COVID-19 LST

Daily COVID-19
Literature Surveillance
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Neuroinfection may potentially contribute to pathophysiology and clinical manifestations of COVID-19.

Steardo, Luca; Steardo, Luca Jr; Zorec, Robert; Verkhratsky, AlexeiActa Physiol (Oxf)

Summary: Ace2 receptors are expressed on neurons and there is evidence of viral spread via neurons. No new data was shown.

Covid-19 and Diabetes Mellitus: Unveiling the Interaction of Two Pandemics

Ernesto Maddaloni 1, Raffaella Buzzetti 1

Abstract

A novel RNA betacoronavirus causing coronavirus disease 2019 (Covid-19) has now been declared pandemic disease by WHO. Guo W et al published the first report of biochemical features in patients with diabetes and the further risk that this disease can determine to the progression of Covid-19. Among different cytokines found significantly higher in patients with diabetes compared to those without, Interleukin-6 (IL-6) which is already increased in conditions of chronic inflammation, may play a more deleterious role in Covid-19 infection. **Targeting the over expression of Il-6 effects with a monoclonal antibody against IL-6 receptor [tocilizumab] or using Janus Kinase inhibitors may be particularly helpful for treatment of Covid-19 pneumonia in diabetes.**

Additional info: Some Italian hospitals used tocilizumab off label for covid-19 patients and currently under study as an ad hoc randomized controlled trial. Also leaves door open for other drugs that inhibit IL-6 and its pathway such as siltuximab (IL-6 inhibitor) and baricitinib, tofacitinib, upadacitinib (jak inhibitors).

The exacerbation of blood glucose instability thought to be result of disproportionately increased infection of liver and pancreas as they widely express ACE2, the receptor for SARS-CoV-2. Writer suggest the possibility of increased autoimmune diabetes in patients who have recovered from Covid-19.

Potential Utilities of Mask Wearing and Instant Hand Hygiene for Fighting SARS-CoV-2

Qing-Xia Ma 1, Hu Shan 1, Hong-Liang Zhang 1, Gui-Mei Li 1, Rui-Mei Yang 1, Ji-Ming Chen

Abstract

Background: The surge of patients in the pandemic of COVID-19 caused by the novel coronavirus

SARS-CoV-2 may overwhelm the medical systems of many countries. Mask wearing and hand washing

can slow the spread of the virus, but currently masks are in shortage in many countries, and timely hand washing is often impossible.

Methods: The efficacy of three types of masks and instant hand wiping was evaluated using avian influenza virus to mock the coronavirus. Virus quantification was performed using real-time RT-PCR. Previous studies on mask wearing were reviewed.

Results: Instant hand wiping using a wet towel soaked in water containing 1.00% soap powder, 0.05% active chlorine, or **0.25% active chlorine from sodium hypochlorite** removed 98.36%, 96.62%, and **99.98%** of the virus from hands, respectively. **N95 masks, medical masks, and homemade masks made of 4-layer kitchen paper and 1-layer cloth could block 99.98%, 97.14%, and 95.15% of the virus in aerosols.** Medical mask wearing which was supported by many studies was opposed by other studies possibly due to erroneous judgment. With these data we propose the approach of mask wearing plus instant hand hygiene (MIH) to slow the exponential spread of the virus. This MIH approach has been supported by the experiences of seven countries in fighting against COVID-19.

TABLE 1 Percentage of AIV removed through instant wiping as compared without wiping

Material for towel soaking	C_t increase ($\overline{X} \pm SD$)	Percentage removed (95% CI)
1.00% soap powder	5.93±1.24	98.36% (96.11–99.31%)
0.05% active chlorine	4.89±0.74	96.62% (94.37–97.97%)
0.25% active chlorine	12.01±1.25	99.98% (99.94–99.99%)

TABLE 2 Percentage of AIV blocked by masks as compared with one layer of cloth

	C_t increase ($\overline{X} \pm SD$)	Percentage blocked (95% CI)
N95 mask	12.49±0.33	99.98% (99.98–99.99%)
Medical mask	5.13±0.98	97.14% (94.36–98.55%)
Homemade mask	4.37±0.90	95.15% (90.97–97.39%)

