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

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polymerase chain reaction (RT-PCR); serum immunoglobulins; screening

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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-PCR tests and 6.7% with positive serological tests during the
first wave of the SARS-CoV-2 pandemic.

Revision note, 8 November 2020

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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.

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

3
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30 **Short title:** Gravids and screening of COVID-19

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36 **Declaration of interest:** none.

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**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

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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-PCR 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

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

14 In asymptomatic pregnant women admitted for delivery, the reported positive
15 SARS-COV-2 screening with the RT-PCR tests is 86-88%, which is similar to those in the
16 general population [7,8]. However, the prevalence of those positive tests are variable
17 depending on the study location and delivery facilities [8-12]. There are different
18 techniques for antibody titration against SARS-CoV-2, including rapid IgM-IgG antibody
19 tests, chemiluminescence immunoassay, and enzyme-linked immunosorbent assay
20 (ELISA), and. The ELISA technique has a sensitivity of 89% and a specificity of 91%
21 [13], although it varies according on the day of analysis since symptoms onset [14].

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

2. Methods

25 This observational retrospective cohort study was conducted between the 31st of
26 March and 31st of August, 2020, at the *Hospital Universitario General de Villalba*, located
27 in the North of Madrid which attends 700-800 deliveries per year. The study was approved
28 by the Fundación Jiménez Díaz Clinical Research Ethics Committee, Madrid, Spain
29 (protocol EO107-20). A total of 266 pregnant women admitted to labor and delivery and to
30 scheduled procedures such as labor induction or caesarean delivery, were screened by RT-
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1 PCR in nasopharyngeal swabs and by a rapid blood antibodies rapid test. In cases with
2 positive RT-PCR or positive antibodies rapid test for IgM and/or IgG, serological testing
3 by ELISA was also carried out to confirm the results.
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5 The RT-PCR measurements were carried out using the MagMAX Viral/Pathogen II
6 Nucleic Acid Isolation reagents in a KinGFisher Flex Purification System. PCR reagents
7 were the Viasure SARS-CoV-2 real time RT-PCR detection it measured in a Bio-Rad
8 CFX96 platform (TaqPath™ COVID-19 Combo Kit Multiplex Real Time RT-PCR). The
9 rapid antibody test is a lateral flow immunochromatographic assay carried out using the test
10 Biozek COVID-19 IgG/IgM Rapid Test Cassette. The ELISA serological presence of Igs
11 was determined for IgG with Abbott reactive and for IgM with Vircell reactive.
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18 We collected demographic, clinical (fever, cough, rhinorrhea, dyspnea, chest pain,
19 diarrhea, myalgia, new anosmia or ageusia), obstetric and perinatal data for each woman
20 admitted, as well as, RT-PCR and serological results. Every woman was classified in one
21 of the three SARS-CoV-2 categories: (i) acute infection (positive RT-PCR); (ii) healed
22 women (negative RT-PCR with positive IgG); (iii) and never infected women (both
23 negative RT-PCR and IgG).
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33 **3. Results**

34 During the period of the study, 266 pregnant women admitted for labor and
35 delivery were submitted to the SARS-Co-V-2 screening with RT-PCRs. The prevalence of
36 acute or healed COVID-19 infection was 9.0 %, corresponding to 18 past SARS-CoV-2
37 exposures and six current infections (**Figure 1**).
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42 There were eight positive RT-PCR for SARS-CoV-2, although two of them were
43 categorized as laboratory misinterpretation of results after women were discharged from
44 the hospital. As expected, these two cases had no clinical symptoms and were negative for
45 ELISA antibody tests. Therefore, we finally counted six positive RT-PCR women, of
46 whom two had COVID-19 symptoms during labor or delivery (one patient was only IgM
47 positive and the other had no serological test), and four were asymptomatic (**Table 1**). One
48 of the two symptomatic cases with positive RT-PCR was diagnosed with intrauterine
49 growth restriction. The four asymptomatic and positive RT-PCR pregnant women were
50 negative in the ELISA study for both IgM and IgG during hospitalization. These four cases
51 were submitted to second ELISA immune tests five to 15 weeks after delivery being
52 negative once again. All six cases were vaginal deliveries without neonatal acidosis, no
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1 newborn required for admission to the Neonatal Intensive Care Unit, and also they all were
2 RT-PCR negative. Symptomatic women were discharged on the third day and evolved
3 favorably, as did their newborns.
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5 All negative RT-PCR cases (n = 260) were asymptomatic throughout the whole
6 hospitalization and 18 of them were positive for IgG, being considered as past SARS-CoV-
7 2 exposure.
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10 11 12 **4. Discussion**

