Daily COVID-19 Literature Surveillance

April 7th, 2020

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Urgent dental care for patients during the COVID-19 pandemic.

PMID: 32251619, Apr 7, 2020
Dave, Manas; Seoudi, Noha; Coulthard, Paul
Lancet
Level of Evidence: 5- Expert opinion
Type of Article: Correspondence

Summary: Because of the risk for aerosolization of potentially infectious body substances, routine dentistry has been suspended in several countries. Without routine dental services, there may be an increased volume of patients that present acutely with compromised airways from dental infections. In this case, the author recommends prioritizing dental extraction of infected teeth over repair and adding dental professionals to the list of healthcare professionals that need high priority COVID-19 testing.

The COVID-19 Pandemic in the US: A Clinical Update.

PMID: 32250388, Apr 7, 2020
Omer, Saad B; Malani, Preeti; Del Rio, Carlos
JAMA
Level of Evidence: 5- Expert opinion
Type of Article: Viewpoint

Summary: Exponential growth phase of COVID-19 epidemic reached. Several concerns remain:

1. What is the true CFR of COVID-19?
   a. Ranges anywhere from 0.7% in Germany and 10.8% in Italy due to the problems associated with finding a true denominator.
2. Testing
   a. The current diagnostic standard for COVID-19 is the PCR test for SARS-CoV2 RNA
   b. But no gold standard exists for diagnosis of COVID-19; hence the sensitivity/specificity of this test remains unknown
   c. There are case reports of patients with CT findings consistent with COVID-19 have had negative and positive tests following CT, suggesting weak diagnostic power of the current PCR test.
   d. With the reliability of PCR test in question, it lends speculation on whether or not patients can get reinfected by the SARS-CoV2 virus or if these case reports reflect patients who were discharged with a false negative test. Other coronaviruses have demonstrated the potential to reinfect but typically requires months to years in between infections.
3. Transmission
   a. SARS-CoV2 spreads primarily through person to person via droplets emitted by infected individuals while coughing, sneezing and talking and land on mucosa.
   b. There is a concern for fomite transmission with evidence of coronaviruses persisting on plastic, metal, glass for up to 9 days at room temperature
      i. Disinfection is best done with 62-71% ethanol, 0.5% hydrogen peroxide or 0.1% sodium hypochlorite for 1 min.
      ii. Chlorhexadine was less effective.
   c. Environmental air sampling in rooms of patients with COVID-19 contained viral particles and **health care providers should consider using airborne precautions.**
   d. Public use of masks may be important to prevent presymptomatic transmission of SARS-CoV2.
4. We need a vaccine
   a. 3 candidates currently in phase 1 human trials with product launch goal of mid 2021.

i.mRNA vaccine
ii.2x adenoviral vector vaccines

Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy.

PMID: 32250385, Apr 7, 2020
Grasselli, Giacomo; Zangrillo, Alberto; Zanella, Alberto; Antonelli, Massimo; Cabrini, Luca; Castelli, Antonio; Cereda, Danilo; Coluccello, Antonio; Foti, Giuseppe; Fumagalli, Roberto; Iotti, Giorgio; Latronico, Nicola; Lorini, Luca; Merler, Stefano; Natalini, Giuseppe; Piatti, Alessandra; Ranieri, Marco Vito; Scandroglio, Anna Mara; Storti, Enrico; Cecconi, Maurizio; Pesenti, Antonio
JAMA
Level of Evidence: Level 4- Retrospective case series
Type of Article: Original Investigation
BLUF: Of 1591 ICU patients, mortality was 26%; with patients over 64 years being significantly more likely to die in the ICU. 99% of these patients required respiratory support (88% endotracheal intubation, 11% non-invasive ventilation).

