Elsevier Editorial System(tm) for European Journal of Obstetrics & Gynecology and Reproductive Biology
Manuscript Draft

Manuscript Number: EJOGRB-20-22875R1

Title: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) universal screening in gravids during labor and delivery

Article Type: SI: Infections in Pregnancy

Section/Category: Obstetrics

Keywords: SARS-CoV-2; COVID-19; delivery; reverse-transcription polymerase chain reaction (RT-PCR); serum immunoglobulins; screening

Corresponding Author: Dr. Ricardo Saviron-Cornudella, M.D.

Corresponding Author's Institution: Hospital General de Villalba

First Author: Ricardo Saviron-Cornudella, M.D.

Order of Authors: Ricardo Saviron-Cornudella, M.D.; Ana Villalba, MD; Javier Zapardiel, MD; Luis M Esteban, MD; Mercedes Andeyro-Garcia, MD; Faustino R Pérez-López, MD

Abstract: Objective: To screen pregnant women at risk of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection during delivery using reverse-transcription polymerase chain reaction (RT-PCR) test and serum immunoglobulin (Ig) testing.
Method: Between March 31st and August 31st of 2020, consecutive pregnant women admitted for labor and delivery in a single hospital were screened for SARS-CoV-2 with nasopharyngeal RT-PCR swab tests and detection of serum IgG and IgM.
Results: We studied 266 pregnant women admitted for labor and delivery. The prevalence of acute or past SARS-CoV-2 infection was 9.0 %, including (i) two cases with respiratory symptoms of SARS-Co-V-2 infection and positive RT-PCR; (ii) four asymptomatic women with positive RT-PCR without clinical symptoms and negative serological tests between two and 15 weeks later; and (iii) two women with false positive RT-PCR due to technical problems. All newborns of the 6 pregnant women with RT-PCR positive had negative RT-PCR and did not require Neonatal Intensive Care Unit admission. There were eighteen asymptomatic women with positive serological IgG tests and negative RT-PCR.
Conclusion: In our cohort of gravids, we found 2.2% of women with positive RT-PRC tests and 6.7% with positive serological tests during the first wave of the SARS-CoV-2 pandemic.

Revision note, 8 November 2020
European Journal of Obstetrics & Gynecology and Reproductive Biology
Ref.: Ms. No. EJOGRB 02745 Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) universal screening in gravids during labor and delivery

Dear Prof. Gupta

We want to thank for the suggestions concerning our manuscript. All comments were appreciated and quite helpful in revising and improving our manuscript. The revised sections are marked in **blue bold** in the manuscript.

We do hope this R1 version be accepted for publication.

Kind regards

Dr. Ricardo Savirón-Cornudella

Reviewer #2: I can not make any clinical or epidemiological relevance of the paper and the authors did not point out any apart from pointing out that their numbers match other observations in their area.

In row 153, we have added the description of Fasset et al., Vintilezos et al., and Knight et al. results in screening in pregnant women.

In row 182, we have added the description of Flannery et al., and Haizler-Cohen et al. results on their serological test studies to give better context to the situation of the current test results.

In row 227, we have highlighted the current clinical and epidemiological importance of the SARS-CoV-2 screening tests.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) universal screening in gravids during delivery

Ricardo Savirón-Cornudella[a*], Ana Villalba[a], Javier Zapardiel[b], Mercedes Andeyro-Garcia[a], Luis M. Esteban[c], Faustino R. Pérez-López[d]

a. Department of Obstetrics and Gynecology, Hospital Universitario General de Villalba, Madrid, Spain

b. Department of Microbiology, Hospital Universitario General de Villalba, Madrid, Spain

c. Escuela Universitaria Politécnica de La Almunia. Universidad de Zaragoza. Zaragoza. Spain.

d. Instituto de Investigación Sanitaria de Aragón and University of Zaragoza Faculty of Medicine, Zaragoza, Spain

*Corresponding Author at Department of Obstetrics and Gynecology. Hospital Universitario General de Villalba. Address: Camino de Moralzarzal M-608 Km. Calle Alpedrete 41. 28400 Collado Villalba. Madrid. Spain. ricardo.saviron@hgvillalba.es

Short title: Gravids and screening of COVID-19

Word count of the main text: 2,071words**; Figure:** One; **Table:** One

Declaration of interest: none.

ORCID Identifications

Ricardo Savirón-Cornudella 0000-0001-9585-0187

Ana Villalba Gutierrez 0000-0001-5259-6940

Javier Zapardiel Ferrero

Mercedes Andeyro-Garcia 0000-0003-3500-8822

Luis M. Esteban 0000-0002-3007-302X

Faustino R. Pérez-López 0000-0002-2801-416X

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) universal screening in gravids during delivery: Detection of virus and antibodies

Short title: SARS-CoV-2 screening during delivery

Word count of the main text: 2,071

Figures: 1

Table: 1

Abstract

Objective: To screen pregnant women at risk of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection during delivery using reverse-transcription polymerase chain reaction (RT-PCR) test and serum immunoglobulin (Ig) testing.
Method: Between March 31st and August 31st of 2020, consecutive pregnant women admitted for labor and delivery in a single hospital were screened for SARS-CoV-2 with nasopharyngeal RT-PCR swab tests and detection of serum IgG and IgM.
Results: We studied 266 pregnant women admitted for labor and delivery. The prevalence of acute or past SARS-CoV-2 infection was 9.0 %, including (i) two cases with respiratory symptoms of SARS-Co-V-2 infection and positive RT-PCR; (ii) four asymptomatic women with positive RT-PCR without clinical symptoms and negative serological tests between two and 15 weeks later; and (iii) two women with false positive RT-PCR due to technical problems. All newborns of the 6 pregnant women with RT-PCR positive had negative RT-PCR and did not require Neonatal Intensive Care Unit admission. There were eighteen asymptomatic women with positive serological IgG tests and negative RT-PCR.
Conclusion: In our cohort of gravids, we found 2.2% of women with positive RT-PRC tests and 6.7% with positive serological tests during the first wave of the SARS-CoV-2 pandemic.
Keywords: SARS-CoV-2; COVID-19; delivery; reverse-transcription polymerase chain reaction (RT-PCR); serum immunoglobulins; screening

1. Introduction

There are several strategies to diagnose the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection related to coronavirus disease (COVID-19) and to identify the current or past infection and immune status. The preferred primary method for screening is the reverse-transcription polymerase chain reaction (RT-PCR) using upper respiratory samples via nasopharyngeal or oropharyngeal swabs [1,2]. The procedure has been demonstrated to be highly specific (95%) [3,4] and sensitive (70%) in samples from non-pregnant women [4]. The RT-PCR may detect the current or past presence of viral material whereas the serological tests assess the formation of antibodies to SARS-CoV-2 and may help to demonstrate a current infection [5]. The antibody tests for serum immunoglobulin (Ig) M (IgM), IgG, and IgA are based in the demonstration of those antibodies in human serum as a diagnostic tool of SARS-Co-V-2. These antibodies can be demonstrated in blood samples of patients RT-PCR positive 2-12 days after symptoms started and depending on sociodemographic factors [6].

