SARS-CoV-2 and the role of vertical transmission from infected pregnant women to their fetuses: systematic review

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Abstract

Background Vertical transmission of SARS-CoV-2 has been reported but appears uncommon. Objectives This study systematically reviewed the evidence on vertical transmission of SARS-CoV-2 from pregnant women to their neonates. Search strategy Literature searches in WHO Covid-19 Database, LitCovid, medRxiv, and Google Scholar for SARS-CoV-2 using keywords and associated synonyms, search date to 20 December 2020; no language restrictions. Selection criteria Studies of any design reporting transmission. Data collection and analysis Two reviewers independently assessed article eligibility and extracted data. Results were reported descriptively; no meta-analyses were possible. Main results 106 studies were included: 40 reviews and 66 primary studies, most conducted in hospitals. 32 case reports were assessed as high risk of bias, due to the study design; across the 34 remaining primary studies, risk of bias was low to moderate. Sixteen case reports described vertical transmission. In cohort studies and case series, 65/2391 (2.7%) neonates born to mothers with a COVID-19 diagnosis tested positive for SARS-CoV-2 within 24 hours of birth; the proportion of positive neonates ranged from 0% to 22%. Twenty studies reported no vertical transmission. Maternal symptomatology and mode of delivery were not correlated with vertical transmission. 7/25 studies of placental tissue identified SARS-CoV-2; vertical transmission was infrequent. No study reported the results of viral culture to detect SARS-CoV-2. Conclusions These findings indicate that vertical transmission is possible, but not frequent. Further high-quality studies are needed to understand vertical transmission. Funding World Health Organization: WHO registration No 2020/1077093.

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Running title: **Vertical transmission of SARS-CoV-2.**

Background

Vertical transmission of SARS-CoV-2 has been reported but appears uncommon.

Objectives

This study systematically reviewed the evidence on vertical transmission of SARS-CoV-2 from pregnant women to their neonates.

Search strategy

Literature searches in WHO Covid-19 Database, LitCovid, medRxiv, and Google Scholar for SARS-CoV-2 using keywords and associated synonyms, search date to 20 December 2020; no language restrictions.

Selection criteria

Studies of any design reporting transmission.

Data collection and analysis

Two reviewers independently assessed article eligibility and extracted data. Results were reported descriptively; no meta-analyses were possible.

Main results

106 studies were included: 40 reviews and 66 primary studies, most conducted in hospitals. 32 case reports were assessed as high risk of bias, due to the study design; across the 34 remaining primary studies, risk of bias was low to moderate. Sixteen case reports described vertical transmission. In cohort studies and case series, 65/2391 (2.7%) neonates born to mothers with a COVID-19 diagnosis tested positive for SARS-CoV-2 within 24 hours of birth; the proportion of positive neonates ranged from 0% to 22%. Twenty studies reported no vertical transmission. Maternal symptomatology and mode of delivery were not correlated with vertical transmission. 7/25 studies of placental tissue identified SARS-CoV-2; vertical transmission was infrequent. No study reported the results of viral culture to detect SARS-CoV-2.

Conclusions

These findings indicate that vertical transmission is possible, but not frequent. Further high-quality studies are needed to understand vertical transmission.

Funding

World Health Organization: WHO registration No 2020/1077093.

Background

Research on previous coronavirus outbreaks of the Middle East respiratory syndrome coronavirus (MERS-CoV) in 2012 and the severe acute respiratory syndrome coronavirus (SARS-CoV-1) in 2002-2003, assessed the risk of vertical transmission from infected mothers to their neonates and to date no cases of vertical transmission were reported[1,2]. For SARS-CoV-2, several studies have assessed vertical transmission with some early reviews reporting no evidence of vertical transmission [3,4], while others reported that vertical transmission was possible and could not be ruled out[4,5] although the risk appeared to be low[6]. This study therefore aims to systematically review the evidence for vertical transmission of SARS-CoV-2.

A WHO scientific brief [2], published in February 2021, based on an evidence synthesis and expert consultation, considered three mechanisms of vertical transmission: (1) *in utero,* where the virus is present in the blood and crosses the maternal-placental interface; (2) intrapartum, occuring during labour and childbirth via contact with maternal blood, vaginal secretions or faeces; and (3) postnatal, via breast milk but can include contact with an infected mother, another infected caregiver or fomites. The WHO review highlighted that defining vertical transmission of SARS-CoV-2 has been challenging, as much of the reported vertical transmission has been based on a single positive neonatal RT-PCR in an upper respiratory tract specimen, with significant variation in the timing of sample collection. A proposed definition of confirmed *in utero* transmission was considered to be a positive RT-PCR test in one or more neonatal samples (including neonatal blood, respiratory swab, stool sample), amniotic fluid or a placental tissue sample; or positive serology, at age <24 hours, where there was evidence of maternal SARS-CoV-2 infection during pregnancy. Another study[7] proposed a definition for vertical transmission as including a positive SARS-CoV-2 test in neonates in the first 24h of life (including respiratory tract swab, neonatal blood, cord blood or amniotic fluid) from mothers who had tested positive for SARS-CoV-2 between 14 days prior to birth and 2 days after birth. The UK Obstetric Surveillance System (UKOSS), however, defined vertical transmission as a positive neonatal sample taken within the first 12 h following birth to a mother with confirmed SARS-CoV-2 infection[8]. Given the challenges in defining vertical transmission and that many studies do not report what criteria were applied to define vertical transmission, in the current review, vertical transmission was considered as a positive test in the neonate (including RT-PCR testing of respiratory tract swabs, blood samples, placenta, amniotic fluid) at birth or up to 24h of life, where the mother had either tested positive for SARS-CoV-2 or had a recorded diagnosis of COVID-19.