Abstract:
Importance: In December 2019, a novel coronavirus (severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]) emerged in China and has spread globally, creating a pandemic. Information about the clinical characteristics of infected patients who require intensive care is limited.
Objective: To characterize patients with coronavirus disease 2019 (COVID-19) requiring treatment in an intensive care unit (ICU) in the Lombardy region of Italy.
Design, Setting, and Participants: Retrospective case series of 1591 consecutive patients with laboratory-confirmed COVID-19 referred for ICU admission to the coordinator center (Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy) of the COVID-19 Lombardy ICU Network and treated at one of the ICUs of the 72 hospitals in this network between February 20 and March 18, 2020. Date of final follow-up was March 25, 2020.
Exposures: SARS-CoV-2 infection confirmed by real-time reverse transcriptase–polymerase chain reaction (RT-PCR) assay of nasal and pharyngeal swabs.
Main Outcomes and Measures: Demographic and clinical data were collected, including data on clinical management, respiratory failure, and patient mortality. Data were recorded by the coordinator center on an electronic worksheet during telephone calls by the staff of the COVID-19 Lombardy ICU Network.
Results: Of the 1591 patients included in the study, the median (IQR) age was 63 (56-70) years and 1304 (82%) were male. Of the 1043 patients with available data, 709 (68%) had at least 1 comorbidity and 509 (49%) had hypertension. Among 1300 patients with available respiratory support data, 1287 (99% [95% CI, 98%-99%]) needed respiratory support, including 1150 (88% [95% CI, 87%-90%]) who received mechanical ventilation and 137 (11% [95% CI, 9%-12%]) who received noninvasive ventilation. The median positive end-expiratory pressure (PEEP) was 14 (IQR, 12-16) cm H_2O, and Fio_2 was greater than 50% in 89% of patients. The median Pao_2/Fio_2 was 160 (IQR, 114-220). The median PEEP level was not different between younger patients (n = 503 aged ≤63 years) and older patients (n = 514 aged ≥64 years) (14 [IQR, 12-15] vs 14 [IQR, 12-16] cm H_2O, respectively; median difference, 0 [95% CI, 0-0]; P = .94). Median Fio_2 was lower in younger patients: 60% (IQR, 50%-80%) vs 70% (IQR, 50%-80%) (median difference, −10% [95% CI, −14% to 6%]; P = .006), and median Pao_2/Fio_2 was higher in younger patients: 163.5 (IQR, 120-230) vs 156 (IQR, 110-205) (median difference, 7 [95% CI, −8 to 22]; P = .02). Patients with hypertension (n = 509) were older than those without hypertension (n = 526) (median [IQR] age, 66 years [60-72] vs 62 years [54-68];

$P < .001$) and had lower Pao_2/Fio_2 (median [IQR], 146 [105-214] vs 173 [120-222]; median difference, −27 [95% CI, −42 to −12]; $P = .005$). Among the 1581 patients with ICU disposition data available as of March 25, 2020, 920 patients (58% [95% CI, 56%-61%]) were still in the ICU, 256 (16% [95% CI, 14%-18%]) were discharged from the ICU, and 405 (26% [95% CI, 23%-28%]) had died in the ICU. Older patients (n = 786; age ≥64 years) had higher mortality than younger patients (n = 795; age ≤63 years) (36% vs 15%; difference, 21% [95% CI, 17%-26%]; $P < .001$).
Conclusions and Relevance: In this case series of critically ill patients with laboratory-confirmed COVID-19 admitted to ICUs in Lombardy, Italy, the majority were older men, a large proportion required mechanical ventilation and high levels of PEEP, and ICU mortality was 26%.

Table 2. Patient Disposition From COVID-Only Intensive Care Units (ICUs), Total and Stratified by History of Hypertension

	Patients by age, y, No. (%)								
	All (N = 1591)	0-20 (n = 4)	21-40 (n = 56)	41-50 (n = 143)	51-60 (n = 427)	61-70 (n = 598)	71-80 (n = 341)	81-90 (n = 21)	91-100 (n = 1)
Overall									
Outcome, No. with data	1581	2	56	142	423	596	340	21	1
Died in ICU	405 (26)	0	4 (7)	16 (11)	63 (15)	174 (29)	136 (40)	11 (52)	1 (100)
Discharged from ICU	256 (16)	0	20 (36)	35 (25)	90 (21)	69 (12)	40 (12)	2 (10)	0
Still in ICU as of 3/25/2020[a]	920 (58)	2 (100)	32 (57)	91 (64)	270 (64)	353 (59)	164 (48)	8 (38)	0

Sample Pooling as a Strategy to Detect Community Transmission of SARS-CoV-2.

PMID: 32250394, Apr 7, 2020
Hogan, Catherine A; Sahoo, Malaya K; Pinsky, Benjamin A
JAMA
Level of evidence: Level 4- Retrospective cohort study
Type of Article: Research Letter
BLUF: Sample pooling can be an effective way to specifically test for SARS-CoV-2 in the population.

Summarizing excerpt:
"A pooled screening strategy was pursued to increase testing throughput, limit use of reagents, and increase overall testing efficiency at an expected slight loss of sensitivity. With only 1 false-positive reading, the strategy was specific. Due to the challenges of restricted access to diagnostic tests and kit supplies across the United States, early testing has largely been limited to symptomatic individuals fulfilling testing criteria. Although this approach facilitates rational use of resources, it may miss individuals in whom COVID-19 risk has not been identified. This study is limited in that it was performed in a single laboratory in a restricted geographical area; additional data are thus required to validate this approach on a larger scale. Furthermore, this screening strategy does not obviate the need for individual diagnostic testing, particularly as community transmission intensifies... Strategies such as pooled screening may facilitate detection of early community transmission of SARS-CoV-2 and enable timely implementation of appropriate infection control measures to reduce spread."

