The Daily COVID-19 Literature Surveillance Summary

October 26, 2020

COVID-19 LST

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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

- Navigating through health care data showed disruption by the COVID-19 pandemic and was found to be variable and potentially unreliable due to the pandemic's effects on health-seeking, patient triage, and overall outcomes. Authors note that analytic methods for many study designs rely on the assumption that these factors are constant over time. They suggest that researchers should be cognizant of this disruption when planning studies and performing analyses in order to prevent potential confounding biases in future research studies.

Management

- Longitudinal profile of laboratory parameters and their application in the prediction for fatal outcome among 642 hospitalized patients infected with SARS-CoV-2 were evaluated and authors found that abnormal lactate dehydrogenase, urea, lymphocyte count, and procalcitonin levels were predictors of death during the acute phase (days 1-9), in addition to abnormal procalcitonin, lactate dehydrogenase, lymphocyte count, monocyte percentage, and cholinesterase being predictors of death in the critical phase (days 10-15). This study suggests that these labs should be followed as markers for prognosis and aggressive care should be considered should abnormalities in these markers arise.

Adjusting Practice During COVID-19

- Powered air purifying respirator (PAPR) restores the N95 face mask induced cerebral hemodynamic alterations among healthcare workers during the COVID-19 outbreak according to a study evaluating cerebral hemodynamic changes using Transcranial Doppler (TCD) of the middle cerebral artery (MCA) flow among 154 COVID-19 healthcare workers, of whom 123/154 developed de-novo headache due to N95 use (38/154 had preexisting migraine co-morbidity). Wearing an N95 increased Mean Flow Velocity (MFV) and ET-CO2, while Pulsatility Index (PI) decreased (p<0.001), whereas 24 participants donning N95 with a PAPR exhibited values nearer to baseline. These results implicate combined use of N95 with PAPR to potentially maintain cerebral homeostasis, mitigating PPE-induced headaches among healthcare workers, although larger trials may be required.

Mental Health & Resilience Needs

- Mental health disorders may be related to COVID-19-related deaths based on a commentary by psychiatrists. The authors cite the Center for Disease Control and Prevention (CDC) June 2020 survey with 40.9% of participants reporting "at least one adverse mental or behavioral health condition," which is 3-4 times higher than one year ago. Health disparities and a distressed healthcare workforce are additional areas of concern. The authors recommend screening (e.g. trauma, grieving, depression, anxiety) by primary care physicians and mental health professionals as well as broad supportive public health strategies (e.g. online resources for grieving families) in an effort to identify and aid those in need of assistance.

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NAVIGATING THROUGH HEALTH CARE DATA DISRUPTED BY THE COVID-19 PANDEMIC

BLUF

Epidemiologists from Yale, Connecticut discuss how data generated during the COVID-19 pandemic is variable and potentially unreliable due to the pandemic's effects on health-seeking, patient triage, and overall outcomes. They note that analytic methods for many study designs rely on the assumption that these factors are constant over time. The authors suggest that researchers should be cognizant of this disruption when planning studies and performing analyses in order to prevent potential confounding biases in future research studies.

ADULTS

HOW TO DEAL WITH CORONAVIRUS DISEASE 2019: A COMPREHENSIVE NARRATIVE REVIEW ABOUT ORAL INVOLVEMENT OF THE DISEASE

BLUF

A narrative review of 23 qualifying publications (Tables 1 & 2) by physicians and dentists from the University of Verona, Italy highlights the oral manifestations related to COVID-19 including: taste alterations, oral ulcers/blisters, and oral symptoms of Kawasaki's Disease (e.g. strawberry tongue). The authors hypothesize that increased expression of the angiotensin-converting enzyme 2 receptors (ACE2) in oral mucosa may be the reason for the development of oral symptoms. The authors recommend experts, namely dermatologists and dentists, to evaluate for oral involvement as a screen for COVID-19.

