between severe COVID-19 disease and increased interactions between epithelial and immune cells. These data further implicate a heightened immune inflammatory response as a pathophysiological mechanism and suggest that dampening of immune hyperactivation, perhaps by targeting common endpoints of signaling pathways such as CCR1 and/or CCR5 pathways, has therapeutic potential.
- Researchers from India hypothesize that the cytokine storm in COVID-19 may be caused by SARS-CoV-2 invasion of the vagus, facial, and glossopharyngeal nerve axons, leading to inflammation of the nucleus tractus solitarius (NTS) and ensuing dysregulation of cholinergic anti-inflammatory pathways and hypothalamic–pituitary–adrenal axis.

Transmission and Prevention:
- An author from the University of California, San Francisco presents a counterargument to a nation-wide antigen and antibody screening program in the US, citing poor test sensitivity, increased risk to healthcare workers administering tests, and lack of correlation between antibody presence and viral neutralization.

Management:
- A group of international researchers evaluating clinical indexes of 75 hospitalized COVID-19 patients in Zhejiang, China found that the proportion of abnormal IL-2, IL-4, and total cholesterol levels were significantly higher in critically-ill patients compared to moderate severity. This is consistent with previous studies, and suggests these may be a useful indicator for identification of severe disease.
- Guidelines developed by Shoham Geriatric Medical Center (SGMC) in Israel to support physical therapy (PT) interventions for geriatric COVID-19 patients recommend direct contact PT treatments, as opposed to tele-rehabilitation, to address both functional and respiratory impairments of geriatric patients with COVID-19.
- An opinion article from the Annals of Emergency Medicine critique the reported findings of the Richardson et. al., 2020 observational case series that found a mortality rate of 88.1% among patients requiring mechanical ventilation. The authors argue that the reported "higher-than-expected mortality" is due to "right censoring" since analysis occurred before most intubated patients had experienced the outcome of the study (death or discharge). They offer two possible solutions (stating the status of all patients at data collection or clarifying the uncertainty in results), illustrating ways future observational studies can avoid presenting disinformation.

Adjusting Practice During COVID-19:
- Recommendations for neonatal and maternal care in low-resource settings during the COVID-19 pandemic included droplet precautions, hand hygiene, and physical spacing, in addition to outlining warning-signs of late-onset neonatal COVID-19 infection. The authors also recommend continuing standard of care with delayed cord clamping in excess of

30 seconds to assure adequate placental transfusion, allowing skin-to-skin contact following appropriate masking, hand-washing, and breast hygiene, and monitoring children for delayed COVID-19 infection after birth in addition to new droplet precautions.

R&D Diagnosis and Treatment:

- Authors associated with Gilead Sciences Inc. present two first-in-human (FIH) phase I studies (a single-dose escalation study and a multiple-dose study) evaluating the safety and pharmacokinetics of IV remdesivir (RDV) in healthy participants for the potential use of RDV in COVID-19 treatment suggesting that a single-dose of RDV daily, whether as a solution or lyophilized formulation, is well-tolerated and safe to use in healthy adults, supporting the continued clinical investigation of RDV in COVID-19 therapy.

TABLE OF CONTENTS

COVID-19 CURRENT CONTROVERSIES

BLUF

An expert in medical ethics and health policy from the Baylor College of Medicine in Houston, Texas presents several ethical controversies that have emerged and been discussed in the literature since the beginning of the COVID-19 pandemic, including:

1. How and when should various laws designed to protect patient rights be used to inform COVID-19 policy development?
2. Should personal privacy be compromised for the greater good?
3. How do we ensure that effective care is delivered safely by healthcare workers in high-risk environments?
4. How do we best distribute personal protective equipment and manage other hospital resources?
5. How do we guarantee the best decision-making for patients who are cognitively impaired?
6. How do we use the data collected by ethicists on pandemic management worldwide?
7. Who is allowed to provide pediatric patient care and how much parental involvement is acceptable?
8. When would it be ethical to consider secondary vaccine trials?

These questions suggest that as the pandemic progresses further, additional ethical concerns will arise and will need to be addressed by adjusting current practices, guidelines, and workplace models.

EXPLORING THE YOUNG DEMOGRAPHIC PROFILE OF COVID-19 CASES IN HONG KONG: EVIDENCE FROM MIGRATION AND TRAVEL HISTORY DATA

BLUF

This study by authors from The Hong Kong University of Science and Technology examines the age demographics and travel histories of confirmed COVID-19 cases in Hong Kong from January 23 to April 16, 2020 and found that the largest incidence occurred in the aged 15-24 group (Figure 1). Further, 3 in 5 confirmed cases (61%) had travel histories from countries with known COVID-19 spread or were infected by another traveling case, with 41.1% of these "imported cases" being in the aged 15-24 group (Figure 2). These findings reveal the importance of demographic analysis of young confirmed cases in addition to older age groups and the importance of travel restrictions/precautions during the pandemic.

ABSTRACT

This paper investigates the profile of COVID-19 cases in Hong Kong, highlighting the unique age structure of confirmed cases compared to other territories. While the majority of cases in most territories around the world have fitted an older age profile, our analysis shows that positive cases in Hong Kong have been concentrated among younger age groups, with the largest incidence of cases reported in the 15-24 age group. This is despite the population's rapidly aging structure and extremely high levels of population density. Using detailed case data from Hong Kong's Centre for Health Department and Immigration Department, we analyze the sex and age distribution of the confirmed cases along with their recent travel histories and immigration flows for the period January to April 2020. Our analysis highlights Hong Kong's high proportion of imported cases and large overseas student population in developing COVID-19 hotspot areas such as the United Kingdom. Combined with community action and targeted and aggressive early policy measures taken to contain the virus, these factors may have contributed to the uniquely younger age structure of COVID-19 cases in the city. Consequently, this young profile of confirmed cases may have prevented fatalities in the territory. Recent research has highlighted the importance of a demographic approach to understanding COVID-19 transmission and fatality rates. The experience in Hong Kong shows that while an older population age structure may be important for understanding COVID-19 fatality, it is not a given. From a social science perspective at least, there is 'no easy answer' to why one area should experience COVID-19 differently from another.
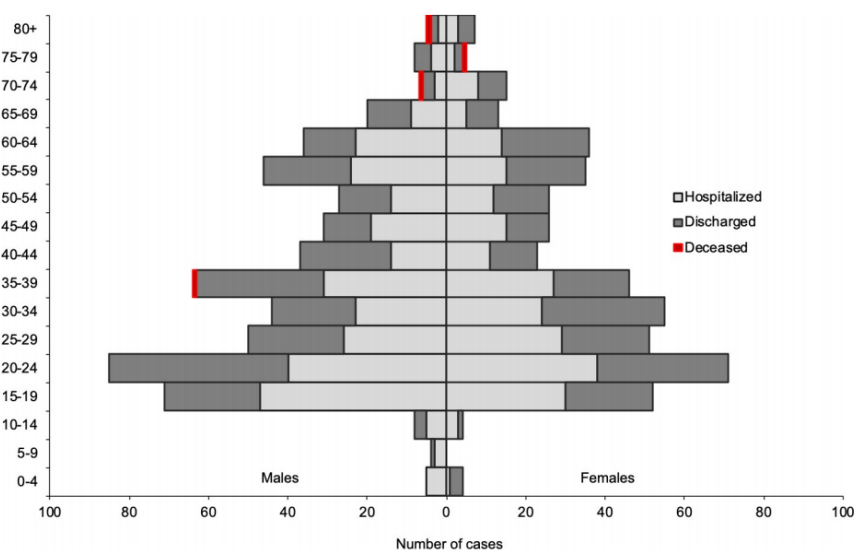
FIGURES

