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SARS-CoV-2 serology levels in pregnant women and their neonates.

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Condensation: SARS-CoV-2 antibody levels in pregnant mothers correlate with presence of maternal symptoms and passive immunity in neonates.

Short Title: SARS-CoV-2 antibody in mothers and neonates

AJOG at a Glance:

A. Why was the study conducted?

- Studies on the serologic response to SARS-CoV-2 viral infection have been focused on the general population but the timing and level of serologic response in pregnant women are not well characterized.
- The passive transmission of maternal antibodies to neonates have not been systematically studied at scale.

B. What are the key findings?

- Asymptomatic pregnant women mount a lower serologic response than symptomatic pregnant women.
- The timing of IgM and IgG antibody response level peaks at 15 days and 30 days post COVID-19 symptoms onset, respectively.
- Maternal IgG antibodies positively correlates with and predicts antibody levels in the neonates.

C. What does this study add to what is already known?

- A comprehensive semiquantitative analysis of the levels and timing of IgM and IgG in the pregnant women
- Mothers with higher antibody levels exhibit higher likelihood of transferring antibodies to their neonates

STRUCTURED ABSTRACT:

Background: Pregnant women and their neonates represent two vulnerable populations highly susceptible to viral infections with an interdependent immune system. The immune response of pregnant women to SARS-CoV-2 and the interplay of how the maternal immune response affects neonatal passive immunity have not been systematically studied.

Objectives: We characterized the serologic response in pregnant women and studied how this serologic response correlates with maternal clinical presentation and with the rate and level of passive immunity from mothers to neonates.

Study Design: Between March 22-May 31, 2020, women giving birth who tested positive for semi-quantitative IgM or IgG detection in a New York City Hospital were included in the study. Retrospective chart review of the cases that met inclusion criteria was conducted for presence of COVID19 symptoms and use of oxygen support. Serology levels between the symptomatic and asymptomatic patients were compared with Welch's two sample t-test. Further chart review of the same patient cohort was conducted in order to identify dates of self-reported onset of COVID-19 symptoms, and the timing of the peak of IgM and IgG antibody levels after symptoms onset were visualized using local polynomial regression smoothing (LOESS) on log2-scaled serological values. To study the neonatal serology response, cord blood samples of neonates born to a subset of all serology positive pregnant women were tested for serology. Maternal antibody levels of serology-positive vs. serology-negative neonates were compared with the Welch's two sample t-test. The relationship between quantitative maternal and quantitative neonatal serologic data was studied using

Pearson correlation and linear regression. Multiple linear regression analysis was conducted using maternal symptoms, maternal serology levels, and maternal use of oxygen support to determine predictors of neonatal IgG levels.

Results: Eighty-eight serology positive pregnant women were included in this study. Antibody levels are higher in symptomatic pregnant women compared to asymptomatic pregnant women. Serology studies in 34 women with symptom onset data reveal that maternal IgM and IgG levels peak around 15 and 30 days post COVID-19 symptoms onset, respectively. Furthermore, studies of fifty neonates born to a subset of serology positive women show that passive immunity in the form of IgG is conferred upon 78% of all neonates. Presence of passive immunity is dependent on maternal antibody levels, and levels of neonatal IgG correlate with maternal IgG levels. Maternal IgG levels and maternal use of oxygen support were predictive of neonatal IgG levels.

Conclusions: We demonstrate that maternal serologies correlate with symptomatic maternal infection, and higher levels of maternal antibodies are associated with passive immunity. Maternal IgG levels and maternal use of oxygen support, a marker of disease severity, predict neonatal IgG levels. These data will further guide the screening for this unique linked population of mothers and their babies, and can aid in developing maternal vaccination strategies.

