The Daily COVID-19 Literature Surveillance Summary

February 12, 2021

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COVID-19 Daily Literature Surveillance

COVID19LST

Bringing you real time, distilled information for guiding best practices during the COVID-19 pandemic

LEVEL OF EVIDENCE

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

Question	Step 1 (Level 1*)	Step 2 (Level 2*)	Step 3 (Level 3*)	Step 4 (Level 4*)	Step 5 (Level 5)
How common is the problem?	Local and current random sample surveys (or censuses)	Systematic review of surveys that allow matching to local circumstances**	Local non-random sample**	Case-series**	n/a
Is this diagnostic or monitoring test accurate? (Diagnosis)	Systematic review of cross sectional studies with consistently applied reference standard and blinding	Individual cross sectional studies with consistently applied reference standard and blinding	Non-consecutive studies, or studies without consistently applied reference standards**	Case-control studies, or "poor or non-independent reference standard**	Mechanism-based reasoning
What will happen if we do not add a therapy? (Prognosis)	Systematic review of inception cohort studies	Inception cohort studies	Cohort study or control arm of randomized trial*	Case-series or case-control studies, or poor quality prognostic cohort study**	n/a
Does this intervention help? (Treatment Benefits)	Systematic review of randomized trials or *n*-of-1 trials	Randomized trial or observational study with dramatic effect	Non-randomized controlled cohort/follow-up study**	Case-series, case-control studies, or historically controlled studies**	Mechanism-based reasoning
What are the COMMON harms? (Treatment Harms)	Systematic review of randomized trials, systematic review of nested case-control studies, *n*-of-1 trial with the patient you are raising the question about, or observational study with dramatic effect	Individual randomized trial or (exceptionally) observational study with dramatic effect	Non-randomized controlled cohort/follow-up study (post-marketing surveillance) provided there are sufficient numbers to rule out a common harm. (For long-term harms the duration of follow-up must be sufficient.)**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning
What are the RARE harms? (Treatment Harms)	Systematic review of randomized trials or *n*-of-1 trial	Randomized trial or (exceptionally) observational study with dramatic effect			
Is this (early detection) test worthwhile? (Screening)	Systematic review of randomized trials	Randomized trial	Non -randomized controlled cohort/follow-up study**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning

*** Level may be graded down on the basis of study quality, imprecision, indirectness (study PICO does not match questions PICO), because of inconsistency between studies, or because the absolute effect size is very small; Level may be graded up if there is a large or very large effect size.**

**** As always, a systematic review is generally better than an individual study.**

How to cite the Levels of Evidence Table

OCEBM Levels of Evidence Working Group*. "The Oxford 2011 Levels of Evidence".

Oxford Centre for Evidence-Based Medicine. http://www.cebm.net/index.aspx?o=5653

** OCEBM Table of Evidence Working Group = Jeremy Howick, Iain Chalmers (James Lind Library), Paul Glasziou, Trish Greenhalgh, Carl Heneghan, Alessandro Liberati, Ivan Moschetti, Bob Phillips, Hazel Thornton, Olive Goddard and Mary Hodgkinson*

EXECUTIVE SUMMARY

Epidemiology

- A phylogenetic analysis of SARS-CoV-2 genomes during the early period of the Boston-area epidemic analyzed the viral strains responsible for two superspreader events. Analysis identified that they occurred at a skilled nursing facility (SNF) and an international business conference. The outbreak at the SNF was found to have higher mortality but limited subsequent community spread, while the conference lead to significant community transmission. This led to subsequent outbreaks, especially in homeless and higher-risk populations throughout Boston and beyond. Genetic analysis of both strains revealed significant variation, implicating mutation as a possible explanation for increased transmissibility. The authors highlight the utility of genomic epidemiology in "understanding the link between individual clusters and wider community spread."

Management

- This retrospective cohort study from the University of Missouri investigates differences in risk factors and outcomes in COVID-19 patients with acute ischemic stroke using de-identified patient data and ICD-10 codes. Results showed that while only 1.3% of COVID-19 patients developed acute ischemic stroke, the presence of stroke and COVID-19 was associated with discharge to a location other than home (relative risk, 2.1, $P<0.0001$). The authors conclude that the incidence of ischemic stroke in patients with COVID-19 is low, and the presence of other risk factors such as hypertension, diabetes, atrial fibrillation and heart failure are better indictors for stroke rather than COVID-19 alone.

- A prospective cohort study conducted at multiple institutions in Spain analyzed 2,225 pregnant persons, 317 of which had evidence of SARS-CoV-2 infection, and found no difference in pregnancy complications but a significant increase in intrapartum fetal distress in SARS-CoV-2-positive women. Rates of preterm delivery, intrapartum fetal distress, and proportion of severe small-for-gestational age newborns were higher in those with symptomatic compared to asymptomatic COVID-19. Presence of SARS-CoV-2 IgG antibodies in umbilical cord blood were found in 61/143 fetuses with infected mothers but no IgM or IgA, signifying uncommon vertical transmission of active infection with IgM antibodies. These findings signify similar overall rates of pregnancy complications in both infected women and non-infected women but an increased prevalence of significant complications among symptomatic women, emphasizing clinical surveillance of COVID-19 in pregnancy/delivery especially with symptomatic patients.