ABSTRACT

OBJECTIVES: The aim of this narrative review was to collect all findings from literature about oral signs and symptoms of COVID-19, in order to draw a picture of oral involvement of this challenging viral infection, to help oral professionals in a better triage and early diagnosis. MATERIAL AND METHODS: The search for international literature was made including articles written in English and reporting about oral manifestations in patients with a diagnosis of COVID-19. The publication time was limited to 2019 and 2020, up to May 20, 2020. A narrative review was performed. RESULTS: Twenty-three articles were included in this review. Three different oral manifestations were found: taste alteration, oral blister and ulcers, and oral lesions associated with Kawasaki-like diseases (erythema, bleeding of lips, "strawberry tongue"). The higher expression of Angiotensin-converting enzyme 2 in the oral cavity and in endothelial cells might be responsible for oral manifestation and the major report of signs and symptoms in the occidental countries. CONCLUSIONS: Detecting oral signs and symptoms of COVID-19 could be useful to perform a better preliminary triage in dental setting, and in recognizing possible early manifestations of the disease. However, considering the outbreak of COVID-19 and the consequent difficulty of undergoing oral examinations, the oral manifestations might be misdiagnosed; then, we would encourage oral professionals to perform other studies about this topic.
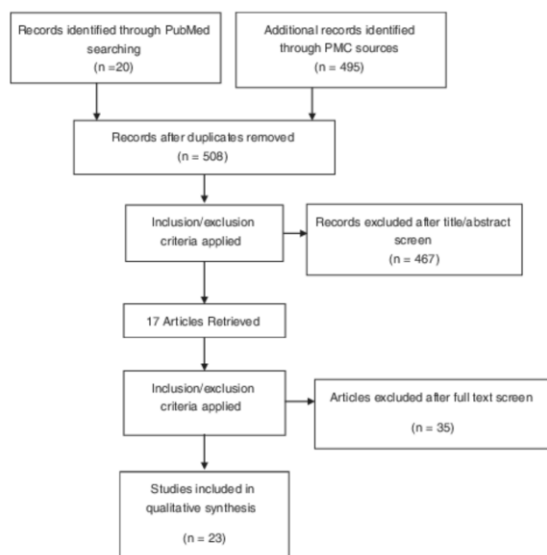
FIGURES

Table 1. Flow chart of literature search

TABLE 2 Synthesis of results

Author, year	Oral manifestation	Country	N. oral manifestation/sample size	Gender (M-F)	Mean age (years)	Study design/other crucial information
Beltrán-Corbellini et al., 2020	Taste alteration	Spain	28/79	48 M-31 F	61.6	Case control/self-reported
Bénézit et al., 2020	Taste alteration	France	63/68	NR	NR	Cross-sectional study/self-reported
Gelardi, Trecca, Cassano, & Ciprandi, 2020	Taste alteration	Italy	52/72	39 M-33 F	49.7	Case series/medical history
Giacomelli et al., 2020	Taste alteration	Italy	17/59	40 M-19 F	60	Cross-sectional study/self-reported
Hjelmesæth & Skaare, 2020	Taste alteration	Norway	3/4	NR	NR	Case series/self-reported. Family cases
Jang et al., 2020	Taste alteration	Korea	1/1	M/42	42	Case report/self-reported
Lechien et al., 2020	Taste alteration	Europe	342/417	154 M-263 F	36.9 ± 11.4	Cross-sectional study/National Health and Nutrition Examination Survey
Lee, Huo, & Huang, 2020	Taste alteration	Korea	488/3.191	1.161 M-2.030 F	44	Retrospective study/self-reported
Mao et al., 2020	Taste alteration	China	12/214	87 M-127 F	52.7	Retrospective study/medical history
Melley, Bress, & Polan, 2020	Taste alteration	USA	1/1	F	59	Case report/medical history-self-reported
Paderno et al., 2020	Taste alteration	Italy	284/508	285 M-223 F	55.15	Cross-sectional study/self-reported
Roland, Gurrola, Loftus, Cheung, & Chang, 2020	Taste alteration	USA	96/145	40 M-105 F	39	Cross-sectional study/self-reported survey
Vaira et al., 2020	Taste alteration	Italy	62/320	NR	NR	Cross-sectional study/medical history
Vaira, Salzano, Deiana, & De Riu, 2020	Taste alteration	Italy	39/72	27 M-45 F	49.2	Cross-sectional study/taste test
Vaira et al., 2020	Taste alteration	Italy	17/33	11 M-22 F	51.8	Cross-sectional study/self-administrate taste test
Villalba et al., 2020	Taste alteration	France	1/2	1 M-1 F	82.5	Case series/medical history
Wee et al., 2020	Taste alteration	Singapore	35/154	NR	NR	Cross-sectional study/self-reported
Yan, Faraji, Prajapati, Ostrander, & DeConde, 2020	Taste alteration	USA	40/59	NR	NR	Cross-sectional study/self-reported
Martín Carreras-Presas, Amaro Sánchez, López-Sánchez, Jané-Salas, & Somacarrera Pérez, 2020	Oral blister and ulcers	Spain	1/3	1 F	65	Case series/EM-like lesion
Hedou et al., 2020	Oral blister and ulcers	France	1/103	32 M-71 F	47	Cross-sectional study/HSV in intubated patient
Jimenez-Cauhe et al., 2020	Oral blister and ulcers	Spain	3/4	4 F	66.65	Case series/EM-like lesion
Rivera-Figueroa, Santos, Simpson, & Garg, 2020	Kawasaki-like disease	USA	1/1	M	5	Case report/incomplete KD
Verdoni et al., 2020	Kawasaki-like disease	Italy	5/10	7 M-3 F	7.5	Retrospective study/4 patients with a classic form and 1 with incomplete had oral manifestation