13 In a group of 266 pregnant women SARS-CoV-2 exposure was screened with RT-
14 PCR tests during delivery. There were eight RT-PCR positive patients including two
15 women with clinical evidence of SARS-CoV-2 infection, four past viral exposure and two
16 false positive due to technical problems. All these 8 neonates were healthy without clinical
17 signs of virus infection and negative RT-PCR tests. Serological IgG specific antibodies
18 addressed against the SARS-CoV-2 were present in 18 women with negative RT-PCR
19 tests. Therefore, the prevalence of acute or past SARS-CoV-2 infection was 9.0 % in our
20 cohort, which is similar to the prevalence in non-pregnant subjects studied by
21 seroprevalence in the Madrid area [15]. The maternal ELISA tests, in the four RT-PCR
22 positive and asymptomatic, repeated 2-15 weeks after delivery were negative.
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32 Dust et al. [16] reported the performance of different commercial SARS-CoV-2
33 RT-PCR assays testing clinical samples and reference material, ranging the sensitivity
34 from 24 copies/mL to 574/mL specimen. However, the RT-PCR sensitivity, specificity,
35 and positive or negative predictive values are still very difficult to determine without clear
36 gold standard tests for SARS-COV-2 [17]. Previous studies have described positive RT-
37 PCR in asymptomatic pregnant women rates ranging between 50% and 89% [8,9,11,12],
38 our 66.7 % in our small sample seems to fit well within reported ranges.
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45 Different studies have addressed the false-negative rate of the RT-PCR tests,
46 ranging from 17.0 to 63.0 % [18]. We did not have patients with negative RT-PCR and
47 symptoms suggestive of COVID-19. Less information is available about the false positive
48 rate. Cohen et al. [19] reported a 2.3% false-positive rate that was most likely related to
49 contamination from other positive samples analyzed at the same time, target genes
50 amplified from prior positive samples or positive controls, or misinterpretation of results.
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56 SARS-CoV-2 serological testing can usually demonstrate IgM from 5th until the
57 21st day of the infection and IgG within 10-20 days after the symptom onset, although it is
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1 still unknown for how long antibodies will be produced [20]. The serological test may
2 reach a specificity of 98.7% depending on the timing of sampling [5].

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

11 There is scarce information concerning the antibody formation dynamic in pregnant
12 women with SARS-Co-V-2 infection around the period of delivery. In an unselected
13 cohort of German pregnant women, Zollkau et al. [23] reported a total of 225 PCRs and
14 180 IgG tests, finding only one case with a positive IgG test. We detected positive IgG
15 serological tests in 18 asymptomatic women. None of our asymptomatic patients with
16 positive RT-PCR developed antibodies during the study period. Pregnant women are
17 considered a relatively low-risk group for COVID-19 since they are generally young [24,
18 25]. However, there are also results suggesting that SARS-Co-V-2 is more likely
19 associated with some adverse clinical conditions due to anatomic and physiological
20 changes during pregnancy [26]. In addition, preeclampsia, excessive body weight and
21 socioeconomic disparities may be potential cofactors to worsen the obstetric and perinatal
22 results [27]. On the other hand, pregnant women during their third trimester of gestation
23 and labor may display atypical features, including the absence of fever as well as
24 leukocytosis. From our own experience, in asymptomatic patients with positive RT-PCR
25 we have to review RT-PCR in search of false positives and take into account perform
26 antibody tests.