Keywords:

antibody levels; asymptomatic infection; baby; convalescent infection; cord blood; COVID19 infection; mother; mother-baby dyads; passive immunity; predictor; prevalence; symptomatic infection; time course

INTRODUCTION:

As the novel SARS-CoV-2 virus spread rapidly through New York City in March 2020 – at that time the global epicenter of the disease – the obstetric unit within a New York City hospital implemented universal testing of all women admitted to labor and delivery to screen this uniquely vulnerable patient population. During this peak of the pandemic, 10-15% of all women admitted to New York City area labor and delivery units tested positive for SARS-CoV-2 by RT-PCR testing.[1,2] An updated report from the CDC in October 2020 found that pregnant women with symptomatic COVID-19 infection were at increased risk of ICU admission, invasive ventilation, extracorporeal membrane oxygenation, and death.[3] Further prospective and retrospective studies have shown that pregnant women infected with SARS-CoV-2 are at increased risk of other morbidities as well, including higher rates of cesarean delivery, increased post-partum complications (including fever, hypoxia, and hospital readmissions post-discharge), as well as placental pathology including fetal vascular malperfusion; however it should be noted that the risk of preterm birth may still require further study.[4–11]

There has been a recent interest in serology testing as a means of detecting exposure to SARS-CoV-2, limiting disease spread, and potentially predicting outcomes.[12–14] Studies have reported that nearly 100% of patients with confirmed SARS-CoV-2 will test positive for IgG and/or IgM within 19 days of exposure, even after RT-PCR results reverted to negative.[15–17] Some data suggests that high levels of IgG are associated with more severe illness,[18] while asymptomatic patients are more likely to convert to seronegative in the convalescent phase of infection.[19] The protective nature of antibodies against SARS-CoV-2 against future infection is still unclear.[20]

Pregnant women and their neonates have a unique interdependent immune system. The interactions between the maternal immune system and fetal placenta result in changes that alter both innate and adaptive host responses to infections.[21] For this reason, current studies on the serologic responses to SARS-CoV-2 may not be applicable to the pregnant population. Studies to date have demonstrated the rate of seropositivity in pregnant women,[22,23] but a detailed analysis of the timing and levels of response in these pregnant patients have not been well characterized.

Passive transfer of antibodies against SARS-CoV-2 has not been systematically studied beyond the demonstration of neonatal antibodies in a small number of cases, and it is not clear whether these antibodies are protective against disease.[24] There have been reports of transplacental transmission of SARS-CoV-2 as well as symptomatic neonates who tested positive for SARS-CoV-2 born to PCR positive mothers.[25–30] However, in these cases, the serologic status of the mother was either negative or not reported. A small case series demonstrated the presence of antibodies in RT-PCR negative asymptomatic neonates born to symptomatic women.[31] However, the rate of transfer of maternal antibodies from mother to neonate and whether even asymptomatic women may transfer antibodies to neonates is not yet established.[32] In this paper, we aimed to systematically explore the serologic responses of mothers and neonates, in both symptomatic and asymptomatic cases.

MATERIALS AND METHODS:

STUDY POPULATION

Eighty-eight pregnant women who tested positive for SARS-CoV-2 specific antibodies (serology positive) at a single institution in New York City were included in this study. 67/88 women were identified to be serology positive from universal serology testing of all women giving birth between April 18, 2020 and May 31, 2020. An additional 21/88 women were identified to be serology positive between March 22 and April 17, 2020 after undergoing testing due to suspicion of SARS-CoV-2 infection or exposure. Neonates born to these mothers were also included in this study and underwent serology testing on cord blood.

LABORATORY TESTING

Patients were tested for IgM and IgG antibodies against SARS-CoV-2 on serum or plasma of peripheral blood (mothers) or on plasma from cord blood (neonates) using a fluorescence-based reporting system which allows for semi-quantitative detection of anti-SARS-CoV-2 antibodies using the clinical testing Pylon 3D platform (ET HealthCare, Palo Alto, CA). This platform utilizes a fluorescence-based reporting system which allows for semi-quantitative detection of anti-SARS-CoV-2 IgG and IgM with a specificity of 99.4% and 98.8% for IgM and IgG, respectively.[8] Antibody levels were expressed as log2(value) + 1.

STATISTICAL ANALYSES

To study the association of symptoms with serologic results, retrospective chart review was conducted in order to identify symptoms at the time of serology testing. Patients with any of the following COVID19 symptoms (self-reported fever, cough, sore throat, rhinorrhea, shortness of breath, diarrhea, other gastrointestinal symptoms, myalgias, loss of sense of taste or smell*)* reported before or at the time of admission were

categorized as symptomatic;[4,24] those without any of the listed symptoms were categorized as asymptomatic. IgM and IgG values of symptomatic and asymptomatic patients were plotted as continuous variables and are expressed as the median (IQR) with error bars representing 95% confidence. The serology levels between the symptomatic and asymptomatic patients were compared with Welch's two sample t-test. P value of < 0.05 was considered statistically significant.