FIGURE 1 The system mocking human breath for evaluation of the efficacy of masks.
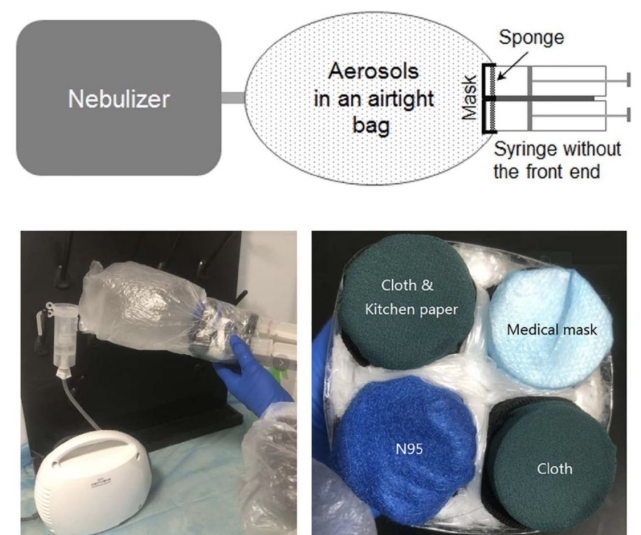
Additional Info:

1. Avian influenza virus was used to mock SARS-CoV-2 because they are both enveloped

and pleomorphic spherical viruses with the diameter around 80−120 nm. These were aerosolized using type 403 nebulizer that creates aerosols with median diameters of 3.9um with 65% of aerosols with diameters <5um
2. Methods for the mask testing are interesting, but I am not sure of its external validity.

COVID-19 Epidemic: Disease Characteristics in Children

She Jiatong 1, **Liu Lanqin** 2 3, **Liu Wenjun** 1 2 3

Main points:

1. Average incubation period for COVID-19 in children under age 15 is 6.5 days, lonnger than the 5.4 days reported in adults

2. An epidemiological analysis of 31 children with

3. COVID-19 in six provinces (autonomous region) of northern China found that 21

4. (68%) had contact with an adult with confirmed disease.

5. Throat swabs of childrenn with covid19 changed from positive to negative in approximately 1 week, but in anal swabs of the same children, it took anywhere from 14 to 51 days. But its ability to infect and transmit fecal-orally is unclear.

6. Whether vertical transmission is possible is unclear; No SARS-CoV2 detected in amniotic fluid, cord blood, neonnatal pharynx swab and breast milk samples at first lactation in mothers with covid19 during late stages of pregnancy. But infants have been known to develop COVID19 after NSVD or CS.

7. Presentation in children

    a. Fever, cough most common with normal or transiently increased CRP (3 cases >23, 27 and 47mg/L)

    b. Of 54 patients with pulmonary imaging data, 38 (70.4%) had **ground glass opacities or exudates,** 4 (7.4%) had enhanced lung texture and 12 (22.2%) had no abnls.

    c. Associated fatigue, myalgia, nasal congestion, rhinorrhea, sneezing, sore throat, headache, dizziness, nausea, vomiting, diarrhea and abdominal pain.

    d. Some exhibit no fever and only cough or diarrhea and rarely some are asymptomatic carriers but children with underlying/co-morbid disease appears to be more likely to have more severe disease

8. Prognosis in children

    a. Mild and/or atypical symptoms, faster recovery, shorter detox time and good prognosis

CD-sACE2 Inclusion Compounds: An Effective Treatment for Corona Virus Disease 2019 (COVID-19)
Pengfei Sun Xiaosheng Lu Chao Xu Yanjin Wang Wenjuan Sun Jianing Xi

Highlights: At present, there are no available drugs or vaccines that can treat or prevent Corona Virus Disease 2019 (COVID-19) effectively. We introduce the mechanisms and drug fabrication methods of CD-sACE2 inclusion compounds for the treatment of COVID-19. It is believed that CD-sACE2 inclusion compounds can effectively treat COVID-19.

The idea being that by aerosolizing sACE2 for inhalation, sACE2 will outcompete replicated viral particles from infected cells and stop their infection of healthy lungs.

