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Correspondence

Is there evidence of intra-uterine vertical transmission potential of COVID-19 infection in samples tested by quantitative RT-PCR?



Dear Editor,

The COVID-19 pneumonia was first reported in Wuhan, Hubei province in China in late December 2019. The disease has since quickly spread worldwide, and has been declared a public health emergency of international concern (PHEIC) by the World Health Organization (WHO) [1]. According to current evidence, COVID-19 is mainly transmitted with close contact through respiratory droplets (such as coughing) and by fomites [2]. Pregnancy presents a unique immunological situation, characterized by increased susceptibility to some infectious diseases, including respiratory pathogens. Pregnant women could hence be at higher risk of severe acute respiratory disease coronavirus 2 (SARS-CoV-2) infection compared to the general population [3]. In previous pandemics such as H1N1, severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS), pregnant women seemed to have poor clinical and obstetric outcomes and higher mortality compared to non-pregnant women [4]. Nonetheless, the even limited data available on COVID-19 in pregnant women would suggest that these patients have similar clinical course as non-pregnant women [5], despite concerns for possibility of increased risk of preterm delivery and low birth weight [6]. The potential of vertical mother-to-child transmission of COVID-19 infection is also still unclear. We therefore analyzed current literature to identify any evidence of vertical transmission.

A systematic electronic search was carried out in Medline (PubMed interface) and China National Knowledge Infrastructure (CNKI) using the keywords “vertical transmission” OR “maternal to

fetal transmission” OR “pregnancy outcomes” AND “coronavirus 2019” OR “2019-nCoV” OR “SARS-CoV-2”, between 2019 and present time (i.e., 11th April, 2020), without applying language restrictions. The title, abstract and full text of all documents identified with these search criteria were assessed to identify studies reporting information vertical transmission of COVID-19. The reference lists of all documents were also analyzed to identify any additional eligible studies. Intra-uterine vertical transmission was defined as positive identification of SARS-CoV-2 in placenta, amniotic fluid, cord blood or neonatal pharyngeal/ throat swabs through reverse transcriptase polymerase chain reaction (RT-PCR) taken immediately after birth.

The initial search produced 40 potentially relevant articles. Following primary screening and assessment by full text for eligibility in the meta-analysis, 35 articles were excluded since they were review articles ($n = 11$), commentaries or other editorial materials ($n = 8$), or did not contain data on vertical transmission of COVID-19 patients ($n = 16$).

Overall, 5 studies ($n = 16$ pregnant COVID-19 patients) were included in the final analysis [5,7–10]. All studies were from China. In all women, the onset of symptoms and subsequent diagnosis with COVID-19 was late in pregnancy (3rd trimester). All but one delivered via caesarian section. None of the specimens tested positive for SARS-CoV-2 (Table 1). These findings therefore suggest that there is currently no evidence of intra-uterine vertical mother to child transmission of SARS-CoV-2 in samples tested by RT-PCR method.

That being said, there are reports on neonatal COVID-19 infections whose mode of transmission is still unclear. For instance, Yu et al., [11] in their retrospective analysis of pregnancy outcomes in COVID-19 patients reported one neonate who tested positive for COVID-19 36 h after delivery. Nucleic tests of placenta and cord blood were negative for SARS-CoV-2, thus indicating the

Table 1
Characteristics of the studies included in the analysis.

Author	Region	No. of patients tested for vertical transmission	Gestational age at onset of symptoms/ diagnosis of COVID-19	Mode of delivery	Specimens tested	Number of positive tests
Lei et al. [7]	China	4 women; 4 neonates	3 rd trimester	Caesarian section	amniotic fluid, umbilical cord blood, neonatal nasopharyngeal swabs	0
Chen et al. [8]	China	3 women	3 rd trimester	Caesarian section	Placenta	0
Chen et al. [8]	China	6 women; 6 neonates	3 rd trimester (36–39 weeks)	Caesarian section	amniotic fluid, cord blood, neonatal throat swab	0
Fan et al. [9]	China	2 women; 2 neonates	3 rd trimester (36 & 37 weeks)	Caesarian section	newborn's nasopharyngeal swab, maternal serum, placenta tissues, umbilical cord blood, amniotic fluid	0
Xiong et al. [10]	China	1 woman; 1 neonate	3 rd trimester (33 weeks)	Vaginal delivery	amniotic fluid, neonatal throat swab	0

unlikely possibility of vertical transmission. Similarly, Dong et al. [12], reported a case of “possible vertical transmission of SARS-CoV-2” based on elevated SARS-CoV-2 specific antibodies (IgG and IgM) in neonatal serum samples taken 2 h after delivery. Since IgM cannot cross the placenta, the possibility of intra-uterine transmission cannot be completely ruled out. Five RT-PCR tests on neonatal nasopharyngeal swabs taken from 2 h to 16 days of age were however negative. Importantly, an optimal COVID-19 testing method for neonates has yet to be established.

In conclusion, there is currently no definitive evidence of intra-uterine vertical transmission of COVID-19 in pregnant women diagnosed in the third trimester. All patients included in the current analysis developed symptoms and were diagnosed with COVID-19 late in pregnancy (3rd trimester). The potential of intra-uterine vertical COVID-19 transmission in the first and second trimester is still unknown. High quality studies are urgently needed to further investigate vertical transmission and risks of severe COVID-19 infections in pregnant women.

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Declaration of Competing Interest

None of the authors have any conflicts of interests with regard to this publication.

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