To study the time course of antibody response at the cohort level, retrospective chart review was conducted in order to identify dates of first COVID-19 symptoms. 34 of the 88 pregnant women had documentation of specific dates of onset of COVID-19 symptoms. IgM and IgG antibody levels were correlated to the number of days elapsed from the date of COVID-19 symptoms onset using local polynomial regression smoothing (LOESS) on log2-scaled serological values.

We studied the relationship between quantitative maternal IgG and quantitative neonatal IgG using Pearson correlation and linear regression. To understand if maternal antibody levels are different between the pregnant women that gave birth to serology positive neonates vs. those who gave birth to serology negative neonates, maternal antibody levels of serology-positive vs. serology-negative neonates were compared using Welch's two sample t-test.

Retrospective chart review was conducted to identify 5 women that required oxygen support (3 women needed nasal canula, 2 women needed non-rebreather) during their hospital course likely as a marker of disease severity. Multiple linear regression analysis was conducted to predict neonatal IgG levels from maternal symptoms (present or absent), maternal IgG level, maternal IgM level, and maternal use of oxygen support.

Statistical analyses were performed using R 3.6.1, RStudio 1.1.463, and SPSS1.0.0.1461 software statistics.

This study was approved by the institutional review board, protocols 20-03021682 and 20-04021792. A waiver of consent was granted by the institutional review board.

RESULTS:

We identified 88 pregnant women with positive SARS-CoV-2 IgM or IgG (10 women IgM positive; 24 IgM and IgG positive; 54 women IgG positive). Retrospective chart analysis of all 88 serology positive mothers showed that 42.0% (37/88) were symptomatic while 58.0% (51/88) of serology positive patients were asymptomatic (Figure 1). Both asymptomatic and symptomatic pregnant women mounted a detectable IgM and IgG response; however, IgG levels were significantly higher in the symptomatic mothers compared to asymptomatic mothers (p=0.029) (Figure 1).

Of all 88 serology positive pregnant women, 34 women had documentation of specific dates of the first COVID-19 symptoms. Analysis of these 34 data points for the elapsed time from the date of symptom onset in relation to antibody levels demonstrates that at the cohort level, IgM levels peak around 15 days post symptom onset, while IgG levels started to peak around 30 days post symptom onset and could last over 90 days (Figure 2).

To better understand passive immunity, we analyzed 50 neonates born to a subset of our cohort of 88 pregnant women with positive serologic results. Of the 50 neonates, 78% (39/50) had positive serologic findings (born to 14 IgM and IgG positive

mothers, 24 IgG positive mothers, and 1 IgM positive mother that was right at the limit of detection for both IgM and IgG). All 39 neonates had IgG only, and none of the neonates had IgM (Figure 3A). RT-PCR analysis of the 39 serology positive neonates showed that 29/39 (74%) neonates were RT-PCR negative, but 10/39 neonates were not tested due to lack of sample capture. To study the factors that dictate passive immunity of SARS-CoV-2 antibodies, we analyzed the IgG levels of these mothers and neonates. Neonates with SARS-CoV-2 specific IgG were born to mothers with significantly higher IgG levels than neonates without IgG ($p=1.7e^{-11}$) (Figure 3B); and of the 39 serology positive neonates, we find that IgG levels positively correlate to maternal IgG levels (Figure 3C). A multiple linear regression analysis was conducted to show that maternal IgG levels ($p<0.0005$) and oxygen supplementation in a limited number of patients ($p=0.001$) were predictive of neonatal IgG levels. However, maternal IgM levels and maternal symptoms were not predictive of neonatal IgG levels ($p=0.290$ and $p=0.506$, respectively). Model statistics: $F(4, 45)=36.686$, $p<0.0005$, $R^2=0.826$.