Fig 1. Age and sex distribution of confirmed COVID-19 cases Hong Kong (n = 1,017, as of April 16, 2020). Data Source: Hong Kong Center for Health Protection, Department of Health.
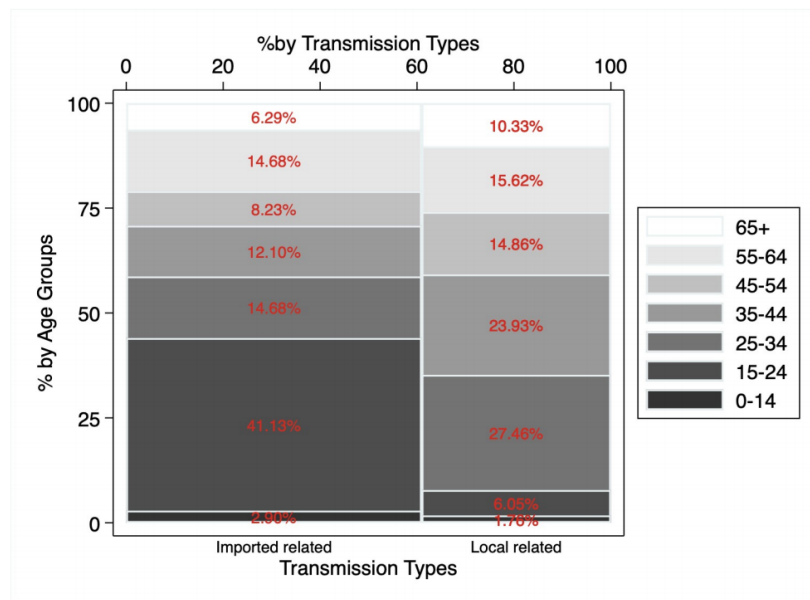
Fig 2. Distribution of confirmed COVID-19 cases by transmission type and by age groups: Hong Kong (n = 1,017, as of April 16, 2020). Data Source: Hong Kong Centre for Health Protection, Department of Health.

SYMPTOMS AND CLINICAL PRESENTATION

ANALYSIS OF CLINICAL FEATURES AND EARLY WARNING SIGNS IN PATIENTS WITH SEVERE COVID-19: A RETROSPECTIVE COHORT STUDY

BLUF

A retrospective cohort study by researchers in China examined 104 COVID-19 patients in the Henan province who either discharged or died prior to 15 February 2020 to identify predictors of severe cases based on initial presentation. Authors found that older age (>63 years [odds ratio, OR=41.0; 95% CI: 2.8, 592.4]), decreased lymphocyte count (≤1.02×10^9/L [OR=6.1; 95% CI: 1.5, 25.2]), and elevated serum CRP (≥65.08 mg/L [OR= 8.9; 95% CI = 1.0, 74.2]) are key predictors during early stage diagnosis for those at high risk of developing severe COVID-19, which could be used to inform physicians about patients who require further monitoring.

SUMMARY

Summary of additional study findings below:
The severe group (n=30) was defined by those who underwent continuous renal replacement therapy, high-flow oxygen absorption, mechanical ventilation, or extracorporeal membrane oxygenation and the remaining patients were assigned to the non-severe group (n=74). All of the following demographic and clinical information was collected retrospectively from the electronic medical records (Table 1):
- 84 patients (80.8%) had history of traveling or residing in Wuhan or surrounding areas, or other communities with reported COVID-19 cases.
- 38 patients (36.5%) had contact with individuals who were experiencing fever or respiratory symptoms and had recently been to Wuhan or other communities with reported cases.
- 24 patients (23.1%) had a history of contact with a COVID-19 patient.
- Fever was the most common initial symptom, seen in 79 patients (76.0%).
- Underlying diseases (respiratory, cardiovascular, neurological) manifested in 13 (43.3%) patients in the severe group, which was higher than in the non-severe group (P<0.05).
- The proportion of patients with dyspnea was significantly higher in the severe group than in the non-severe group (P <0.05).
- Direct bilirubin, lactate dehydrogenase, CRP, and procalcitonin levels were significantly higher in the severe group than in the non-severe group (P <0.05) and the absolute value of lymphocyte count was significantly lower in the severe group than in

the non-severe group (P <0.05).
- An analysis of the receiver operating characteristics (ROC) curves with multiple predictors indicate that age, lymphocyte count, and CRP are independent predictors for an increased risk of severe COVID-19 (Figure 5).

ABSTRACT

Coronavirus disease 2019 (COVID-19) was first identified in Wuhan, China, in December 2019. Although previous studies have described the clinical aspects of COVID-19, few studies have focused on the early detection of severe COVID-19. Therefore, this study aimed to identify the predictors of severe COVID-19 and to compare clinical features between patients with severe COVID-19 and those with less severe COVID-19. Patients admitted to designated hospital in the Henan Province of China who were either discharged or died prior to February 15, 2020 were enrolled retrospectively. Additionally, patients who underwent at least one of the following treatments were assigned to the severe group: continuous renal replacement therapy, high-flow oxygen absorption, noninvasive and invasive mechanical ventilation, or extracorporeal membrane oxygenation. The remaining patients were assigned to the non-severe group. Demographic information, initial symptoms, and first visit examination results were collected from the electronic medical records and compared between the groups. Multivariate logistic regression analysis was performed to determine the predictors of severe COVID-19. A receiver operating characteristic curve was used to identify a threshold for each predictor. Altogether,104 patients were enrolled in our study with 30 and 74 patients in the severe and non-severe groups, respectively. Multivariate logistic analysis indicated that patients aged >=63 years (odds ratio = 41.0; 95% CI: 2.8, 592.4), with an absolute lymphocyte value of <=1.02x109/L (odds ratio = 6.1; 95% CI = 1.5, 25.2) and a C-reactive protein level of >=65.08mg/L (odds ratio = 8.9; 95% CI = 1.0, 74.2) were at a higher risk of severe illness. Thus, our results could be helpful in the early detection of patients at risk for severe illness, enabling the implementation of effective interventions and likely lowering the morbidity of COVID-19 patients.
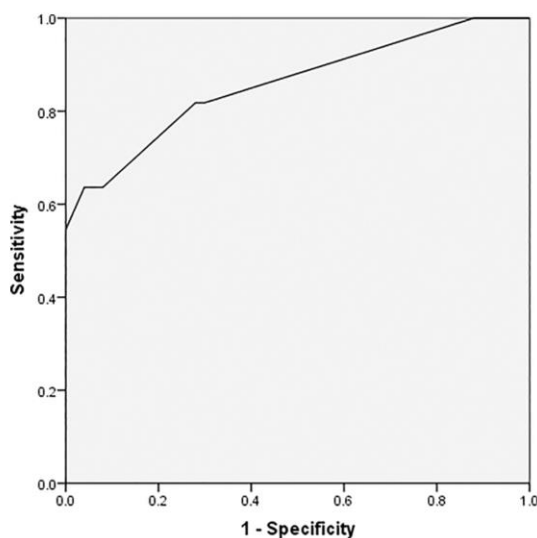
FIGURES

Figure 5: Receiver operating characteristic curve of the multivariate prediction model.

Table 1

Baseline demographics and epidemiological and clinical status of participants.