Abbreviations: EM-like lesion, Erythema Multiforme-like eruption; F, female; HSV, Herpes simplex virus; KD, Kawasaki disease; M, male; NR, not reported.

PEDIATRICS

SEVERE COVID-19 INITIALLY PRESENTING AS MESENTERIC ADENOPATHY

BLUF

This case report by physicians from the University of Washington is of a 17 y/o male patient who developed hypoxemia secondary to COVID-19 after initially being diagnosed with mesenteric adenopathy. The authors suggest that mesenteric adenopathy may be an atypical gastrointestinal presentation of COVID-19, as the patient tested negative for many other common infectious agents (Table 1). The authors recommend consideration of COVID-19 on the differential diagnosis during the pandemic given its many systemic manifestations, of which we are still discovering.

SUMMARY

A 17 year-old Caucasian male patient presented with 3 days of severe right lower quadrant abdominal pain, vomiting, and fever. Abdominal imaging and workup revealed mesenteric adenopathy. COVID-19 PCR testing via nasal swab was negative. The patient was admitted to the ED 2 days later with worsening abdominal pain, productive cough, and headache. An abdominal pelvic CT scan revealed new peripheral basilar ground-glass opacities, interlobular septal thickening, and consolidation, suggestive of potential COVID-19 infection. The patient developed hypoxemia requiring admission to the pediatric ICU and was managed with non-invasive positive pressure support and diuretics. A repeat COVID-19 PCR test via nasal swab was negative, but a PCR sputum sample was positive for COVID-19. Labs were significant for elevated BNP and hyper-inflammatory response (increase CRP, ESR, IL-6). Cardiac, renal, and liver function tests were normal. Treatment with Remdesivir was tried, but stopped due to elevation of liver enzymes. The patient was discharged on the sixth day upon return to near baseline, with residual cough and fatigue.

ABSTRACT

Coronavirus disease 2019 (COVID-19) can present with abdominal pain in children and adults. Most imaging findings have been limited to characteristic lung findings, as well as one report of bowel-ischemia-related findings in adults. We report a case of COVID-19 in a healthy teenager who initially presented with isolated mesenteric adenopathy, typically a self-limited illness, which progressed to severe illness requiring intensive care before complete recovery. The boy tested negative for COVID-19 twice by polymerase chain reaction (PCR) from upper respiratory swabs before sputum PCR resulted positive. A high index of suspicion should be maintained for COVID-19 given the continued emergence of new manifestations of the disease.

FIGURES

Nasal swab PCR testing	Blood viral testing	Stool testing
Multiplex respiratory PCR:	Adenovirus PCR:	Stool multiplex PCR:
Adenovirus	HIV antigen and antibody	*Campylobacter (jejuni, coli, upsaliensis)*
Coronavirus 229E	CMV IgG and IgM	*Plesiomonas shigelloides*
Coronavirus HKU1	EBV PCR	Salmonella species
Coronavirus NL63	EBV IgG, IgM, nuclear	*Yersinia enterocolitica*
Coronavirus OC43	antibody, early	Enterotoxigenic *E. coli* (ETEC)
Human metapneumovirus	antigen antibody	*E. coli* O157 STEC
Human rhinovirus/ enterovirus		*E. coli* NON O157 STEC
Influenza A		Shigella species
Influenza A subtype H1		*Vibrio (parahaemolyticus,*
Influenza A subtype 2009 H1		*vulnificus, cholerae)*
Influenza A subtype H3		Cryptosporidium
Influenza B		*Cyclospora cayetanensis*
Parainfluenza virus 1		*Entamoeba histolytica*
Parainfluenza virus 2		*Giardia duodenalis*
Parainfluenza virus 3		Adenovirus F 40/41
Parainfluenza virus 4		Astrovirus
Respiratory syncytial virus		Norovirus
Mycoplasma pneumoniae		Rotavirus
Bordetella pertussis		Sapovirus
Chlamydophila pneumoniae		
Methicillin-resistant *Staphylococcus aureus* PCR screen		