In asymptomatic pregnant women admitted for delivery, the reported positive SARS-COV-2 screening with the RT-PCR tests is 86-88%, which is similar to those in the general population [7,8]. However, the prevalence of those positive tests are variable depending on the study location and delivery facilities [8-12]. There are different techniques for antibody titration against SARS-CoV-2, including rapid IgM-IgG antibody tests, chemiluminescence immunoassay, and enzyme-linked immunosorbent assay (ELISA), and. The ELISA technique has a sensitivity of 89% and a specificity of 91% [13], although it varies according on the day of analysis since symptoms onset [14].

The objective of the present study is to evaluate the clinical manifestations and the performance of two different tests, RT-PCR and serological testing, for screening of pregnant women admitted to the maternity ward for delivery.

2. Methods

This observational retrospective cohort study was conducted between the 31st of March and 31st of August, 2020, at the *Hospital Universitario General de Villalba*, located in the North of Madrid which attends 700-800 deliveries per year. The study was approved by the Fundación Jiménez Díaz Clinical Research Ethics Committee, Madrid, Spain (protocol EO107-20). A total of 266 pregnant women admitted to labor and delivery and to scheduled procedures such as labor induction or caesarean delivery, were screened by RT-

PCR in nasopharyngeal swabs and by a rapid blood antibodies rapid test. In cases with positive RT-PCR or positive antibodies rapid test for IgM and/or IgG, serological testing by ELISA was also carried out to confirm the results.

The RT-PCR measurements were carried out using the MagMAX Viral/Pathogen II Nucleic Acid Isolation reagents in a KinGFisher Flex Purification System. PCR reagents were the Viasure SARS-CoV-2 real time RT-PCR detection it measured in a Bio-Rad CFX96 platform (TaqPath™ COVID-19 Combo Kit Multiplex Real Time RT-PCR). The rapid antbody test is a lateral flow immunochromatographic assay carried out using the test Biozek COVID-19 IgG/IgM Rapid Test Cassette. The ELISA serological presence of Igs was determined for IgG with Abbott reactive and for IgM with Vircell reactive.

We collected demographic, clinical (fever, cough, rhinorrhea, dyspnea, chest pain, diarrhea, myalgia, new anosmia or ageusia), obstetric and perinatal data for each woman admitted, as well as, RT-PCR and serological results. Every woman was classified in one of the three SARS-CoV-2 categories: (i) acute infection (positive RT-PCR); (ii) healed women (negative RT-PCR with positive IgG); (iii) and never infected women (both negative RT-PCR and IgG).

3. Results

During the period of the study, 266 pregnant women admitted for labor and delivery were submitted to the SARS-Co-V-2 screening with RT-PCRs. The prevalence of acute or healed COVID-19 infection was 9.0 %, corresponding to 18 past SARS-CoV-2 exposures and six current infections (**Figure 1**).

There were eight positive RT-PCR for SARS-CoV-2, although two of them were categorized as laboratory misinterpretation of results after women were discharged from the hospital. As expected, these two cases had no clinical symptoms and were negative for ELISA antibody tests. Therefore, we finally counted six positive RT-PCR women, of whom two had COVID-19 symptoms during labor or delivery (one patient was only IgM positive and the other had no serological test)**,** and four were asymptomatic (**Table 1**). One of the two symptomatic cases with positive RT-PCR was diagnosed with intrauterine growth restriction. The four asymptomatic and positive RT-PCR pregnant women were negative in the ELISA study for both IgM and IgG during hospitalization. These four cases were submitted to second ELISA immune tests five to 15 weeks after delivery being negative once again. All six cases were vaginal deliveries without neonatal acidosis, no

newborn required for admission to the Neonatal Intensive Care Unit, and also they all were RT-PCR negative. Symptomatic women were discharged on the third day and evolved favorably, as did their newborns.

All negative RT-PCR cases (n = 260) were asymptomatic throughout the whole hospitalization and 18 of them were positive for IgG, being considered as past SARS-CoV-2 exposure.

4. Discussion

In a group of 266 pregnant women SARS-CoV-2 exposure was screened with RT-PCR tests during delivery. There were eight RT-PCR positive patients including two women with clinical evidence of SARS-CoV-2 infection, four past viral exposure and two false positive due to technical problems. All these 8 neonates were healthy without clinical signs of virus infection and negative RT-PCR tests. Serological IgG specific antibodies addressed against the SARS-CoV-2 were present in 18 women with negative RT-PCR tests. Therefore, the prevalence of acute or past SARS-CoV-2 infection was 9.0 % in our cohort, which is similar to the prevalence in non-pregnant subjects studied by seroprevalence in the Madrid area [15]. The maternal ELISA tests, in the four RT-PCR positive and asymptomatic, repeated 2-15 weeks after delivery were negative.

Dust et al. [16] reported the performance of different commercial SARS-CoV-2 RT-PCR assays testing clinical samples and reference material, ranging the sensitivity from 24 copies/mL to 574/mL specimen. However, the RT-PCR sensitivity, specificity, and positive or negative predictive values are still very difficult to determine without clear gold standard tests for SARS-COV-2 [17]. Previous studies have described positive RT-PCR in asymptomatic pregnant women rates ranging between 50% and 89% [8,9,11,12], our 66.7 % in our small sample seems to fit well within reported ranges.

Different studies have addressed the false-negative rate of the RT-PCR tests, ranging from 17.0 to 63.0 % [18]. We did not have patients with negative RT-PCR and symptoms suggestive of COVID-19. Less information is available about the false positive rate. Cohen et al. [19] reported a 2.3% false-positive rate that was most likely related to contamination from other positive samples analyzed at the same time, target genes amplified from prior positive samples or positive controls, or misinterpretation of results.

SARS-CoV-2 serological testing can usually demonstrate IgM from 5th until the 21st day of the infection and IgG within 10-20 days after the symptom onset, although it is

still unknown for how long antibodies will be produced [20]. The serological test may reach a specificity of 98.7% depending on the timing of sampling [5].

SARS-CoV-2 serology is complementary to RT-PCR for the COVID-19 diagnosis during at least 14 days after clinical infection initiation [21]. In a meta-analysis, the pooled ELISA methods have a sensitivity of 84% for measuring IgG or IgM as compared to lateral flow immunoassays of 66.0% and chemiluminescent immunoassays of 97.8% in the general population [22]. Total antibody determination has low sensitivity during the first weeks with clinical symptoms (30.1%), increasing during the second week to reach the highest levels during the third week. There is limited information beyond 35 days post-initiation of clinical symptoms [5].

There is scarce information concerning the antibody formation dynamic in pregnant women with SARS-Co-V-2 infection around the period of delivery. In an unselected cohort of German pregnant women, Zollkau et al. [23] reported a total of 225 PCRs and 180 IgG tests, finding only one case with a positive IgG test. We detected positive IgG serological tests in 18 asymptomatic women. None of our asymptomatic patients with positive RT-PCR developed antibodies during the study period. Pregnant women are considered a relatively low-risk group for COVID-19 since they are generally young [24, 25]. However, there are also results suggesting that SARS-Co-V-2 is more likely associated with some adverse clinical conditions due to anatomic and physiological changes during pregnancy [26]. In addition, preeclampsia, excessive body weight and socioeconomic disparities may be potential cofactors to worsen the obstetric and perinatal results [27]. On the other hand, pregnant women during their third trimester of gestation and labor may display atypical features, including the absence of fever as well as leukocytosis. From our own experience, in asymptomatic patients with positive RT-PCR we have to review RT-PCR in search of false positives and take into account perform antibody tests.