Definition Vertical transmission: positive test for SARS-CoV-2 in a neonate up to 24 hours of life, including RT-PCR testi

Methods

We have been undertaking an open evidence review investigating factors and circumstances that impact on the transmission of SARS-CoV-2, based on our published protocol last updated on 1 December 2020 (Supplementary files, Protocol). This review aims to identify, appraise, and summarize the evidence (from peer-reviewed studies or studies awaiting peer review) assessing the occurrence of vertical transmission of SARS-CoV-2 from mothers to their babies in utero. We are conducting an ongoing literature search in the WHO Covid-19 Database, LitCovid, medRxiv, and Google Scholar for SARS-CoV-2 for keywords and associated synonyms. The search for this review was conducted up to 20 December 2020. We did not impose any language restrictions. (See Supplementary files for the search strategies).

Studies of any design (including reviews and case reports) reporting vertical transmission were included. For the included primary studies, the risk of bias was assessed using five domains from the QUADAS-2 criteria [9]; we adapted this tool because the included studies were not primarily designed as diagnostic accuracy studies. Due to the intrinsic difference in study designs, we did not conduct a quality appraisal of case reports reporting on only one or up to two cases, and data from these studies is reported separately in the Results. We checked the methodology of included reviews and recorded whether they fulfilled systematic review methodology; we did not perform formal assessments of the quality of included systematic reviews but summarized their findings, including quality of their included studies as reported by the authors. We extracted the following information from included primary studies: the country, setting and included population; study design; symptoms reported in mothers (including timing of symptoms if reported); the mode of delivery of babies (if reported); sample sources for SARS-CoV-2 testing for mothers and babies and SARS-CoV-2; and the numbers of neonates testing positive for SARS-CoV-2 from mothers with a COVID-19 positive diagnosis, as well as live culture results and any other relevant results (e.g. assessment of the placenta using histopathology and /or culture and/or immunostaining). We also extracted information on methodology used for RT-PCR, cycle threshold (Ct), and viral culture if reported. We defined "vertical transmission" as a positive test in the neonate within 24h of life, unless otherwise stated.

One reviewer (EAS) assessed the risk of bias from the primary studies (cohort and case series with > 2 cases) and these judgments were independently verified by a second reviewer (AP). Two reviewers (AP and EAS) extracted data from the included primary studies (including the case reports), each extracting data from half of the studies and independently verifying the data extraction of the other studies. One reviewer (AP) extracted data from the included systematic reviews, and which were independently checked by a second reviewer (EAS). Disagreements in the data extraction or bias assessments were resolved by consensus. A third author (IJO) was available in case consensus could not be reached. Results are presented in tabular format and a bar chart was used to represent the percentage of neonates testing positive for SARS-CoV-2 within 24h of birth: these were neonates born to mothers with a SARS-CoV-2 positive test or with a recorded COVID-19 diagnosis which included imaging or X-ray. We did not conduct meta-analysis because of substantial heterogeneity across the included studies.

Results

We found 123 studies assessing vertical transmission of SARS-CoV-2 from pregnant women to their neonates (Figure 1. PRISMA flow diagram). The studies assessed included 40 reviews and 83 primary studies. Laboratory studies, studies on breast milk only, one study describing a spa outbreak that did not report data for pregnant women, two case reports that did not provide data for testing of the baby, one study on oocytes, and one study that reported a subset of data of another included study[10] were excluded (see Supplementary files, List of excluded studies). After removing duplicates we included a total of 106 studies: 40 reviews and 66 primary studies.

Amongst the 66 primary studies or reports (Table 1. Characteristics of included studies), 32 were case reports (describing either single cases only or up to 2 cases) and the remaining 34 studies included prospective and retrospective cohort studies, prospective and retrospective case series, observational studies (including asymptomatic screening), database studies and a quality improvement project. Most studies reported results from testing of neonates, however one cohort study (Smithgall MC 2020) and one case series (Zhang P 2020) reported only on placental samples. Forty eight primary studies reported testing respiratory samples in neonates; in 10 studies the neonatal sample source was not clearly reported; the remainder of the studies examined placental, amniotic, umbilical and skin swab samples. The main findings of the reviews are shown in Table 2. Included reviews and those of the primary studies are shown in Table 4. Main findings of included studies.

Quality of the evidence

We assessed the methodology of included reviews and documented whether they fulfilled systematic review methodology; we did not otherwise assess their quality. Of 40 reviews, 21 fulfilled systematic review methodology, including risk of bias assessment of included studies; the others are considered narrative reviews (Table 2. Included reviews). We did not assess the quality of case reports and we did not formally assess the quality of the reviews. The risk of bias of the included primary studies is shown in Table 3. Quality of included primary studies. Almost all studies adequately reported the methods to allow replication of the study with only 5 studies rated as unclear in this domain (although it is to be noted that laboratory testing methods reporting was significantly limited as outlined below). One study did not report information on sample sources and six studies were rated as unclear in this domain, with 5/6 of these studies not reporting the sample sources used for SARS-CoV-2 testing from the mothers, and one not reporting the sample source for the neonates. Analysis and reporting was appropriate for almost all studies with only 2/34 rating as unclear in this domain. Bias was not addressed in 27/34 studies and only 2 studies specifically addressed bias, with the remainder having an unclear rating. We judged the overall risk of bias across the 32 case reports as high; the overall risk of bias across the remaining 34 studies was low to moderate. It is notable that almost all studies were conducted in a hospital setting and thus only women attending hospital were included in these studies, which may introduce bias regarding the included population in terms of presenting for rapid and accessible SARS-CoV-2 testing, as well as limitations in understanding vertical transmission in the out-of-hospital setting.

