

# Passive immunity in newborn from SARS-CoV-2-infected mother

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## Abstract

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) vertical transmission is an open issue. Recent reports call into question in utero or peripartum viral transmission to the offspring. Few data are available on immunoglobulin G (IgG) and/or IgM in newborns. Insufficient evidence is available regarding passive immunity in neonates born from SARS-CoV-2 infected women. We report a case of a neonate showing the presence of blood specific IgG and the absence of IgM and negative nasopharyngeal swab. He was born from an asymptomatic SARS-CoV-2-infected mother with positive IgG and IgM. The transplacental passage of specific IgG antibodies from the affected mother to the unaffected fetus highlights neonatal passive immunity.

## KEYWORDS

coronavirus, passive immunity, SARS-CoV-2, vertical transmission

## 1 | INTRODUCTION

In January 2020, Huang et al.<sup>1</sup> reported a new cluster of pneumonia cases in Wuhan, China, in December 2019 caused by a novel coronavirus, named 2019-nCoV—severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Pregnant women and infants “a priori” deserve special attention during a viral pandemic and evidence on this virus has been steadily increasing.

The risk of SARS-CoV-2 vertical transmission and fetoneonatal passive immunity are still open questions. At first, evidence pointed to a lack of vertical transmission<sup>2–6</sup> due to the absence of the virus in the placenta, cord blood, and amniotic fluid samples. However, recent case reports revealed the presence of SARS-CoV-2 in the placenta,<sup>7–9</sup> the positivity of the real-time polymerase chain reaction (RT-PCR) on nasopharyngeal swabs and of the serological antibody tests in newborns.<sup>10–14</sup>

No conclusive data has been published regarding specific newborn passive immunity, consisting in the transplacental immunoglobulin G (IgG) antibodies passage from the affected mother

to her fetus during pregnancy, following the kinetics model well studied in maternal vaccination (dTpa and influenza immunization) during pregnancy.<sup>15,16</sup>

We speculate on the presence of passive immunity in a neonate born from a SARS-CoV-2-infected pregnant woman.

## 2 | CASE

A low-risk 34-year-old woman (gravida 1, para 0) without symptoms suggestive of COVID-19 was admitted to our Hospital at 37<sup>+2</sup> weeks of gestational age (GA) due to premature rupture of membranes. A 3320 g healthy male (9–10 Apgar Index) was vaginally delivered 26 h after admission.

Due to the presence of IgG and IgM in the serological maternal test, although the pre-partum nasopharyngeal swab for SARS-CoV-2 (RNA extraction and PCR test were performed, using STARMag Universal Cartridge kit and Allplex 2019-nCoV kit, respectively) was negative, a second swab (post-partum) was repeated showing a positive result.

In the puerperium, maternal blood exams (complete blood count and differential, markers of inflammation, D-dimer, kidney and liver function tests) and chest X-ray were performed, all showing normal results except for D-dimer that increased from Day IV to Day VI after delivery and started decreasing on Day VIII. Prophylactic LMWH was prescribed for 7 days. The nasopharyngeal swab still showed positive results on Day VII after delivery and was negative on Day XIV.

With regard to the newborn, delayed cord clamping and skin-to-skin contact were allowed, breastfeeding was encouraged with the use of hand hygiene and maternal masking and the crib was placed at almost 2 m of distance from his mother.

Neonatal tests showed: (1) virus absence in the nasopharyngeal swab performed at Days II, III, and VII after birth; (2) SARS-CoV-2 antibodies presence in serum, with positive IgG and negative IgM titres at Day VII; (3) RT-PCR on breast milk was negative for SARS-CoV-2.

Six weeks after delivery both IgG and IgM antibodies were absent in the neonate (IgG 4.8 IgM 0.3 AU/ml) and only IgG were detected in the mother (IgG 10.4 IgM 2.2 AU/ml) (cut-off value:  $\geq 10$  AU/ml).