Basic information	Statistics			P
	All patients	Non-severe group	Severe group	
Age, median (IQR)	42.0 (31.0–55.0)	40.0 (32.0–55.0)	55.0 (31.0–72.0)	0.005
Sex				0.509
Male, n (%)	63(60.6)	43 (58.1)	20 (66.7)	-
Female, n (%)	41(39.4)	31 (41.9)	10 (33.3)	-
Exposure history				
Travelling in Wuhan, n (%)	84 (80.8)	65 (87.8)	19 (63.3)	0.006
Contact with patient in Wuhan, n (%)	38 (36.5)	31 (41.9)	7 (23.3)	0.115
Clustered onset, n (%)	17 (16.3)	13 (17.6)	4 (13.3)	0.772
Contact with COVID-19, n (%)	24 (23.1)	17 (23.0)	7 (23.3)	1.000
Unknown exposure, n (%)	6 (5.8)	0 (0.0)	6 (20%)	<0.001
Incubation period, n (min-max)	5.0 (3.0–9.0)	5.0 (2.0–9.0)	5.0 (3.0–8.0)	0.956
Comorbidity, n (%)	29 (27.9)	16 (21.6)	13 (43.3)	0.032
Respiratory disease, n (%)	10 (9.6)	6 (8.1)	4 (13.3)	0.426
Metabolic disease, n (%)	12 (11.5)	6 (8.1)	6 (20.0)	0.099
Cardiovascular disease, n (%)	23 (22.1)	12 (16.2)	11 (36.7)	0.036
Neurological disease, n (%)	1 (1.0)	1 (1.4)	0 (0.0)	1.000
Others, n (%)	2 (1.9)	1 (1.4)	1 (3.3)	0.496
Symptoms				
Fever, n (%)	96 (92.3)	66 (89.2)	30 (100)	0.065
Fatigue, n (%)	50 (48.1)	37 (50.0)	13 (43.3)	0.665
Cough, n (%)	66 (63.5)	45 (60.8)	21 (70.0)	0.501
Expectoration, n (%)	33 (31.7)	24 (32.4)	9 (30.0)	0.822
Asthma, n (%)	12 (11.5)	6 (8.1)	6 (20.0)	0.099
Nasal obstruction, n (%)	7 (6.7)	4 (5.4)	3 (10.0)	0.670
Runny nose, n (%)	9 (8.7)	6 (8.1)	3 (10.0)	1.000
Pharyngalgia, n (%)	15(14.4)	13 (17.6)	2(6.7)	0.221

[a]Quantitative data are expressed as median and interquartile range (IQR); qualitative data are expressed as count and percentages.

NEW INSIGHTS INTO THE NEUROLOGICAL EFFECTS OF COVID-19

Wood H.. Nat Rev Neurol. 2020 Jun 26. doi: 10.1038/s41582-020-0386-7. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

An article from Nature Reviews Neurology highlights three different studies conducted by researchers from the US and Europe that have provided significant evidence of CNS damage in patients with COVID-19. While patients with COVID-19 have exhibited various neurological symptoms, further research still needs to be done to distinguish if these symptoms are a result of direct SARS-CoV-2 invasion of the brain parenchyma or if other mechanisms are at play.

ADULTS

THE DEFINITION AND RISKS OF CYTOKINE RELEASE SYNDROME IN 11 COVID-19-AFFECTED CRITICALLY ILL PATIENTS WITH PNEUMONIA: ANALYSIS OF DISEASE CHARACTERISTICS

Wang W, Liu X, Wu S, Chen S, Li Y, Nong L, Lie P, Huang L, Cheng L, Lin Y, He J.. J Infect Dis. 2020 Jun 30:jiaa387. doi: 10.1093/infdis/jiaa387. Online ahead of print.
Level of Evidence: 4 - Case-series

BLUF

In order to better understand the characteristics of cytokine release syndrome (CRS) in the setting of COVID-19, authors analyzed data from 11 COVID-19 patients with pneumonia and subsequent acute respiratory distress syndrome (ARDS) who received care at the First Affiliated Hospital of Guangzhou Medical University in China from January 26th, 2020 through February 18th, 2020. The analysis indicated that eight out of the 11 patients developed CRS (Figure 1) with characteristics including a continuous fever, organ and tissue damage caused by the cytokine-related immune reaction, and coagulation dysfunction. The authors also noted a substantial increase of interleukin 6 (IL-6) in their peripheral blood, which could potentially act as a prognostic factor for CRS development in COVID-19 patients with severe pneumonia.

ABSTRACT

Corona Virus Disease 2019(COVID-19)-affected patients with severe immune abnormalities have a risk of cytokine release syndrome. The definition, prevention, and treatment of symptoms of cytokine release syndrome in critically ill patients with COVID-19 are important problems. This was a single-center case series of 11 COVID-19 patients with acute respiratory distress syndrome (ARDS) from The First Affiliated Hospital of Guangzhou Medical University in China from January 26, 2020 to February 18, 2020. The termination date of follow-up was February 19, 2020. In this single-center analysis of 11 critically ill patients with COVID-19, 8 patients were determined to have characteristics of cytokine release syndrome (CRS), including pulmonary inflammation, fever, and dysfunction of non-pulmonary organs; an increase of- Interleukin-6 (IL-6) in peripheral blood was the highest risk factor and an early indicator of CRS in COVID-19.

FIGURES
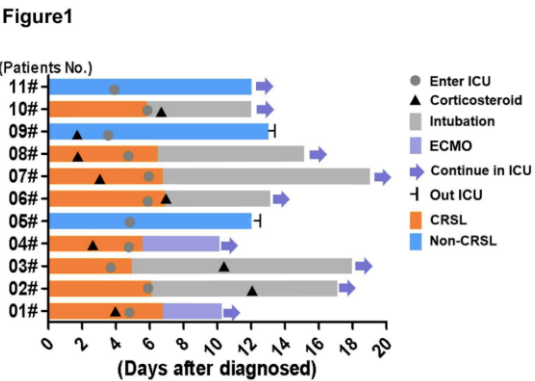
Figure 1. Timeline of disease course according to days from definitive diagnosis of illness and days from entering ICU. Before entering the ICU, nine patients received corticosteroid therapy. In the treatment and nursing process of ICU, six patients were intubated, two patients were given extracorporeal membrane oxygenation (ECMO), and eight patients had CRS symptoms; two of the patients who had non-CRS symptoms were transferred out of ICU.

COVID-19 SEVERITY CORRELATES WITH AIRWAY EPITHELIUM-IMMUNE CELL INTERACTIONS IDENTIFIED BY SINGLE-CELL ANALYSIS

Chua RL, Lukassen S, Trump S, Hennig BP, Wendisch D, Pott F, Debnath O, Thürmann L, Kurth F, Völker MT, Kazmierski J, Timmermann B, Twardziok S, Schneider S, Machleidt F, Müller-Redetzky H, Maier M, Krannich A, Schmidt S, Balzer F, Liebig J, Loske J, Suttorp N, Eils J, Ishaque N, Liebert UG, von Kalle C, Hocke A, Witzenrath M, Goffinet C, Drosten C, Laudi S, Lehmann I, Conrad C, Sander LE, Eils R.. Nat Biotechnol. 2020 Jun 26. doi: 10.1038/s41587-020-0602-4. Online ahead of print.
Level of Evidence: 4 - Case-series or casecontrol studies, or poor quality prognostic cohort study

BLUF

Immunologic analysis of 24 patients (19 SARS-CoV-2 positive and five controls) conducted by a multidisciplinary group of researchers from Germany found that immune marker expression profiles show that severe cases of COVID-19, when compared to moderate cases, involved much stronger interactions between epithelial and immune cells (Figures 1, 4). These data support the hypothesis that severe COVID-19 disease may be in part due to a heightened immune inflammatory response and that dampening of immune hyperactivation, perhaps by targeting common endpoints of a variety of immunological signaling pathways such as CCR1 and/or CCR5 pathways, has potential as a treatment strategy.

SUMMARY

Additional key findings from the study include:
1. Three times increased angiotensin-converting enzyme 2 (ACE2) expression in airway epithelial cells of COVID-19 infected patients compared to controls ($p < 0.001$). ACE2 is known to have a role as the SARS-CoV-2 entry receptor.
2. Moderate COVID-19 disease patients showed significantly higher expression of CXCL1, CXCL3, CXCL6, CXCL16, and CXCL17 when compared to controls ($p < 0.05$ for all)
The authors also note that this study could not include patients with very mild or asymptomatic COVID-19 since these patients would not seek/need hospitalization, precluding a true comparison between the severity spectrum of the disease at the cellular level. Future research must include these patients to further elucidate cytokine and RNA profiles.