Reviews

We included 40 reviews assessing the possibility of vertical maternal-fetal transmission of SARS-CoV-2 (Table 2. Main findings of included reviews). Half (21/40) of the reviews applied at least some systematic review methodology, including appraisal of the risk of bias of included studies, while the remaining reviews were narrative reviews or literature overviews. The systematic review with the most recent search date, up to 31 October 2020, included 70 studies with a total of 1457 pregnant women diagnosed with COVID-19 (Amaral W 2020). This review identified 21 studies including 39 (3.7%) newborns who tested positive for SARS-CoV-2, and reported the detection of SARS-CoV-2 RNA in the placenta (n = 13). However, only 6 studies in the review reported positive tests for newborns within 24h (n = 13 cases, <1%). The majority (n = 58) of the included studies in the review were judged by the authors to be of low or very low quality using the GRADE quality of evidence assessment, with only one included cohort study judged to be of high quality. Overall 21 reviews (*Amaral W 2020,Bellos I 2020,Bwire GM 2020,Caparros-Gonzalez RA 2020,Cavalcante de Melo 2020,Chi J 2020,Deniz M 2020,Dhir SK 2020,Di Toro F 2020,Dube R 2020,Goh XL 2020,Khalil A 2020,Kotlyar AM 2020,Pettirosso E 2020,Raschetti R 2020,Rodrigues C 2020,Romeo G 2020,Sheth S 2020, Tripella G 2020,Turan O 2020,Walker KF 2020*) found evidence of vertical transmission, reporting transmission rates between 1% and 5%. Fifteen reviews did not find any evidence for vertical transmission (using a broader definition of vertical transmission including peribirth and post birth), although some stated vertical transmission could not be ruled out despite the lack of evidence (*Abd EW 2020,Akhtar H 2020,AlQahtani MA 2020,Della Gatta AN 2020,Diriba K 2020,Gao Y 2020,Han Y 2020,Hessami K 2020,Huntley BJF 2020,Juan J 2020,Novoa RH 2020,Sampieri CL 2020,Shrestha R 2020,Thomas P 2020, Yoon SH 2020*). However, for the majority of these reviews, the search end date was until April 2020 or May 2020, with the latest search date being July 2020 for one non-systematic review (*Hessami K 2020*). The remaining reviews did not specifically report vertical transmission rates. One review reported data solely on transmission via breast milk (*Centeno-Tablante E 2020*) and found no evidence of SARS-CoV-2 transmission through breast milk. Two reviews focused specifically on maternal characteristics and clinical outcomes and reported that pregnant women did not appear to be more affected by the respiratory complications of COVID-19, compared with non-pregnant women (*Figueiro-Filho EA 2020*) and that SARS-CoV-2 infection was not specifically shown to increase the risk of maternal, fetal, and neonatal complications (*Salem D 2020*), although other included reviews have reported the potential for higher risk of complications, depending on the maternal disease course (*Amaral W 2020*). One review assessed diagnostic methodologies to determine vertical transmission, finding a lack of consensus on the diagnostic strategy for congenital infection (*Mahyuddin AP 2020*).

Case reports

There were 32 case reports included in this review, of which 28 reports were of single cases and 4 reports included 2 cases. Sixteen case reports reported vertical transmission, with babies testing positive for SARS-CoV-2 by RT-PCR within 24h, while 13 did not find vertical transmission (Table 4. Main findings of included primary studies). Three studies did not report results for testing of neonates: three assessed amniotic fluid samples from SARS-CoV-2 PCR positive women only due to death of the fetus, with 2 reporting the presence of SARS-CoV-2 RNA using PCR in amniotic fluid and placental cell supernatant (*Shende P 2020*, 1 case;*Pulinx B 2020*, 2 cases) and one reporting a negative test for SARS-CoV-2 RNA (*Rubio Lorente AMR 2020*). The symptom status of the mother did not directly correlate with whether the baby tested positive, as some asymptomatic women were reported to have a neonate who tested positive for SARS-CoV-2.

Primary studies

We included 34 primary studies that were not case reports. The primary studies included eight case series (*Chaudhary S 2020,Liu W 2020,Masmejan S 2020,Olivini N 2020,Pereira A 2020,Pissarra S 2020,Zhang L 2020,Zhang P 2020*), 21 cohort studies (either prospective or retrospective) (*Anand P 2020,Ayed A 2020,Bachani S 2020,Barbero P 2020,Gale C 2020,Fenizia B 2020,He Z 2020, Hu X 2020,Luo Q 2020,Khan MA 2020,Nayak AH 2020,Ogamba I 2020,Oncel MY 2020,Maraschini A 2020,Popofsky S 2020,Schwartz DA 2020,Smithgall MC 2020,Tang F 2020,Vinuela MC 2020,Vouga M 2020,Yang R 2020*), 2 retrospective obser-