CMV cytomegalovirus, *E. coli* *Escherichia coli*, *EBV* Epstein–Barr virus, *HIV* human immunodeficiency virus, *IgG* immunoglobulin G, *PCR* polymerase chain reaction, *STEC* Shiga toxin-producing E. coli

Table 1 Nasopharyngeal, blood and stool tests (all with negative results) performed in addition to cultures and COVID-19 testing

COVID-19 VACCINE: A COMPREHENSIVE STATUS REPORT

BLUF

A review by microbiologists from India provides a succinct report on the status of COVID-19 vaccine development which includes 158 vaccine candidates with varying mechanisms (Figure 1) at different stages of development, ranging from preclinical to phase III trials. The review includes a written update on the most promising candidates, including ChAdOx1, which is a recombinant adenovirus vaccine currently in phase III trials which had an adequate safety profile in the phase I/II clinical trials, and an anti-spike IgG response in 91% of participants.

ABSTRACT

The current COVID-19 pandemic has urged the scientific community internationally to find answers in terms of therapeutics and vaccines to control SARS-CoV-2. Published investigations mostly on SARS-CoV and to some extent on MERS has taught lessons on vaccination strategies to this novel coronavirus. This is attributed to the fact that SARS-CoV-2 uses the same receptor as SARS-CoV on the host cell i.e. human Angiotensin Converting Enzyme 2 (hACE2) and is approximately 79% similar genetically to SARS-CoV. Though the efforts on COVID-19 vaccines started very early, initially in China, as soon as the outbreak of novel coronavirus erupted and then world-over as the disease was declared a pandemic by WHO. But we will not be having an effective COVID-19 vaccine before September, 2020 as per very optimistic estimates. This is because a successful COVID-19 vaccine will require a cautious validation of efficacy and adverse reactivity as the target vaccinee population include high-risk individuals over the age of 60, particularly those with chronic co-morbid conditions, frontline healthcare workers and those involved in essentials industries. Various platforms for vaccine development are available namely: virus vectored vaccines, protein subunit vaccines, genetic vaccines, and monoclonal antibodies for passive immunization which are under evaluations for SARS-CoV-2, with each having discrete benefits and hindrances. The COVID-19 pandemic which probably is the most devastating one in the last 100 years after Spanish flu mandates the speedy evaluation of the multiple approaches for competence to elicit protective immunity and safety to curtail unwanted immune-potentiation which plays an important role in the pathogenesis of this virus. This review is aimed at providing an overview of the efforts dedicated to an effective vaccine for this novel coronavirus which has crippled the world in terms of economy, human health and life.
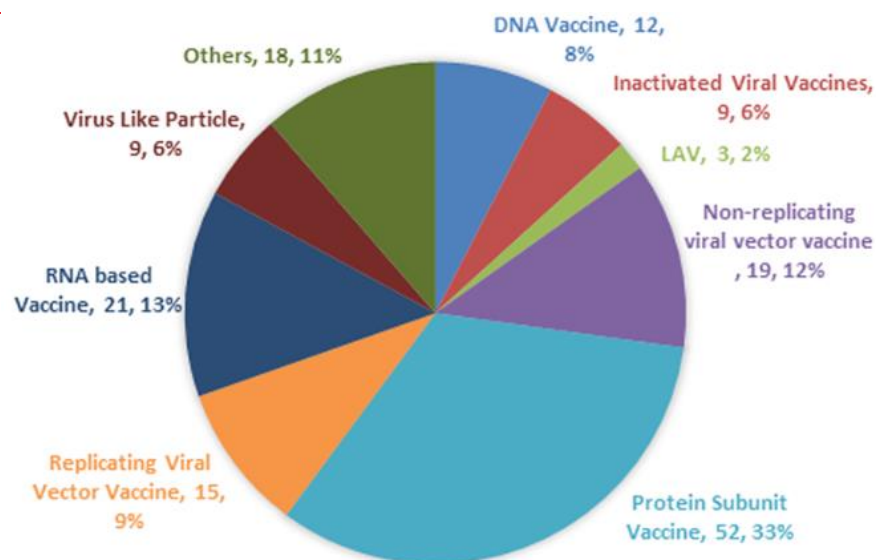
FIGURES

Fig. 1. Pie Chart showing the different categories of SARS-CoV-2 vaccines under research (Anon, 2020c).