ABSTRACT

To investigate the immune response and mechanisms associated with severe coronavirus disease 2019 (COVID-19), we performed single-cell RNA sequencing on nasopharyngeal and bronchial samples from 19 clinically well-characterized patients with moderate or critical disease and from five healthy controls. We identified airway epithelial cell types and states vulnerable to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. In patients with COVID-19, epithelial cells showed an average three-fold increase in expression of the SARS-CoV-2 entry receptor ACE2, which correlated with interferon signals by immune cells. Compared to moderate cases, critical cases exhibited stronger interactions between epithelial and immune cells, as indicated by ligand-receptor expression profiles, and activated immune cells, including inflammatory macrophages expressing CCL2, CCL3, CCL20, CXCL1, CXCL3, CXCL10, IL8, IL1B and TNF. The transcriptional differences in critical cases compared to moderate cases likely contribute to clinical observations of heightened inflammatory tissue damage, lung injury and respiratory failure. Our data suggest that pharmacologic inhibition of the CCR1 and/or CCR5 pathways might suppress immune hyperactivation in critical COVID-19.
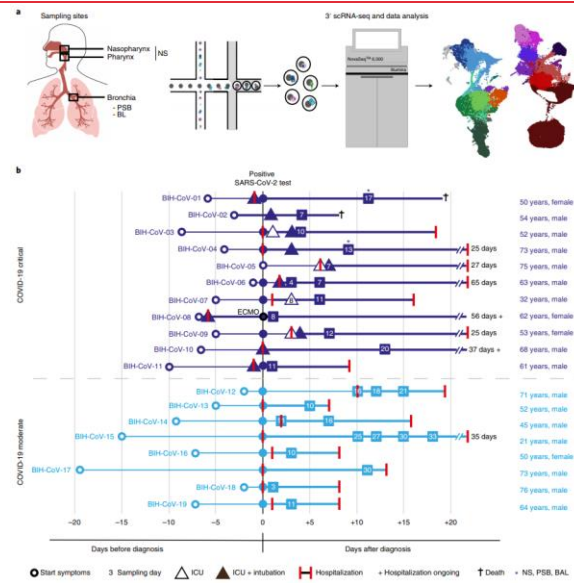
Figure 1. Illustration of the experimental setup and the patient cohort used in this study. A. Schematic representation of the experimental workflow. Depicted are the sampling sites (left) and the 3′ scRNA-seq library preparation using 10X Genomics (middle) followed by data analysis revealing cell type identity (right). B. Overview of the patient cohort. Given are age, sex and COVID-19 severity as well as onset of symptoms, hospitalization duration and sampling time points in days after onset of symptoms, with all patients being temporally aligned to the day of positive SARS-CoV-2 test. Admission to the ICU is also depicted if applicable. One patient required extracorporeal membrane oxygenation (ECMO). We obtained nasopharyngeal/pharyngeal swabs (NS) from all patients and, in addition, bronchial protected specimen brushes (PSB) and bronchial lavages (BL) from patients BIH-CoV-01 and BIH-CoV-04 (marked with *). The sampling day relative to the onset of symptoms is given as a number in a square or triangle.
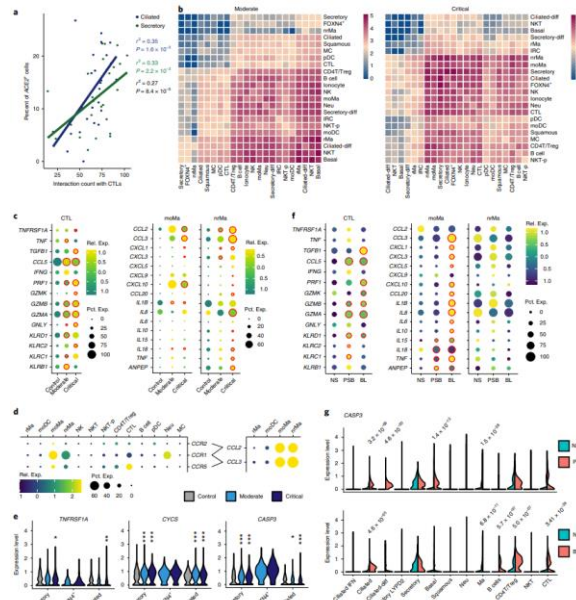

Figure 4. Immune–epithelial cell interaction in COVID-19. A. Scatter plot of ACE2 expression in secretory and ciliated cells versus their interaction strength with CTLs in patients and controls, excluding samples with fewer than 20 cells per cell type (n= 19 patients and 27 samples). Spearman's ρ2 and corresponding P values indicated for CTL interaction with secretory cells (green), ciliated cells (blue) and both combined (black). B. Heat map depicting cell–cell communications between all identified cell types derived from log-scaled ligand–receptor interaction counts in moderate (left, n= 8 patients and 14 samples) and critical (right, n= 11 patients and 13 samples) patients. Interaction strengths are color coded. C. Dot plots of pro-inflammatory and cytotoxic mediators in CTL, moMa and nrMa. Significantly altered expression (Benjamini–Hochberg adjusted two-tailed, negative-binomial P < 0.05) in critical versus moderate (circles around critical) and moderate versus controls (circles around moderate) is marked by a red circle. D. Dot plots of chemokine/receptor expression in the different immune cells of patients

with critical COVID-19 (n= 11). Scaling according to Extended Data Fig. 4. E. Expression of apoptosis-related genes in epithelial cells comparing critical cases, moderate cases and controls (n= 5 controls, 8 moderate and 11 critical). Asterisks above critical indicate P values for critical versus control; asterisks above moderate indicate significance of moderate versus control. *P < 0.05, **P < 0.01, ***P < 0.001. Statistics as in C. F. Dot plots of inflammatory and cytotoxic mediators from NS, PSB and BL collected from patients with critical COVID-19 (BIH-CoV-01 and BIH-CoV-04). Visualization as in C. G. CASP3 expression in immune and epithelial cell subtypes of these patients. Comparing PSB versus NS (top) and BL versus NS (bottom). Significant decreases (nasal versus other sampling site) are indicated. Rel. Exp. = relative gene expression; Pct. Exp. = percentage of cells expressing the gene.

CYTOKINE STORM IN COVID19: A NEURAL HYPOTHESIS

BLUF

Authors affiliated with the UR Anoop Research Group in India hypothesize that the cytokine storm in COVID-19 may be caused by SARS-CoV-2 invasion of the vagus, facial, and glossopharyngeal nerve axons, leading to inflammation of the nucleus tractus solitarius (NTS) and ensuing dysregulation of cholinergic anti-inflammatory pathways and hypothalamic–pituitary–adrenal axis (Figure 1). Further investigation into SARS-CoV-2-mediated inflammation of the NTS is needed to confirm this hypothesis and to determine optimal early interventions for this potential mode of entry.