R&D: Diagnosis & Treatments

- This health journalism piece discusses a new technology from the University of California, San Francisco, utilizing clustered regularly interspaced short palindromic repeats (CRISPR) gene editing technology to detect SARS-CoV-2 RNA viral particles from patient nasal swabs. The test, which quantifies viral load based off time to detection, is not available for mass use by the public as it currently requires RNA extraction and medical-grade equipment. However the research team, including Jennifer Doudna, PhD, who holds a Nobel Prize for developing CRISPR-based gene editing, is hoping to make this technology available to the public in the future, potentially adding another testing modality.

TABLE OF CONTENTS

EPIDEMIOLOGY

MODELING

PHYLOGENETIC ANALYSIS OF SARS-COV-2 IN BOSTON HIGHLIGHTS THE IMPACT OF SUPERSPREADING EVENTS

Lemieux JE, Siddle KJ, Shaw BM, Loreth C, Schaffner SF, Gladden-Young A, Adams G, Fink T, Tomkins-Tinch CH, Krasilnikova LA, DeRuff KC, Rudy M, Bauer MR, Lagerborg KA, Normandin E, Chapman SB, Reilly SK, Anahtar MN, Lin AE, Carter A, Myhrvold C, Kemball ME, Chaluvadi S, Cusick C, Flowers K, Neumann A, Cerrato F, Farhat M, Slater D, Harris JB, Branda JA, Hooper D, Gaeta JM, Baggett TP, O'Connell J, Gnirke A, Lieberman TD, Philippakis A, Burns M, Brown CM, Luban J, Ryan ET, Turbett SE, LaRocque RC, Hanage WP, Gallagher GR, Madoff LC, Smole S, Pierce VM, Rosenberg E, Sabeti PC, Park DJ, MacInnis BL.. Science. 2021 Feb 5;371(6529):eabe3261. doi: 10.1126/science.abe3261. Epub 2020 Dec 10.
Level of Evidence: 5 - Modeling

BLUF

A phylogenetic analysis of SARS-CoV-2 genomes during the early period of the Boston-area epidemic (March-May 2020) analyzed the viral strains responsible for two superspreader events. Analysis identified that they occurred at a skilled nursing facility (SNF) and an international business conference. The outbreak at the SNF was found to have higher mortality but limited subsequent community spread, while the conference lead to significant community transmission. This led to subsequent outbreaks, especially in homeless and higher-risk populations throughout Boston and beyond (Figures 1-3). Genetic analysis of both strains revealed significant variation, implicating mutation as a possible explanation for increased transmissibility. The authors highlight the utility of genomic epidemiology in "understanding the link between individual clusters and wider community spread".

ABSTRACT

Analysis of 772 complete SARS-CoV-2 genomes from early in the Boston area epidemic revealed numerous introductions of the virus, a small number of which led to most cases. The data revealed two superspreading events. One, in a skilled nursing facility, led to rapid transmission and significant mortality in this vulnerable population but little broader spread, while other introductions into the facility had little effect. The second, at an international business conference, produced sustained community transmission and was exported, resulting in extensive regional, national, and international spread. The two events also differed significantly in the genetic variation they generated, suggesting varying transmission dynamics in superspreading events. Our results show how genomic epidemiology can help understand the link between individual clusters and wider community spread.

