# The Daily COVID-19 Literature Surveillance Summary

## February 24, 2021

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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

**Epidemiology**

- This case series conducted by Italian nephrologists studied the ability of 210 adult patients on chronic hemodialysis (HD) to mount a detectable and persistent antibody response to SARS-CoV-2. They found that all symptomatic survivors of COVID-19 developed an initial immune response, but there was a subsequent decline in persistent seropositivity at 6 months. They also found that in individuals with asymptomatic or mild COVID-19, the virus induced a stronger memory T cell response than humoral immune response, and therefore, seroprevalence may be a poor indicator of protection against the virus. This study is the first of its kind and provides valuable information as to the ability of anti-SARS-CoV-2 spikes IgG to protect against a virus re-infection.

**Understanding the Pathology**

- Obstetricians and pathologists from Maimonides Medical Center collaborate on this case control study, which compared histopathological findings in placental tissue from 150 patients (85 SARS-CoV-2 positive via RT-PCR) using the Amsterdam consensus group criteria. After analyzing various variables such as vascular perfusion, fibrin concentrations, and chorangiosis, the authors found no statistically significant histopathological difference between the two groups nor did they identify any immunohistochemical presence of SARS-CoV-2 within the placentas of COVID-19 patients. These findings, which are congruent with current literature, suggest that direct viral invasion of placental tissue is not a pathophysiological mechanism of COVID-19 in pregnancy, although larger studies are needed to determine variations in chronic inflammatory lesions such as basal chronic villitis and chronic deciduitis.

**Adjusting Practice During COVID-19**

- This research letter from the University of Texas, Austin, discusses how the executive order to postpone non-essential surgeries until April 21, 2020 due to the COVID-19 pandemic has affected abortions in Texas. Results revealed a 38% decrease overall in abortions at Texas clinics as well as greater numbers of residents receiving out-of-state abortion care. Additionally, they found increases in medically managed abortions from 39% the year prior to 80% in this period and an 82.6% increase in abortions at or after 12 weeks gestational age after the ban was lifted. The authors conclude that overall trends in delays seeking care during this pandemic were likely exacerbated by the effects of the ban in this population.

# TABLE OF CONTENTS

# CLIMATE

## GLOBAL

### SARS-COV-2 VARIANTS OF CONCERN IN THE UNITED STATES-CHALLENGES AND OPPORTUNITIES

Walensky RP, Walke HT, Fauci AS.. JAMA. 2021 Feb 17. doi: 10.1001/jama.2021.2294. Online ahead of print.
Level of Evidence: 5 - Expert Opinion

#### BLUF

This expert opinion article from researchers with the US Centers for Disease Control and Prevention discusses three concerning SARS-CoV-2 variants (B.1.1.7, B.1.351, and P.1), which have increased propensity for transmission, severity of disease, and lessened protection from the COVID-19 vaccine. They highlight the need for adapting the public health response to include increased genomic surveillance and ongoing investigation into vaccination efficacy against novel mutations. They also advocate for accelerating vaccination efforts globally to decrease SARS-CoV-2 transmission and the importance of continuing preventative practices such as masking, physical distancing, and decreased travel, which are critical for a concerted and well-coordinated effort at controlling the trajectory of the pandemic.

# ADULTS

## THE HUMORAL IMMUNE RESPONSE TO SARS-COV-2 MOUNTS AND IS DURABLE IN SYMPTOMATIC HEMODIALYSIS PATIENTS

La Milia V, Tonolo S, Luzzaro F, Bonato C, Cavalli A, Foglieni B, Debiase C, Limardo M, Longhi S, Ravasi C, Viganò S..
Nephrol Dial Transplant. 2021 Feb 19:gfab047. doi: 10.1093/ndt/gfab047. Online ahead of print.
Level of Evidence: 4 - Local non-random sample

### BLUF

This case series conducted by Italian nephrologists studied the ability of 210 adult patients on chronic hemodialysis (HD) to mount a detectable and persistent antibody response to SARS-CoV-2. They found that all symptomatic survivors of COVID-19 developed an initial immune response, but there was a subsequent decline in persistent seropositivity at 6 months (Figure 1). They also found that in individuals with asymptomatic or mild COVID-19, the virus induced a stronger memory T cell response than humoral immune response, and therefore, seroprevalence may be a poor indicator of protection against the virus. This study is the first of its kind and provides valuable information as to the ability of anti-SARS-CoV-2 spikes IgG to protect against a virus re-infection.