LONGITUDINAL PROFILE OF LABORATORY PARAMETERS AND THEIR APPLICATION IN THE PREDICTION FOR FATAL OUTCOME AMONG PATIENTS INFECTED WITH SARS-COV-2: A RETROSPECTIVE COHORT STUDY

Zeng HL, Lu QB, Yang Q, Wang X, Yue DY, Zhang LK, Li H, Liu W, Li HJ.. Clin Infect Dis. 2020 Oct 13:ciaa574. doi: 10.1093/cid/ciaa574. Online ahead of print.
Level of Evidence: 3 - Cohort study or control arm of randomized trial

BLUF

A retrospective cohort study conducted at Tongji Hospital in Wuhan, China from January 17th - March 5th, 2020 trended lab results in 642 hospitalized COVID-19 patients and found that abnormal lactate dehydrogenase, urea, lymphocyte count, and procalcitonin levels were predictors of death during the acute phase (days 1-9), in addition to abnormal procalcitonin, lactate dehydrogenase, lymphocyte count, monocyte percentage, and cholinesterase being predictors of death in the critical phase (days 10-15) (Figure 2). This study suggests that these labs should be followed as markers for prognosis and aggressive care should be considered should abnormalities in these markers arise.

ABSTRACT

BACKGROUND: Patients with coronavirus disease 2019 (COVID-19) experience a wide clinical spectrum, with over 2% developing fatal outcome. The prognostic factors for fatal outcome remain sparsely investigated. METHODS: A retrospective cohort study was performed in a cohort of patients with confirmed COVID-19 in one designated hospital in Wuhan, China, from 17 January-5 March 2020. The laboratory parameters and a panel of cytokines were consecutively evaluated until patients' discharge or death. The laboratory features that could be used to predict fatal outcome were identified. RESULTS: Consecutively collected data on 55 laboratory parameters and cytokines from 642 patients with COVID-19 were profiled along the entire disease course, based on which 3 clinical stages (acute stage, days 1-9; critical stage, days 10-15; and convalescence stage, day 15 to observation end) were determined. Laboratory findings based on 75 deceased and 357 discharged patients revealed that, at the acute stage, fatality could be predicted by older age and abnormal lactate dehydrogenase (LDH), urea, lymphocyte count, and procalcitonin (PCT) level. At the critical stage, the fatal outcome could be predicted by age and abnormal PCT, LDH, cholinesterase, lymphocyte count, and monocyte percentage. Interleukin 6 (IL-6) was remarkably elevated, with fatal cases having a more robust production than discharged cases across the whole observation period. LDH, PCT, lymphocytes, and IL-6 were considered highly important prognostic factors for COVID-19-related death. CONCLUSIONS: The identification of predictors that were routinely tested might allow early identification of patients at high risk of death for early aggressive intervention.
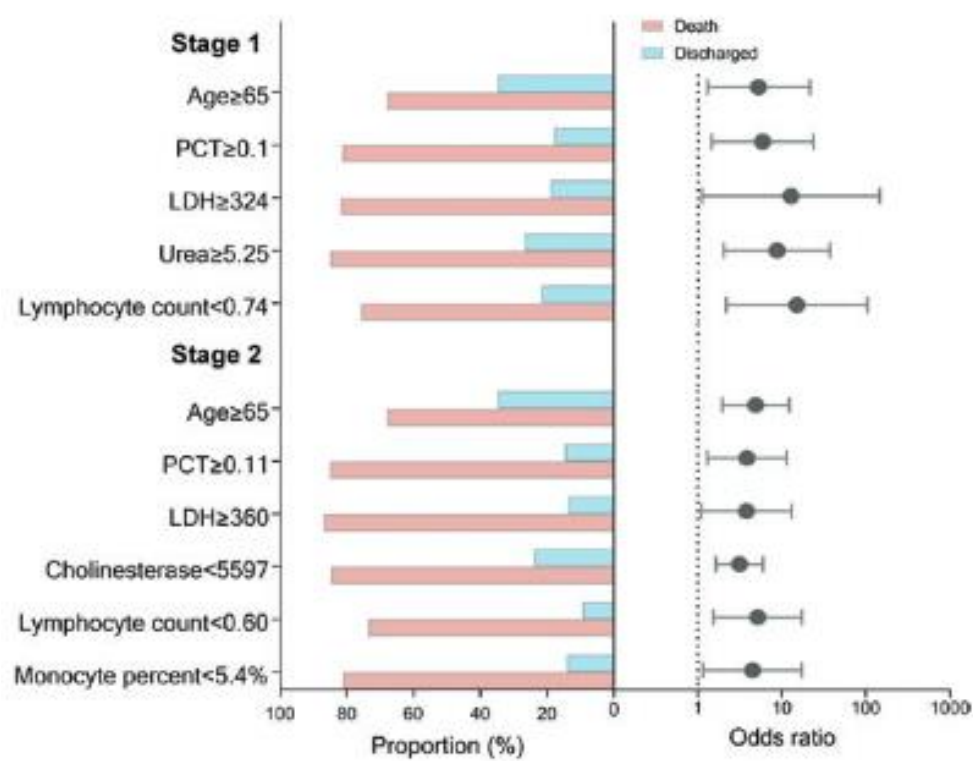
Figure 2. The proportion of deaths and adjusted ORs for deaths of patients with COVID-19 by age and laboratory signs. The black points show the adjusted ORs for death and the error bars represent the 95% CIs. ORs were adjusted for age, sex, and preexisting conditions. The dotted line indicates an adjusted OR of 1. Abbreviations: CI, confidence interval; LDH, lactate dehydrogenase; OR, odds ratio; PCT, procalcitonin.