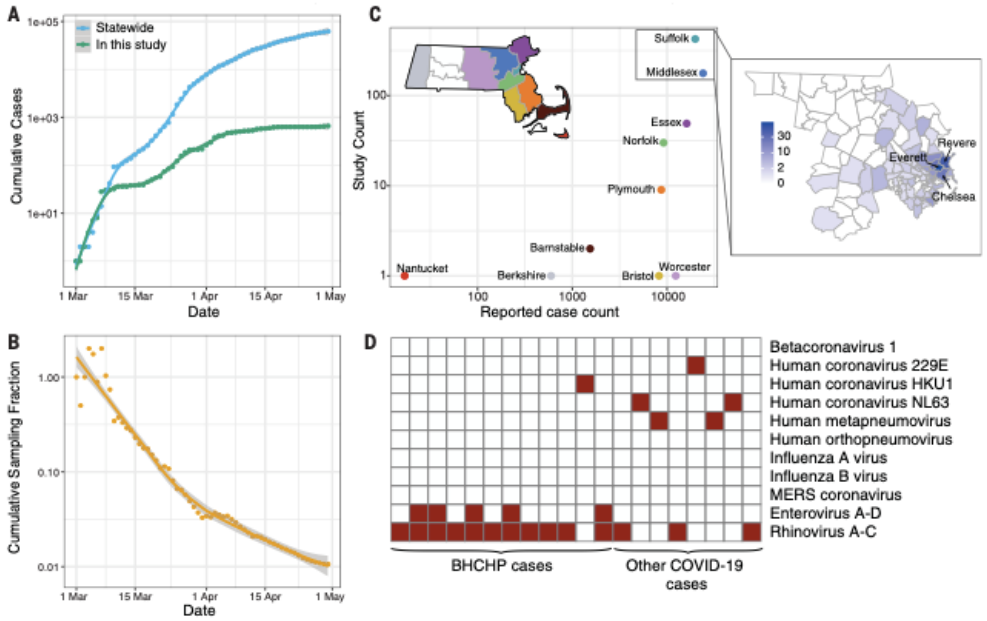

Fig. 1. Epidemiology of SARS-CoV-2 in Massachusetts and of sequenced viral genomes. (A) Cumulative confirmed and presumed cases reported statewide in Massachusetts (10) from 1 March through 1 May 2020 and the number of these cases that successfully yielded complete genomes with >98% coverage (green) in this study. (B) Cumulative proportion of all Massachusetts confirmed positive cases with complete genome sequences from distinct individuals that are part of this dataset over time. (C) Total number of cases
compared with cases in this study by Massachusetts county. Points are colored by state as shown in the state map. Suffolk and Middlesex counties are shown in detail to the right, with counts from this study shown by ZIP code. (D) Detection of common respiratory viruses from metagenomic sequencing data. Samples with more than 10 reads that mapped to at least one of these viruses by using Kraken2 are shown in red. Enterovirus and Rhinovirus species have been grouped owing to the difficulty in discriminating at the sequence level.

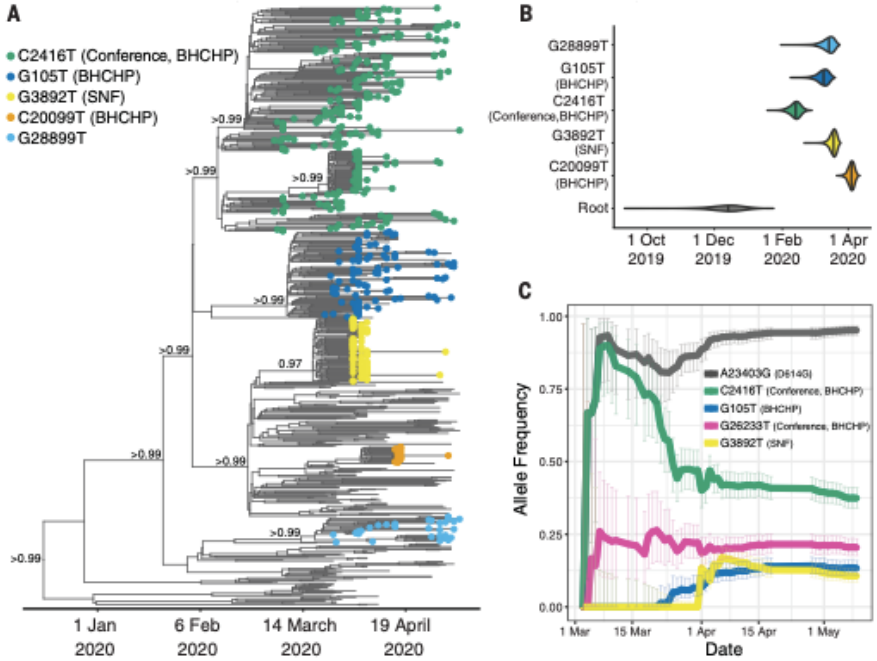

Fig. 3. SARS-CoV-2 spread in the Boston area. (A) Time-measured maximum clade credibility tree of 772 Massachusetts genomes with tips labeled by clade. Nodes with posterior support >0.8 are labeled. (B) Violin plots of tMRCA for the major Boston-area clades. (C) Estimated allele frequency in sequenced genomes over time for major Boston-area clades. Boston

Healthcare for the Homeless Program, BHCHP; skilled nursing facility, SNF; international business conference, Conference.