COMMENT:

Principal Findings: IgG antibody response in symptomatic pregnant women was significantly higher compared to the asymptomatic pregnant women. In pregnant women, IgM and IgG levels peaked at 15 days and 30 days post COVID-19 symptoms onset, respectively. Passive immunity in the form of IgG was demonstrated in 78% of neonates, and serology levels in mothers correlated with serology levels of matched neonates. Serology levels in mothers, and oxygen supplementation in a limited number of mothers, predicted serology levels in the matched neonates.

Results: This study provides semi-quantitative and separate IgM and IgG data for a cohort of 88 pregnant women as well as 50 of their neonates. The timing of IgM response and IgG response among pregnant women mirrors that seen in the general population and the expected classic pattern of IgM and IgG antibody response to infections.[15–17,33] Asymptomatic women mount an immune response, albeit weaker than symptomatic women, which is consistent with similar findings in non-pregnant individuals.[9] Passive immunity has been demonstrated in small cohorts or case studies, but our semi-quantitative study on a large mother-baby dyad cohort demonstrates that there is a correlation between maternal antibody levels and the amount of IgG demonstrated in neonatal cord blood. Furthermore, we demonstrate that maternal IgG and maternal oxygen supplementation—a marker of disease severity--predict neonatal IgG.

Clinical Implications: We found that both symptomatic and asymptomatic women mounted a detectable antibody response; however, symptomatic women mounted a higher IgG response. Since asymptomatic non-pregnant patients are more likely to convert to seronegative in the convalescent phase of infection,[19] and since a large cohort of the pregnant women are also asymptomatic, these data hint at a potential faster conversion to seronegative in many pregnant women implying that even women with documented infections could be antibody negative by the time of birth particularly if they were infected early in their pregnancies. Whether the antibodies are protective, and if so, at what antibody levels are correlated with protection as well as how long that protection lasts are critical next areas of investigation.

We demonstrate that the timeline of antibody response in pregnant women is similar to that of the non-pregnant patient population and does not deviate from classic patterns of IgM and IgG response. [15–17,33] Given the difficulty to enroll pregnant women in vaccination studies, these data confirming the classic patterns of IgM and IgG response in SARS-CoV-2 infection may enable the ability to work off of frameworks from previously established maternal vaccination protocols.

This study strongly suggests that maternal SARS CoV-2 specific IgG is transferred to the neonate particularly when the mother has a high IgG level. This implies that maternal SARS CoV-2 infection stimulates IgG antibody production that readily crosses the placenta, consistent with other maternal infections. These data suggest that if the mother mounts an antibody response secondary to a vaccination against SARS-CoV-2, then those antibodies could also cross the placenta into the neonate, potentially protecting both the mother and her neonate(s) from future infection. It is not known how protective this maternally derived IgG antibody is for the neonate and how long the protection lasts.

Research Implications: Using the methodologies described here, a larger cohort of mothers could be tested, and serial studies on the same mothers could be conducted in order to understand the timeline of antibody production and clearance. Follow-up studies on neonates could be conducted to study whether maternal antibodies provide protection, and would allow better understanding of the clearance curve of the antibodies post birth. These studies will ultimately inform the potential benefit of maternal vaccination when it becomes available.

Strengths and Limitations: Our study has multiple strengths. Our cohort is large with consistent clinical data available. In addition, we utilized semi-quantitative independent analysis of both IgM and IgG in mothers and their matched neonates. A limitation is that we did not have data on all neonates born to our serology positive cohort due lack of sample capture given that this was not a prospective collection study.

The inclusion of serology positive women both from those identified from universal serology testing as well as those identified due to suspicion for COVID-19 infection may contribute sampling bias of more severe patients; however, analysis done on only the cohort of patients identified from the universal serology testing also led to the same rate of symptomatic vs. asymptomatic women. The findings on serologic differences between symptomatic and asymptomatic women is limited by the fact that we only captured symptoms data on 34 women and there may be lack of data capture or recall bias. The serologic difference may also be due to differences in the timing of their infections. Asymptomatic women maybe have a lower IgG antibody level due to a more recent infection compared to women who were symptomatic, and thus these women may in time develop both higher antibody levels as well as symptoms. The data on timing of serologic response from symptom onset are dependent on self-reported dates of symptoms which introduces recall bias and are more representative of the symptomatic populations. The analysis from the time of symptom onset fails to capture the delay between when a woman becomes infected until when she becomes symptomatic; however, it is difficult to ascertain true timing of infection in a clinical study setting. Given the lack of serial sampling of each individual patient to study the time

course of serologic response, we rely on the overall trend of the entire cohort of pregnant women.