ABSTRACT

Cytokine storm in COVID-19 is characterized by an excessive inflammatory response to SARS-CoV-2 that is caused by a dysregulated immune system of the host. We are proposing a new hypothesis that SARS-CoV-2 mediated inflammation of nucleus tractus solitarius (NTS) may be responsible for the cytokine storm in COVID 19. The inflamed NTS may result in a dysregulated cholinergic anti-inflammatory pathway and hypothalamic-pituitary-adrenal axis.
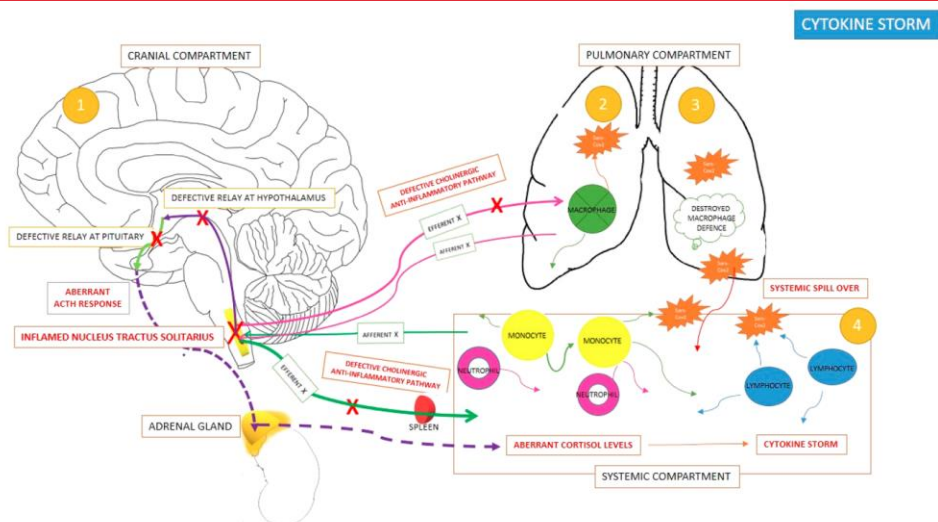
FIGURES

Figure 1. NTS as the coordinating center for the cholinergic anti-inflammatory pathway and the HPA axis.

SCREENING THE GENERAL POPULATION FOR SARS COV-2 VIRUS AND COVID-19 ANTIBODIES: A COUNTER-ARGUMENT

BLUF

An author from the University of California, San Francisco argues against the idea of a national antigen and antibody screening program for SARS-CoV-2 in the United States. The author reasons that further research is needed to address the lack of sensitivity of antibody testing kits and to establish assays that specifically target neutralizing viral antibodies before mass antibody screening is implemented.

DETECTION AND ANALYSIS OF CLINICAL FEATURES OF PATIENTS WITH DIFFERENT COVID-19 TYPES

Zhao Y, Zhou J, Pan L, Zhang Y, Wang H, Wu W, He J, Chen J, Huang H.. J Med Virol. 2020 Jun 26. doi: 10.1002/jmv.26225. Online ahead of print.
Level of Evidence: 3 - Cohort study or control arm of randomized trial

BLUF

In this study, a group of international researchers evaluate the clinical indexes, including blood indexes, immune indexes, and liver, kidney, and myocardial indexes, of 75 hospitalized COVID-19 patients in the Zhejiang province of China. They found that the proportion of abnormal IL-2, IL-4, and total cholesterol levels was significantly higher in critically severe patients compared to that of patients with moderate symptoms, which is consistent with previous studies. These results provide insight into the disease progression of COVID-19 and can be a reference for identification of patients with severe disease.

ABSTRACT

OBJECTIVE: This study was designed to investigate the change of various indexes in patients with different types of coronavirus disease 2019 (COVID-19). METHODS: 75 COVID-19 patients were collected from the First Affiliated Hospital, Zhejiang University School of Medicine, and they were classified into moderate, severe and critically severe types according to the disease severity. The basic information, blood routine, pneumonia-related blood indexes, immune-related indexes along with liver, kidney and myocardial indexes in patients with different types were analyzed. RESULTS: The analysis of immune-related indexes showed that the proportions of critically severe patients with abnormal IL-2 and IL-4 were higher than those of severe and moderate patients. In addition, the proportion of patients with abnormal total cholesterol increased as the severity of disease increased, and the proportion in critically severe patients was significantly higher than that in moderate patients. CONCLUSIONS: The patients with a more severe COVID-19 are older and more likely to have a history of hypertension. With the progression of COVID-19, the abnormal proportion of total white blood cell, neutrophils, lymphocytes, IL-2, IL-4 and total cholesterol increased. The change of these indexes in patients with different COVID-19 types could provide reference for the disease severity identification and diagnosis of COVID-19. In addition, the change in the total cholesterol level suggested that COVID-19 would induce some liver function damage in patients. This article is protected by copyright. All rights reserved.

DECISION MAKING: PHYSICAL THERAPIST INTERVENTION FOR PATIENTS WITH COVID-19 IN A GERIATRIC SETTING

Levi N, Ganchrow K, Gheva M.. Phys Ther. 2020 Jun 26:pzaa116. doi: 10.1093/ptj/pzaa116. Online ahead of print.
Level of Evidence: Other - Guidelines and Recommendations

BLUF

This report outlines guidelines developed by Shoham Geriatric Medical Center (SGMC) in Israel to support physical therapy (PT) interventions for geriatric COVID-19 patients (Figure 1). The authors recommended direct contact PT treatments, as opposed to tele-rehabilitation based on the findings detailed below and urge other PT providers to adopt similar guidelines to address both functional and respiratory impairments of geriatric patients with COVID-19.

SUMMARY

- COVID-19 patients admitted to COVID-19 unit at SGMC were characterized as having mild COVID-19 where most were asymptomatic. Several patients with mild COVID-19 diagnosis had moderate to a severe deficit in function compared to their baseline functional status (Table 1).
- Geriatric patients were divided into three mobility groups based on functional deterioration and respiratory condition (1. Independent/Modified Independent/ Supervision (I/ Mod I/ Sup); 2. Minimal/Moderate Assistance (Min / Mod A); 3. Maximal/ Total Assistance (Max / Total A)) (Figure 1).
- During the 5-week course, 108 treatments were provided (89 direct contact treatment in the unit, 19 tele-rehabilitation). Although not clearly evaluated, the authors claim that direct contact treatment was the preferred modality for patients in the

Min/Mod A and Max/Total A groups.

- Treatments took place in negative pressure rooms and were provided by staff who wore appropriate personal protective equipment for airborne precautions (i.e., N95 masks, face shields, full-body suit).

- Authors report limited efficacy with tele-rehabilitation for geriatric patients in the COVID-19 unit due to limited patient familiarity with technology, lack of hands on assessments, and concern for patient safety.
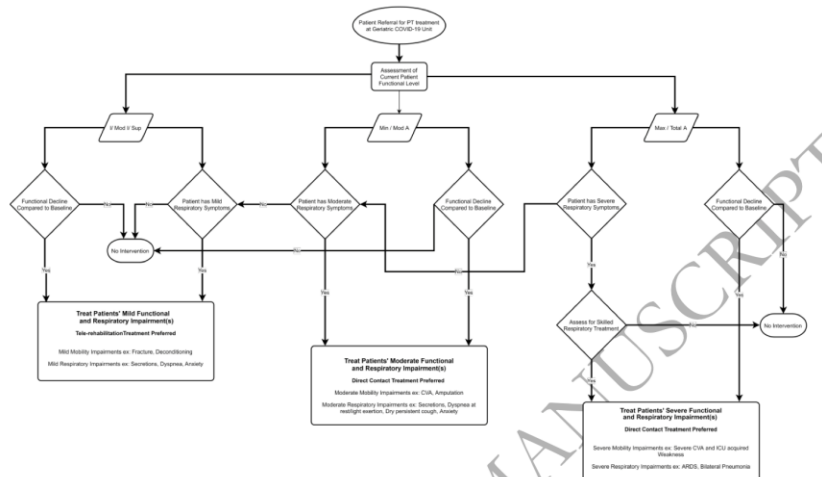
FIGURES

Figure 1 Decision making tree.

Table: Demographic Characteristics SGMC COVID-19 Unit[a]

Characteristic	N = 47
Sex	
Male	14
Female	33
Age (y)	
Age range	38-96
Average age	80.8
Median age	83.0
Patient origin of admission	
Acute hospital	8
Dementia care unit	13
Long term care facility	22
Skilled nursing facility	2
Assisted living facility	2
Patient functional level on arrival	
I/ Mod I/ Sup	16
Min / Mod A	12
Max / Total A	19
Number of treatments	
Direct contact treatment	89
Tele-rehabilitation	19
Average hospitalization (Days)	21.9

[a]April 6, 2020 – May 14, 2020.