Key points:

1. ACE2
    a. metalloproteinase that is the main active enzyme in the RAS system.
    b. Expressed in lungs, heart, kidneys and testes
    c. 3 main functions
        i. Negative regulator of RAS, its substrate is angiotensin II
        ii. Important for amino acid absorption in kidneys and gut
        iii. Main receptors for SARS-CoV and SARS-CoV2
    d. They think that by providing ACE2 to infected cells, that it could out compete for viral binding
2. Cyclodextrin
    a. Encloses highly hydrophobic molecules and typically used to improve water solubility of drugs and for controlled drug release systems.
    b. Can complex with soluble ACE2 to atomize for inhalation

**Hypertension, 2020 Mar 25[Online ahead of print]**

Renin-Angiotensin System Blockers and the COVID-19 Pandemic: At Present There Is No Evidence to Abandon Renin-Angiotensin System Blockers

A H Jan Danser 1, Murray Epstein 2, Daniel Batlle 3

Abstract

During the spread of the severe acute respiratory syndrome coronavirus-2, some reports of data still emerging and in need of full analysis indicate that certain groups of patients are at risk of COVID-19. This includes patients with hypertension, heart disease, diabetes mellitus, and clearly the elderly. Many of those patients are treated with reninangiotensin system blockers. Because the ACE2 (angiotensin-converting enzyme 2) protein is the receptor that facilitates coronavirus entry into cells, the notion has been popularized that treatment with renin-angiotensin system blockers might increase the risk of developing a severe and fatal severe acute respiratory syndrome coronavirus-2 infection. The present article discusses this concept. ACE2 in its full-length form is a membrane-bound enzyme, whereas its shorter (soluble) form circulates in blood at very low levels. As a mono-carboxypeptidase, ACE2 contributes to the degradation of several substrates including angiotensins I and II. ACE (angiotensin-converting enzyme) inhibitors do not inhibit ACE2 because ACE and ACE2 are different enzymes. Although angiotensin II type 1 receptor blockers have been shown to upregulate ACE2 in experimental animals, the evidence is not always consistent and differs among the diverse angiotensin II type 1 receptor blockers and differing organs. Moreover, there are no data to support the notion that ACE inhibitor or angiotensin II type 1 receptor blocker administration facilitates coronavirus entry by increasing ACE2 expression in either animals or humans. Indeed, animal data support elevated ACE2 expression as conferring potential protective pulmonary and cardiovascular effects. **In summary, based on the currently available evidence, treatment with renin-angiotensin system blockers should not be discontinued because of concerns with coronavirus infection.**
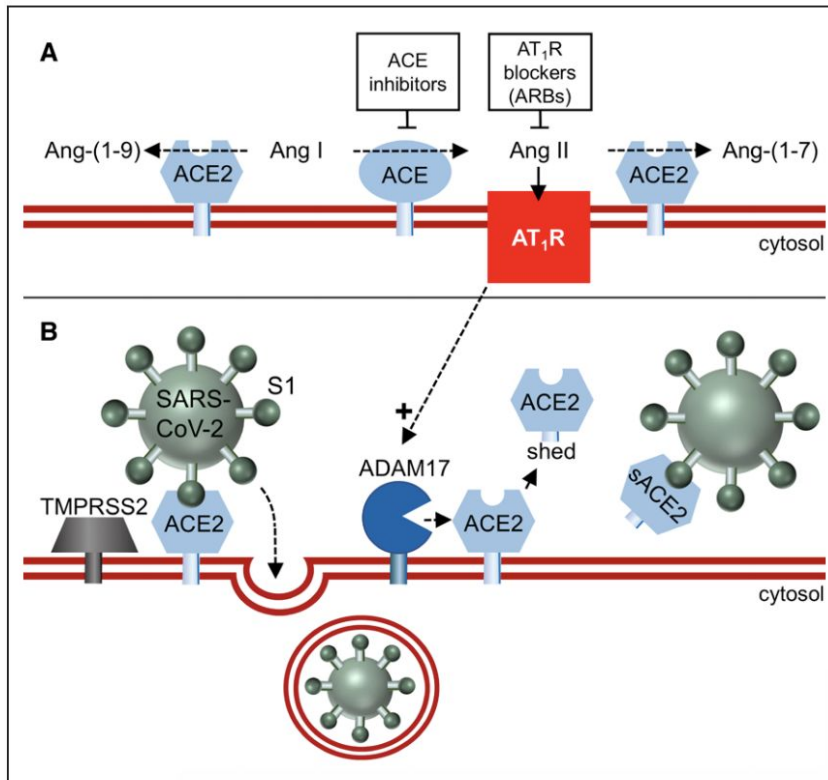
Figure. The carboxypeptidase ACE2 (angiotensin-converting enzyme 2) converts Ang II (angiotensin II) to Ang-(1–7) and Ang I to Ang-(1–9) (**A**), yet is not blocked by ACE (angiotensin-converting enzyme) inhibitors, which prevent the conversion of Ang I to Ang II. ACE2 also binds and internalizes SARS-Cov-2 (severe acute respiratory syndrome coronavirus-2; **B**), after priming by the serine protease TMPRSS2 (transmembrane protease, serine 2). Shedding of membrane-bound ACE2 by a disintegrin and metalloprotease 17 (ADAM17) results in the occurrence of soluble (s) ACE2, which can no longer mediate SARS-Cov-2 entry and which might even prevent such entry by keeping the virus in solution. AT_1R (Ang II, via its type 1 receptor) upregulates ADAM17, and AT_1R blockers (ARBs) would prevent this.