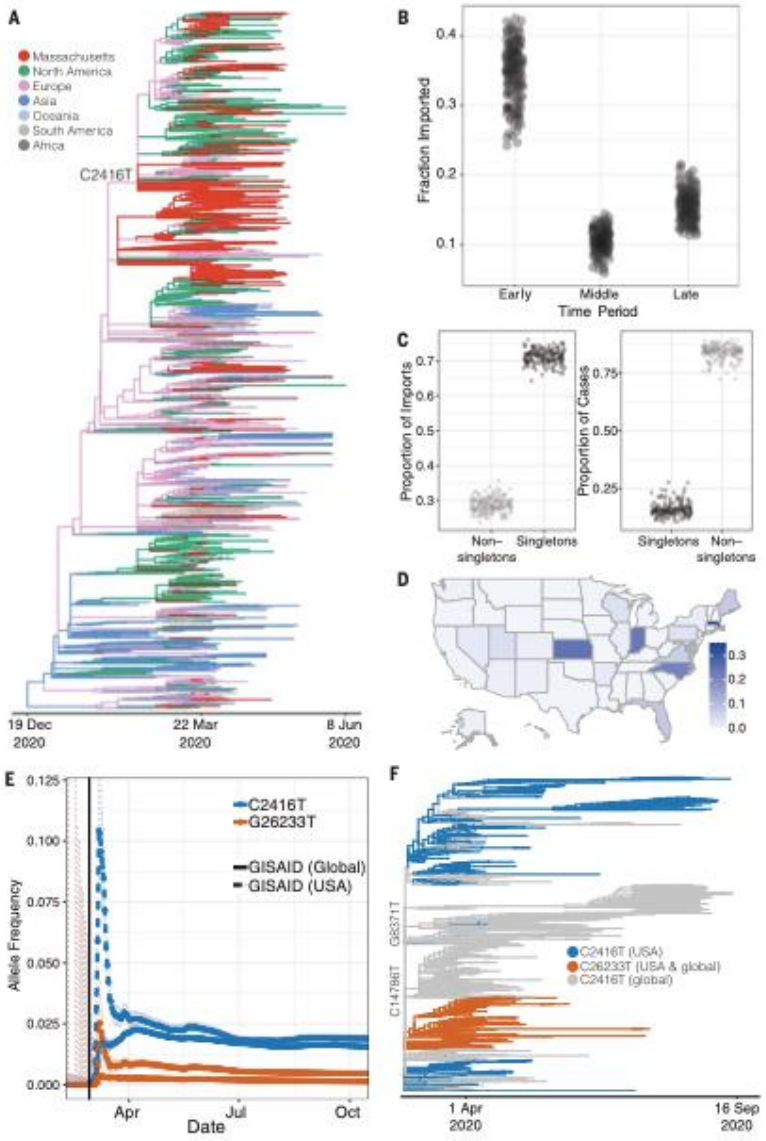

Fig. 2. Introductions of SARS- CoV-2 into Massachusetts.
(A) Time tree of 772 Massachusetts genomes and a global set of 4011 high-quality genomes from GISAID. An interactive version of this tree and more information on specific subgroupings within the Massachusetts dataset is available at https://auspice. broadinstitute.org. (B) Propor- tion of genomes that were inferred as imported (ancestral state as not from Massachusetts) in the early (before 28 March 2020), middle (28 March to 14 April 2020), and late (after 15 April 2020) time periods of the Massachusetts epidemic. (C) The proportion of importation events and cases that were associated with singleton introductions (importation events associated with a single case in Massachusetts) into the Boston area over subsampled trees. (D) Allele frequency of the C2416T mutation by state. (E) Allele frequency of the C2416T and C26233T alleles in 159,043 GISAID samples reported through 17 October 2020. The vertical black line denotes the end of the business conference on 27 February. (F) Time tree of all sequences containing the C2416T variant collected before 30 September 2020.

UNDERSTANDING THE PATHOLOGY

MICROVASCULAR INJURY IN THE BRAINS OF PATIENTS WITH COVID-19

Lee MH, Perl DP, Nair G, Li W, Maric D, Murray H, Dodd SJ, Koretsky AP, Watts JA, Cheung V, Masliah E, Horkayne-Szakaly I, Jones R, Stram MN, Moncur J, Hefti M, Folkerth RD, Nath A.. N Engl J Med. 2021 Feb 4;384(5):481-483. doi: 10.1056/NEJMc2033369. Epub 2020 Dec 30.
Level of Evidence: 3 - Local non-random sample

BLUF

An interdisciplinary group of neurologists and pathologists analyzed 13 post-mortem COVID-19 patients with high-resolution MRI and corresponding histopathologic examination. They found multifocal microvascular injury throughout brain and olfactory bulbs, but no evidence of active viral infection, perivascular inflammation, or large vessel occlusion (Figure 1). The authors propose that these findings of diffuse microvascular thrombotic injury may correspond with the well documented MRI findings of punctate hyperintensities and linear hypointensities seen in patients with COVID-19.