Limitations

We had two false positive RT-PCR for misinterpreting the test during the period of maximum incidence of the pandemic and probably related to initial learning curve of the technique. The false positive RT-PCR results may have a negative impact on clinical practice and emotional for pregnant women and their families, increasing specific assistance for a suspicious women and epidemiological statistics. Previous studies have reported both false positive and false negative rates for RT-PCR. Cohen and Kessel [19]

meta-analyzed studies reporting at least 100 negative RT-PCR tests with a global 3.2% rate for false positive results which could at least partially explain reports of large numbers of asymptomatic carriers of SARS-CoV-2.

Our two positive RT-PCR women were asymptomatic during the follow up with and were negative in the control serological tests. We do not know if we have had any false negative RT-PCR in asymptomatic patients, although we did not have positive IgM serologies in these cases either. It is interesting to note that asymptomatic cases with positive RT-PCR have shown negative IgM and IgG SARS-COV-2 antibodies by ELISA testing during hospitalization and four weeks after. There are several possible explanations, including (i) false positive RT-PCR cases for sample contamination for the false negative of antibody testing cases; (ii) true positive RT-PCR patients that have not developed antibodies because of the theoretical B-cell response against SARS-COV-2 [28] or with lower viral load, which has been associated to lower rates of seropositivity [29].

New methods are currently under development to detect SARS-CoV-2 combining simplified extraction of RNA with reverse transcription followed by isothermal amplification and clustered regularly interspaced short palindromic repeats mediated detection. This new approach has a sensitivity of 93.1% and a specificity of 98.5% [30].

Stregths of the study

Our study point out the relevance in that RT-PCR and antibody serologies are techniques that can be complementary in some circumstances. In particular, antibodies would be indicated in symptomatic patients or with positive chest images with negative RT-PCR and in asymptomatic patients with positive RT-PCR to clarify false positives and negatives. The performance of antibodies has also allowed us to know which patients have overcome the disease.

Conclusion

The pandemic nature of the COVID-19 has allowed designing different strategies to manage pregnant women according to available resources in different health care systems. We found that the systematic RT-PCR assessment and serological studies of SARS-CoV-2 seem appropriated to identify women at risk during labor and delivery. There were 2.2% of women with positive RT-PRC tests and 6.7% with positive serological tests during the first wave of the SARS-CoV-2 pandemic in Madrid. There is a need to contrast different

international experiences to effectively define the better models of clinical assistance during pregnancy and delivery since the pandemic nature of the virus.

Author contributions

RSC, JZ, MAG and FRPL contributed to the conception of the study. RSC, AV, LME and FRPL contributed to the design of the work. JZ and AV carried out data acquisition. All authors were involved in the interpretation of the study results, and the drafting and revision of the manuscript, and all approved the final version to be published.

Disclosure statement

The authors report no conflicts of interest and are alone responsible for the content and the writing of the article.

Funding / Source of support

This research did not receive any specific grant or was funded by any commercial or non-profit organization or public agency.

Details of ethics approval

The study was approved by the Fundación Jiménez Díaz Clinical Research Ethics Committee, Madrid, Spain (protocol EO107-20).

Data statement

The present study was based on clinical results obtained during the COVID-19 pandemic.

Declaration of Competing Interest

The authors report no conflicts of interest and are alone responsible for the content and the writing of the article.

Acknowledgments

None

References

1. Savirón-Cornudella R, Altamirano-Barcia IE, Chedraui P, Andeyro-García M, Tajada M, Pérez-López FR. The coronavirus disease (COVID) 2019 and human pregnancy: A scoping review. Gynecological and Reproductive Endocrinology and Metabolism 2020; 1(2):70-75 https://gremjournal.com/journal/02-2020/the-coronavirus-disease-covid-2019-and-human-pregnancy-a-scoping-review/
2. Pascarella G, Strumia A, Piliego C, et al. COVID-19 diagnosis and management: a comprehensive review. J Intern Med. 2020;288(2):192-206. doi:10.1111/joim.13091
3. Ai T, Yang Z, Hou H et al. Correlation of chest CT and RT-PCR testing in coronavirus disease 2019 (COVID-19) in China: a report of 1014 cases. Radiology. 2020 Aug;296(2):E32-E40.
4. Wang W, Xu Y, Gao R, et al. Detection of SARS-CoV-2 in different types of clinical specimens. JAMA. 2020 May 12;323(18):1843-1844.
5. Deeks JJ, Dinnes J, Takwoingi Y, et al. Antibody tests for identification of current and past infection with SARS-CoV-2. Cochrane Database Syst Rev. 2020 Jun 25;6(6):CD013652. doi: 10.1002/14651858.CD013652.
6. Flannery DD, Gouma S, Dhudasia MB, et al. SARS-CoV-2 seroprevalence among parturient women in Philadelphia. Sci Immunol. 2020 Jul 29;5(49):eabd5709. doi: 10.1126/sciimmunol.abd5709.
7. Li R, Pei S, Chen B, et al. Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (SARS-CoV2). Science. 2020 May 28;382(22):2163-2164.
8. 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 May 28;382(22):2163-2164.
9. Ceulemans D, Thijs I, Schreurs A, et al. Screening for COVID-19 at childbirth: is it effective?. Ultrasound Obstet Gynecol. 2020;56(1):113-114. doi:10.1002/uog.22099
10. Fassett MJ, Lurvey LD, Yasumura L, et al. Universal SARS-Cov-2 Screening in Women Admitted for Delivery in a Large Managed Care Organization. Am J Perinatol. 2020 Sep;37(11):1110-1114.
11. Herraiz I, Folgueira D, Villalaín C, Forcén L, Delgado R, Galindo A. Universal screening for SARS-CoV-2 before labor admission during Covid-19 pandemic in Madrid. J Perinat Med. 2020;/j/jpme.ahead-of-print/jpm-2020-0236/jpm-2020-0236.xml. doi:10.1515/jpm-2020-0236
12. 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. 2020;10.1111/1471-0528.16403. doi:10.1111/1471-0528.16403
13. Zullo F, Di Mascio D, Saccone G. COVID-19 Antibody Testing in Pregnancy. Am J Obstet Gynecol MFM. 2020;2(3):100142. doi: 10.1016/j.ajogmf.2020.100142
14. Zhao J, Yuan Q, Wang H, et al. Antibody responses to SARS-CoV-2 in patients of novel

coronavirus disease 2019. Clin Infect Dis. 2020 Mar 28:ciaa344.