POWERED AIR PURIFYING RESPIRATOR (PAPR) RESTORES THE N95 FACE MASK INDUCED CEREBRAL HEMODYNAMIC ALTERATIONS AMONG HEALTHCARE WORKERS DURING COVID-19 OUTBREAK

Bharatendu C, Ong JJY, Goh Y, Tan BYQ, Chan ACY, Tang JZY, Leow AS, Chin A, Sooi KWX, Tan YL, Hong CS, Chin BZ, N g E, Foong TW, Teoh HL, Ong ST, Lee P, Khoo D, Tsivgoulis G, Alexandrov AV, Sharma VK.. J Neurol Sci. 2020 Oct 15;417:117078. doi: 10.1016/j.jns.2020.117078. Epub 2020 Aug 3.
Level of Evidence: 3 - Non-randomized controlled cohort/follow-up study

BLUF

A cross-sectional study by neurologists from Singapore spanning February - April, 2020 evaluated cerebral hemodynamic changes using Transcranial Doppler (TCD) of middle cerebral artery (MCA) flow among 154 COVID-19 healthcare workers (Table 1), of whom 123/154 developed de-novo headache due to N95 use (38/154 had preexisting migraine co-morbidity). Wearing an N95 increased Mean Flow Velocity (MFV) and ET-CO2, while Pulsatility Index (PI) decreased (p<0.001), whereas 24 participants donning N95 with a Powered Air Purifying Respirator (PAPR) exhibited values nearer to baseline (Table 3, Figure 1). These results implicate combined use of N95 with PAPR to potentially maintain cerebral homeostasis, mitigating PPE-induced headaches among healthcare workers, although larger trials may be required.

ABSTRACT

BACKGROUND AND AIM: COVID-19 pandemic has resulted in an unprecedented increased usage of Personal protective equipment (PPE) by healthcare-workers. PPE usage causes headache in majority of users. We evaluated changes in cerebral hemodynamics among healthcare-workers using PPE. METHODS: Frontline healthcare-workers donning PPE at our tertiary center were included. Demographics, co-morbidities and blood-pressure were recorded. Transcranial Doppler (TCD) monitoring of middle cerebral artery was performed with 2-MHz probe. Mean flow velocity (MFV) and pulsatility index (PI) were recorded at baseline, after donning N95 respirator-mask, and after donning powered air-purifying respirator (PAPR), when indicated. End-tidal carbon-dioxide (ET-CO2) pressure was recorded for participants donning PAPR in addition to the N95 respirator-mask. RESULTS: A total of 154 healthcare-workers (mean age 29 +- 12 years, 67% women) were included. Migraine was the commonest co-morbidity in 38 (25%) individuals while 123 (80%) developed de-novo headache due to N95 mask. Donning of N95 respirator-mask resulted in significant increase in MFV (4.4 +- 10.4 cm/s, p < 0.001) and decrease in PI (0.13 +- 0.12; p < 0.001) while ET-CO2 increased by 3.1 +- 1.2 mmHg (p < 0.001). TCD monitoring in 24 (16%) participants donning PAPR and N95 respirator mask together showed normalization of PI, accompanied by normalization of ET-CO2 values within 5-min. Combined use of N95 respirator-mask and PAPR was more comfortable as compared to N95 respirator-mask alone. CONCLUSION: Use of N95 respirator-mask results in significant alterations in cerebral hemodynamics. However, these effects are mitigated by the use of additional PAPR. We recommend the use of PAPR together with the N95 mask for healthcare-workers doing longer duties in the hospital wards.