The majority of our neonate samples utilized cord blood which may risk maternal blood contamination; however, we believe these findings are not due to maternal blood contamination because 1) these samples were utilized for neonatal blood typing without any issues or maternal blood typing confusion, 2) none of the neonates born to IgM positive mothers tested IgM positive as would be expected if contamination did occur, and 3) peripheral blood samples available in some neonates served as confirmation that the presence of IgG was not due to maternal blood contamination (data not shown).

The findings on predictors of neonatal serology levels are limited by clinical data capture, and the sample size may obscure other predictors of neonatal serology response. In addition, the data on maternal oxygen supplementation used in the multiple linear regression analysis was limited to a small number of patients, and we suspect that oxygen supplementation in the mothers is a marker of disease severity.

Conclusions. These data on the timing of the IgG and IgM response following infection and the duration of the antibody response during pregnancy may help inform the use of a protective vaccine for pregnant women. Our findings suggest that maternal vaccination that stimulates maternal IgG response may confer protection to the neonate. Furthermore, a certain level of maternal IgG may be necessary to transfer sufficient antibody to the neonate.

References

1. Sutton D, Fuchs K, D'Alton M, Goffman D. Universal Screening for SARS-CoV-2 in Women Admitted for Delivery. *N Engl J Med*. 2020;382(22):2163-2164. doi:10.1056/nejmc2009316
2. Campbell KH, Tornatore JM, Lawrence KE, et al. Prevalence of SARS-CoV-2 Among Patients Admitted for Childbirth in Southern Connecticut. *JAMA*. 2020:E1-E2. doi:10.1056/nejmc2009316
3. Zambrano LD, Ellington S, Strid P, et al. Update: Characteristics of Symptomatic Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status — United States, January 22–October 3, 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69(44):1641-1647. doi:10.15585/mmwr.mm6944e3
4. Prabhu M, Cagino K, Matthews KC, et al. Pregnancy and postpartum outcomes in a universally tested population for SARS-CoV-2 in New York City: A prospective cohort study. *BJOG An Int J Obstet Gynecol*. 2020;127(12):1548-1556. doi:10.1111/1471-0528.16403
5. DeBolt CA, Bianco A, Limaye MA, et al. Pregnant women with severe or critical COVID-19 have increased composite morbidity compared to non-pregnant matched controls. *Am J Obstet Gynecol*. 2020:19-21. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7657940/pdf/main.pdf.
6. Pirjani R, Hosseini R, Soori T, et al. Maternal and neonatal outcomes in COVID-19 infected pregnancies: A prospective cohort study. *J Travel Med*. 2020;27(7). doi:https://doi.org/10.1093/jtm/taaa158
7. Marín Gabriel MA, Reyne Vergeli M, Caserío Carbonero S, et al. Maternal,

Perinatal and Neonatal Outcomes With COVID-19: A multicenter study of 242 pregnancies and their 248 infant newborns during their first month of life. *Pediatr Infect Dis J*. 2020;39(12):e393-e397. doi:10.1097/inf.0000000000002902

8. Antoun L, El N, Ahmed I, Patni S, Honest H. Maternal COVID-19 infection, clinical characteristics, pregnancy, and neonatal outcome: A prospective cohort study. *Eur J Obstet Gynecol Reprod Biol*. 2020;252:559-562. doi:10.1016/j.ejogrb.2020.07.008

9. Allotey J, Stallings E, Bonet M, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: Living systematic review and meta-analysis. *BMJ*. 2020;370(m3320). doi:10.1136/bmj.m3320

10. Di Toro F, Gjoka M, Di Lorenzo G, et al. Impact of COVID-19 on maternal and neonatal outcomes: a systematic review and meta-analysis. *Clin Microbiol Infect*. 2021;27(1):36-46. doi:10.1016/j.cmi.2020.10.007

11. Ellington S, Strid P, Tong VT, et al. Characteristics of Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status - United States, January 22-June 7, 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69(25):769-775. https://www.uptodate.com/contents/coronavirus-disease-2019-covid-19-pregnancy-issues/print.