27 ***Limitations***

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

1 meta-analyzed studies reporting at least 100 negative RT-PCR tests with a global 3.2% rate
2 for false positive results which could at least partially explain reports of large numbers of
3 asymptomatic carriers of SARS-CoV-2.
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5 Our two positive RT-PCR women were asymptomatic during the follow up with
6 and were negative in the control serological tests. We do not know if we have had any false
7 negative RT-PCR in asymptomatic patients, although we did not have positive IgM
8 serologies in these cases either. It is interesting to note that asymptomatic cases with
9 positive RT-PCR have shown negative IgM and IgG SARS-COV-2 antibodies by ELISA
10 testing during hospitalization and four weeks after. There are several possible explanations,
11 including (i) false positive RT-PCR cases for sample contamination for the false negative
12 of antibody testing cases; (ii) true positive RT-PCR patients that have not developed
13 antibodies because of the theoretical B-cell response against SARS-COV-2 [28] or with
14 lower viral load, which has been associated to lower rates of seropositivity [29].
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24 New methods are currently under development to detect SARS-CoV-2 combining
25 simplified extraction of RNA with reverse transcription followed by isothermal
26 amplification and clustered regularly interspaced short palindromic repeats mediated
27 detection. This new approach has a sensitivity of 93.1% and a specificity of 98.5% [30].
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32 ***Strengths of the study***

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

49 The pandemic nature of the COVID-19 has allowed designing different strategies to
50 manage pregnant women according to available resources in different health care systems.
51 We found that the systematic RT-PCR assessment and serological studies of SARS-CoV-2
52 seem appropriated to identify women at risk during labor and delivery. There were 2.2% of
53 women with positive RT-PCR tests and 6.7% with positive serological tests during the first
54 wave of the SARS-CoV-2 pandemic in Madrid. There is a need to contrast different
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1 international experiences to effectively define the better models of clinical assistance
2 during pregnancy and delivery since the pandemic nature of the virus.
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5 **Author contributions**

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

17 The authors report no conflicts of interest and are alone responsible for the content
18 and the writing of the article.
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24 This research did not receive any specific grant or was funded by any commercial
25 or non-profit organization or public agency.
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31 **Details of ethics approval**

32 The study was approved by the Fundación Jiménez Díaz Clinical Research Ethics
33 Committee, Madrid, Spain (protocol EO107-20).
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38 **Data statement**

39 The present study was based on clinical results obtained during the COVID-19
40 pandemic.
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45 **Declaration of Competing Interest**

46 The authors report no conflicts of interest and are alone responsible for the content
47 and the writing of the article.
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52 **Acknowledgments**

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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 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.