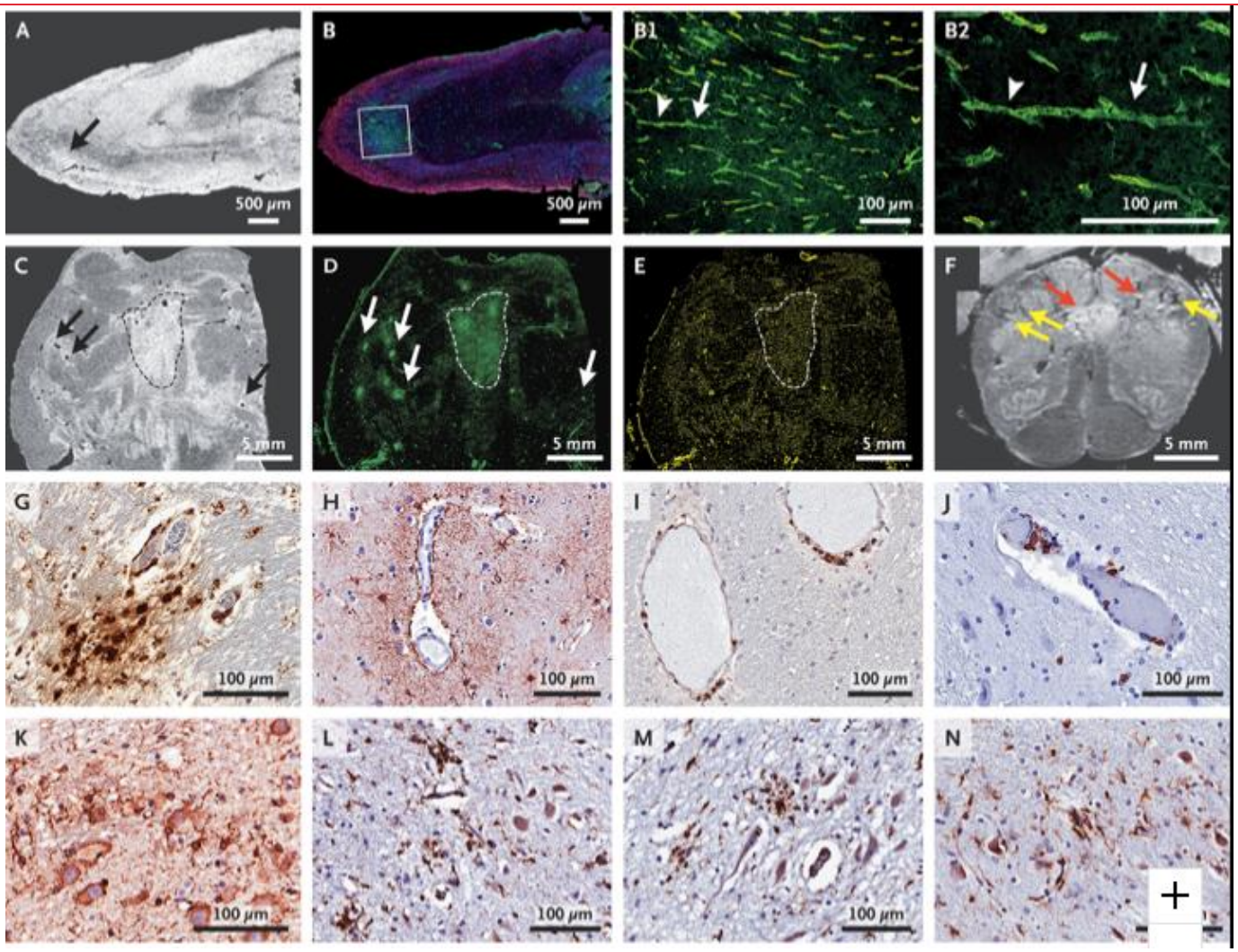

Figure 1. Pathological Studies of Microvascular Injury in the Brains of Patients Who Died from Covid-19.
Panel A (magnetic resonance microscopy of the olfactory bulb) shows an area of hyperintense signal (arrow). Panel B shows the corresponding area on multiplex immunofluorescence imaging, which revealed a focal area of fibrinogen leakage (in the box, fibrinogen is shown in green, collagen IV is shown in yellow, and nuclei are shown in blue). Panel B1 shows diffuse leakage of fibrinogen in the parenchyma (an enlarged view showing marked blood vessel staining for collagen IV is shown in Panel B2). Panel B2 (collagen IV immunostaining) shows intact (arrowhead) and thinned (arrow) basal lamina with fibrinogen leakage into the parenchyma. Panel C shows magnetic resonance microscopy of the pons, and Panel D (fibrinogen staining) shows areas of increased signal intensity corresponding to the vascular leakage visible on magnetic resonance microscopy. The arrows and the area within the dashed lines in Panels C and D indicate the vascular leakage. Panels A through E represent imaging performed in Patient IA1. Panel E (collagen IV immunostaining) shows areas of fibrinogen leakage in blood vessels in Patient IA1. Panel F shows magnetic resonance microscopy of the medulla in Patient IA3. The yellow arrows indicate linear hypointense signals, and the red arrows indicate linear hyperintense signals. Panel G shows CD68+ perivascular macrophages in the pons in Patient NY6. Panel H shows perivascular astrocytosis in the basal ganglia in Patient NY5. Panel I shows perivascular CD3+ cells in the cerebellum in Patient IA1. Panel J shows intraluminal and perivascular CD8+ cells in the pons in Patient NY6. Panel K shows perineuronal IBA1 cells in the pons in Patient NY6. Panel L shows CD68+ cells in the dorsal motor nucleus of the vagus nerve in Patient IA1. Panel M shows a solitary nucleus in the medulla and Panel N shows a pre-Bötzinger complex in Patient IA1. (Diaminobenzidine staining was used in Panels G through N.)

MANAGEMENT

ACUTE CARE

NEUROLOGY

ACUTE ISCHEMIC STROKE AND COVID-19: AN ANALYSIS OF 27 676 PATIENTS

Qureshi AI, Baskett WI, Huang W, Shyu D, Myers D, Raju M, Lobanova I, Suri MFK, Naqvi SH, French BR, Siddiq F, Gomez CR, Shyu CR.. Stroke. 2021 Feb 4:STROKEAHA120031786. doi: 10.1161/STROKEAHA.120.031786. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

This retrospective cohort study from the University of Missouri investigates differences in risk factors and outcomes in COVID-19 patients with acute ischemic stroke using de-identified patient data and ICD-10 codes (Figure 1). Results showed that while only 1.3% of COVID-19 patients developed acute ischemic stroke, the presence of stroke and COVID-19 was associated with discharge to a location other than home (relative risk, 2.1, P<0.0001, Table 2). The authors conclude that the incidence of ischemic stroke in patients with COVID-19 is low, and the presence of other risk factors such as hypertension, diabetes, atrial fibrillation and heart failure are better indictors for stroke rather than COVID-19 alone.