Covid-19 in South Korea - Challenges of Subclinical Manifestations.

PMID: 32251568, Apr 7, 2020
Song, Joon-Young; Yun, Jin-Gu; Noh, Ji-Yun; Cheong, Hee-Jin; Kim, Woo-Joo
N Engl J Med
Level of Evidence: Level 5- expert opinion

Type of Article: Correspondence
Summary: SARS-CoV-2 is likely more transmissible than MERS-CoV due to higher R_0 and shorter estimated serial interval distribution. Despite high suggestion of subclinical presentations, there is little data on viral shedding from patients with various symptom severity.

Structural Variations in Human ACE2 may Influence its Binding with SARS-CoV-2 Spike Protein.

PMID: 32249956, Apr 7, 2020
Hussain, Mushtaq
Journal of Medical Virology
Level of Evidence: 5 - Expert opinion, basic biology analysis and knowledge
Type of Article: Scientific Study
BLUF: Variations in ACE2 alleles may lead to resistance patterns to COVID-19 due to varied intermolecular interactions between the receptor and the virus, however statistically different data was not observed to explain the difference in immune response or susceptibility to COVID-19 among patients.

Abstract: The recent pandemic of COVID-19, caused by SARS-CoV-2, is unarguably the most fearsome compared to the earlier outbreaks caused by other coronaviruses, SARS-CoV and MERS-CoV. Human ACE2 is now established as a receptor for the SARS-CoV-2 spike protein. Where variations in the viral spike protein in turn lead to the cross species transmission of the virus, genetic variations in the host receptor ACE2, may also contribute to the susceptibility and/or resistance against the viral infection. This study aims to explore the binding of the proteins encoded by different human ACE2 allelic variants with SARS-CoV-2 spike protein. Briefly, coding variants of ACE2 corresponding to the reported binding sites for its attachment with coronavirus spike protein were selected and molecular models of these variants were constructed by homology modelling. The models were then superimposed over the native ACE2 and ACE2-spike protein complex, to observe structural changes in the ACE2 variants and their intermolecular interactions with SARS-CoV-2 spike protein respectively. Despite strong overall structural similarities, spatial orientation of the key interacting residues varies in the ACE2 variants compared to the wild type molecule. Most ACE2 variants showed similar binding affinity for SARS-CoV-2 spike protein as observed in the complex structure of wild type ACE2 and SARS-CoV-2 spike protein. However, ACE2 alleles, rs73635825 (S19P) and rs143936283 (E329G) showed noticeable variations in their intermolecular interactions with the viral spike protein. In summary, our data provide structural basis of potential resistance against SARS-CoV-2 infection driven by ACE2 allelic variants.

An Analysis of Spatiotemporal Pattern for COIVD-19 in China based on Space-Time Cube.

PMID: 32249952, Apr 7, 2020
Mo, Chunbao

Journal of Medical Virology
Level of Evidence: 5 - Expert opinion, base knowledge and methodology
Type of Article: Scientific Article

BLUF: Spatial-temporal clustering models may be put to use to predict trends in viral transmission and the effects of viral containment measures during this rapidly evolving pandemic. However, their accuracy and utility remains unproven and requires further study.

Abstract: This study seeks to examine and analyze the spatial and temporal patterns of COVID-19 outbreaks and identify the spatiotemporal distribution characteristics and changing trends of cases. Hence, local outlier analysis and emerging spatiotemporal hot spot analysis were performed to analyze the spatiotemporal clustering pattern and cold\hot spot trends of COVID-19 cases based on space-time cube during the period from January 23, 2020 to February 24, 2020. The main findings are as follows. 1) The outbreak had spread rapidly throughout the country within a short time and the current totality incidence rate has decreased. 2) The spatiotemporal distribution of cases was uneven. In terms of the spatiotemporal clustering pattern, Wuhan and Shiyan city were the center as both cities had high–high clustering pattern with a surrounding unstable multiple type pattern in partial areas of Henan, Anhui, Jiangxi, and Hunan provinces, and Chongqing city. Those regions are continuously in the hot spot on the spatiotemporal tendency. 3) The spatiotemporal analysis technology based on the space-time cube can analyze comprehensively the spatiotemporal pattern of epidemiological data and produce a visual output of the consequences, which can reflect intuitively the distribution and trend of data in space–time. Therefore, the Chinese government should strengthen the prevention and control efforts in a targeted manner to cope with a highly changeable situation.