### FIGURES

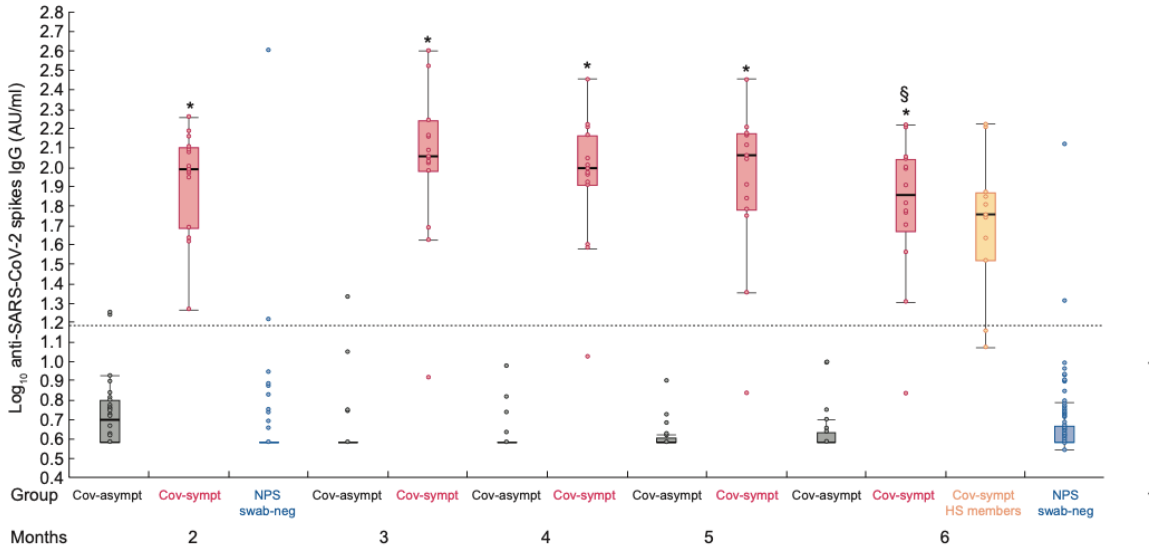


Figure 1. Anti-SARS-CoV-2 spikes IgG titer in CoV-asympt, CoV-sympt survivors, NPS swab- negative and CoV-sympt health staff members group during 6 months follow-up.

The horizontal line within the box represents the median sample value; the ends of the box represent the 75th and 25th quantiles, respectively; the distance or the difference between the 75th and 25th, also expressed as 3rd and 1st quartile, is the interquartile range; each box has lines, called whiskers, that extend from each end; the whiskers extend from ends of the box to outermost data point that falls within the distances computed as follows: 3rd quartile + 1.5*(interquartile range), 1st quartile - 1.5*(interquartile range), if the data points do not reach the computed ranges, then the whiskers are determined by the upper and lower data point values (not including outliers). The dashed black line represents the sensitivity threshold of the anti-SARS-CoV-2 spikes IgG dosing method.

*P<0.0001 vs CoV-asympt and NPS swab negative group; §p=0.5 vs CoV-sympt health care staff members

## HISTOLOGIC AND IMMUNOHISTOCHEMICAL EVALUATION OF 65 PLACENTAS FROM WOMEN WITH POLYMERASE CHAIN REACTION-PROVEN SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2 (SARS-COV-2) INFECTION

Levitan D, London V, McLaren RA, Mann JD, Cheng K, Silver M, Balhotra KS, McCalla S, Loukeris K.. Arch Pathol Lab Med. 2021 Feb 17. doi: 10.5858/arpa.2020-0793-SA. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

### BLUF

Obstetricians and pathologists from Maimonides Medical Center collaborate on this case control study, which compared histopathological findings in placental tissue from 150 patients (85 SARS-CoV-2 positive via RT-PCR) using the Amsterdam consensus group criteria. After analyzing various variables such as vascular perfusion, fibrin concentrations, and chorangiosis, the authors found no statistically significant histopathological difference between the two groups (Table 2), nor did they identify any immunohistochemical presence of SARS-CoV-2 within the placentas of COVID-19 patients. These findings, which are congruent with current literature, suggest that direct viral invasion of placental tissue is not a pathophysiological mechanism of COVID-19 in pregnancy, although larger studies are needed to determine variations in chronic inflammatory lesions such as basal chronic villitis and chronic deciduitis.