Takeaways:
1. ACE ≠ ACE2, active sites are different
2. Some limited evidence for ACE inhibitors changing ACE2 expression levels in heart and kidney, but ARBs seem to upregulate ACE2 more consistently in animal and in vitro studies
   a. Yet, required high ARB doses, different ARBs had different efficacies on ACE2 expression and unclear if this reflects not true levels of ACE2 expression but the change in the proportion of sACE2 vs membrane bound ACE2.
3. Despite these concerns for increased ACE2 expression in lung tissue via ARB use, during acute lung injury, alveolar ACE2 is downregulated, which causes decreased angiotensin II metabolism, increasing circulating and local levels of angiotensin II causing worsening hypertension, increased alveolar permeability and lung injury, "**in which case use of an ARB may actually be protective during the course of a SARS-CoV2 infection**"

Headaches Associated With Personal Protective Equipment - A Cross-sectional Study Amongst Frontline Healthcare Workers During COVID-19 (HAPPE Study)
Jonathan Jy Ong 1 2, Chandra Bharatendu 1 2, Yihui Goh 1, Jonathan Zy Tang 2 3, Kenneth Wx Sooi 1, Yi Lin Tan 1, Benjamin Yq Tan 1 2, Hock-Luen Teoh 1 2, Shi Ting Ong 3, David M Allen 2 4, Vijay K Sharma 1 2

 Abstract

Background: COVID-19 is an emerging infectious disease of pandemic proportions. Healthcare workers in Singapore working in high-risk areas were mandated to wear personal protective equipment (PPE) such as N95 face-mask and protective eyewear while attending to patients.

Objectives: We sought to determine the risk factors associated with the development of de novo PPE-associated headaches as well as the perceived impact of these headaches on their personal health and work performance. The impact of COVID-19 on pre-existing headache disorders was also investigated.

Methods: This is a cross-sectional study amongst healthcare workers at our tertiary institution who were working in high-risk hospital areas during COVID-19. All respondents completed a self-administered questionnaire.

Results: A total of 158 healthcare workers participated in the study. Majority [126/158 (77.8%)] were aged 21-35 years. Participants included nurses [102/158 (64.6%)], doctors [51/158 (32.3%)] and paramedical staff [5/158 (3.2%)]. Pre-existing primary headache diagnosis was present in about a third [46/158 (29.1%)] of respondents. Those based at the emergency department had higher average daily duration of combined PPE exposure compared to those working in isolation wards [7.0 (SD 2.2) vs 5.2 (SD 2.4) hours, p<0.0001] or medical ICU [7.0 (SD 2.2) vs 2.2 (SD 0.41) hours, p<0.0001]. Out of 158 respondents, 128 (81.0%) respondents developed de novo PPE-associated headaches. A pre-existing primary headache diagnosis (OR=4.20, 95% CI 1.48-15.40; p=0.030) and combined PPE usage for >4 hours per day (OR 3.91, 95% CI 1.35-11.31; p=0.012) were independently associated with de novo PPE-associated headaches. Since COVID-19 outbreak, 42/46 (91.3%) of respondents with pre-existing headache diagnosis either 'agreed' or 'strongly agreed' that the increased PPE usage had affected the control of their background headaches, which affected their level of work performance.