vational studies (*Gao X 2020,Moreno SC 2020*). and one quality improvement project (*Cojocaru L 2020*), one longitudinal surveillance study (*Woodworth KR 2020*), and one multi-centre retrospective chart review (*Marin Gabriel MA 2020.* Across these primary studies we extracted the data reporting the number of neonates testing positive for SARS-CoV-2 by RT-PCR within 24h of birth (typically from a nasopharyngeal swab), who were born to mothers who either had a positive test for SARS-CoV-2 (RT-PCR or serologic testing) or who were diagnosed as having COVID-19 based on clinical assessment including imaging or chest X-ray. Twenty studies reported no positive neonatal cases for neonates tested within 24h of birth (Figure 2. Percentage neonates positive for SARS-CoV-2 within 24h). Two studies reporting the higher percentage of SARS-CoV-2 cases amongst neonates (22% and 11%) were cohort studies that had specifically selected only neonates with a positive test within 28 days (*Gale C 2020)* or within 35 days (*Schwartz DA 2020*) of birth as the included population, where some but not all had been born to mothers with known SARS-CoV-2 infection. These latter studies therefore constituted a selected population. The study reporting 15% positivity for neonates was a small study (n=20) including neonates with a positive SARS-CoV-2 test (antibody or RT-PCR) within 14 days after birth or mothers with a positive COVID-19 test in the third trimester (*Tang F 2020*). These latter studies therefore also constitute a more selected population. The remaining studies reported percentages of positive neonates between 0.8% and 10.8%. Overall there were a total of 2391 neonates included in the analysis of which 65 (2.7%) had a positive RT-PCR test for SARS-CoV-2 within 24h of birth.

The studies included symptomatic and asymptomatic women; however there did not seem to be a specific correlation between symptom status of the mothers and the likelihood of a positive test in the babies, with some studies reporting on women who had symptoms of COVID-19 either immediately prior to or during hospitalisation, some with severe symptoms, where none of the babies tested positive within 24h of birth (e.g.*Liu W 2020,Luo Q 2020,Masmejan S 2020,Moreno SC 2020,Ogamba I 2020,Popofsky S 2020*) (See Table 1a). Similarly, the mode of delivery (vaginal birth, caesarean section, emergency caesarean section) did not seem to be correlated to positivity rate amongst neonates; across the included cohort and case series studies, for the 6188 cases where mode of delivery was reported, 3939 were by vaginal delivery, 2122 by caesarean section, and 127 reported as emergency caesarean (Table 1b). The overall rate of caesarean section across the included studies thus appears higher than rates generally reported, for example in the UK a recent study reported the rate of caesarean section delivery to range from 13.6% to 31.9% across 146 English NHS trusts[11], although rates may be context dependent. This may relate to a cautious approach being taken, particularly in the early stages of the pandemic where there was a lack of evidence to inform practice. As noted by others it is reasonable to question whether caesarean delivery for pregnant patients with COVID-19 as the indication, is warranted (*Della Gatta AN 2020*).

We considered mothers' test results up to 5 days pre delivery and 8 days post delivery, and mothers' symptomatology in that same time period (as the relevant time period of likely infectiousness). We also looked at studies' reports of SARS-CoV-2 testing in the neonates up to or at 24 hours of life, as the most relevant indicator of possible vertical transmission. Testing in mothers was not reported in 4 studies; timing for the mothers' testing was not reported in 23/79 studies, and the timing was unclear in 1 study. Timing of mothers' symptomatology was not reported or unclear in 28/83 studies. 75/83 studies reported testing of neonates within 24 hours of life for SARS-CoV-2: among these 75 studies, 144 neonates/1,545 total neonates tested positive within 24h of life. Among those neonates with a positive testing mother within 5 days pre delivery and 8 days post delivery, the number of neonates testing positive was 19/199. For neonates of women with a positive test and symptoms within that time window, 13/32 neonates tested positive within 24h of life. The number of neonates with a positive test within 24h\soutours, born to women with a negative test within 5 days pre and 8 days post delivery, was 4 of 5 neonates.

The focus of this review was to assess the evidence for vertical transmission and did not specifically address the question of maternal and fetal outcomes. Other reviews addressing this question have concluded that SARS-CoV-2 infection was not specifically shown to increase the risk of maternal, fetal, and neonatal complications (*Salem D 2020*), although some reviews have reported the potential for higher risk of complications, depending on the maternal disease course (*Amaral W 2020*). The cohort and case series studies in

this review reported some cases of neonatal admission to intensive care, but this was not always related to symptoms of SARS-CoV-2 and several studies reported no symptoms in neonates who had tested positive for SARS-CoV-2 (Table 3. Main findings of included cohort and case series studies).

Detection of virus in the placenta using PCR and immunostaining

Of the included studies, 25 studies reported assessment of the placenta and of these, 18 were case studies (*Alamar I 2020* ,*Birindwa EK 2020*, *Ferraiolo A 2020*,*Grimminck K 2020*,*Kulkarni R 2020*,*Hsu AL 2020*,*Lv Y 2020*,*Palalioglu RM 2020*,*Pulinx B 2020*,*Rebello CM 2020*,*Shende P 2020*,*Sisman J 2020*,*Stonoga E 2020*,*Tang J 2020*,*Vivanti AJ 2020*,*Von Kohorn I 2020*,*Zaigham M 2020.Zheng T 2020*), 2 were retrospective case series (*Liu W 2020*,*Masmejan S 2020*), 3 were cohort studies (*Fenizia B 2020* ,*Ogamba I 2020*,*Oncel MY 2020*) and 2 were a cohort and a case series specifically studying placental samples (*Smithgall MC 2020*,*Zhang P 2020*) (Table 5. Findings of studies reporting placenta analysis). Seven studies reported placentas testing positive for SARS-CoV-2 by in situ hybridisation or immunohistochemistry (*Alamar I 2020* ,*Hsu AL 2020*,*Pulinx B 2020*,*Shende P 2020*,*Vivanti AJ 2020*,*Zaigham M 2020*,*Zhang P 2020*), although not all of these reported vertical transmission to the neonate. Some studies only tested placentas for the presence of SARS-CoV-2 by RT-PCR and did not perform histopathology, while others assessed general inflammation of the placenta, but did not conduct immunostaining for viral presence (Supplementary file Table 4.Findings of studies reporting placenta analysis). One case study conducted whole genome sequencing of viral samples from the mother, placenta and neonate and reported the presence of a single variant of the virus in the mother and placenta. Interestingly, the neonate displayed a SARS-CoV-2 population which included the strain identical to that identified in the mother and placenta, as well as a population with one single-nucleotide polymorphism difference, and they are probably the same strain. This finding suggests vertical transmission for this case and the potential for a minor intrapatient genetic drift (*Zaigham M 2020*).