### ABSTRACT

CONTEXT: -Coronavirus disease 2019 (COVID-19) has been shown to have effects outside of the respiratory system. Placental pathology in the setting of maternal severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection remains a topic of great interest as earlier studies have shown mixed results. OBJECTIVE: -To ascertain whether maternal SARS-CoV-2 infection is associated with any specific placental histopathology, and to evaluate the virus's propensity for direct placental involvement. DESIGN: -Placentas from 65 women with polymerase chain reaction-proven SARS-CoV-2 infection underwent histologic evaluation using Amsterdam consensus group criteria and terminology. Another 85 placentas from women without SARS-CoV-2 constituted the negative control group. Sixty-four of the placentas from the SARS-CoV-2-positive group underwent immunohistochemical staining for SARS-CoV-2 nucleocapsid protein. RESULTS: -Pathologic findings were divided into maternal vascular malperfusion, fetal vascular malperfusion, chronic inflammatory lesions, amniotic fluid infection sequence, increased perivillous fibrin, intervillous thrombi, increased subchorionic fibrin, meconium-laden macrophages within fetal membranes, and chorangiosis. There was no statistically significant difference in prevalence of any specific placental histopathology between the SARS-CoV-2-positive and negative groups. There was no immunohistochemical evidence of SARS-CoV-2 virus in any of the 64 placentas that underwent staining for viral nucleocapsid protein. CONCLUSIONS: -Our study results and a literature review suggest that there is no characteristic histopathology in the majority of placentas from women with SARS-CoV-2 infection. Likewise, direct placental involvement by SARS-CoV-2 is a rare event.

**Table 2. Prevalence of MVM**

| | SARS-CoV-2-Positive (n = 65) | | | SARS-CoV-2-Negative (n = 85) | | | *P* Values | *P* Values |
|---|---|---|---|---|---|---|---|---|
| MVM | Total | PEC/gHTN+ (n = 9) | PEC/gHTN- (n = 56) | Total | PEC/gHTN+ (n = 13) | PEC/gHTN- (n = 72) | (totals) | (PEC/gHTN-) |
| DA | 6 (9%) | 0 | 6 (11%) | 8 (9%) | 4 (33%) | 4 (6%) | >.99 | .33 |
| DVH | 3 (5%) | 1 (11%) | 2 (4%) | 8 (9%) | 1 (8%) | 7 (10%) | .35 | .30 |
| ISK | 8 (12%) | 1 (11%) | 7 (13%) | 11 (13%) | 5 (42%) | 6 (8%) | >.99 | .56 |
| VA | 1 (1.5%) | 0 | 1 (2%) | 9 (10.5%) | 1 (8%) | 8 (11%) | .04 | .08 |
| VI | 8 (12%) | 2 (22%) | 6 (11%) | 14 (16%) | 4 (33%) | 10 (14%) | .64 | .79 |
| RPH | 2 (3%) | 0 | 2 (4%) | 3 (3.5%) | 0 | 3 (4%) | >.99 | >.99 |
| Total MVM | 23 (35%) | 4 (44%) | 19 (34%) | 31 (36%) | 8 (67%) | 22 (30%) | >.99 | .71 |

Abbreviations: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; MVM, maternal vascular malperfusion; DA, decidual arteriopathy; DVH, distal villous hypoplasia; ISK, increased syncytial knots; VA, villous agglutination; VI, villous infarction; RPH, retroplacental hemorrhage; PEC/gHTN, preeclampsia/gestational hypertension.