FIGURES

Variables	Values
Mean Age in years (SD)	29.6 (12.1)
Female gender, *n* (%)	103 (66.9)
Co-morbidities, *n* (%)	
Hypertension	3 (1.9)
Diabetes mellitus	0 (0.0)
Hyperlipidaemia	1 (0.6)
Pre-existing migraine	38 (24.7)
De novo headache	123 (79.9)
Coronary artery disease	0 (0.0)
Congestive heart failure	0 (0.0)
Chronic obstructive pulmonary disease	0 (0.0)

Table 1: Baseline characteristics of the study population (n = 154).

Parameter	Baseline	N95 alone	Change[a]	P	N95 + PAPR	Change[b]	p
Mean MFV (SD) in cm/s	54.5 (8.7)	61.4 (8.2)	+7.0 (6.9)	< 0.001	59.9 (8.8)	+5.5 (8.4)	0.004
PI (SD)	0.92 (0.06)	0.81 (0.06)	− 0.10 (0.04)	< 0.001	0.91 (0.06)	0.00 (0.04)	0.694
Mean ET-CO2 (SD) in mmHg	37.3 (1.3)	40.4 (1.6)	+3.1 (1.2)	< 0.001	37.3 (1.3)	0.0 (1.2)	1.000

MFV: mean flow velocity, PI: pulsatility index, SD: standard deviation, ET-CO2: end-tidal carbon dioxide.

[a] Absolute change between baseline and after donning N95.

[b] Absolute change between baseline and after donning PAPR.

3

Table 3: Cerebral hemodynamic parameters after donning N95 respirator mask alone together with powered air purifying respirator (PAPR) (n = 24).
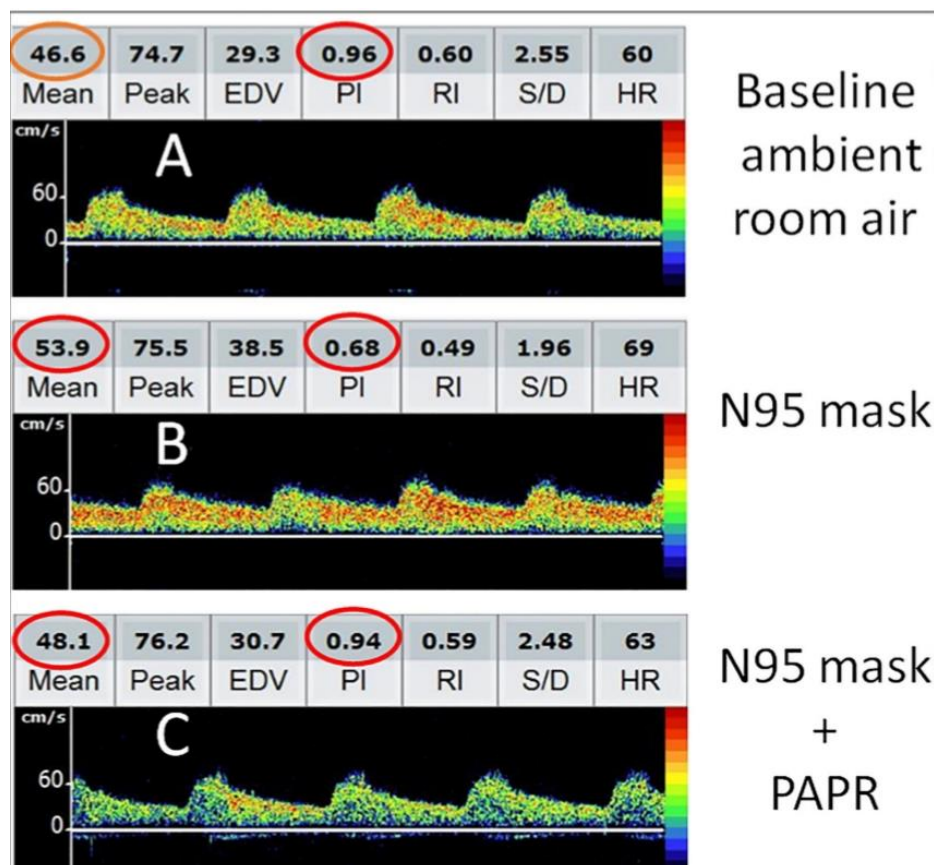

Figure 1: Serial transcranial Doppler (TCD) changes during donning of N95 respirator mask alone and together with powered air purifying respirator (PAPR). While breathing ambient room air, Doppler spectra from right middle cerebral artery showed mean flow velocity (MFV) 46.6 cm/s and pulsatility index (PI) 0.96 (A). After donning N95 respirator mask for 5-minutes, MFV increased to 53.9 cm/s while PI decreased to 0.68 (B). However, both MFV and PI returned to near-baseline 5minutes after donning PAPR and N95 respirator mask together (C).