About the origin of the first two Sars-CoV-2 infections in Italy: inference not supported by appropriate sequence analysis.

PMID: 32249944, Apr 7, 2020
Carletti, Fabrizio
Journal of Medical Virology
Level of Evidence: 5 - Expert opinion, basic biology analysis and knowledge
Type of Article: Commentary, including a report on scientific data

BLUF: Phylogenetic evolutionary reconstruction can only be made based on long sequences in COVID-19 due to high levels of conservation. The sequences used to indicate origins in the paper published by Giovannetti were too short to provide reliable analysis and the data reported cannot be independently validated.

Abstract: In the 5th February 2020 issue of Journal of Medical Virology a paper was published by Giovannetti et al., entitled "The first two cases of 2019-nCoV in Italy: where they come from?"(1) . In this paper a phylogenetic and evolutionary analysis was applied to the virus identified in the first two subjects diagnosed in Italy with 2019-nCoV infection, recently renamed SARS-CoV-2(2) , two Chinese spouses arrived in Italy for tourism. The diagnosis was performed by the virology team under

direction of Maria R. Capobianchi, at the National Institute of Infectious Diseases (INMI) in Rome, Italy, where the patients are currently hospitalized.

A comparative-descriptive analysis of clinical characteristics in 2019- Coronavirus -infected children and adults.

PMID: 32249943, Apr 7, 2020
Han, Ya-Nan
Journal of Medical Virology
Level of Evidence: 3 - Cross-sectional analysis without controls
Type of Article: Scientific Study

BLUF: Children show a statistically significant increase in diarrhea and decrease in duration of fever (1 vs 4 days) compared to adults. Leukocytosis, elevated procalcitonin, and elevated creatine kinase were more common in children, with leukopenia and hypoalbuminemia more common in adults. Patients were not necessarily confirmed to have COVID-19 by PCR.

Abstract: Acute respiratory disease (ARD) caused by 2019 novel coronavirus (2019-nCoV) has rapidly spread throughout China. Children and adults show a different clinical course. The purpose of the current study is to comparatively analyze the clinical characteristics of 2019-nCoV infection in children and adults and to explore the possible causes for the discrepancies present. The medical records of 25 adults and 7 children confirmed cases of 2019-nCoV ARD were reviewed retrospectively. All children were family clusters. The total adult patients were differentiated into: the local residents of Wuhan, a history of travel to Wuhan and direct contact with people from Wuhan. The numbers were 14 (56%), 10 (40%) & 1 (4%), respectively. The median incubation period of children and adults was 5 days (range 3-12 days) and 4 days (range 2-12 days), respectively. Diarrhoea and/or vomiting (57.1%) were more common in children, whereas for adults it was myalgia or fatigue (52%). On admission, the percentage of children having pneumonia (5, 71.4%) was roughly the same as adults (20, 80%). 20% of adults had leucopoenia, but leukocytosis was more frequently in children (28.6%, P=0.014). A higher number of children had elevated creatine kinase isoenzyme (57.1% vs. 4%, P=0.004). Antiviral therapy was given to all adult patients but to none of the children. In summary, knowledge of these differences between children and adults will not only be helpful for the clinical diagnosis of 2019 novel coronavirus disease (COVID-19), but also for a future discussion on age-specific coronavirus infection.

Baricitinib for COVID-19: a suitable treatment? - Authors' reply.

PMID: 32251639, Apr 7, 2020
Richardson, Peter J; Corbellino, Mario; Stebbing, Justin
Lancet
Level of Evidence: 5 - Expert opinion
Type of Article: Correspondence

BLUF: Cytokine inhibitors should not be implemented in wide use as a cure all drug for hospitalized COVID-19 patients, as proven data is not available to prove they do more good than harm.

Summary: SARS patients who developed hypoxemia and died in hospital were shown to have high levels of interferons involved in the JAK-STAT pathway, compared with low levels in those who recovered. This could represent a cytokine storm effect that could be treated using a JAK1/JAK2 inhibitor such as baricitinib during the late stages of the disease. However, more data needs to be collected to determine the utility of a cytokine inhibitor in COVID-19 and the authors caution against promoting it as a cure or using it empirically across all hospitalized patients. Randomized controlled trials are necessary to produce the most reliable data regarding drug efficacy in treating this and other viruses.

Baricitinib for COVID-19: a suitable treatment?