Conclusion: Most healthcare workers develop de novo PPE-associated headaches or exacerbationof their pre-existing headache disorders.

Table 5. Univariate logistic regression analysis of factors (demographic variables, primary location of PPE usage, pre-existing primary headache diagnosis, and PPE usage) in respondents with and without *de novo* PPE-associated headaches (n=158)

Demographic variables	With *de novo* PPE-related headaches N =128 (%)	Without *de novo* PPE-related headaches N=30 (%)	OR (95% CI)	p-value[1]
Gender, Female	92 (71.9)	19 (63.3)	1.14 (0.85-1.52)	0.380
Age (years)				
21-40	111 (86.7)	27 (90.0)	0.96 (0.84-1.11)	0.770
>40	17 (13.3)	3 (10.0)		
Ethnicity				
Chinese	72 (56.3)	20 (66.7)	0.84 (0.63-1.13)	0.410
Non-Chinese	56 (43.8)	10 (33.3)		
Occupation				
Doctors and Nurses	125 (97.7)	28 (93.3)	1.05 (0.95-1.16)	0.241
Paramedical staff	3 (2.3)	2 (6.7)		
Underlying co-morbidities	23 (18.0)	3 (10.0)	1.80 (0.57-5.60)	0.414
Originating department of healthcare workers				
Emergency department	51 (39.8)	5 (16.7)	2.39 (1.05-5.47)	**0.019***
Others: Medicine, Nursing, ICU	77 (60.2)	25 (83.3)		
Pre-existing primary headache diagnosis	43 (33.6)	3 (10.0)	3.44 (1.14-10.32)	**0.013***
Duration of N95 face-mask wear per day				
>4 h	115 (89.8)	17 (56.7)	1.59 (1.15-2.18)	**<0.001***
1-4 h	13 (10.2)	13 (43.3)		
Frequency of N95 face-mask wear per month				
>15 d	97 (75.8)	17 (56.7)	1.34 (0.96-1.86)	0.061
3-15 d	31 (24.2)	13 (43.3)		
Duration of protective eyewear use per day				
>4 h	109 (85.2)	16 (53.3)	1.60 (1.13-2.25)	**<0.001***
1-4 h	19 (14.8)	14 (46.7)		
Frequency of protective eyewear use per month				
>15 d	96 (75.0)	15 (50.0)	1.50 (1.03-2.18)	**0.013***
3-15 d	32 (25.0)	15 (50.0)		
Duration of combined N95 face-mask & eyewear use per day				
>4 h	109 (85.2)	17 (56.7)	1.50 (1.09-2.07)	**0.002***
1-4 h	19 (14.8)	13 (43.3)		
Frequency of combined N95 face-mask & eyewear use per month				
>15 d	94 (73.4)	15 (50.0)	1.47 (1.01-2.13)	**0.016***
3-15 d	34 (26.6)	15 (50.0)		

[1] Chi-square analyses (statistically significant if p<0.05).
*Statistically significant results.

Diagnostic Performance of Chest CT to Differentiate COVID-19 Pneumonia in Non-High-Epidemic Area in Japan
Yuki Himoto 1, Akihiko Sakata 2, Mitsuhiro Kirita 2, Takashi Hiroi 2, Ken-Ichiro Kobayashi 3, Kenji Kubo 3, Hyunjin Kim 2, Azusa Nishimoto 2, Chikara Maeda 2, Akira Kawamura 2, Nobuhiro Komiya 3, Shigeaki Umeoka 2

Abstract

Purpose: To evaluate the diagnostic performance of chest CT to differentiate coronavirus disease 2019 (COVID-19) pneumonia in non-high-epidemic area in Japan.