15. Pollán M, Pérez-Gómez B, Pastor-Barriuso R, et al. Prevalence of SARS-CoV-2 in Spain (ENE-COVID): a nationwide, population-based seroepidemiological study. Lancet. 2020 Aug 22;396(10250):535-544.
16. Dust K, Hedley A, Nichol K, et al. Comparison of Commercial Assays and Laboratory Developed Tests for Detection of SARS-CoV-2. J Virol Methods. 2020;113970. doi:10.1016/j.jviromet.2020.113970
17. Mahendiratta S, Batra G, Sarma P, et al. Molecular diagnosis of COVID-19 in different biologic matrix, their diagnostic validity and clinical relevance: A systematic review. Life Sci. 2020 Oct 1;258:118207.
18. Kelly JC, Dombrowksi M, O'Neil-Callahan M, Kernberg AS, Frolova AI, Stout MJ. False-negative testing for severe acute respiratory syndrome coronavirus 2: consideration in obstetrical care. Am J Obstet Gynecol MFM. 2020;2(3):100130. doi:10.1016/j.ajogmf.2020.100130
19. Cohen A.N., Kessel B. False positives in reverse-transcription PCR testing for SARS-CoV-2. medRxiv. 2020 doi: 10.1101/2020.04.26.20080911.
20. Long Q, Liu B, Deng H, et al. Antibody responses to SARS-CoV-2 in patients with COVID-19. Nat Med. 2020 Jun;26(6):845-848. doi: 10.1038/s41591-020-0897-1. Epub 2020 Apr 29. PMID: 32350462.
21. Marlet J, Petillon C, Ragot E, et al. Clinical performance of four immunoassays for antibodies to SARS-CoV-2, including a prospective analysis for the diagnosis of COVID-19 in a real-life routine care setting. J Clin Virol. 2020;132:104633. doi:10.1016/j.jcv.2020.104633
22. Lisboa Bastos M, Tavaziva G, Abidi SK, et al. Diagnostic accuracy of serological tests for covid-19: systematic review and meta-analysis. BMJ. 2020;370:m2516. doi:10.1136/bmj.m2516
23. Zöllkau J, Baier M, Scherag A, Schleußner E, Groten T. Periodenprävalenz von SARS-CoV-2 in einer unselektierten Stichprobe schwangerer Frauen in Jena, Thüringen [Period Prevalence of SARS-CoV-2 in an Unselected Sample of Pregnant Women in Jena, Thuringia]. Z Geburtshilfe Neonatol. 2020;224(4):194-198. doi:10.1055/a-1206-1033
24. Huntley BJF, Huntley ES, Di Mascio D, Chen T, Berghella V, Chauhan SP. Rates of Maternal and Perinatal Mortality and Vertical Transmission in Pregnancies Complicated by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-Co-V-2) Infection: A Systematic Review. Obstet Gynecol. 2020;136(2):303-312. doi:10.1097/AOG.0000000000004010
25. Khalil A, Kalafat E, Benlioglu C, et al. SARS-CoV-2 infection in pregnancy: A systematic review and meta-analysis of clinical features and pregnancy outcomes. EClinicalMedicine. 2020;25:100446. doi:10.1016/j.eclinm.2020.100446

26. Diriba K, Awulachew E, Getu E. The effect of coronavirus infection (SARS-CoV-2, MERS-CoV, and SARS-CoV) during pregnancy and the possibility of vertical maternal-fetal transmission: a systematic review and meta-analysis. Eur J Med Res. 2020;25(1):39. Published 2020 Sep 4. doi:10.1186/s40001-020-00439-w

27. Barbero P, Mugüerza L, Herraiz I, et al. SARS-CoV-2 in pregnancy: characteristics and outcomes of hospitalized and non-hospitalized women due to COVID-19. J Matern Fetal Neonatal Med. 2020;1-7. doi:10.1080/14767058.2020.1793320

28. Soresina A, Moratto D, Chiarini M, et al. Two X-linked agammaglobulinemia patients develop pneumonia as COVID-19 manifestation but recover. Pediatr Allergy Immunol. 2020 Apr 22:10.1111/pai.13263. doi: 10.1111/pai.13263. PMID: 32319118; PMCID: PMC7264678.

29. Wellinghausen N, Plonné D, Voss M, Ivanova R, Frodl R, Deininger S. SARS-CoV-2-IgG response is different in COVID-19 outpatients and asymptomatic contact persons. J Clin Virol. 2020;130:104542. doi:10.1016/j.jcv.2020.104542

30. Joung J, Ladha A, Saito M, et al. Detection of SARS-CoV-2 with SHERLOCK One-pot testing. New Engl J Med 2020; DOI: 10.1056/NEJMc2026172

Tables and figures

Table 1. Reverse transcription polymerase chain reaction (RT-PCR) positive cases in pregnant women (n = 8/266) admitted for delivery, maternal and newborn outcomes, and analytical results.

Figure 1. Flowchart of the SARS-CoV-2 screening and results in 266 pregnant women during delivery.

Table

Table 1. Reverse transcription polymerase chain reaction (RT-PCR) positive cases in pregnant women (n = 8/266) admitted for delivery, maternal and newborn outcomes, and analytical results.

Case	Maternal age (years), parity, delivery (weeks)	Maternal symptoms	Delivery	Newborn sex	Birth weight (grams)	Arterial umbilical cord blood pH	Apgar test 5´	Maternal RT-PCR	Maternal IgG[b] and IgM[a] (ELISA[c])	Maternal IgG[b] and IgM[a] control (ELISA[c])
1	26, 2, 37	Yes (fever and cough)	Vaginal	Female	2525	7.28	10	+	Not done	Not done
2	35, 1, 40	Yes (fever and cough)	Vaginal	Male	3480	7.30	10	+	+ / +	Not done
3	26, 3, 39	No	Vaginal	Female	3425	7.27	10	+	Not done	- (15 weeks)
4	32, 0, 40	No	Vaginal	Male	2805	7.20	10	+	- / -	- (2 weeks)
5	21, 0, 39	No	Vaginal	Male	3350	7.33	10	+	+ / -	- (12 weeks)
6	27, 0, 39	No	Vaginal	Female	3054	7.33	10	+	- / -	- (15 weeks)
7	31, 0, 40	No	Cesarean section (induction failure)	Male	3950	7.31	10	+ (false positive)	- / -	Not done
8	25, 0, 41	No	Vaginal	Female	3915	7.19	9	+ (false positive)	- / -	Not done