PMID: 32251638, Apr 7, 2020
Favalli, Ennio G
Lancet
Level of Evidence: 5 - Expert opinion
Type of Article: Correspondence
Summary: Baricitinib use in COVID-19 patients should be used with caution due to the many adverse effects of the drug and potential inhibition of antiviral response in patients. There is also a risk of reactivation of latent viral infections which could lead to viral pneumonia not due to COVID-19 in immunocompromised patients.

From China: hope and lessons for COVID-19 control.

PMID: 32251637, Apr 7, 2020
Azman, Andrew S; Luquero, Francisco J
Lancet
Level of Evidence: 5 - Expert opinion
Type of Article: Comment
BLUF: Data transparency will enable increased epidemiological analysis to generate well-supported response parameters to the COVID-19 pandemic to enable rapid diminished transmission around the globe.

Summary: The rapid quelling of local viral transmission in numerous Chinese provinces outside of Hubei is likely “due to the strict government imposed restrictions on movement of people and social gatherings, widespread symptom screening, testing and quarantine programmes, and the strong emphasis on personal behaviour change (eg, hand hygiene, mask use, and physical distancing) to reduce the risk of transmission”. Data transparency from China was vital in enabling the study by Juanjuan Zhang that reported these findings and more openness regarding data on viral transmission, cases, testing availability and criteria are needed from across the globe to enable more

studies to better track the nature of the virus and an appropriate response to mitigate transmission. If data continues to show that drastic measures to shut-down society help to create a rapid decrease in viral transmission it may be more likely that governments will implement similar responses to rapidly end the pandemic.

Maternal and neonatal outcomes of pregnant women with COVID-19 pneumonia: a case-control study.

PMID: 32249918, Apr 7, 2020
Li, Na
Clinical Infectious Diseases
Level of Evidence: 2 - Case-control study
Type of Article: Scientific Study

BLUF: Pregnant patients with confirmed COVID-19 or suspected COVID-19 (with negative PCR, but typical CHEST CT findings) may show mild symptoms, so adequate screening is vital. No severe complications were noted in women with COVID-19 or neonates born to COVID-19 patients regardless of delivery method. There was a significant increase in premature birth and low birth weight in confirmed and suspected COVID-19 patients.

Abstract:
BACKGROUND: The ongoing epidemics of coronavirus disease 2019 (COVID-19) have caused serious concerns about its potential adverse effects on pregnancy. There are limited data on maternal and neonatal outcomes of pregnant women with COVID-19 pneumonia.
METHODS: We conducted a case-control study to compare clinical characteristics, maternal and neonatal outcomes of pregnant women with and without COVID-19 pneumonia.
RESULTS: During January 24 to February 29, 2020, there were sixteen pregnant women with confirmed COVID-19 pneumonia and eighteen suspected cases who were admitted to labor in the third trimester. Two had vaginal delivery and the rest took cesarean section. Few patients presented respiratory symptoms (fever and cough) on admission, but most had typical chest CT images of COVID-19 pneumonia. Compared to the controls, COVID-19 pneumonia patients had lower counts of white blood cells (WBC), neutrophils, C-reactive protein (CRP), and alanine aminotransferase (ALT) on admission. Increased levels of WBC, neutrophils, eosinophils, and CRP were found in postpartum blood tests of pneumonia patients. There were three (18.8%) and three (16.7%) of the mothers with confirmed or suspected COVID-19 pneumonia had preterm delivery due to maternal complications, which were significantly higher than the control group. None experienced respiratory failure during hospital stay. COVID-19 infection was not found in the newborns and none developed severe neonatal complications.
CONCLUSION: Severe maternal and neonatal complications were not observed in pregnant women with COVID-19 pneumonia who had vaginal delivery or caesarean section. Mild respiratory symptoms of pregnant women with COVID-19 pneumonia highlight the need of effective screening on admission.

China empowers Internet hospital to fight against COVID-19.

PMID: 32251688, Apr 7, 2020
Sun, Shuangyi
Journal of Infection
Level of Evidence: 6 - Critical data uncited
Type of Article: Letter

BLUF: Internet hospitals can decrease COVID-19 spread by conducting care remotely and providing drug delivery to patients who do not need to be seen in a hospital acutely.

Summary: Patients with comorbidities have shown to have higher mortality from COVID-19. However, routine medical treatment for conditions other than COVID-19 have been less accessible during the pandemic. Internet hospitals have been utilized in China to enable remote care without risk of viral transmission in traditional clinics. Internet hospitals can also be used to triage patients who show viral symptoms, but may not have COVID-19 or be good candidates for at-home quarantine and symptomatic treatment. In China, these hospitals have been incorporated into the insurance structure and offer drug delivery to patients to ease accessibility.