SARS-CoV-2 testing methodology

None of the included studies reported results of viral culture to detect SARS-CoV-2. All studies used RT-PCR (alone or in combination with clinical and/or immunologic tests) to determine the presence of SARS-CoV-2 infection in the mothers and the babies. However, the majority of studies did not report details of the methods used, nor did they report Ct values. Fourteen studies reported RT-PCR methodological information, including the gene probes used (*Anand P 2020*,*Bachani S 2020*,*Demirjian A 2020*,*Fenizia B 2020*,*Gao X 2020*,*Hinojosa-Velasco A 2020*,*Luo Q 2020*,*Pulinx B 2020*,*Shende P 2020*,*Tang F 2020*,*Vinuela MC 2020*,*Vivanti AJ 2020*,*Von Kohorn I 2020*,*Zaigham M 2020*), although only 9 studies reported the cycle threshold (Ct) with reported Ct ranging from 13-41 (*Bachani S 2020* ,*Demirjian A 2020*,*Hinojosa-Velasco A 2020*,*Pulinx B 2020*,*Shende P 2020*,*Vinuela MC 2020*,*Vivanti AJ 2020*,*Von Kohorn I 2020*,*Zaigham M 2020*). Two studies provided an estimate of viral load based on RT-PCR Ct (*Bachani S 2020* ,*Hinojosa-Velasco A 2020*), citing a Ct of 15 and 23, respectively, as "high viral load", and one study reported the viral load of each sample, expressed as log copies/mL or per million of cells as appropriate (*Vivanti AJ 2020*).

Discussion

We identified 40 reviews and 66 primary studies assessing vertical transmission of SARS-CoV-2 from pregnant women to their neonates. Overall, the results of these studies indicate that vertical transmission is possible, but is not frequent, and factors affecting whether vertical transmission occurs are unknown. The analysis of the included primary studies that were not case reports found that overall of the 2391 included neonates, 65 (2.7%) had a positive RT-PCR test for SARS-CoV-2 within 24h of birth; this may not be a representative population of pregnant women and neonates. Other systematic reviews included in this study have reported similar results, for example*Amaral W 2020*reported a positivity rate for newborns within 24h of less than 1%,*Cavalcante de Melo 2020* reported 2% positivity rate and*Dhir SK 2020* reported 5% positivity rate. When considering other viruses or microbial pathogens known to be transmitted from mothers to infants, a systematic review of mother-to child transmission of HIV including 18 studies and 6253 participants reported an estimated pooled prevalence of mother-to-child transmission of HIV of 11.4%

(95% CI = 9.1-13.7)[12]; a systematic review of vertical transmission of Chikungunya virus including 42 studies and 266 infected neonates reported a vertical transmission rate of 50%[13]; and a retrospective analysis of mid-trimester amniocentesis performed in pregnancies with diagnosed maternal infection by cytomegalovirus (CMV), rubella or *Toxoplasma gondii* reported a transmission rate of 17.3% in cases with infection from CMV, 9.5% from *Toxoplasma gondii* and 7.8% from rubella[14].

All of the included studies in this review used RT-PCR (alone or in combination with clinical and/or immunologic tests) to determine the presence of SARS-CoV-2 infection in the mothers and neonates, but most studies did not report details of the PCR methods used nor did they report Ct values. Notably none of the studies reported results of viral culture to detect SARS-CoV-2 and only one case report conducted whole genome sequencing of viral samples from the mother and neonate, reporting the presence of a single variant of the virus, indicating vertical transmission (*Zaigham M 2020*). In addition, in most studies no definition was provided as to what constituted "vertical transmission" and the maternal disease course was not always described in relation to testing, therefore it is possible that some cases identified as vertical transmission in the included studies could have been attributable to an alternative source of infection.

The majority of studies utilised PCR testing to assess vertical transmission. Whilst these studies suggest that vertical transmission is possible and may occur in a minority of pregnancies, these data in themselves can not discern whether infection takes place in utero, during the birth process, or via contact with the mother or health care workers at or shortly after birth.

This review did not specifically assess maternal and fetal outcomes. Some early reviews that have assessed this question found that SARS-CoV-2 infection was not specifically shown to increase the risk of maternal, fetal, and neonatal complications (*Salem D 2020*), while others have reported the potential for higher risk of complications for both mothers and their neonates, depending on the maternal disease course (*Amaral W 2020*). One recent large multinational cohort study assessing maternal and neonatal morbidity and mortality, comparing pregnant women with and without a COVID-19 diagnosis, found higher rates of adverse outcomes, including maternal mortality, preeclampsia, and preterm birth, in women with COVID-19 (*Villar et al 2021*) and further investigation is warrranted.

The presence of positive tests in both mother and neonate does not unequivocally demonstrate direct transfer of virus from mother to neonate, nor can it demonstrate the biological process by which virus may be transferred. For neonates testing positive for SARS-CoV-2, the virus may have been transmitted directly from mother to neonate across the placenta, but other infection routes may also occur. For example, one study examining fecal samples of mother-neonate dyads found that although the majority of the bacterial microbiome mirrored that of the mother, only a small proportion of the virus population found in a neonate's fecal samples matched that of the mother. This would be expected given that the gut flora in neonates will be very different from the mother, but this also suggests virus transfer via other routes such as skin contact, breastmilk, or local contamination (*Maqsood et al 2019*).