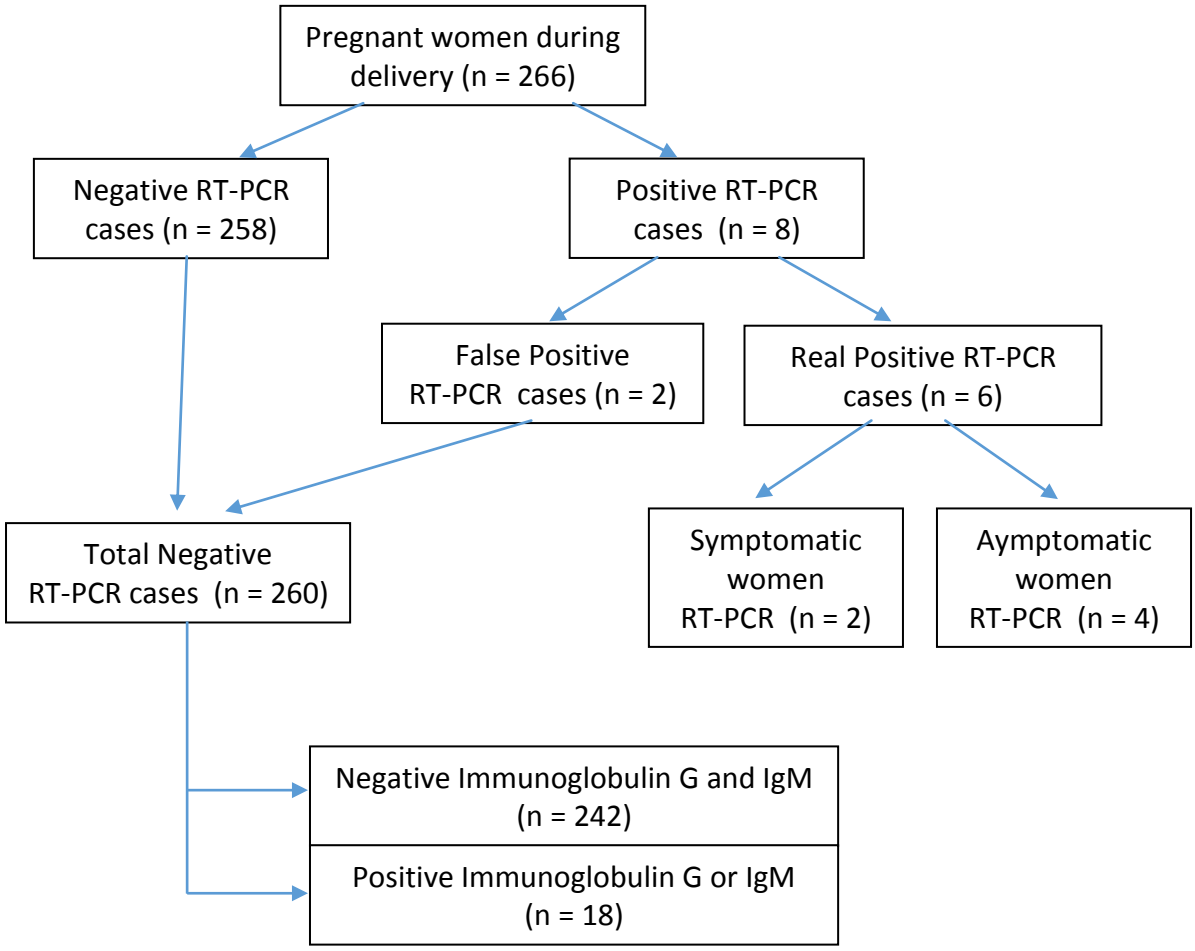
[a.] IgM: immunoglobulin M

[b.] IgG: immunoglobulin G

[c.] ELISA: enzyme-linked immunosorbent assay

Figure

Figure 1. Flowchart of the SARS-CoV-2 screening and results in 266 pregnant women during delivery.



Conflict of interest

The authors report no conflicts of interest. The authors alone are esponsible for the content and the writing of the article.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) universal screening in gravids during labor and delivery

Ricardo Savirón-Cornudella[a*], Ana Villalba[a], Javier Zapardiel[b], Mercedes Andeyro-Garcia[a], Luis M. Esteban[c], Faustino R. Pérez-López[d]

a. Department of Obstetrics and Gynecology, Hospital Universitario General de Villalba, Madrid, Spain

b. Department of Microbiology, Hospital Universitario General de Villalba, Madrid, Spain

c. Escuela Universitaria Politécnica de La Almunia. Universidad de Zaragoza. Zaragoza. Spain.

d. Instituto de Investigación Sanitaria de Aragón and University of Zaragoza Faculty of Medicine, Zaragoza, Spain

*Corresponding Author at Department of Obstetrics and Gynecology. Hospital Universitario General de Villalba. Address: Camino de Moralzarzal M-608 Km. Calle Alpedrete 41. 28400 Collado Villalba. Madrid. Spain. ricardo.saviron@hgvillalba.es

Short title: Gravids and screening of SARS-CoV-2

Word count of the main text: 2,255words**; Figure:** One; **Table:** One

Declaration of interest: none.

ORCID Identifications

Ricardo Savirón-Cornudella 0000-0001-9585-0187

Ana Villalba Gutierrez 0000-0001-5259-6940

Javier Zapardiel Ferrero 0000-0002-7680-4502

Mercedes Andeyro-Garcia 0000-0003-3500-8822

Luis M. Esteban 0000-0002-3007-302X

Faustino R. Pérez-López 0000-0002-2801-416X

Abstract

Objective: To screen pregnant women at risk of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection during delivery using reverse-transcription polymerase chain reaction (RT-PCR) test and serum immunoglobulin (Ig) testing.
Method: Between March 31st and August 31st of 2020, consecutive pregnant women admitted for labor and delivery in a single hospital were screened for SARS-CoV-2 with nasopharyngeal RT-PCR swab tests and detection of serum IgG and IgM.
Results: We studied 266 pregnant women admitted for labor and delivery. The prevalence of acute or past SARS-CoV-2 infection was 9.0 %, including (i) two cases with respiratory symptoms of SARS-Co-V-2 infection and positive RT-PCR; (ii) four asymptomatic women with positive RT-PCR without clinical symptoms and negative serological tests between two and 15 weeks later; and (iii) two women with false positive RT-PCR due to technical problems. All newborns of the 6 pregnant women with RT-PCR positive had negative RT-PCR and did not require Neonatal Intensive Care Unit admission. There were eighteen asymptomatic women with positive serological IgG tests and negative RT-PCR.
Conclusion: In our cohort of gravids, we found 2.2% of women with positive RT-PRC tests and 6.7% with positive serological tests during the first wave of the SARS-CoV-2 pandemic.
Keywords: SARS-CoV-2; COVID-19; labor and delivery; reverse-transcription polymerase chain reaction (RT-PCR); serum immunoglobulins; screening

1. Introduction

There are several strategies to diagnose the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection related to coronavirus disease (COVID-19) and to identify the current or past infection and immune status. The preferred primary method for screening is the reverse-transcription polymerase chain reaction (RT-PCR) using upper respiratory samples via nasopharyngeal or oropharyngeal swabs [1,2]. The procedure has been demonstrated to be highly specific (95%) [3,4] and sensitive (70%) in samples from non-pregnant women [4]. The RT-PCR may detect the current or past presence of viral material whereas the serological tests assess the formation of antibodies to SARS-CoV-2 and may help to demonstrate a current infection [5]. The antibody tests for serum immunoglobulin (Ig) M (IgM), IgG, and IgA are based in the demonstration of those antibodies in human serum as a diagnostic tool of SARS-Co-V-2. These antibodies can be demonstrated in blood samples of patients RT-PCR positive 2-12 days after symptoms started and depending on sociodemographic factors [6].

In asymptomatic pregnant women admitted for delivery, the reported positive SARS-COV-2 screening with the RT-PCR tests is 86-88%, which is similar to those in the general population [7,8]. However, the prevalence of those positive tests are variable depending on the study location and delivery facilities [8-12]. There are different techniques for antibody titration against SARS-CoV-2, including rapid IgM-IgG antibody tests, chemiluminescence immunoassay, and enzyme-linked immunosorbent assay (ELISA), and. The ELISA technique has a sensitivity of 89% and a specificity of 91% [13], although it varies according on the day of analysis since symptoms onset [14].