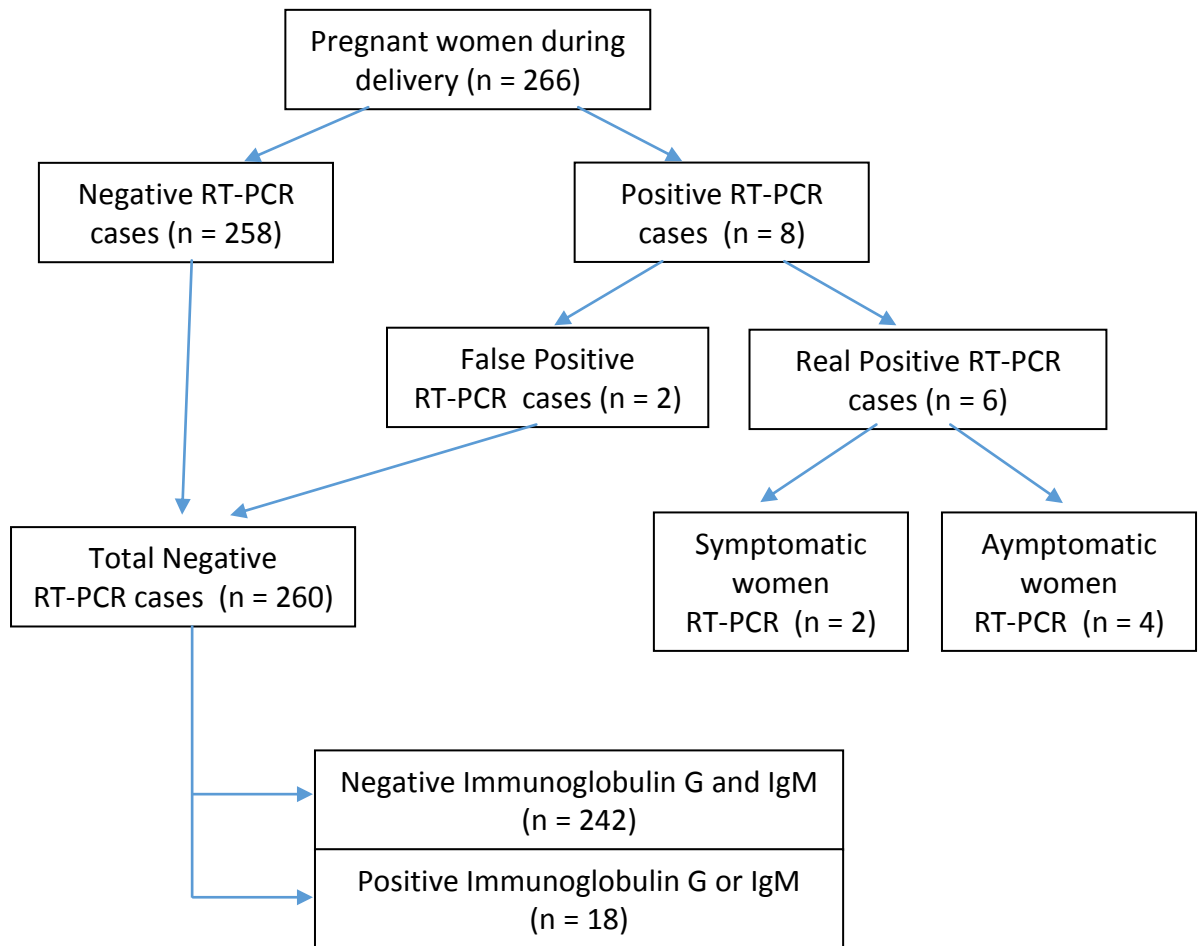
Case	Maternal age (years), parity, delivery (weeks)	Maternal symptoms	Delivery	Newborn sex	Birth weight (grams)	Arterial umbilical cord blood pH	Apgar test 5'	Maternal RT-PCR	Maternal IgG ^b and IgM ^a (ELISA ^c)	Maternal IgG ^b and IgM ^a control (ELISA ^c)
1	26, 2, 37	Yes (fever and cough)	Vaginal	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 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 responsible for the content and the writing of the article.

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

3
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34

35 **Abstract**

36 *Objective:* To screen pregnant women at risk of severe acute respiratory syndrome
37 coronavirus 2 (SARS-CoV-2) infection during delivery using reverse-transcription
38 polymerase chain reaction (RT-PCR) test and serum immunoglobulin (Ig) testing.

39 *Method:* Between March 31st and August 31st of 2020, consecutive pregnant women
40 admitted for labor and delivery in a single hospital were screened for SARS-CoV-2 with
41 nasopharyngeal RT-PCR swab tests and detection of serum IgG and IgM.

42 *Results:* We studied 266 pregnant women admitted for labor and delivery. The prevalence
43 of acute or past SARS-CoV-2 infection was 9.0 %, including (i) two cases with respiratory
44 symptoms of SARS-Co-V-2 infection and positive RT-PCR; (ii) four asymptomatic
45 women with positive RT-PCR without clinical symptoms and negative serological tests
46 between two and 15 weeks later; and (iii) two women with false positive RT-PCR due to
47 technical problems. All newborns of the 6 pregnant women with RT-PCR positive had
48 negative RT-PCR and did not require Neonatal Intensive Care Unit admission. There were
49 eighteen asymptomatic women with positive serological IgG tests and negative RT-PCR.