EMERGENCY MEDICINE

AVOIDING DISINFORMATION TRAPS IN COVID-19: JULY 2020 ANNALS OF EMERGENCY MEDICINE JOURNAL CLUB

BLUF

Two physicians critique the reported findings of Richardson et. al., 2020 observational case series that included 5,700 SARS-CoV-2 positive patients in 12 New York hospitals and found a mortality rate of 88.1% among patients requiring mechanical

ventilation. The authors argue that the reported "higher-than-expected mortality" is due to "right censoring" since analysis occurred before most intubated patients had experienced the outcome of the study (death or discharge). They offer two possible solutions (stating the status of all patients at data collection or clarifying the uncertainty in results), illustrating ways future observational studies can avoid presenting disinformation.

MEDICAL SUBSPECIALTIES

ENDOCRINOLOGY

SUCCESSFUL BLOOD GLUCOSE MANAGEMENT OF A SEVERE COVID-19 PATIENT WITH DIABETES: A CASE REPORT

BLUF

A case study describing a 64-year-old woman with COVID-19 hospitalized in Guizhou, China on February 19, 2020 with productive cough, COVID-19 related pulmonary infection, and type 2 diabetes (T2DM). Abnormal laboratory results included: blood glucose 17.4 mmol/L, interleukin-6 61.31 pg/mL, erythrocyte sedimentation rate 75 mm/h and she was placed in ICU on high-flow oxygen therapy for critical COVID-19 infection, and comprehensive measures to control blood glucose (see below for details). Per the authors, this is the first reported case detailing blood glucose management in a patient with severe COVID-19 patient and diabetes.

SUMMARY

The authors aim to describe successful blood glucose control in a patient with severe COVID-19 requiring ICU-level care. They point to a number of interventions they believe contributed to the patient's recovery:
- Blood sugar control with 10-28 units of aspart before dinner and 10 to 28 units of glargine before bed, targeting postprandial glucose of 6-8 mmol/L and postprandial of 8-14 mmol/L (Figure 1).
- Establishment of a multidisciplinary team (critical care, pulmonology, endocrinology, nursing) to establish care plans.
- Adherence to a strict diabetic diet plan formulated by endocrinology & nutrition.
- A plan for activity including body position changes, early physical activity, and respiratory therapy.
- Substantial efforts to maintain good mental health.
- Frequent blood glucose monitoring (seven times daily) and include patient's involvement.

ABSTRACT

RATIONALE: Coronavirus disease 2019 (COVID-19) has emerged as a rapidly spreading communicable disease affecting individuals worldwide. Patients with diabetes are more vulnerable to the disease, and the mortality is higher than in those without diabetes. We reported a severe COVID-19 patient with diabetes and shared our experience with blood glucose management. PATIENT CONCERNS: A 64-year-old female diabetes patient was admitted to the intensive care unit due to productive coughing for 8 days without any obvious cause. The results of blood gas analysis indicated that the partial pressure of oxygen was 84 mm Hg with oxygen 8 L/min, and the oxygenation index was less than 200 mm Hg. In addition, postprandial blood glucose levels were abnormal (29.9 mmol/L). DIAGNOSES: The patient was diagnosed with COVID-19 (severe type) and type 2 diabetes. INTERVENTIONS: Comprehensive interventions including establishing a multidisciplinary team, closely monitoring her blood glucose level, an individualized diabetes diet, early activities, psychological care, etc, were performed to control blood glucose while actively treating COVID-19 infection. OUTCOMES: After the comprehensive measures, the patient's blood glucose level gradually became stable, and the patient was discharged after 20 days of hospitalization. LESSONS: This case indicated that the comprehensive measures performed by a multidisciplinary team achieved good treatment effects on a COVID-19 patient with diabetes. Targeted treatment and nursing methods should be performed based on patients' actual situations in clinical practice.
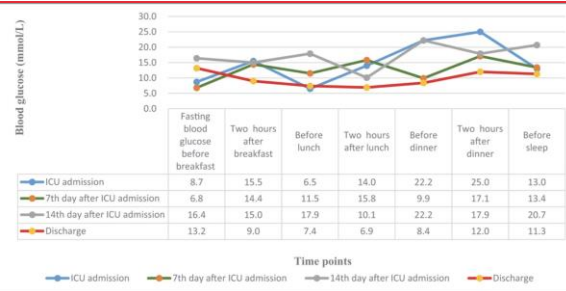
FIGURES

Figure 1. Changes trends of blood glucose in the patient throughout the day from the beginning of her ICU admission to discharge

ADJUSTING PRACTICE DURING COVID-19

INCREASED BURN CENTER ADMISSIONS DURING COVID 19 PANDEMIC

Williams FN, Nazimani R, Chrisco L, King BT.. J Burn Care Res. 2020 Jul 1:iraa112. doi: 10.1093/jbcr/iraa112. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

Authors from North Carolina Jaycee Burn Center compared admissions data from March 1, 2020 to present (specific end point unspecified) to the same time period the year prior and found a 7% rise in total burn admissions, a 35% increase in pediatric admissions, a 114% rise in burn injuries in school aged children, a 70% increase in pediatric contact injuries, and a 15% increase in pediatric scald injuries. Based on these observations, the authors stress the importance for ongoing provision of resources and staff to manage burn patients during the COVID-19 pandemic.

SURGICAL SUBSPECIALTIES

ADAPTING PROTOCOLS FOR THE CARE OF SURGICAL PATIENTS DURING THE COVID-19 PANDEMIC

. AORN J. 2020 Jul;112(1):P15-P18. doi: 10.1002/aorn.13126.
Level of Evidence: Other - Expert Opinion

BLUF

In an interview with Debra Dunn (MSN, MBA, RN, CNOR, education specialist) of Holy Name Medical Center, New Jersey regarding adapting protocols in caring for surgical patients during the COVID-19 pandemic, Dunn discusses:
-The implementation of a detailed workflow to limit viral exposure including detailed surgery steps, personal protective equipment (PPE) to be worn, a list of necessary supplies, and staff members permitted in the OR.
-Construction of new devices, such as negative pressure hoods to be placed over the patient's head with embedded gloved slots for intubation and extubation (Figure 1) and a transportation isopod ("bubble") used to move COVID-19 patients (positive/presumed) on beds within the hospital while keeping hospital personnel safe (Figure 2).
-The most notable challenges were described as adjusting to a "new normal" and adapting as the situation evolved, but ultimately staff members seemingly gained the ability to provide care with confidence.

FIGURES

Figure 1: Transportation isopod used to move patients positive for COVID-19.

Figure 2: Transportation isopod used to move patients positive for COVID-19.

OBGYN

MANAGEMENT OF MOTHERS AND NEONATES IN LOW RESOURCES SETTING DURING COVID-19 PANDEMIA

Trevisanuto D, Weiner G, Lakshminrusimha S, Azzimonti G, Nsubuga JB, Velaphi S, Seni AHA, Tylleskär T, Putoto G.. J Matern Fetal Neonatal Med. 2020 Jun 30:1-12. doi: 10.1080/14767058.2020.1784873. Online ahead of print.
Level of Evidence: Other - Guidelines and Recommendations

BLUF

Recommendations for neonatal and maternal care in low-resource settings during the COVID-19 pandemic were published by a group of international experts, recommending droplet precautions, hand hygiene, and physical spacing, in addition to outlining warning-signs of late-onset neonatal COVID-19 infection (Figure 3). The authors also recommend continuing standard of care with delayed cord clamping in excess of 30 seconds to assure adequate placental transfusion, allowing skin-to-skin contact following appropriate masking, hand-washing, and breast hygiene, and monitoring children for delayed COVID-19 infection after birth in addition to new droplet precautions (Figure 1). These guidelines can aid in minimizing COVID-19 spread and transmission to neonates in low-resource settings.