The objective of the present study is to evaluate the clinical manifestations and the performance of two different tests, RT-PCR and serological testing, for screening of pregnant women admitted to the maternity ward for delivery.

2. Methods

This observational retrospective cohort study was conducted between the 31st of March and 31st of August, 2020, at the *Hospital Universitario General de Villalba*, located in the North of Madrid which attends 700-800 deliveries per year. The study was approved by the Fundación Jiménez Díaz Clinical Research Ethics Committee, Madrid, Spain (protocol EO107-20). A total of 266 pregnant women admitted to labor and delivery and to scheduled procedures such as labor induction or caesarean delivery, were screened by RT-

PCR in nasopharyngeal swabs and by a rapid blood antibodies rapid test. In cases with positive RT-PCR or positive antibodies rapid test for IgM and/or IgG, serological testing by ELISA was also carried out to confirm the results.

The RT-PCR measurements were carried out using the MagMAX Viral/Pathogen II Nucleic Acid Isolation reagents in a KinGFisher Flex Purification System. PCR reagents were the Viasure SARS-CoV-2 real time RT-PCR detection it measured in a Bio-Rad CFX96 platform (TaqPath™ COVID-19 Combo Kit Multiplex Real Time RT-PCR). The rapid antibody test is a lateral flow immunochromatographic assay carried out using the test Biozek COVID-19 IgG/IgM Rapid Test Cassette. The ELISA serological presence of immunoglobulins was determined for IgG with Abbott reactive and for IgM with Vircell reactive.

We collected demographic, clinical (fever, cough, rhinorrhea, dyspnea, chest pain, diarrhea, myalgia, new anosmia or ageusia), obstetric and perinatal data for each woman admitted, as well as, RT-PCR and serological results. Every woman was classified in one of the three SARS-CoV-2 categories: (i) acute infection (positive RT-PCR); (ii) healed women (negative RT-PCR with positive IgG); (iii) and never infected women (both negative RT-PCR and IgG).

3. Results

During the period of the study, 266 pregnant women admitted for labor and delivery were submitted to the SARS-Co-V-2 screening with RT-PCRs. The prevalence of acute or healed COVID-19 infection was 9.0 %, corresponding to 18 past SARS-CoV-2 exposures and six current infections (**Figure 1**).

There were eight positive RT-PCR for SARS-CoV-2, although two of them were categorized as laboratory misinterpretation of results after women were discharged from the hospital. As expected, these two cases had no clinical symptoms and were negative for ELISA antibody tests. Therefore, we finally counted six positive RT-PCR women, of whom two had COVID-19 symptoms during labor or delivery (one patient was only IgM positive and the other had no serological test)**,** and four were asymptomatic (**Table 1**). One of the two symptomatic cases with positive RT-PCR was diagnosed with intrauterine growth restriction. The four asymptomatic and positive RT-PCR pregnant women were negative in the ELISA study for both IgM and IgG during hospitalization. These four cases were submitted to second ELISA immune tests five to 15 weeks after delivery being negative once again. All six cases were vaginal deliveries without neonatal acidosis, no

newborn required for admission to the Neonatal Intensive Care Unit, and also they all were RT-PCR negative. Symptomatic women were discharged on the third day and evolved favorably, as did their newborns. All negative RT-PCR cases (n = 260) were asymptomatic throughout the whole hospitalization and 18 of them were positive for IgG, being considered as past SARS-CoV-2 exposure.

4. Discussion

In a group of 266 pregnant women SARS-CoV-2 exposure was screened with RT-PCR tests during delivery. There were eight RT-PCR positive patients including two women with clinical evidence of SARS-CoV-2 infection, four past viral exposure and two false positive due to technical problems. All these 8 neonates were healthy without clinical signs of virus infection and negative RT-PCR tests. Serological IgG specific antibodies addressed against the SARS-CoV-2 were present in 18 women with negative RT-PCR tests. Therefore, the prevalence of acute or past SARS-CoV-2 infection was 9.0 % in our cohort, which is similar to the prevalence in non-pregnant subjects studied by seroprevalence in the Madrid area [15]. The maternal ELISA tests, in the four RT-PCR positive and asymptomatic, repeated 2-15 weeks after delivery were negative.

Dust et al. [16] reported the performance of different commercial SARS-CoV-2 RT-PCR assays testing clinical samples and reference material, ranging the sensitivity from 24 copies/mL to 574/mL specimen. However, the RT-PCR sensitivity, specificity, and positive or negative predictive values are still very difficult to determine without clear gold standard tests for SARS-COV-2 [17]. Previous studies have described positive RT-PCR in asymptomatic pregnant women rates ranging between 50% and 89% [8,9,11,12], our 66.7 % in our small sample seems to fit well within reported ranges. Different studies have addressed the false-negative rate of the RT-PCR tests, ranging from 17.0 to 63.0 % [18]. We did not have patients with negative RT-PCR and symptoms suggestive of COVID-19. Less information is available about the false positive rate. Cohen et al. [19] reported a 2.3% false-positive rate that was most likely related to contamination from other positive samples analyzed at the same time, target genes amplified from prior positive samples or positive controls, or misinterpretation of results.

Fasset et al. [10] reported a retrospective cohort study of 3,923 asymptomatic pregnant women screened for SARS-CoV-2 at labor and delivery in 15 hospitals in Southern California, reporting 17 women with a positive RT-PCR test, 24 had a fever on admission, and none developed the viral infection during the following 14 days.

Besides, neonates were negative for SARS-CoV-2 tests during the first day postpartum. Vintzileos et al. [20] reported a retrospective cohort describing a screening program for all pregnant adolescents and women admitted in labor and delivery (n = 161) in a single Hospital in New York using RT-PCR tests. They found that 20% (n = 32) of admitted women were positive for SARS-CoV-2 infection and 66% of these women were asymptomatic and all neonates were negative for viral infection. Another more recent publication reported prospective results from 3 other hospitals from New York including 675 women admitted at delivery [12]. They reported high rates of cesarean delivery in symptomatic COVID-19 (46.7%), asymptomatic COVID-19 (45.5%) and in women without COVID-19. In all these 3 studies from the United States SARS-CoV-2 serological tests were not used. Knight et al. [21] reported clinical outcomes of 427 pregnant women with confirmed SARS-CoV-2 infection from the United Kingdom National population cohort, including gravids admitted to hospital with confirmed SARS-CoV-2 infection by RT-PCR tests.

