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Letter to the Editor

# SARS-COV-2 excretion and maternal-fetal transmission: Virological data of French prospective multi-center cohort study COVIPREG during the first wave



Keywords: SARS-CoV-2 Pregnancy Transmission rate RT-PCR

# Objective

Our objective was to evaluate SARS-CoV-2 excretion in different maternal sites at delivery and during the postpartum period. We also aimed to evaluate the materno-fetal transmission rate according to the WHO classification.

#### Study design

COVIPREG study is a prospective study conducted in France (The study was approved by the national ethics comity, the CPP SUD MED-ITERRANEE (2020-A00924–35) on April 23, 2020, and recorded in the clinical trial registry (NCT04355234) during the first two waves of COVID-19 pandemic (inclusion between 04/28/2020 and 01/13/2021) and before vaccines availability. A written consent was obtained from both parents. In women with positive SARS-CoV-2 nasopharyngeal RT-PCR at any time during pregnancy, several samples were collected at delivery or in the 48H later, for RT-PCR analysis (vagina (VS), rectum (RS), Maternal blood (MB), nasopharynx (NP), Placenta (P), Amniotic fluid (AF) and milk (M)). In the neonate, Umbilical Cord Blood (UCB), NP, gastric fluid (GF), urine (U), and RS were collected to investigate transmission rate. A total of 12 samples could be collected from either the mother or the child. (Methods in Supplemental Data).

#### Results

310 women/child pairs were included in the study but unfortunately not all 12 samples were collected for each pair: in 297 pairs at least one maternal and one neonatal sample (excluding blood samples) was available (Fig. 1).

In our series, we identified a total of 31 women with at least one positive SARS-CoV-2 RT-PCR in one sample at delivery or in the post-partum period. Among those 7/31 (22.5%) were infected more than 5 weeks before delivery between 11.4 WG and 31.4 WG. The main maternal excretion sites were RS (20/272, 7.4%), followed by VS (5/255, 2.0%) and P (7/262, 2.7%). AF and M were

found positive only once in two different mothers (1/176, 0.6%; 1/197, 0.5%). NP RT-PCR at delivery were negative for all mothers. There was no correlation between the different excretion sites.

At birth or during the first 48 h of life, 8/289 (2.8%) neonates had at least one SARS-CoV-2 positive RT-PCR in one sample site, and according to WHO classification, 5/289 (1.7%) cases of proven materno-fetal infection were diagnosed.

Among the 31 women with at least one positive SARS-CoV-2 RT-PCR and the 8 neonates with at least one positive SARS-CoV-2 RT-PCR, 5 women/child pairs both had at least one positive RT-PCR, 26 women had at least one positive RT-PCR without positive RT-PCR in their children and 3 children had at least one positive RT-PCR with an unknown mother's status at delivery. Among the 34 positive pairs (31 mother with a positive sample + 3 neonates with a positive sample with a mother without positive sample). 25positive mothers had symptoms.23/25 symptomatic mothers had a positive sample. 7 neonates had a positive sample (5/7 congenital infections, for 5 positive women/child pairs and 2 positive neonates with an unknown mother status). Ten mothers were hospitalized, 9 had a positive sample and 4 neonates had a positive sample (one positive neonate with an unknown woman status). Therefore, for the five identified neonates with congenital infections all mothers were symptomatic and 2/5 were hospitalized.

#### Discussion

Excretion in these different sites has been reported in small series in the literature (5 to 56 patients) [1–4]. Therefore, our series is the larger to date. Furthermore, in these series the delay between maternal SARS-CoV-2 infection and delivery was not stated.

Interestingly, none of the mothers whose neonate had a congenital infection, had positive RT-PCR in blood. However, all had either VS or RS positive RT-PCR. This observation suggests transmission mainly occurs during delivery. One neonate was positive at 48 h of life but was negative at birth, suggesting an immediate postnatal infection. Three neonates were positive at birth but negative in a RT-PCR later, suggesting a superficial exposure to SARS-CoV-2 (one mother had three positive samples (VS, RS and P), and two did not have any RT-PCR positive among samples collected). The rate of transmission we observe (1.7%) is similar to that was reported in the review of Poblete et al. [5].

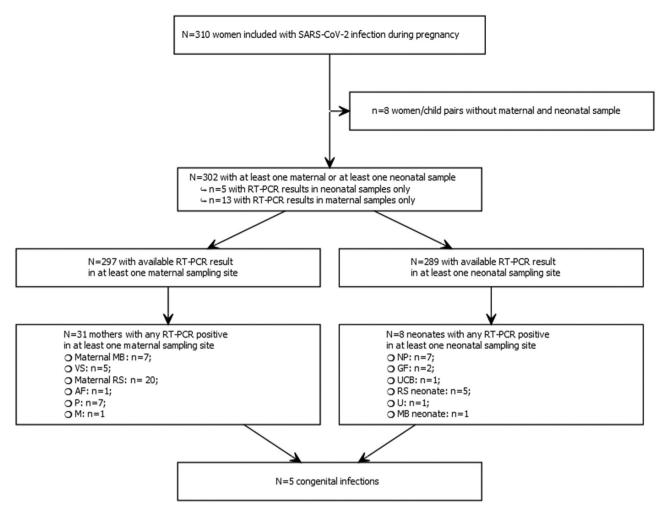


Fig. 1. flowchart of positive RT-PCR for each compartment for the mother and the newborn. vagina (VS), rectum (RS), Maternal blood (MB), nasopharynx (NP), Placenta (P), Amniotic fluid (AF), milk (M), Umbilical Cord Blood (UCB), NP, gastric fluid (GF), urine (U).

#### Conclusion

Our cohort is the largest one before the anti-SARS-CoV-2 vaccination era, and it aimed to evaluate maternal viral excretion at delivery and in the post-partum period. Routes of transmission remain to be confirmed but materno-fetal transmission is a rare event.

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#### **Declaration of Competing Interest**

C.V.F. has obtained a grand from Ferring pharmaceutics for the COVIPREG study.

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# Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jogoh.2023.102547.

# References

- [1] Schwartz A, Yogev Y, Zilberman A, Alpern S, Many A, Yousovich R, Gamzu R. Detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in vaginal swabs of women with acute SARS-CoV-2 infection: a prospective study. BJOG 2021;128(1):97–100.
- [2] Fenizia C, Saulle I, Di Giminiani M, Vanetti C, Trabattoni D, Parisi F, Biasin M, Savasi V. Unlikely SARS-CoV-2 transmission during vaginal delivery. Reprod Sci 2021;28 (10):2939–41.
- [3] Sinaci S, Ocal DF, Seven B, Anuk AT, Besimoglu B, Keven MC, Goncu Ayhan S, Akin MS, Tayman C, Keskin HL, Yapar Eyi EG, Dinc B, Moraloglu Tekin O, Sahin D. Vertical transmission of SARS-CoV-2: a prospective cross-sectional study from a tertiary center. J Med Virol 2021;93(10):5864–72.
- [4] Wu Y, Liu C, Dong L, Zhang C, Chen Y, Liu J, Zhang C, Duan C, Zhang H, Mol BW, Dennis C-L, Yin T, Yang J, Huang H. Coronavirus disease 2019 among pregnant Chinese women: case series data on the safety of vaginal birth and breastfeeding. BIOG 2020:127(9):1109–15.
- [5] Poblete CA, Bancalari AM. Vertical transmission of Covid 19. What does the evidence say? Andes Pediatr. 2021;92(5):790-8.

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