12. Zullo F, Di Mascio D, Saccone G. COVID-19 Antibody Testing in Pregnancy. *Am J Obstet Gynecol*. 2020;Pre-print.

13. Peeling RW, Wedderburn CJ, Garcia PJ, et al. Serology testing in the COVID-19 pandemic response. *Lancet Infect Dis*. 2020;3099(20):1-5. doi:10.1016/S1473-

3099(20)30517-X

14. Villalaín C, Herraiz I, Luczkowiak J, et al. Seroprevalence analysis of SARS-CoV-2 in pregnant women along the first pandemic outbreak and perinatal outcome. *PLoS One*. 2020;15(11):e0243029. doi:10.1371/journal.pone.0243029

15. Yang HS, Racine-Brzostek SE, Lee WT, et al. SARS-CoV-2 antibody characterization in emergency department, hospitalized and convalescent patients by two semi-quantitative immunoassays. *Clin Chim Act*. 2020;Oct(509):117-125. doi:10.1016/j.cca.2020.06.004

16. Long QX, Liu BZ, Deng HJ, et al. Antibody responses to SARS-CoV-2 in patients with COVID-19. *Nat Med*. 2020. doi:10.1038/s41591-020-0897-1

17. To KKW, Tsang OTY, Leung WS, et al. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. *Lancet Infect Dis*. 2020;20(5):565-574. doi:10.1016/S1473-3099(20)30196-1

18. Zhang B, Zhou X, Zhu C, et al. Immune phenotyping based on neutrophil-to-lymphocyte ratio and IgG predicts disease severity and outcome for patients with COVID-19. *medRxiv*. 2020. doi:10.1101/2020.03.12.20035048

19. Long QX, Tang XJ, Shi QL, et al. Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections. *Nat Med*. 2020. doi:10.1038/s41591-020-0965-6

20. Winter AK, Hegde ST. The important role of serology for COVID-19 control. *Lancet Infect Dis*. 2020. doi:10.1016/S1473-3099(20)30322-4

21. Mor G, Cardenas I. The immune system in pregnancy: A Unique Complexity. *Am*

J Reprod Immunol. 2011;63(6):425-433. doi:10.1111/j.1600-0897.2010.00836.x.The

22. Crovetto F, Crispi F, Llurba E, Figueras F, Gómez-Roig MD, Gratacós E. Seroprevalence and presentation of SARS-CoV-2 in pregnancy. *Lancet*. 2020;396(10250):530-531. doi:10.1016/S0140-6736(20)31714-1

23. Flannery DD, Gouma S, Dhudasia MB, et al. SARS-CoV-2 seroprevalence among parturient women in Philadelphia. *Sci Immunol*. 2020;5(49):1-6. doi:10.1126/sciimmunol.abd5709

24. Pettirosso E, Giles M, Cole S, Rees M. COVID-19 and pregnancy: A review of clinical characteristics, obstetric outcomes and vertical transmission. *Aust New Zeal J Obstet Gynaecol*. 2020:1-20. doi:10.1111/ajo.13204

25. Vivanti AJ, Vauloup-Fellous C, Prevot S, et al. Transplacental transmission of SARS-CoV-2 infection. *Nat Commun*. 2020;11(3572):1-7. doi:10.1038/s41467-020-17436-6

26. Alzamora MC, Paredes T, Caceres D, Webb CM, Valdez LM, La Rosa M. Severe COVID-19 during Pregnancy and Possible Vertical Transmission. *Am J Perinatol*. 2020;1(212). doi:10.1055/s-0040-1710050

27. Dong L, Tian J, He S, et al. Possible Vertical Transmission of SARS-CoV-2 From an Infected Mother to Her Newborn. *JAMA*. 2020;323(18):1846-1848. doi:10.1093/phe/phw039

28. Zeng L, Xia S, Yuan W, et al. Neonatal Early-Onset Infection with SARS-CoV-2 in 33 Neonates Born to Mothers with COVID-19 in Wuhan, China. *JAMA Pediatr*. 2020;23(77):2-4. doi:10.1001/jamapediatrics.2020.0878

29. Lamouroux A, Attie-Bitach T, Martinovic J, Leruez-Ville M, Ville Y. Evidence for and against vertical transmission for severe acute respiratory syndrome coronavirus 2. *Am J Obstet Gynecol*. 2020;223(1):91.e1-e91.e4. http://repositorio.unan.edu.ni/2986/1/5624.pdf.