Evidence of SARS-CoV-2 RNA in placental samples does not demonstrate placental infection by the virus, nor that transmission via the placental barrier has occurred or can potentially occur (*Wastnedge et al 2020*). In these studies, positive PCR for SARS-CoV-2 in placentas did not necessarily correlate with positive PCR tests of the neonate. Some studies however showed intervillositis in the placenta and positive immunostaining for SARS-CoV-2 (*Pulinx B 2020 ,Shende P 2020,Vivanti AJ 2020,Zaigham M 2020*), which suggests the presence of SARS-CoV-2 in the placenta, and recent work has reported cultivatable SARS-CoV-2 from placental tissue with positive histopathology and whole genome sequencing supporting true vertical transmission (*Vayalumkal et al 2021*). Overall, viral invasion of the placenta appears to be likely, given the reports in some studies of intervillositis in the placenta and positive immunostaining for SARS-CoV-2; however more high quality information is needed for a clearer understanding of placental infection, the possibility of the virus being transmitted via the placental barrier, and the risk of transmission at the different stages of pregnancy. Nonetheless the demonstration in multiple studies of intervillositis in the placenta and positive immunostaining for SARS-CoV-2 would be strong enough evidence to suggest policy development against placentophagy in the setting of a mother who delivers and has active SARS-CoV-2 infection.

Strengths and limitations of the study

We conducted a comprehensive search of the literature on vertical transmission of SARS-CoV-2, also including studies that had not yet undergone peer review. We also accounted for the reporting quality of included primary studies. However, we may have missed some relevant studies and recognise that several studies may have been published after December 2020, which was the end date for the search. For example, there may now be more high quality cohort studies as much of the early evidence, as identified in this review, constituted single case studies. The aim of this review was to assess the evidence for vertical transmission and we did not specifically address maternal and fetal outcomes as a primary outcome measure. We did not systematically search for studies reporting this in our review and any conclusions around maternal and fetal outcomes should be interpreted with caution. The definition of vertical transmission varied across studies, with many not reporting the definition of vertical transmission used in the study. It should also be noted that all studies were conducted in the hospital setting, therefore this review does not provide evidence regarding transmission in the out-of-hospital setting.

It is also well known that sample contamination is a hazard of performing PCR testing which is sufficiently sensitive to detect very low concentrations of nucleic acids; for example, to avoid contamination, a study of vertical transmission of HPV used separate buildings for collecting and testing samples (*Smith et al 2010*). To reduce uncertainty about transmission based on evidence from PCR testing alone, steps for avoiding contamination should be clearly performed and reported. In the studies reviewed here, we found little data relating to PCR procedures and so are unable to evaluate any potential risk of contamination.

Implications for further research

Evidence of replicable virus as indicated by serial culture with confirmed virus identification, along with concordance in the results of whole genome sequencing for samples from mother and neonate, would substantially reduce uncertainty about the mode of transmission[15].

Whilst this currently available evidence suggests that vertical transmission is possible and appears to take place infrequently, there is very little information to explain what affects transmission, and therefore how risk can best be mitigated. The risk of vertical transmission is also uncertain when the SARS-CoV-2 infection occurs in the first or second trimester (especially if the mother is asymptomatic). Prospective studies are needed to recruit pregnant women and follow the perinatal and neonatal time course, collecting clinical and exposure information at multiple stages and utilising standardised methods to identify viral infection.

Conclusion

In conclusion, this review found evidence that vertical transmission can occur, but does not happen frequently. Among neonates born to women with a SARS-CoV-2 positive test or a recorded COVID-19 diagnosis, the great majority do not test positive for SARS-CoV-2 within the first 24 hours of life, indicating a low rate of vertical transmission. From the data we examined, it is not possible to establish what factors may affect vertical transmission.

Competing Interests

TJ was in receipt of a Cochrane Methods Innovations Fund grant to develop guidance on the use of regulatory data in Cochrane reviews (2015-018). In 2014–2016, he was a member of three advisory boards for Boehringer Ingelheim. TJ was a member of an independent data monitoring committee for a Sanofi Pasteur clinical trial on an influenza vaccine. TJ is occasionally interviewed by market research companies about phase I or II pharmaceutical products for which he receives fees (current). TJ was a member of three advisory boards for Boehringer Ingelheim (2014-16). TJ was a member of an independent data monitoring committee for a Sanofi Pasteur clinical trial on an influenza vaccine (2015-2017). TJ is a relator in a False Claims Act lawsuit on behalf of the United States that involves sales of Tamiflu for pandemic stockpiling. If resolved in the United States favor, he would be entitled to a percentage of the recovery. TJ is coholder of a Laura and John Arnold Foundation grant for development of a RIAT support centre (2017-2020) and Jean Monnet Network Grant, 2017-2020 for The Jean Monnet Health Law and Policy Network. TJ is an unpaid collaborator to the project

Beyond Transparency in Pharmaceutical Research and Regulation led by Dalhousie University and funded by the Canadian Institutes of Health Research (2018-2022). TJ consulted for Illumina LLC on next generation gene sequencing (2019-2020). TJ was the consultant scientific coordinator for the HTA Medical Technology programme of the Agenzia per i Servizi Sanitari Nazionali (AGENAS) of the Italian MoH (2007-2019). TJ is Director Medical Affairs for BC Solutions, a market access company for medical devices in Europe. TJ was funded by NIHR UK and the World Health Organization (WHO) to update Cochrane review A122, Physical Interventions to interrupt the spread of respiratory viruses. TJ is funded by Oxford University to carry out a living review on the transmission epidemiology of COVID-19. Since 2020, TJ receives fees for articles published by The Spectator and other media outlets. TJ is part of a review group carrying out Living rapid literature review on the modes of transmission of SARS-CoV-2 (WHO Registration 2020/1077093-0). He is a member of the WHO COVID-19 Infection Prevention and Control Research Working Group for which he receives no funds. TJ is funded to co-author rapid reviews on the impact of Covid restrictions by the Collateral Global Organisation. He is also an editor of the Cochrane Acute Respiratory Infections Group.