SARS-CoV-2 serological testing can usually demonstrate IgM from 5th until the 21st day of the infection and IgG within 10-20 days after the symptom onset, although it is still unknown for how long antibodies will be produced [22]. The serological test may reach a specificity of 98.7% depending on the timing of sampling [5]. SARS-CoV-2 serology is complementary to RT-PCR for the COVID-19 diagnosis during at least 14 days after clinical infection initiation [23]. In a meta-analysis, the pooled ELISA methods have a sensitivity of 84% for measuring IgG or IgM as compared to lateral flow immunoassays of 66.0% and chemiluminescent immunoassays of 97.8% in the general population [24]. Total antibody determination has low sensitivity during the first weeks with clinical symptoms (30.1%), increasing during the second week to reach the highest levels during the third week. There is limited information beyond 35 days post-initiation of clinical symptoms [5]. **Flannery et al. [6] performed serological tests in 1,293 women admitted at labor and delivery in Philadelphia, reporting that 6.2% had specific IgG and/or IgM against SARS-CoV-2. It is important to mention that of the 72 seropositive women, 46 (64%) were also RT-PCR positive. Haizler-Cohen et al. [25] postulated that PCR and serological tests may allow to establish the timing of infection: (i) the acute infection may displays a positive RT-PCR with negative serological testing; (ii) the past infection may have a negative RT-PCR and positive serological testing; (iii) when both tests are positive, the case may be a recent or past infection. It is accepted that a RT-PCR may remain positive for weeks after SARS-CoV-2 infection.**

There is scarce information concerning the antibody formation dynamic in pregnant women with SARS-Co-V-2 infection around the period of delivery. In an unselected cohort of German pregnant women, Zollkau et al. [26] reported a total of 225 PCRs and 180 IgG tests, finding only one case with a positive IgG test. We detected positive IgG serological tests in 18 asymptomatic women. None of our asymptomatic patients with positive RT-PCR developed antibodies during the study period. Pregnant women are considered a relatively low-risk group for COVID-19 since they are generally young [27, 28]. However, there are also results suggesting that SARS-Co-V-2 is more likely associated with some adverse clinical conditions due to anatomic and physiological changes during pregnancy [29]. In addition, preeclampsia, excessive body weight and socioeconomic disparities may be potential cofactors to worsen the obstetric and perinatal results [30]. On the other hand, pregnant women during their third trimester of gestation and labor may display atypical features, including the absence of fever as well as leukocytosis. From our own experience, in asymptomatic patients with positive RT-PCR we have to review RT-PCR in search of false positives and take into account perform antibody tests.

Limitations

We had two false positive RT-PCR for misinterpreting the test during the period of maximum incidence of the pandemic and probably related to initial learning curve of the technique. The false positive RT-PCR results may have a negative impact on clinical practice and emotional for pregnant women and their families, increasing specific assistance for a suspicious women and epidemiological statistics. Previous studies have reported both false positive and false negative rates for RT-PCR. Cohen and Kessel [19] meta-analyzed studies reporting at least 100 negative RT-PCR tests with a global 3.2% rate for false positive results which could at least partially explain reports of large numbers of asymptomatic carriers of SARS-CoV-2.

Our two positive RT-PCR women were asymptomatic during the follow up with and were negative in the control serological tests. We do not know if we have had any false negative RT-PCR in asymptomatic patients, although we did not have positive IgM serologies in these cases either. It is interesting to note that asymptomatic cases with positive RT-PCR have shown negative IgM and IgG SARS-COV-2 antibodies by ELISA testing during hospitalization and four weeks after. There are several possible explanations, including (i) false positive RT-PCR cases for sample contamination for the false negative

of antibody testing cases; (ii) true positive RT-PCR patients that have not developed antibodies because of the theoretical B-cell response against SARS-COV-2 [31] or with lower viral load, which has been associated to lower rates of seropositivity [32].

New methods are currently under development to detect SARS-CoV-2 combining simplified extraction of RNA with reverse transcription followed by isothermal amplification and clustered regularly interspaced short palindromic repeats mediated detection. This new approach has a sensitivity of 93.1% and a specificity of 98.5% [33].

Stregths of the study

Our study point out the relevance in that RT-PCR and antibody serologies are techniques that can be complementary in some circumstances. In particular, antibodies would be indicated in symptomatic patients or with positive chest images with negative RT-PCR and in asymptomatic patients with positive RT-PCR to clarify false positives and negatives. The performance of antibodies has also allowed us to know which patients have overcome the disease.

Conclusion

The pandemic nature of the COVID-19 has allowed designing different strategies to manage pregnant women according to available resources in different health care systems. We found that the systematic RT-PCR assessment and serological studies of SARS-CoV-2 seem appropriated to identify women at risk during labor and delivery. There were 2.2% of women with positive RT-PRC tests and 6.7% with positive serological tests during the first wave of the SARS-CoV-2 pandemic in Madrid. **However, every diagnosis proposal should bring something meaningful for the clinical management of SARS-CoV 2 infected patients. There is a need to contrast different international experiences to effectively define the better diagnostic model of clinical assistance during pregnancy and delivery since the pandemic nature of the virus.**

Author contributions

RSC, JZ, MAG and FRPL contributed to the conception of the study. RSC, AV, LME and FRPL contributed to the design of the work. JZ and AV carried out data acquisition. All authors were involved in the interpretation of the study results, and the drafting and revision of the manuscript, and all approved the final version to be published.

Disclosure statement

The authors report no conflicts of interest and are alone responsible for the content and the writing of the article.

Funding / Source of support

This research did not receive any specific grant or was funded by any commercial or non-profit organization or public agency.

Details of ethics approval

The study was approved by the Fundación Jiménez Díaz Clinical Research Ethics Committee, Madrid, Spain (protocol EO107-20).

Data statement

The present study was based on clinical results obtained during the COVID-19 pandemic.

Declaration of Competing Interest

The authors report no conflicts of interest and are alone responsible for the content and the writing of the article.

Acknowledgments

None

References

1. Savirón-Cornudella R, Altamirano-Barcia IE, Chedraui P, Andeyro-García M, Tajada M, Pérez-López FR. The coronavirus disease (COVID) 2019 and human pregnancy: A scoping review. Gynecological and Reproductive Endocrinology and Metabolism 2020; 1(2):70-75 https://gremjournal.com/journal/02-2020/the-coronavirus-disease-covid-2019-and-human-pregnancy-a-scoping-review/
2. Pascarella G, Strumia A, Piliego C, et al. COVID-19 diagnosis and management: a comprehensive review. J Intern Med. 2020;288(2):192-206. doi:10.1111/joim.13091
3. Ai T, Yang Z, Hou H et al. Correlation of chest CT and RT-PCR testing in coronavirus disease 2019 (COVID-19) in China: a report of 1014 cases. Radiology. 2020;296(2):E32-E40.
4. Wang W, Xu Y, Gao R, et al. Detection of SARS-CoV-2 in different types of clinical