ABSTRACT

The coronavirus disease (COVID-19) epidemic started in the Hubei province of China, but is rapidly spreading all over the world. Much of the information and literature have been centered on the adult population while a few reports pertaining to COVID-19 and neonates have been published so far. Actual guidelines are based on expert opinion and show significant differences among the official neonatal societies around the world. Recommendations for the care of neonates born to suspected or confirmed COVD-19 positive mothers in low-resource settings are very limited. This perspective aims to provide practical support for the planning of delivery, resuscitating, stabilizing, and providing postnatal care to an infant born to a mother with suspected or confirmed COVID-19 in low-resource settings where resources for managing emergency situations are limited.
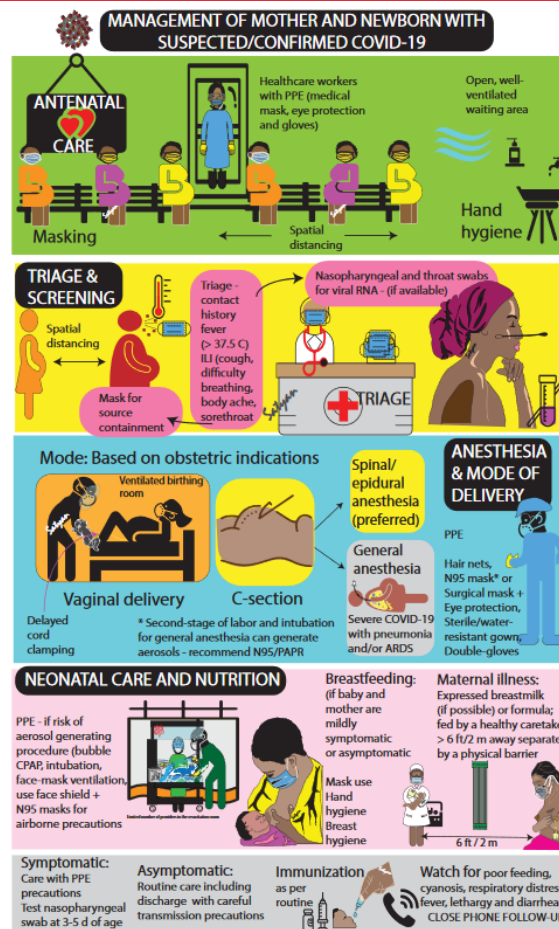
Figure 1. Infographic showing the approach to neonates born to mothers with suspected or confirmed COVID-19. ARDS, acute respiratory distress syndrome; ILI, influence-like illness; PAPR, powered air-purifying respirator; PPE, personal protective equipment; SARS-CoV-2, severe acute respiratory syndrome–coronavirus 2. Image Courtesy: Satyan Lakshminrusimha.
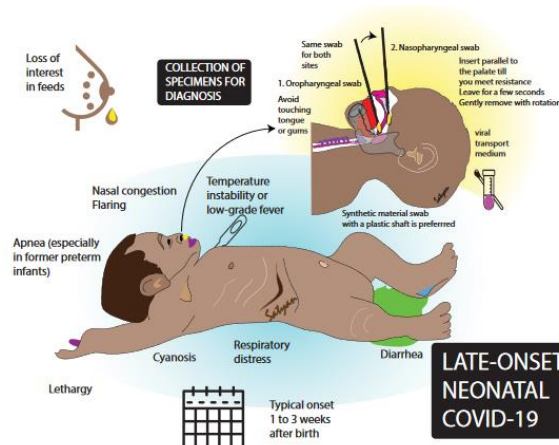

Figure 3. Late-onset neonatal COVID-19–warning signs and diagnostic measures. Image Courtesy: Satyan Lakshminrusimha.

SAFETY, TOLERABILITY, AND PHARMACOKINETICS OF REMDESIVIR, AN ANTIVIRAL FOR TREATMENT OF COVID-19, IN HEALTHY SUBJECTS

BLUF
Authors associated with Gilead Sciences Inc. present two first-in-human (FIH) phase I studies (a single-dose escalation study and a multiple-dose study) evaluating the safety and pharmacokinetics of IV remdesivir (RDV) in healthy participants for the potential use of RDV in COVID-19 treatment. The findings of these two studies (illustrated below) suggest that a single-dose of RDV daily, whether as a solution or lyophilized formulation, is well-tolerated and safe to use in healthy adults, supporting the continued clinical investigation of RDV in COVID-19 therapy.

SUMMARY
The design and findings of the two FIH phase I studies are summarized below:

Single-dose escalation study:
• 96 healthy adults were randomized to 9 cohorts receiving placebo or certain IV doses of RDV: 3mg-225 mg (cohort 1-6), lyophilized formulation 75 mg (cohort 7 and 9), or lyophilized formulation 150 mg (cohort 8).
• Among the cohorts, the dose escalation was well-tolerated with adverse events only at a grade 1 or 2
• lyophilized and solution formulations showed similar pharmacokinetic parameters, as measured by RDV metabolites (Figure 1).
• high intracellular concentrations were obtained with infusion of 75mg or 150mg lyophilized formulation for greater than 30 minutes or 2 hours (Figure 1).

Multiple-dose study:
• 24 healthy adults received 150mg RDV or placebo for a 1-hour period daily for either 7 days (cohort 1) or 14 days (cohort 2).
• All adverse events grade I severity, and RDV did not accumulate with multiple dose regimen.
• multiple-doses exhibited a similar pharmacokinetic profile to single-drug dose (Figure 2).

ABSTRACT
Remdesivir (RDV), a single diastereomeric monophosphoroamidate prodrug that inhibits viral RNA polymerases, has potent in vitro antiviral activity against SARS-CoV2. RDV received FDA's emergency use authorization in United States and approval in Japan for treatment of severe COVID-19 patients. This report describes two phase 1 studies that evaluated the safety and pharmacokinetics (PK) of single escalating and multiple intravenous (IV) doses of RDV (solution or lyophilized formulation) in healthy subjects. Lyophilized formulation was evaluated for potential future use in clinical trials due to its storage stability in resource-limited settings. All adverse events were Grade 1 or 2 in severity. Overall, RDV exhibited a linear profile following single-dose IV administration over 2 hours of RDV solution formulation across the dose range of 3 to 225mg. Both lyophilized and solution formulations provided comparable PK parameters. High intracellular concentrations of the active triphosphate (approximately 220 to 370- fold higher than the in vitro EC50 against SARS-CoV-2 clinical isolate) were achieved following infusion of 75 mg or 150 mg lyophilized formulation over 30 minutes or 2 hours. Following multiple-doses of RDV 150mg once daily for 7 or 14 days, RDV exhibited a PK profile similar to single-dose administration. Metabolite GS-441524 accumulated approximately 1.9-fold after daily dosing. Overall, RDV exhibited favorable safety and PK profiles that supported once-daily dosing.
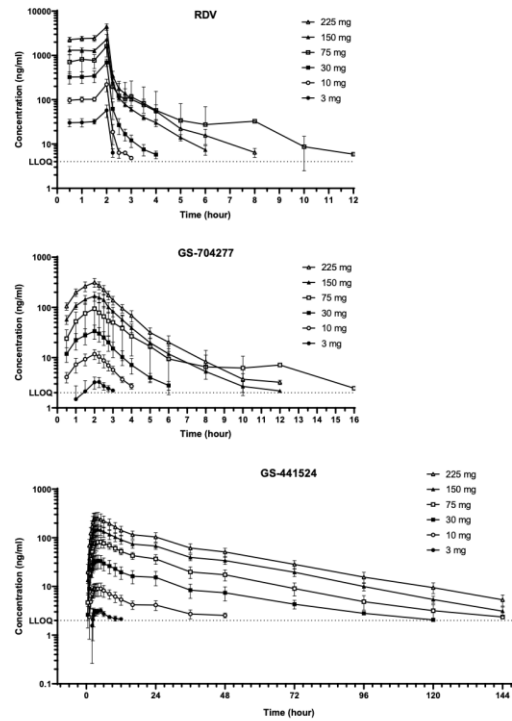
Figure 1: Plasma Concentration-vs-Time Profiles following RDV Single-Dose Administration;
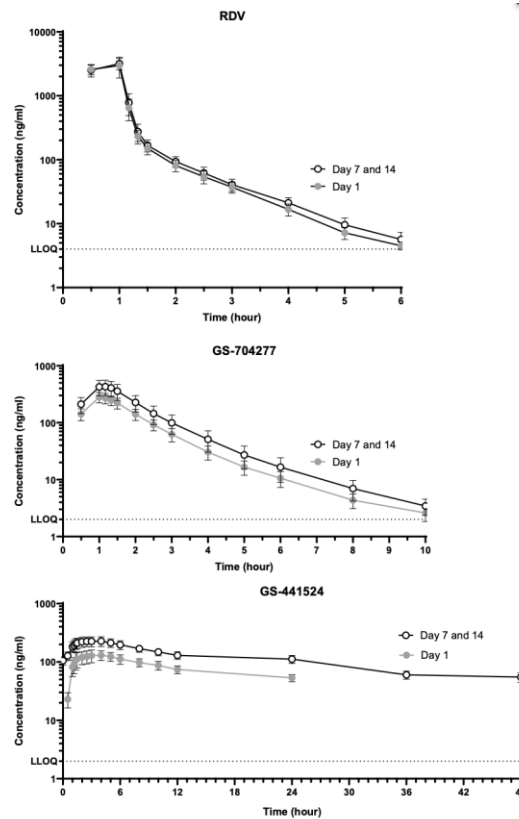Mean (±SD) values are plotted