WHAT CHANCES DO CHILDREN HAVE AGAINST COVID-19? IS THE ANSWER HIDDEN WITHIN THE THYMUS?

BLUF

An expert commentary by pediatricians from the Kahramanmaras Sutcu Imam University postulate that the reason why there are less COVID-19 cases (and decreased severity in clinical course) in the pediatric population could be due to effective thymus and T-lymphocyte function, namely the immunomodulatory effects of regulatory T-cells, in children prior to thymic involution beginning in adolescence. Based on this hypothesis, the authors compiled a list of thymus stimulating agents as potential solutions to preventing COVID-19 (Table 1).

ABSTRACT

A new type of coronavirus named as SARS-CoV-2 pandemic has begun to threaten human health. As with other types of coronaviruses, SARS-CoV-2 affects children less frequently, and it has been observed that the disease is mild. In the pathogenesis of a standard viral infection, the pathogen's contact with the mucosa is initially followed by an innate immunity response. T cells are the primary decisive element in adaptive immunity capability. For this reason, the adaptive immune response mediated by the thymus is a process that regulates the immune response responsible for preventing invasive damage from a virus. Regulatory T cells (T-reg) are active during the early periods of life and have precise roles in immunomodulation. The thymus is highly active in the intrauterine and neonatal period; it begins to shrink after birth and continues its activity until adolescence. The loss of T-reg function by age results in difficulty with the control of the immune response, increased inflammation as shown in coronavirus disease (COVID-19) as an inflammatory storm. Also, the thymus is typically able to replace the T cells destroyed by apoptosis caused by the virus. Thymus and T cells are the key factors of pathogenesis of SARS-CoV-2 in children.Conclusion: We speculated that thymus activity and T lymphocyte function in children protect them against the virus effects. Stimulating and preventing the inhibition of the thymus can be possible treatment components against COVID-19. What is Known: The SARS-CoV-2 infection does not often progress with an invasive clinic in children.   Thymus activity and T lymphocyte functions are highly active in children. What is New: Effective thymus activity and T lymphocyte function in children protect them against the invasive SARS-CoV-2 infection.   Stimulating and preventing the inhibition of the thymus can be possible treatment components against COVID-19.

FIGURES

Molecule/therapy option	Treatment	Effects
Zinc	Oral supplement	Lowers age-associated thymic atrophy with partial recovery of lymphocyte functions, as measured by mitogen responsiveness and NK cell activity on mice, and serves as a co-factor of thymulin which is associated with both intrathymic and extrathymic T cell differentiation
Antioxidants	Vitamin E, high-dose vitamin C and N-acetyl cysteine	Reduces thymic atrophy
IL-7	Recombinant human IL-7	Increased TCR diversity in clinical studies in humans, in vitro proliferation of peripheral T cells and increased thymic output in aged mice
Glucocorticoids	Inhibition of glucocorticoids	Glucocorticoids reduce thymic cell count during *Salmonella typhimurium* and *Francisella tularensis* infections in mice; therapies with thymopoeitic potential are known to reduce GCs.
Leptin		It reduces thymic atrophy, increases intrathymic IL-7, and decreases pro-inflammatory cytokine release in mice, but not all conditions are suitable for administration.
Keratinocyte growth factor		Increases thymic output and naive T cell pool in aged mice.
Ghrelin, an appetite-stimulant hormone		Improvement in thymocyte numbers, thymic output, and T cell activation in aged mice

Table 1: Treatment options that can prevent thymic atrophy or stimulate thymus.

MENTAL HEALTH DISORDERS RELATED TO COVID-19-RELATED DEATHS

Simon NM, Saxe GN, Marmar CR.. JAMA. 2020 Oct 12. doi: 10.1001/jama.2020.19632. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

A commentary by psychiatrists from the NYU Grossman School of Medicine discuss the incoming wave of anxiety and mental health illnesses stemming from the COVID-19 pandemic. The authors cite the Center for Disease Control and Prevention (CDC) June 2020 survey with 40.9% of participants reporting "at least one adverse mental or behavioral health condition," which is 3-4 times higher than one year ago. Health disparities and a distressed healthcare workforce are additional areas of concern. The authors recommend screening (e.g. trauma, grieving, depression, anxiety) by primary care physicians and mental health professionals as well as broad supportive public health strategies (e.g. online resources for grieving families) in an effort to identify and aid those in need of assistance (Figure 1).

FIGURES

Figure 1: Potential Strategies to Manage the Coming Wave of Grief and Distress Following Coronavirus Disease 2019 (COVID-19)–Related Deaths.