### 3 | DISCUSSION

Vertical viral transmission after maternal infection usually occurs during intrauterine life via trans-placenta, at delivery via ingestion or aspiration of cervicovaginal secretions, and in the postpartum via breastfeeding.<sup>17</sup>

Several authors have investigated the trans-placental passage of novel coronavirus. At first, case reports and case series published did not demonstrate SARS-CoV-2 presence in the placenta, amniotic fluid, and cord blood samples<sup>2,3,18–26</sup> in contrast with more recent reports that describe positive RT-PCR in amniotic fluid<sup>13,27</sup> and placenta swabs positivity for SARS-CoV-2.<sup>7,8,27</sup> Moreover, Algarroba<sup>9</sup> identified in one case coronavirus virions invading into syncytiotrophoblasts in placental villi using electron microscopy and SARS-CoV-2 was demonstrated in placental tissue using nucleocapsid-specific monoclonal antibody<sup>28</sup> and by in-situ hybridization.<sup>29,30</sup>

Vaginal delivery is not contraindicated as it doesn't seem to increase the risk of peripartum transmission to the newborn.<sup>31</sup> The majority of published papers didn't demonstrate the virus in the vaginal secretions, neither in pregnant<sup>32</sup> nor in nonpregnant<sup>33,34</sup> women, however, Scorzolini et al.<sup>35</sup> demonstrated the presence of the virus in the vaginal secretions of nonpregnant women.

Breastfeeding is not contraindicated as it is not considered a mode of transmission.<sup>31</sup>

Authors have reported of neonates immediately isolated from the SARS-CoV-2-infected mother who showed a positive nasopharyngeal swab soon after birth and negative serology.<sup>10,36–38</sup> This evidence raises the doubt of possible vertical transmission of SARS-CoV-2 and question whether this occurrence may happen during intrauterine life or peripartum.

With regard to SARS-CoV-2 antibodies in neonates born from infected women, only a few cases have been reported up to now in the literature. Dong et al.<sup>11</sup> and Zeng et al.<sup>12</sup> described a total of six newborns delivered by caesarean section and isolated from the mothers of which three showed positive IgG and IgM and three positive IgG titers, all with negative nasopharyngeal swabs. IgM detection immediately after birth is in favor of the hypothesis of intrauterine passage of the virus, despite another possible explanation, postulated by Zeng, that speculates the passage of maternal IgM through a damaged placenta. Although IgG antibodies can pass through the placenta, and therefore may reflect neonatal passive immunity, IgM are usually not transferred via the placenta because of a larger macromolecular structure, suggesting an infection of the offspring.

Recently Toner et al.<sup>39</sup> reported a case to assess passive immunity in a SARS-CoV-2 positive pregnant woman failing to demonstrate specific IgG in fetal cord blood samples.

As far as our case is concerned, the hypothesis is the presence of passive immunity as the newborn resulted IgG positive/IgM negative and negative at repeated swabs and considering the IgG and IgM positivity in the mother. The antibodies in the maternal circulation suggest the presence of SARS-CoV-2 for more than 1 week. Studies on antibodies kinetics for SARS-CoV-2 in adults demonstrate that IgM and IgG need at least 5–7 days to be produced.<sup>40</sup>

The presence of antibodies in maternal circulation due to the SARS-CoV-2 infection could explain IgG detected in the newborn and suggest the transplacental passage of specific antibodies from the mother to the fetus. The disappearance of IgG antibodies in the newborn at 6 weeks of life corroborates this hypothesis. This is the first case with follow up evidence of the clearance in the newborn of the IgG acquired by the mother.

Unfortunately, we don't have the numerical value (quantity) of IgG and IgM at diagnosis. RT-PCR on amniotic fluid and placenta samples were not performed as at the time of delivery the first nasopharyngeal swab was negative and the patient was completely asymptomatic.

It is our opinion that to investigate vertical transmission and passive immunity from SARS-CoV-2, it is necessary to apply the SARS-CoV-2 screening to a large number of pregnant women using both RT-PCR on nasopharyngeal swabs and serological tests. In cases of positive results (1) maternal qualitative and quantitative serology, (2) placenta, amniotic fluid, cord blood, breast milk virus testing and (3) neonatal swab and serology should be performed. More collaborative studies are needed to investigate newborn transient passive immunity, as well as to define the persistence of IgG transmitted from mother to fetus.

### CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

### AUTHOR CONTRIBUTIONS

Dr. Cavaliere, Dr. Vasarri, Dr. Marchi, Dr. Aquilini and Dr. Brunelli conceptualized and designed the study, drafted the manuscript,

reviewed and revised the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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