50 *Conclusion:* In our cohort of gravids, we found 2.2% of women with positive RT-PCR
51 tests and 6.7% with positive serological tests during the first wave of the SARS-CoV-2
52 pandemic.

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

55

56 **1. Introduction**

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

70 In asymptomatic pregnant women admitted for delivery, the reported positive
71 SARS-COV-2 screening with the RT-PCR tests is 86-88%, which is similar to those in the
72 general population [7,8]. However, the prevalence of those positive tests are variable
73 depending on the study location and delivery facilities [8-12]. There are different
74 techniques for antibody titration against SARS-CoV-2, including rapid IgM-IgG antibody
75 tests, chemiluminescence immunoassay, and enzyme-linked immunosorbent assay
76 (ELISA), and. The ELISA technique has a sensitivity of 89% and a specificity of 91%
77 [13], although it varies according on the day of analysis since symptoms onset [14].

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

81

82 **2. Methods**

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

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

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

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

106

107 **3. Results**

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

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

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

128

129 **4. Discussion**

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

140 Dust et al. [16] reported the performance of different commercial SARS-CoV-2
141 RT-PCR assays testing clinical samples and reference material, ranging the sensitivity
142 from 24 copies/mL to 574/mL specimen. However, the RT-PCR sensitivity, specificity,
143 and positive or negative predictive values are still very difficult to determine without clear
144 gold standard tests for SARS-COV-2 [17]. Previous studies have described positive RT-
145 PCR in asymptomatic pregnant women rates ranging between 50% and 89% [8,9,11,12],
146 our 66.7 % in our small sample seems to fit well within reported ranges. Different studies
147 have addressed the false-negative rate of the RT-PCR tests, ranging from 17.0 to 63.0 %
148 [18]. We did not have patients with negative RT-PCR and symptoms suggestive of
149 COVID-19. Less information is available about the false positive rate. Cohen et al. [19]
150 reported a 2.3% false-positive rate that was most likely related to contamination from other
151 positive samples analyzed at the same time, target genes amplified from prior positive
152 samples or positive controls, or misinterpretation of results.

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

157 **Besides, neonates were negative for SARS-CoV-2 tests during the first day**
158 **postpartum. Vintzileos et al. [20] reported a retrospective cohort describing a**
159 **screening program for all pregnant adolescents and women admitted in labor and**
160 **delivery (n = 161) in a single Hospital in New York using RT-PCR tests. They found**
161 **that 20% (n = 32) of admitted women were positive for SARS-CoV-2 infection and**
162 **66% of these women were asymptomatic and all neonates were negative for viral**
163 **infection. Another more recent publication reported prospective results from 3 other**
164 **hospitals from New York including 675 women admitted at delivery [12]. They**
165 **reported high rates of cesarean delivery in symptomatic COVID-19 (46.7%),**
166 **asymptomatic COVID-19 (45.5%) and in women without COVID-19. In all these 3**
167 **studies from the United States SARS-CoV-2 serological tests were not used. Knight et**
168 **al. [21] reported clinical outcomes of 427 pregnant women with confirmed SARS-**
169 **CoV-2 infection from the United Kingdom National population cohort, including**
170 **gravids admitted to hospital with confirmed SARS-CoV-2 infection by RT-PCR tests.**

171 SARS-CoV-2 serological testing can usually demonstrate IgM from 5th until the
172 21st day of the infection and IgG within 10-20 days after the symptom onset, although it is
173 still unknown for how long antibodies will be produced [22]. The serological test may
174 reach a specificity of 98.7% depending on the timing of sampling [5]. SARS-CoV-2
175 serology is complementary to RT-PCR for the COVID-19 diagnosis during at least 14 days
176 after clinical infection initiation [23]. In a meta-analysis, the pooled ELISA methods have
177 a sensitivity of 84% for measuring IgG or IgM as compared to lateral flow immunoassays
178 of 66.0% and chemiluminescent immunoassays of 97.8% in the general population [24].
179 Total antibody determination has low sensitivity during the first weeks with clinical
180 symptoms (30.1%), increasing during the second week to reach the highest levels during
181 the third week. There is limited information beyond 35 days post-initiation of clinical
182 symptoms [5]. **Flannery et al. [6] performed serological tests in 1,293 women admitted**
183 **at labor and delivery in Philadelphia, reporting that 6.2% had specific IgG and/or**
184 **IgM against SARS-CoV-2. It is important to mention that of the 72 seropositive**
185 **women, 46 (64%) were also RT-PCR positive. Haizler-Cohen et al. [25] postulated**
186 **that PCR and serological tests may allow to establish the timing of infection: (i) the**
187 **acute infection may displays a positive RT-PCR with negative serological testing; (ii)**
188 **the past infection may have a negative RT-PCR and positive serological testing; (iii)**
189 **when both tests are positive, the case may be a recent or past infection. It is accepted**
190 **that a RT-PCR may remain positive for weeks after SARS-CoV-2 infection.**