TJ's competing interests are also online*https://restoringtrials.org/competing-interests-tom-jefferson*

CH holds grant funding from the NIHR, the NIHR School of Primary Care Research, the NIHR BRC Oxford and the World Health Organization for a series of Living rapid review on the modes of transmission of SARs-CoV-2 reference WHO registration No2020/1077093. He has received financial remuneration from an asbestos case and given legal advice on mesh and hormone pregnancy tests cases. He has received expenses and fees for his media work including occasional payments from BBC Radio 4 Inside Health and The Spectator. He receives expenses for teaching EBM and is also paid for his GP work in NHS out of hours (contract Oxford Health NHS Foundation Trust). He has also received income from the publication of a series of toolkit books and for appraising treatment recommendations in non-NHS settings. He is Director of CEBM, an NIHR Senior Investigator and an advisor to Collateral Global. He is also an editor of the Cochrane Acute Respiratory Infections Group

DHE holds grant funding from the Canadian Institutes for Health Research and Li Ka Shing Institute of Virology relating to the development of Covid-19 vaccines as well as the Canadian Natural Science and Engineering Research Council concerning Covid-19 aerosol transmission. He is a recipient of World Health Organization and Province of Alberta funding which supports the provision of BSL3-based SARS-CoV-2 culture services to regional investigators. He also holds public and private sector contract funding relating to the development of poxvirus-based Covid-19 vaccines, SARS-CoV-2-inactivation technologies, and serum neutralization testing.

JMC holds grants from the Canadian Institutes for Health Research on acute and primary care preparedness for COVID 19 in Alberta, Canada and was the primary local Investigator for a *Staphylococcus aureus*vaccine study funded by Pfizer for which all funding was provided only to the University of Calgary. He is a co investigator on a WHO funded study using integrated human factors and ethnography approaches to identify and scale innovative IPC guidance implementation supports in primary care with a focus on low resource settings and using drone aerial systems to deliver medical supplies and PPE to remote First Nations communities during the COVID 19 pandemic. He also received support from the Centers for Disease Control and Prevention (CDC) to attend an Infection Control Think Tank Meeting. He is a member and Chair of the WHO Infection Prevention and Control Research and Development Expert Group for COVID 19 and a member of the WHO Health Emergencies Programme (WHE) Ad hoc COVID 19 IPC Guidance Development Group, both of which provide multidisciplinary advice to the WHO, for which no funding is received and from which no funding recommendations are made for any WHO contracts or grants. He is also a member of the Cochrane Acute Respiratory Infections Group.

JB is a major shareholder in the Trip Database search engine (*www.tripdatabase.com*) as well as being an employee. In relation to this work Trip has worked with a large number of organisations over the years, none have any links with this work. The main current projects are with AXA and Collateral Global.

ECR was a member of the European Federation of Neurological Societies(EFNS) / European Academy of

Neurology (EAN) Scientist Panel – Subcommittee of Infectious Diseases (2013-2017). Since 2021, she is a member of the International Parkinson and Movement Disorder Society (MDS) Multiple System Atrophy Study Group and the Mild Cognitive Impairment in Parkinson Disease Study Group. She was an External Expert and sometimes Rapporteur for COST proposals (2013, 2016, 2017, 2018, 2019) for Neurology projects.

AP is Senior Research Fellow at the Centre for Evidence-Based Medicine and reports grant funding from NIHR School of Primary Care Research (NIHR SPCR ESWG project 390 and project 461), during the conduct of the study; and occasionally receives expenses for teaching Evidence-Based Medicine.

IJO, EAS have no interests to disclose.

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Data Availability

All data included in the review are provided in the tables or in the supplemental files.

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Table 1. Characteristics of included studies

Study	**Country**	**Population**	**Method**	**Patient numbers**	**Symptoms in mothers, including timing (if reported)**
Alamar I 2020	USA	1 mother with fever, mild chills, fatigue, anosmia and dysgeusia beginning 1 day before presentation, with positive COVID-19 test	case study	1 mother baby dyad	Mother at 35+6 gestational age presented with vaginal bleeding & contractions; subjective fever, mild chills, fatigue, dysgeusia, anosmia beginning 1 day before presentation.

Anand P 2020	India	69 COVID19 + mothers, 65 infants (1 abortion, 4 still births). 51 mothers had symptoms and of these 45 had mild symptoms	cohort study	39/69 mothers had positive test; 2 deaths attributed to COVID-19	Among 7 positive-testing women: 1. critically ill & died 3 days postpartum, symptoms & timing NR; 2. fever 13 days pre-delivery, negative test day prior to delivery, time to diagnosis NR; 3. symptoms days 4 postpartum, time to diagnosis NR; 4. fever before delivery led to testing positive, time to diagnosis NR; 5. tested day 4 postpartum, symptoms NR; 6. symptoms day 12 postpartum; 7. day 10 symptoms so tested, time to diagnosis NR.