Figure 2: Plasma Concentration-vs-Time Profiles following RDV Multiple-Dose Administration;
Mean (±SD) values are plotted

COVID-19'S IMPACT ON HEALTHCARE WORKFORCE

FACTORS ASSOCIATED WITH POST-TRAUMATIC STRESS DISORDER OF NURSES EXPOSED TO CORONA VIRUS DISEASE 2019 IN CHINA

BLUF

A cross-sectional and correlational study conducted in China between February 2020 and March 2020 surveyed 202 nurses exposed to COVID-19 with the PTSD Checklist-Civilian questionnaire (PCL-C) and Simplified Coping Questionnaire (SCSQ). Results found 7.42% of nurses (n=15) suffered from some degree of PTSD and 9.41% (n=19) from definitively diagnosed PTSD. Further analysis found a negative correlation between PTSD incidence and positive coping and a positive correlation between PTSD and negative coping (Table 5). These findings suggest that PTSD may be prevalent in healthcare providers who care for COVID-19 patients and that mental health resources should be made available.

ABSTRACT

Quantitative studies using validated questionnaires on post-traumatic stress disorder (PTSD) of Nurses exposed to corona virus disease 2019 (COVID-19) in China are rare and the baseline PTSD must first be evaluated before prevention. This study aimed to investigate the factors potentially involved in the level of PTSD of Nurses exposed to COVID-19 in China.In this cross-sectional study, male and female Nurses (n = 202) exposed to COVID-19 from HuBei China were included in the final sample. The PTSD Checklist-Civilian (PCL-C) questionnaire and Simplified Coping Style Questionnaire (SCSQ) were used for evaluation. Multivariate stepwise linear regression analysis and spearman correlation test were performed to assess the association between various factors associated with PTSD.The incidence of PTSD in Nurses exposed to COVID-19 was 16.83%, the PCL-C score was 27.00 (21.00-34.00), and the highest score in the three dimensions was avoidance dimension 9.50 (7.00-13.25); multivariable stepwise linear regression analysis showed that job satisfaction and gender were independently associated with lower PCL-C scores (both P < .001); PCL-C scores were correlated with positive coping (r = -0.151, P = .032), negative coping (r = 0.154, P = .029).Nurses exposed to COVID-19 from HuBei China with job satisfaction, male and positive coping had low PCL-C scores which necessitate reducing the PTSD level by ways of improving job satisfaction, positive response, and strengthening the psychological counseling of female nurses in order to reduce the risk of psychological impairment.

FIGURES

Table 5. Associations between PCL-C Scores and scores in the 2 dimensions of SCSQ in nurses (n=202) exposed to COVID-19 in Tertiary Hospitals in China.

IMPACT ON PUBLIC MENTAL HEALTH

HOW THE COVID-19 PANDEMIC IS FOCUSING ATTENTION ON LONELINESS AND SOCIAL ISOLATION

BLUF

Public health researchers propose that the increase in social isolation and loneliness in Australia during the pandemic provides an opportunity to recognize the health benefits of social connection. After reviewing previous interventions for social isolation and loneliness (befriending schemes, one-to-one and group therapies, etc.), the authors note that there is no singular, effective strategy in mitigating these conditions. The researchers argue for interdisciplinary efforts to investigate factors (predictors, maintenance factors, etc.) related to social isolation and loneliness for establishment of evidence-based initiatives.

ABSTRACT

The effects of the coronavirus disease 2019 (COVID-19) pandemic upon human health, economic activity and social engagement have been swift and far reaching. Emerging evidence shows that the pandemic has had dramatic mental health impacts, bringing about increased anxiety and greater social isolation due to the physical distancing policies introduced to control the disease. In this context, it is possible to more deeply appreciate the health consequences of loneliness and social isolation, which researchers have argued are enduring experiences for many people and under-recognised contributors to public health. In this paper, we examine the social and psychological consequences of the COVID-19 pandemic, with a focus on what this has revealed about the need to better understand and respond to social isolation and loneliness as public health priorities. Social isolation and loneliness are understood to be distinct conditions, yet each has been found to predict premature mortality, depression, cardiovascular disease and cognitive decline. Estimates of the prevalence and distribution of social isolation and loneliness vary, possibly ranging from one-in-six to one-in-four people, and the lack of knowledge about the extent of these conditions indicates the need for population monitoring using standardised methods and validated measures. Reviews of the evidence relating to social isolation and loneliness interventions have found that befriending schemes, individual and group therapies, various shared activity programs, social prescription by healthcare providers, and diverse strategies using information and communication technologies have been tried. There remains uncertainty about what is effective for different population groups, particularly for prevention and for addressing the more complex condition of loneliness. In Australia, a national coalition - Ending Loneliness Together - has been established to bring together researchers and service providers to facilitate evidence gathering and the mobilisation of knowledge into practice. Research-practice partnerships and cross-disciplinary collaborations of this sort are essential for overcoming the public health problems of loneliness and social isolation that have pre-existed and will endure beyond the COVID-19 pandemic.

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CONTINGENCY PLANNING IN THE CLINICAL LABORATORY: LESSONS LEARNED AMIDST COVID-19

BLUF

American physicians outline recommendations for best practices in clinical laboratories during the pandemic that include 1) varying staffing models, 2) prioritizing testing orders, 3) preparing for a surge of COVID-19 patients, and 4) maintaining communication with hospital leadership (Table 1). These recommendations may prepare clinical laboratories for high COVID-19 testing demand and the possibility of staffing shortages due to infection.

FIGURES

Vary staffing models
Alter shift hours
Preemptively scale back on-site workers
Alternate teams for remote vs. on-site work
Approve overtime to call in off-shift workers
Cross-train professionals from other clinical lab areas
Prioritize testing menu for emergent testing
Define necessary/urgently needed tests
Prioritize FTEs to necessary tests
Batch or temporarily discontinue non-prioritized tests
Mask non-prioritized tests from provider order system
Prepare for surge of COVID-19 patients
Amplify inventory of reagents for prioritized tests
Support point-of-care testing
Recruit medical trainees or researchers for lab assistant roles
Maintain communication with hospital and medical leadership
Define expected practices for laboratory testing
Communicate daily lab staffing status and test menu availability

Table 1. Strategies for contingency planning in the clinical laboratory amidst the COVID-19 pandemic.

ACKNOWLEDGEMENTS