ABSTRACT

BACKGROUND AND PURPOSE: Acute ischemic stroke may occur in patients with coronavirus disease 2019 (COVID-19), but risk factors, in-hospital events, and outcomes are not well studied in large cohorts. We identified risk factors, comorbidities, and outcomes in patients with COVID-19 with or without acute ischemic stroke and compared with patients without COVID-19 and acute ischemic stroke. METHODS: We analyzed the data from 54 health care facilities using the Cerner deidentified COVID-19 dataset. The dataset included patients with an emergency department or inpatient encounter with discharge diagnoses codes that could be associated to suspicion of or exposure to COVID-19 or confirmed COVID-19. RESULTS: A total of 103 (1.3%) patients developed acute ischemic stroke among 8163 patients with COVID-19. Among all patients with COVID-19, the proportion of patients with hypertension, diabetes, hyperlipidemia, atrial fibrillation, and congestive heart failure was significantly higher among those with acute ischemic stroke. Acute ischemic stroke was associated with discharge to destination other than home or death (relative risk, 2.1 [95% CI, 1.6-2.4]; P<0.0001) after adjusting for potential confounders. A total of 199 (1.0%) patients developed acute ischemic stroke among 19 513 patients without COVID-19. Among all ischemic stroke patients, COVID-19 was associated with discharge to destination other than home or death (relative risk, 1.2 [95% CI, 1.0-1.3]; P=0.03) after adjusting for potential confounders. CONCLUSIONS: Acute ischemic stroke was infrequent in patients with COVID-19 and usually occurs in the presence of other cardiovascular risk factors. The risk of discharge to destination other than home or death increased 2-fold with occurrence of acute ischemic stroke in patients with COVID-19.

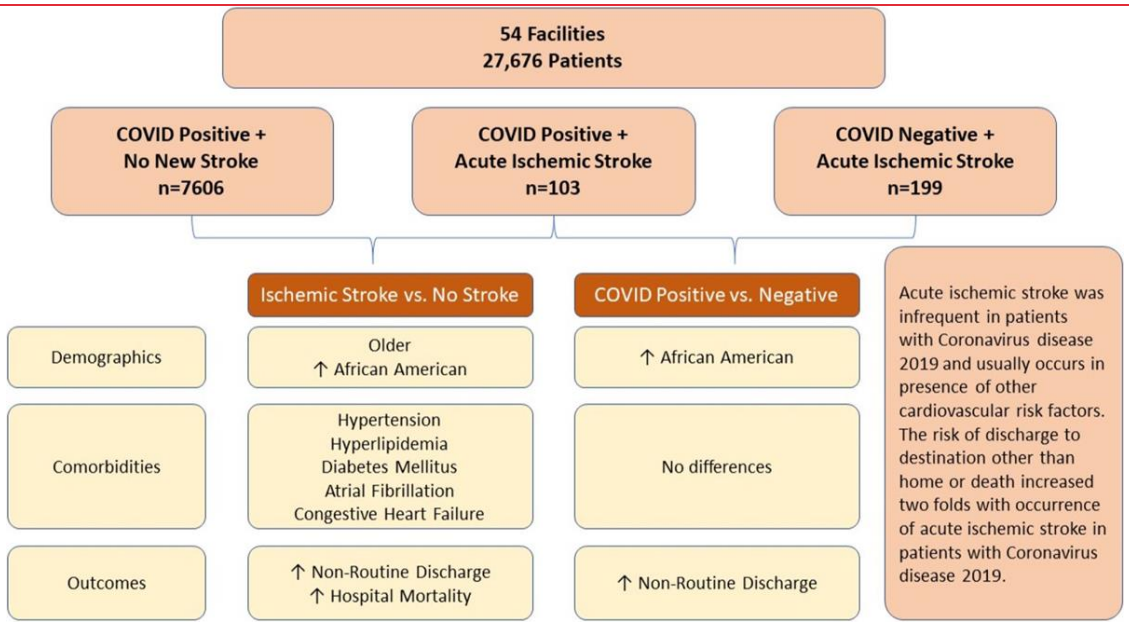

Figure 1.

Outcome	Patients with COVID-19 and acute ischemic stroke (n=103)	Patients with COVID-19 but without any stroke (n=7606)	Patients with acute ischemic stroke without COVID-19 (n=199)
Discharge home*	19 (18.5%)	4939 (64.9%)	60 (30.2%)
Discharge to destination other than home*†	64 (62.1%)	2215 (29.1%)	96 (48.2%)
In-hospital death*†	20 (19.4%)	474 (6.2%)	43 (21.6%)

COVID-19 indicates coronavirus disease 2019.
*Significant difference between patients with COVID-19 and acute ischemic stroke compared with those without any stroke.
†Significant difference between acute ischemic patients with COVID-19 compared with those without COVID-19.

Table 2. Outcomes of Patients

IMPACT OF SARS-COV-2 INFECTION ON PREGNANCY OUTCOMES: A POPULATION-BASED STUDY

Crovetto F, Crispi F, Llurba E, Pascal R, Larroya M, Trilla C, Camacho M, Medina C, Dobaño C, Gomez-Roig MD, Figueras F, Gratacos E; KidsCorona Pregnancy COVID-19 group.. Clin Infect Dis. 2021 Feb 8:ciab104. doi: 10.1093/cid/ciab104. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

A prospective cohort study conducted at multiple institutions in Spain from March 15 to May 31, 2020 analyzed 2,225 pregnant persons, 317 of which had evidence of SARS-CoV-2 infection, and found no difference in pregnancy complications (See Table 2) but a significant increase in intrapartum fetal distress in SARS-CoV-2-positive women. Rates of preterm delivery, intrapartum fetal distress, and proportion of severe small-for-gestational age newborns were higher in those with symptomatic compared to asymptomatic COVID-19 (Table 3). Presence of SARS-CoV-2 IgG antibodies in umbilical cord blood were found in 61/143 fetuses with infected mothers but no IgM or IgA, signifying uncommon vertical transmission of active infection with IgM antibodies. These findings signify similar overall rates of pregnancy complications in both infected women and non-infected women but an increased prevalence of significant complications among symptomatic women, emphasizing clinical surveillance of COVID-19 in pregnancy/delivery especially with symptomatic patients.