Materials and methods: This retrospective study included 21 patients clinically suspected COVID-19 pneumonia and underwent chest CT more than 3 days after the symptom onset: six patients confirmed COVID-19 pneumonia by real-time reverse-transcription polymerase chain reaction (RT-PCR) and 15 patients proved uninfected. Using a Likert scale and its receiver operating characteristic curve analysis, two radiologists (R1/R2) evaluated the diagnostic performance of the five CT criteria: (1) ground glass

opacity (GGO)-predominant lesions, (2) GGO- and peripheral-predominant lesions, (3) bilateral GGO-predominant lesions; (4) bilateral GGO- and peripheral-predominant lesions, and (5) bilateral GGO- and peripheral-predominant lesions without nodules, airway abnormalities, pleural effusion, and mediastinal lymphadenopathy.

Results: All patients confirmed COVID-19 pneumonia had **bilateral GGO- and peripheral-predominant lesions without airway abnormalities, mediastinal lymphadenopathy, and pleural effusion.** The five CT criteria showed moderate to excellent diagnostic performance with area under the curves (AUCs) ranging 0.77-0.88 for R1 and 0.78-0.92 for R2. The criterion (e) showed the highest AUC.

Abstract

With the outbreak of unknown pneumonia in Wuhan, China, in December 2019, a new coronavirus, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), aroused the attention of the entire world. The current outbreak of infections with SARS-CoV-2 is termed Coronavirus Disease 2019 (COVID-19). The World Health Organization declared COVID-19 in China as a Public Health Emergency of International Concern. Two other coronavirus infections-SARS in 2002-2003 and Middle East Respiratory Syndrome (MERS) in 2012-both caused severe respiratory syndrome in humans. All 3 of these emerging infectious diseases leading to a global spread are caused by β-coronaviruses. Although coronaviruses usually infect the upper or lower respiratory tract, viral shedding in plasma or serum is common. Therefore, there is still a theoretical risk of transmission of coronaviruses through the transfusion of labile blood products. **Because more and more asymptomatic infections are being found among COVID-19 cases, considerations of blood safety and coronaviruses have arisen especially in endemic areas.** In this review, we detail current evidence and understanding of the transmission of

SARS-CoV, MERS-CoV, and SARS-CoV-2 through blood products as of February 10, 2020, and also discuss pathogen inactivation methods on coronaviruses.

Key takeaways (super well written article, so this is copy and paste):

1. viral RNA in plasma or serum could be detected in COVID-19 patients on the first 2 or 3 days after onset of symptoms;
2. Most patients, especially younger adults who can donate blood, had milder symptoms than the older adults;
3. patients with no fever and asymp-tomatic carriers have been identified in China, which increase the possi-bility that a COVID-19 patient or virus carrier could donate blood
4. The rate of infectivity of patients who are in the incubation period re-mains uncertain, and there are no data on the viral load in plasma,serum, or lymphocytes among individuals in the incubation period.
5. Therefore, whether the risk of transfusion transmission of SARS-CoV-2is higher than other coronaviruses, especially in endemic areas such asWuhan, China, should be further explored as soon as possible.

Recommends :

1. Taking body temperature before blood donation;
2. additional questions in the donor screening questionnaire regarding whether the donor or rel-atives have related symptoms, have traveled to areas with local trans-mission of SARS-CoV-2 (Wuhan or Hubei province) within 28 days, or are donors with high risk;
3. calling back all blood donors and asking the donors and their family about their current physical condition after donation;
4. recalling untransfused blood products from in-fected donors[57].
5. However, given the differences between SARS-CoV,MERS-CoV, and SARS-CoV-2, it is not known if the prior recommenda-tions used for SARS and MERS are sufficient.

Clin Infect Dis 2020 Mar 31[Online ahead of print]

Computed Tomographic Imaging of 3 Patients With Coronavirus Disease 2019 Pneumonia With Negative Virus Real-time Reverse-Transcription Polymerase Chain Reaction Test

Junqing Xu 1, Ruodai Wu 1, Hua Huang 1, Weidong Zheng 2, Xinling Ren 3, Nashan Wu 1, Bin Ji 1, Yungang Lv 1, Yumeng Liu 1, Rui Mi 1

Abstract

We reported computed tomographic (CT) imaging findings of 3 patients with coronavirus disease 2019 (COVID-19) pneumonia with initially negative results before CT examination and finally confirmed positive for the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by real-time reverse-transcription polymerase chain reaction assay.