191 There is scarce information concerning the antibody formation dynamic in pregnant
192 women with SARS-Co-V-2 infection around the period of delivery. In an unselected
193 cohort of German pregnant women, Zollkau et al. [26] reported a total of 225 PCRs and
194 180 IgG tests, finding only one case with a positive IgG test. We detected positive IgG
195 serological tests in 18 asymptomatic women. None of our asymptomatic patients with
196 positive RT-PCR developed antibodies during the study period. Pregnant women are
197 considered a relatively low-risk group for COVID-19 since they are generally young [27,
198 28]. However, there are also results suggesting that SARS-Co-V-2 is more likely
199 associated with some adverse clinical conditions due to anatomic and physiological
200 changes during pregnancy [29]. In addition, preeclampsia, excessive body weight and
201 socioeconomic disparities may be potential cofactors to worsen the obstetric and perinatal
202 results [30]. On the other hand, pregnant women during their third trimester of gestation
203 and labor may display atypical features, including the absence of fever as well as
204 leukocytosis. From our own experience, in asymptomatic patients with positive RT-PCR
205 we have to review RT-PCR in search of false positives and take into account perform
206 antibody tests.

207

208 *Limitations*

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

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

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

228 New methods are currently under development to detect SARS-CoV-2 combining
229 simplified extraction of RNA with reverse transcription followed by isothermal
230 amplification and clustered regularly interspaced short palindromic repeats mediated
231 detection. This new approach has a sensitivity of 93.1% and a specificity of 98.5% [33].
232

233 *Strengths of the study*

234 Our study point out the relevance in that RT-PCR and antibody serologies are
235 techniques that can be complementary in some circumstances. In particular, antibodies
236 would be indicated in symptomatic patients or with positive chest images with negative
237 RT-PCR and in asymptomatic patients with positive RT-PCR to clarify false positives and
238 negatives. The performance of antibodies has also allowed us to know which patients have
239 overcome the disease.
240

241 *Conclusion*

242 The pandemic nature of the COVID-19 has allowed designing different strategies to
243 manage pregnant women according to available resources in different health care systems.
244 We found that the systematic RT-PCR assessment and serological studies of SARS-CoV-2
245 seem appropriated to identify women at risk during labor and delivery. There were 2.2% of
246 women with positive RT-PCR tests and 6.7% with positive serological tests during the first
247 wave of the SARS-CoV-2 pandemic in Madrid. **However, every diagnosis proposal
248 should bring something meaningful for the clinical management of SARS-CoV 2
249 infected patients. There is a need to contrast different international experiences to
250 effectively define the better diagnostic model of clinical assistance during pregnancy
251 and delivery since the pandemic nature of the virus.**
252

253 *Author contributions*

254 RSC, JZ, MAG and FRPL contributed to the conception of the study. RSC, AV,
255 LME and FRPL contributed to the design of the work. JZ and AV carried out data
256 acquisition. All authors were involved in the interpretation of the study results, and the
257 drafting and revision of the manuscript, and all approved the final version to be published.
258

259 Disclosure statement

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

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265 or non-profit organization or public agency.

266

267 Details of ethics approval

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

270

271 Data statement

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

274

275 Declaration of Competing Interest

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

278

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281

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382

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.

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