ABSTRACT

BACKGROUND: A population-based study to describe the impact of SARS-CoV-2 infection on pregnancy outcomes. METHODS: Prospective, population-based study including pregnant women consecutively attended at first/second trimester or at delivery at three hospitals in Barcelona, Spain. SARS-CoV-2 antibodies (IgG and IgM/IgA) were measured in all participants and nasopharyngeal RT-PCR was performed at delivery. The primary outcome was a composite of pregnancy complications in SARS-CoV-2 positive versus negative women: miscarriage, preeclampsia, preterm delivery, perinatal death, small-for-gestational age, neonatal admission. Secondary outcomes were components of the primary outcome plus abnormal fetal growth, malformation, intrapartum fetal distress. Outcomes were also compared between positive symptomatic and positive asymptomatic SARS-CoV-2 women. RESULTS: Of 2,225 pregnant women, 317 (14.2%) were positive for SARS-CoV-2 antibodies (n=314, 99.1%) and/or RT-PCR (n=36, 11.4%). Among positive women, 217 (68.5%) were asymptomatic, 93 (29.3%) had mild COVID-19 and 7 (2.2%) pneumonia, of which 3 required intensive care unit admission. In women with and without SARS-CoV-2 infection, the primary outcome occurred in 43 (13.6%) and 268 (14%), respectively [risk difference -0.4%, (95% CI: -4.1% to 4.1)]. As compared with non-infected women, women with symptomatic COVID-19 had increased rates of preterm delivery (7.2% vs. 16.9%, p=0.003) and intrapartum fetal distress (9.1% vs. 19.2%, p=0.004), while asymptomatic women had similar rates to non-infected cases. Among 143 fetuses from infected mothers, none had anti-SARS-CoV-2 IgM/IgA in cord blood. CONCLUSIONS: The overall rate of pregnancy complications in women with SARS-CoV-2 infection was similar to non-infected women. However, symptomatic COVID-19 was associated with modest increases in preterm delivery and intrapartum fetal distress.

	SARS-CoV-2 negative	SARS-CoV-2 positive	Risk difference (95% CI)
Primary outcome			
Overall pregnancy complication[#]	268 (14%)	43 (13.6%)	-0.4% (-4.1 to 4.1)
Early pregnancy complication[†]	15 (1.9%)	2 (1.4%)	-0.5% (-3.2 to 2.1)
Late pregnancy complication[§]	253 (22.4%)	41 (23.3%)	0.9% (-5.3 to 8.1)
Secondary outcomes			
Miscarriage[†]	15 (1.9%)	2 (1.4%)	-0.5% (-3.2 to 2.1)
Abnormal fetal growth† at 20-24 weeks'[¶]	6 (2.6%)	1 (1.9%)	-0.7% (-7.4 to 4)
Fetal malformation at 20-24 weeks'[¥]	16 (3.5%)	3 (3.8%)	0.3% (-3 to 7.2)
Preeclampsia[§]	40 (3.5%)	8 (4.5%)	1% (-1.5 to 5.3)
Preterm delivery[§]	81 (7.2%)	20 (11.4%)	4.2% (-0.03 to 9.9)
Perinatal death[*]	6 (0.5%)	1 (0.6%)	0.1% (-0.7 to 2.7)
Small-for-gestational age[*]	168 (14.5%)	25 (14%)	-0.5% (-5.7 to 5.3)
Intrapartum fetal distress[*]	105 (9.1%)	25 (14%)	4.9% (0.2 to 11)
Admission to high-dependency neonatal care[*]	63 (5.4%)	11 (6.2%)	0.8% (-2.3 to 5.5)
Exploratory outcomes			
Induction of labour[§]	464 (41.1%)	66 (37.5%)	-3.6% (-4.3 to 11)
Caesarean section[§]	311 (27.6%)	54 (30.7%)	3.1% (-3.8 to 10.7)
Gestational age at delivery, weeks[§]	39.3 (2.6)	39.1 (2.1)	-0.2 (-0.6 to 0.2)
Birth weight, g[*]	3198 (609)	3245 (581)	47 (-49 to 143)
Severe small-for-gestational age[*]	55 (4.7%)	8 (4.5%)	-0.2% (-4.1 to 2.8)
Neonatal metabolic acidosis[**]	115 (12.7%)	10 (8.3%)	-4.4% (-2.2 to 8.8)
Maternal breastfeeding[§]	1050 (93.1%)	160 (90.9%)	-2.2% (-1.6 to 7.5)

Table 2. Pregnancy and perinatal outcomes in women with and without evidence of SARS-CoV-2 infection.
Data are n (%) or mean (SD). CI: Confidence interval.
#Including all pregnancies (n=2,225: 1,908 SARS-CoV-2 negative; 317 SARS-CoV-2 positive)
†Including all early pregnancies (n=921: 780 SARS-CoV-2 negative; 141 SARS-CoV-2 positive)
§Including all late pregnancies (n=1,304: 1,128 SARS-CoV-2 negative; 176 SARS-CoV-2 positive)
¶Data are calculated over 285 consecutive scans completed at the time of data analysis (n=231 SARS-CoV-2 negative, n=54 SARS-CoV-2 positive).
¥Data calculated over 540 consecutive scans completed at the time of data analysis (n=460 SARS-CoV-2 negative, n=80 SARS-CoV-2 positive).
*Including multiple gestation (n=1,338: 1,1160 SARS-CoV-2 negative; 178 SARS-CoV-2 positive) **Including 1024 neonates (n=903 SARS-CoV-2 negative, n=121 SARS-CoV-2 positive).
Accepted Manus