30. Shah PS, Diambomba Y, Acharya G, Morris SK, Bitnun A. Classification system and case definition for SARS-CoV-2 infection in pregnant women, fetuses, and neonates. *Acta Obstet Gynecol Scand*. 2020;99(5):565-568. doi:10.1111/aogs.13870

31. Zeng H, Xu C, Fan J, et al. Antibodies in Infants Born to Mothers With COVID-19 Pneumonia. *JAMA*. 2020;323(18):1848-1849. doi:10.1038/2101070a0

32. Toner LE, Gelber SE, Pena JA, Fox NS, Rebarber A. A Case Report to Assess Passive Immunity in a COVID Positive Pregnant Patient. *Am J Perinatol*. 2020;10029:98-100. doi:10.1055/s-0040-1715643

33. Sethuraman N, Jeremiah SS, Ryo A. Interpreting Diagnostic Tests for SARS-CoV-2. *JAMA - J Am Med Assoc*. 2020;Pre-print:E1-E3. doi:10.1001/jama.2020.8259

FIGURE LEGENDS:

Figure 1: IgG and IgM levels in symptomatic and asymptomatic pregnant women. Comparison of the level of IgG (**A**) and IgM (**B**) serology values in asymptomatic (beige, N=51) and symptomatic (green, N=37) pregnant women. All positive serology cutoff is 1 (dashed line). Values are shown on $\log_2$ scale.

Figure 2: Timing of Serologic Response in Pregnant women.

Serologic results were plotted as a function of time to better understand the timing of antibody response. **A,** IgG (blue) and IgM (red) values per pregnant woman plotted as a function of elapsed time from first COVID-19 symptoms. All positive serology cutoff is 1 (dashed line). Values are shown on $\log_2$ scale. Data is plotted as a LOESS curve for each group. Shaded regions indicate 95% confidence intervals derived during LOESS.

Fig. 3: Passive immunity and the serology levels in neonates.

Neonates were tested for serology in order to understand the rate of passive immunity and the pattern of passive immunity between mother to child. **A,** Neonates that are serology negative (beige) vs. IgG positive (purple). No neonates were IgM positive. **B,** Maternal IgG antibody levels grouped by those mothers who gave birth to serology positive neonates (purple, N=39) or the mothers that gave birth to serology negative neonates (beige, N=11). **C,** IgG levels of mothers vs. IgG levels of neonates. All positive serology cutoff is 1 (dashed line). Values are shown on $\log_2$ scale.