specimens. JAMA. 2020;323(18):1843-1844.
5. Deeks JJ, Dinnes J, Takwoingi Y, et al. Antibody tests for identification of current and past infection with SARS-CoV-2. Cochrane Database Syst Rev. 2020;6(6):CD013652. doi: 10.1002/14651858.CD013652.
6. Flannery DD, Gouma S, Dhudasia MB, et al. SARS-CoV-2 seroprevalence among parturient women in Philadelphia. Sci Immunol. 2020;5(49):eabd5709. doi: 10.1126/sciimmunol.abd5709.
7. Li R, Pei S, Chen B, et al. Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (SARS-CoV2). Science. 2020;382(22):2163-2164.
8. 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.
9. Ceulemans D, Thijs I, Schreurs A, et al. Screening for COVID-19 at childbirth: is it effective?. Ultrasound Obstet Gynecol. 2020;56(1):113-114. doi:10.1002/uog.22099
10. Fassett MJ, Lurvey LD, Yasumura L, et al. Universal SARS-Cov-2 Screening in Women Admitted for Delivery in a Large Managed Care Organization. Am J Perinatol. 2020;37(11):1110-1114.
11. Herraiz I, Folgueira D, Villalaín C, Forcén L, Delgado R, Galindo A. Universal screening for SARS-CoV-2 before labor admission during Covid-19 pandemic in Madrid. J Perinat Med. 2020;/j/jpme.ahead-of-print/jpm-2020-0236/jpm-2020-0236.xml. doi:10.1515/jpm-2020-0236
12. 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. 2020; 127(12):1548-1556. doi: 10.1111/1471-0528.16403
13. Zullo F, Di Mascio D, Saccone G. COVID-19 Antibody Testing in Pregnancy. Am J Obstet Gynecol MFM. 2020;2(3):100142. doi: 10.1016/j.ajogmf.2020.100142
14. Zhao J, Yuan Q, Wang H, et al. Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019. Clin Infect Dis. 2020 Mar 28:ciaa344.
15. Pollán M, Pérez-Gómez B, Pastor-Barriuso R, et al. Prevalence of SARS-CoV-2 in Spain (ENE-COVID): a nationwide, population-based seroepidemiological study. Lancet. 2020 Aug 22;396(10250):535-544.
16. Dust K, Hedley A, Nichol K, et al. Comparison of Commercial Assays and Laboratory Developed Tests for Detection of SARS-CoV-2. J Virol Methods. 2020;113970. doi:10.1016/j.jviromet.2020.113970
17. Mahendiratta S, Batra G, Sarma P, et al. Molecular diagnosis of COVID-19 in different biologic matrix, their diagnostic validity and clinical relevance: A systematic review. Life Sci. 2020 Oct 1;258:118207.
18. Kelly JC, Dombrowksi M, O'Neil-Callahan M, Kernberg AS, Frolova AI, Stout MJ. False-negative testing for severe acute respiratory syndrome coronavirus 2: consideration in

obstetrical care. Am J Obstet Gynecol MFM. 2020;2(3):100130. doi:10.1016/j.ajogmf.2020.100130

19. Cohen A.N., Kessel B. False positives in reverse-transcription PCR testing for SARS-CoV-2. medRxiv. 2020 doi: 10.1101/2020.04.26.20080911.
20. **Vintzileos WS, Muscat J, Hoffmann E, John NS, Vertichio R, Vintzileos AM, Vo D. Screening all pregnant women admitted to labor and delivery for the virus responsible for coronavirus disease 2019. Am J Obstet Gynecol. 2020;223(2):284-286. doi: 10.1016/j.ajog.2020.04.024.**
21. **Knight M, Bunch K, Vousden N, Morris E, Simpson N, Gale C, O'Brien P, Quigley M, Brocklehurst P, Kurinczuk JJ; UK Obstetric Surveillance System SARS-CoV-2 Infection in Pregnancy Collaborative Group. Characteristics and outcomes of pregnant women admitted to hospital with confirmed SARS-CoV-2 infection in UK: national population based cohort study. BMJ. 2020;369:m2107. doi: 10.1136/bmj.m2107.**
22. Long Q, Liu B, Deng H, et al. Antibody responses to SARS-CoV-2 in patients with COVID-19. Nat Med. 2020 Jun;26(6):845-848. doi: 10.1038/s41591-020-0897-1. Epub 2020 Apr 29. PMID: 32350462.
23. Marlet J, Petillon C, Ragot E, et al. Clinical performance of four immunoassays for antibodies to SARS-CoV-2, including a prospective analysis for the diagnosis of COVID-19 in a real-life routine care setting. J Clin Virol. 2020;132:104633. doi:10.1016/j.jcv.2020.104633
24. Lisboa Bastos M, Tavaziva G, Abidi SK, et al. Diagnostic accuracy of serological tests for covid-19: systematic review and meta-analysis. BMJ. 2020;370:m2516. doi:10.1136/bmj.m2516
25. **Haizler-Cohen L, Davidov A, Blitz MJ, Fruhman G. Severe acute respiratory syndrome coronavirus 2 antibodies in pregnant women admitted to labor and delivery units. Am J Obstet Gynecol. 2020 Sep 21:S0002-9378(20)31101-7. doi: 10.1016/j.ajog.2020.09.022.**
26. Zöllkau J, Baier M, Scherag A, Schleußner E, Groten T. Periodenprävalenz von SARS-CoV-2 in einer unselektierten Stichprobe schwangerer Frauen in Jena, Thüringen [Period Prevalence of SARS-CoV-2 in an Unselected Sample of Pregnant Women in Jena, Thuringia]. Z Geburtshilfe Neonatol. 2020;224(4):194-198. doi:10.1055/a-1206-1033
27. Huntley BJF, Huntley ES, Di Mascio D, Chen T, Berghella V, Chauhan SP. Rates of Maternal and Perinatal Mortality and Vertical Transmission in Pregnancies Complicated by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-Co-V-2) Infection: A Systematic Review. Obstet Gynecol. 2020;136(2):303-312. doi:10.1097/AOG.0000000000004010
28. Khalil A, Kalafat E, Benlioglu C, et al. SARS-CoV-2 infection in pregnancy: A systematic review and meta-analysis of clinical features and pregnancy outcomes. EClinicalMedicine. 2020;25:100446. doi:10.1016/j.eclinm.2020.100446

29. Diriba K, Awulachew E, Getu E. The effect of coronavirus infection (SARS-CoV-2, MERS-CoV, and SARS-CoV) during pregnancy and the possibility of vertical maternal-fetal transmission: a systematic review and meta-analysis. Eur J Med Res. 2020;25(1):39. Published 2020 Sep 4. doi:10.1186/s40001-020-00439-w
30. Barbero P, Mugüerza L, Herraiz I, et al. SARS-CoV-2 in pregnancy: characteristics and outcomes of hospitalized and non-hospitalized women due to COVID-19. J Matern Fetal Neonatal Med. 2020;1-7. doi:10.1080/14767058.2020.1793320
31. Soresina A, Moratto D, Chiarini M, et al. Two X-linked agammaglobulinemia patients develop pneumonia as COVID-19 manifestation but recover. Pediatr Allergy Immunol. 2020 Apr 22:10.1111/pai.13263. doi: 10.1111/pai.13263. PMID: 32319118; PMCID: PMC7264678.
32. Wellinghausen N, Plonné D, Voss M, Ivanova R, Frodl R, Deininger S. SARS-CoV-2-IgG response is different in COVID-19 outpatients and asymptomatic contact persons. J Clin Virol. 2020;130:104542. doi:10.1016/j.jcv.2020.104542
33. Joung J, Ladha A, Saito M, et al. Detection of SARS-CoV-2 with SHERLOCK One-pot testing. New Engl J Med 2020; DOI: 10.1056/NEJMc2026172

383 **Tables and figures**

384

385 **Table 1**. Reverse transcription polymerase chain reaction (RT-PCR) positive cases in
386 pregnant women (n = 8/266) admitted for delivery, maternal and newborn outcomes, and
387 analytical results.

388

389 **Figure 1.** Flowchart of the SARS-CoV-2 screening and results in 266 pregnant women
390 during delivery.

391