	SARS-CoV-2 negative	SARS-CoV-2 positive		
		asymptomatic	symptomatic	Risk difference (95% CI)
Early pregnancy				
Miscarriage[§]	15 (1.9%)	1 (0.9%)	1 (3.4%)	2.5% (-2.4 to 16.2)
Abnormal fetal growth† at 20-24 weeks[‖¶]	6 (2.6%)	1 (2.1%)	0 (0%)	-2.1% (-33.4 to 11.1)
Fetal malformation at 20-24 weeks[‖¶¶]	16 (3.5%)	3 (4.8%)	0 (0%)	-4.8% (-13.9 to 13.1)
Late pregnancy and delivery				
Preeclampsia[¶]	40 (3.5%)	6 (5.6%)	2 (2.8%)	-2.8% (-4.7 to 9.3)
Preterm delivery[¶]	81 (7.2%)	8 (7.6%)	12 (16.9%)[#]	9.3% (-0.4 to 20.3)
Induction of labour[¶]	464 (41.1%)	36 (34.3%)	30 (42.3%)	8% (-6.4 to 22.3)
Intrapartum fetal distress[¶]	105 (9.1%)	11 (10.5%)	14 (19.2%)[†]	8.7% (-1.7 to 20.1)
Caesarean section[¶]	311 (27.6%)	33 (31.4%)	21 (29.6%)	-1.8% (-12.2 to 15.1)
Gestational age at delivery, weeks[¶]	39.1 (2.6)	39.2 (2.1)	39.0 (2.2)	-0.2 (-0.8 to 0.4)
Birth weight, g[¥]	3198 (609)	3299 (535)	3166 (636)	-133 (-307 to 41)
Birth weight centile[¥§§]	47 (30.8)	53 (30.6)	51 (32.6)	-0.2 (-11.4 to 7.5)
Small-for-gestational age[¥]	168 (14.5%)	13 (12.4%)	12 (16.4%)	4% (-6.2 to 15.3)
Severe small-for-gestational age[¥]	55 (4.7%)	1 (1%)	7 (9.6%)[*]	8.6% (2.1 to 17.5)
Neonatal metabolic acidosis[¥¥]	115 (12.7%)	6 (8.1%)	4 (8.5%)	0.4% (-9.5 to 12.6)
Admission to high-dependency neonatal care[¶]	63 (5.4%)	6 (5.7%)	5 (6.8%)	1.1% (-6.2 to 9.8)
Perinatal death[¶]	6 (0.5%)	1 (1%)	0 (0%)	-1% (-4.1 to 5.3)
Maternal breastfeeding[¶]	1050 (93.1%)	96 (91.4%)	64 (90.1%)	-1.3% (-7.2 to 11.1)

Data are n (%) or mean (SD). CI: Confidence interval.

Table 3. Pregnancy and perinatal outcomes in women SARS-CoV-2 infected during pregnancy according to the presence or absence of COVID-19 symptoms.

#Statistically significant difference between SARS-CoV-2 negative vs. positive symptomatic (p=0.003) †Statistically significant difference between SARS-CoV-2 negative vs. positive symptomatic (p=0.004)
*Statistically significant difference between SARS-CoV-2 positive asymptomatic vs. positive symptomatic (p=0.006)
§Including all early pregnancies (n=921: 780 negative, 112 positives asymptomatic; 29 positives symptomatic)
§§Data are calculated over 285 consecutive scans completed at the time of data analysis (n=231 negative, n=47 positive asymptomatic, n=7 positive symptomatic).
§§§Data calculated over 540 consecutive scans completed at the time of data analysis (n=460 negative, n=63 positive asymptomatic, n=17 positive symptomatic).
¶Including all late pregnancies (n=1,304: 1,1128 negative, 105 positives asymptomatic; 71 positives symptomatic)
¥Including multiple gestation (n=1,338: 1,1160 negative, n= 105 positives asymptomatic; 73 positives symptomatic)
¥¥Including 1024 neonates (n=903 negative, n= 74 positives asymptomatic; 47 positives symptomatic)

CRISPR-BASED COVID-19 SMARTPHONE TEST IN DEVELOPMENT

Abbasi J.. JAMA. 2021 Feb 9;325(6):522. doi: 10.1001/jama.2021.0493.
Level of Evidence: 5 - Opinion

BLUF

This health journalism piece discusses a new technology from the University of California, San Francisco, utilizing clustered regularly interspaced short palindromic repeats (CRISPR) gene editing technology to detect SARS-CoV-2 RNA viral particles from patient nasal swabs. The test, which quantifies viral load based off time to detection, is not available for mass use by the public as it currently requires RNA extraction and medical-grade equipment. However the research team, including Jennifer Doudna, PhD, who holds a Nobel Prize for developing CRISPR-based gene editing, is hoping to make this technology available to the public in the future, potentially adding another testing modality.

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