Table 2. Prevalence of MVM (maternal vascular malperfusion)

# CHANGES IN ABORTION IN TEXAS FOLLOWING AN EXECUTIVE ORDER BAN DURING THE CORONAVIRUS PANDEMIC

White K, Kumar B, Goyal V, Wallace R, Roberts SCM, Grossman D.. JAMA. 2021 Feb 16;325(7):691-693. doi: 10.1001/jama.2020.24096.
Level of Evidence: 3 - Local non-random sample

## BLUF

This research letter from the University of Texas, Austin, discusses how the executive order to postpone non-essential surgeries until April 21, 2020 due to the COVID-19 pandemic has effected abortions in Texas. Results revealed a 38% decrease overall in abortions at Texas clinics as well as greater numbers of residents receiving out-of-state abortion care (from 157 in February 2020 to 947 in April 2020). Additionally, they found increases in medically managed abortions from 39% the year prior to 80% in this period and an 82.6% increase in abortions at or after 12 weeks gestational age after the ban was lifted (Table 2). The authors conclude that overall trends in delays seeking care during this pandemic were likely exacerbated by the effects of the ban in this population.

## FIGURES

Table 2. Distribution of Abortion Type and Percent Change in Number of Abortions in Texas, February-May 2019 and February-May 2020

| | No. (%)[a] | | % (95% CI) | |
|---|---|---|---|---|
| | 2019 | 2020 | Month-specific change, 2019-2020[b] | Deviation from trend since January 2019[c] |
| **Medication abortion (≤10.0 wk GA)** | | | | |
| February-May | 7097 (38.8) | 8754 (53.5) | | |
| February | 1620 (37.8) | 1928 (41.5) | 19.0 (11.4 to 27.1) | −9.1 (−23.9 to 8.4) |
| March | 1905 (38.7) | 1980 (49.6) | 3.9 (−2.4 to 10.7) | −7.5 (−23.6 to 12.0) |
| April | 1808 (39.2) | 2297 (80.4) | 27.0 (19.5 to 35.1) | 17.4 (−7.1 to 48.4) |
| May | 1764 (39.6) | 2549 (52.6) | 44.5 (36.0 to 53.5) | 29.2 (0.0 to 67.0) |
| **Procedural abortion (<12.0 wk GA)** | | | | |
| February-May | 8943 (49.0) | 5395 (33.0) | | |
| February | 2123 (49.5) | 2113 (45.4) | −0.5 (−6.3 to 5.7) | −4.8 (−16.3 to 8.4) |
| March | 2322 (47.2) | 1482 (37.1) | −36.2 (−40.2 to −31.9) | −32.9 (−41.8 to −22.6) |
| April | 2318 (50.3) | 317 (11.1) | −86.3 (−87.8 to −84.6) | −84.9 (−87.6 to −81.6) |
| May | 2180 (49.0) | 1483 (30.6) | −32.0 (−36.3 to −27.3) | −28.9 (−41.2 to −14.1) |
| **Procedural abortion (≥12.0 wk GA)** | | | | |
| February-May | 2228 (12.2) | 2200 (13.5) | | |
| February | 544 (12.7) | 610 (13.1) | 12.1 (−0.1 to 25.9) | −4.2 (−17.6 to 11.5) |
| March | 695 (14.1) | 533 (13.3) | −23.3 (−31.5 to −14.1) | −14.7 (−27.8 to 0.8) |
| April | 482 (10.5) | 242 (8.5) | −49.8 (−57.0 to −41.4) | −46.7 (−57.5 to −33.3) |
| May | 507 (11.4) | 815 (16.8) | 60.7 (43.9 to 79.6) | 82.6 (46.7 to 127.4) |

Abbreviation: GA, gestational age.

[a] Percent of all abortions in month and year.

[b] Percent change in February, March, April, and May 2020 vs 2019 estimated from negative binomial regression models.

[c] Deviation from trend estimated from negative binomial regression models projecting the linear trend in abortion type from January 2019 through May 2020. Models also controlled for number of facilities and abortion seasonality.

Table 2.  Distribution of Abortion Type and Percent Change in Number of Abortions in Texas, February-May 2019 and February-May 2020.

# ACKNOWLEDGEMENTS


## CONTRIBUTORS

Renate Meckl
Sarala Kal
Sokena Zaidi

## EDITORS

Stephen Ferraro

## SENIOR EDITORS

Justin Doroshenko

## SENIOR EXECUTIVE EDITOR

Sangeetha Thevuthasan

## CHIEF EDITOR

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