Key takeaways:

1. 3 patients in Shenzhen University General Hospital with definitive history of close contact with confirmed patients with covid19.
2. Let symptoms, exam and CT findings take precedence over a negative PCR.

Day 0= last day of known covid19 exposure

Cutaneous manifestations in COVID-19: a first perspective.

S. Recalcati First published:26 March 2020 https://doi.org/10.1111/jdv.16387
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Summary: Italian dermatologists studied 88 covid19 patients in Lecco Hospital, Lombardy, Italy without recent onset of new medications (<15 days prior to symptoms). OF these 18 (20.4%) developed cutaneous symptoms at onset of URI symptoms, 10 patients developed them after hospitalization. Cutaneous manifestations ranged from erythematous rash (14 patients), widespread uriticaria (3 patients) and chicken pox- like vesicles (1 patient) with low level or no itching. Lesions self resolved in a few days and was not predictive of disease severity.

I personally also saw 2 people who broke out in vesicular lesions along lip and the vermillion border with concomitant covid symptoms who tested positive for covid19.

Risks of Novel Coronavirus Disease (COVID-19) in Pregnancy; A Narrative Review

Latif Panahi 1, Marzieh Amiri 2, Somaye Pouy 1

Abstract

Introduction: The outbreak of the new Coronavirus in China in December 2019 and subsequently in various countries around the world has raised concerns about the possibility of vertical transmission of the virus from mother to fetus. The present study aimed to review published literature in this regard.

Methods: In this narrative review, were searched for all articles published in various databases including PubMed, Scopus, Embase, Science Direct, and Web of Science using MeSH-compliant keywords including COVID-19, Pregnancy, Vertical transmission, Coronavirus 2019, SARS-CoV-2 and 2019-nCoV from December 2019 to March 18, 2020 and reviewed them. All type of articles published about COVID-19 and vertical transmission in pregnancy were included.

Results: A review of 13 final articles published in this area revealed that **COVID-19 can cause fetal distress, miscarriage, respiratory dist**
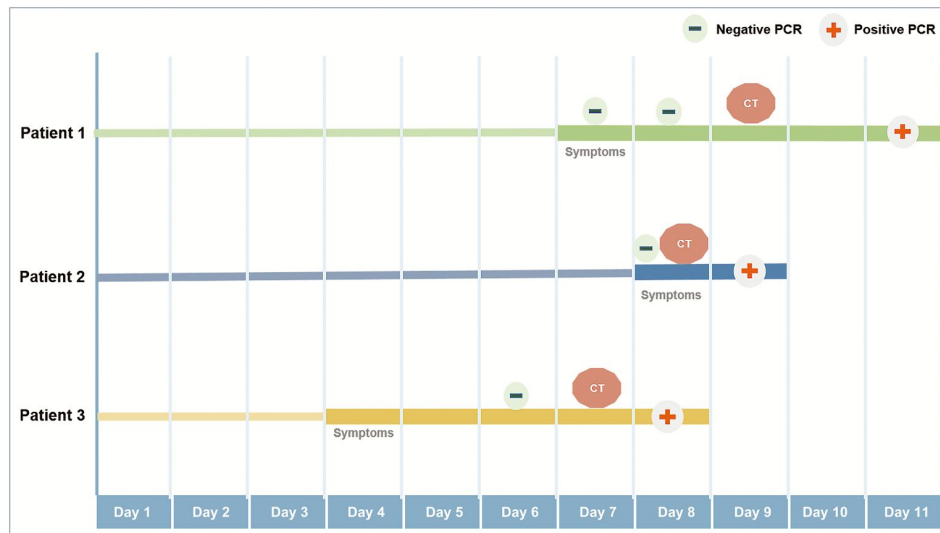
ress and preterm delivery in pregnant women but does not infect newborns. **There has been no report of vertical transmission in pregnancy,** and it has been found that clinical symptoms of COVID-19 in pregnant women are not different from those of non-pregnant women.

Conclusion: Overall, due to lack of appropriate data about the effect of COVID-19 on pregnancy, it is necessary to monitor suspected pregnant women before and after delivery. For confirmed cases both the mother and the newborn child should be followed up comprehensively.