Figure 1

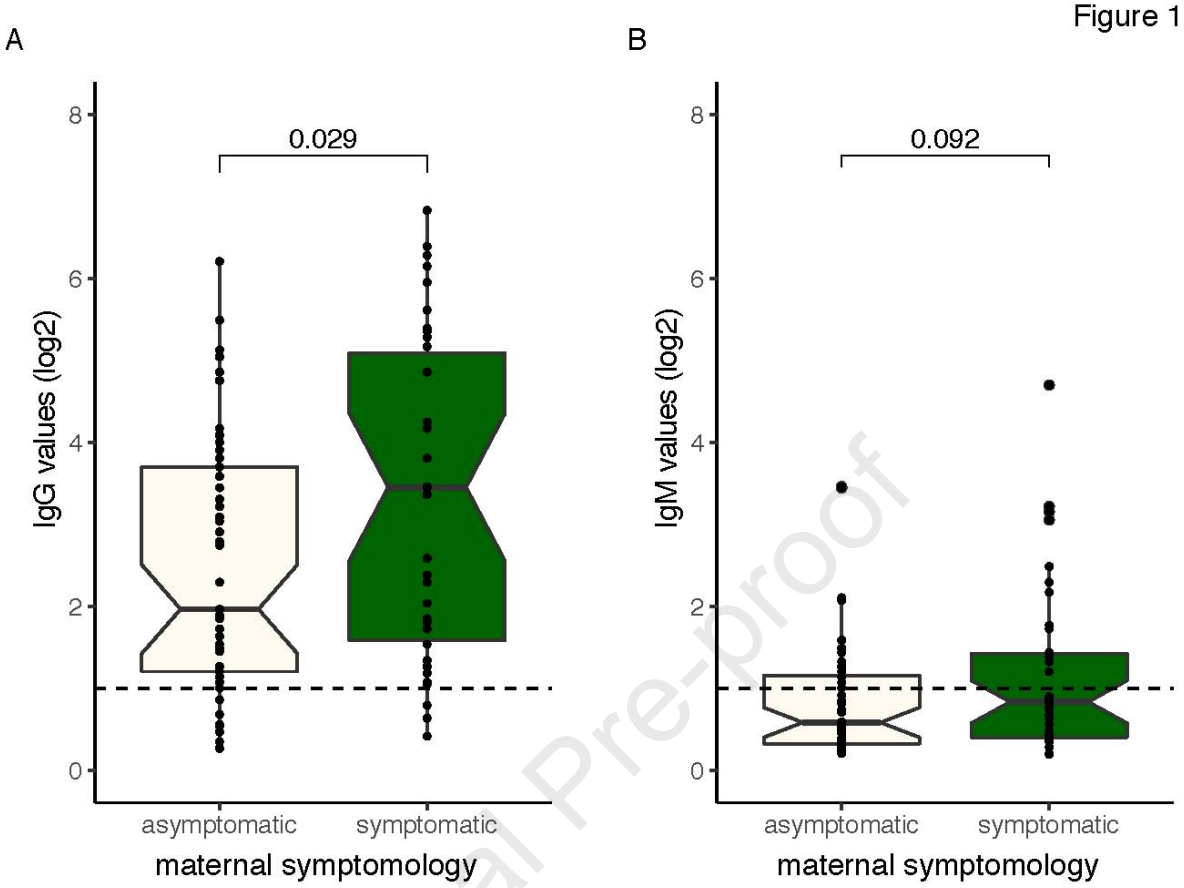

Figure 2

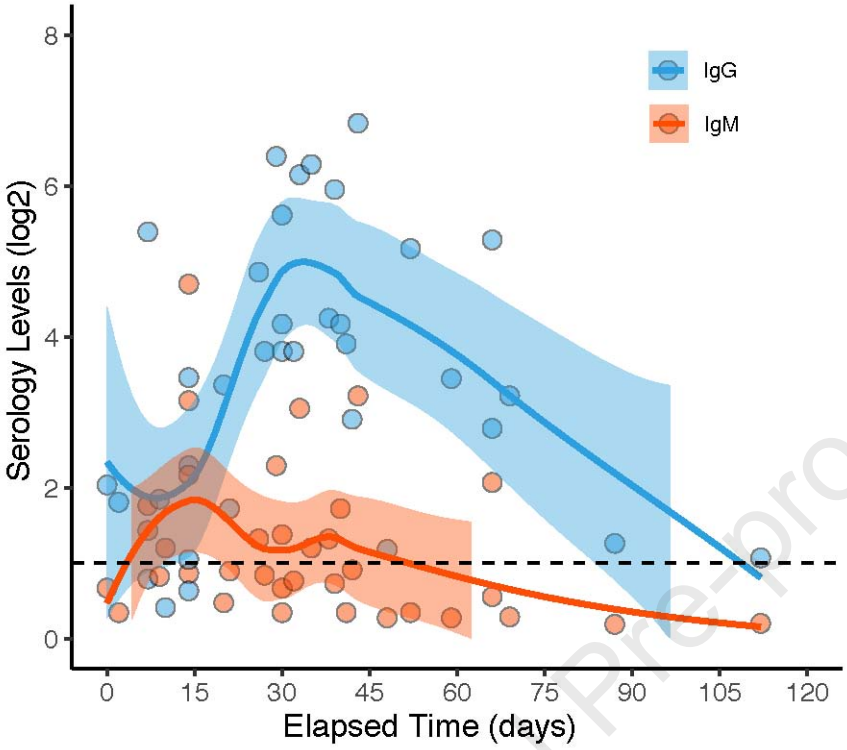

Figure 3