Ayed A 2020	Kuwait	185 pregnant women with PCR confirmed SARS-CoV-2 infection (median age 31; median gestation at diagnosis 29 weeks). 88% had mild symptoms, (fever and cough the most common presenting symptoms). During the study period 40 (21.6%) gave live birth, 3 (1.6%) had a miscarriage, and 1 (0.54%) had intrauterine fetal death, which was not related to COVID19. Only 2 (1.1%) patients developed severe pneumonia and required intensive care. Most of the neonates were asymptomatic, and only 2 (5%) of them tested positive on day 5 .	retrospective study, medical records	185 women testing positive; no deaths	88% of the patients had mild symptoms, with fever (58%) being most common presenting symptom followed by cough (51%). Time to diagnosis NR; tested on admission to maternity services.

Bachani S 2020	India	348 pregnant women tested for SARS-CoV-2, 57 women (16.3%) confirmed positive. Three maternal deaths were associated with comorbidities. Five neonates tested positive for SARS-CoV-2,	retrospective study	57/348 pregnant women positive; 3 deaths (comorbidities, 2 classed as COVID-19-related complications; 1 classed as COVID-19-related)	Most women that tested positive experienced mild infection (45/57; 78.9%), with one or two spikes of low-grade fever, cough, and/or diarrhoea that resolved in 2-3 days. Three (5.2%) women had moderate symptoms (fever and breathlessness). Timing of symptoms in relation to testing and/or delivery NR.
Bandyopadhyay T 2020	India	1 mother, mild grade fever, close contact of positive case (husband)	case study	1	Mild grade fever, pharyngeal swab taken that day and found positive for SARS-CoV-2 by RT-PCR; admitted to hospital for isolation then became asymptomatic one day later. Delivery 1 month after symptoms. Negative by PCR before delivery.

Barbero P 2020	Spain	91 women with COVID-19 symptoms (fever (37.8 C), dry cough, shortness of breath or dyspnea,chills and myalgia, headache, coryza and new onset of loss of taste or smell) and diagnosed with SARS-CoV-2 infection during pregnancy and postpartum (<40 days after giving birth). 46.2% rate of hospitalization,	retrospective cohort study	91 women	Symptoms preceded & led to testing. Timing in relation to delivery NR. 40/91 developed pneumonia, and 4/91 required ICU admission

Birindwa EK 2020	DR Congo	1 woman positive for SARS-Cov-2	case report	1 mother baby dyad	3 weeks before admission, woman complained of fever, not responding to acetaminophen; fever persisted; swab test done 2 weeks later confirming SARS-CoV-2 positive by RT-PCR. She was admitted. 4 days later a rapid antigen test was negative for SARS-CoV-2. Preterm labour commenced and C-section was performed.
Bordbar A 2020	Iran	1 women, gestational diabetes, no COVID-19 symptoms; tested 2 days after giving birth	case report	1 mother baby dyad	no fever, cough, dyspnea or GI symptoms
Chaudhary S 2020	Pakistan	26 women, RT-PCR COVID-19 positive; 10 asymptomatic, 16 symptomatic; all mild disease, 1 pneumonia	case series	26; 14 deliveries during study period	16/26 positive tested women were symptomatic: 14/16 fever, 11/16 cough; 1 severe pneumonia leading to death. Timing of symptoms NR.

Cojocaru L 2020	US	1989 women were screened for SARS-CoV-2, from which 86 (0.04%) tested positive and 34 delivered during the study period (3 excluded from analysis). 5 women in analysis admitted to ICU	quality improvement project, prospective	31	5/31 admitted to ICU. Other symptoms, and timing of symptoms, NR.
Demirjian A 2020	UK	1 woman, fever and respiratory symptoms, tested for COVID on day 6 of admission	case report	1	Fever and respiratory symptoms on admission; condition deteriorated to severe, leading to C-section 7 days after admission.
Farsi Z 2020	Iran	1 women, pregnant with triplets, symptoms of cough, fever, myalgia	case report	1 mother, 3 babies	Woman had hypothyroidism, gestational hypertension (HTN), and gestational diabetes mellitus; also recent symptoms of cough, fever and myalgia 3 days before delivery.

Fenizia B 2020	Italy	31 laboratory-confirmed COVID19+ women, also radiological assessment and signs and symptoms; 4 severe cases requiring ICU admission	cohort study, multicentre	31 mothers, 31 babies	4/31 women had severe COVID-19 (defined by the need of urgent delivery for the deterioration of maternal conditions or by ICU/sub-intensive care admission). Radiological confirmation of interstitial pneumonia was obtained on admission or antepartum for all 4 severe cases and in 10 (32%) of the mild cases.
Ferraiolo A 2020	Italy	1 woman, no symptoms, breach presentation	case report	1 mother baby dyad	Hospitalized in order to undergo C-section. No symptoms on admission of fever/ respiratory/ GI symptoms, myalgia, malaise, ageusia/ anosmia
Gale C 2020	UK	babies with a diagnosis of SARS-CoV-2 within 28 days	prospective cohort study	66 SARS-CoV-2 positive babies; 21 diagnosed with SARS-CoV-2 in the first 7 days,	maternal symptoms NR
Gao W 2020	China	1 asymptomatic woman	case report	1 mother baby dyad	no fever or cough; thoracic CT showed no abnormality

Gao X 2020	China	14 pregnant women with lab-confirmed COVID-19	retrospective observational study	14 women? (numbers unclear as not consistent in reporting)	11/14 women had fever, 6/14 had cough; all 14 had abnormalities evident by thoracic CT. 8/14 were given oxygen via nasal cannula; none was treated with respirator or mechanical ventilation.
Grimminck K 2020	The Netherlands	1 pregnant woman, OP swab RT-PCR positive for COVID-19, immunosuppressed (lupus)	case report	1 mother baby dyad	cough developed prior to admission
He Z 2020	China	22 newborns born to pregnant women with COVID-19	retrospective cohort study	22 newborns	NR
Hinojosa-Velasco A 2020	Mexico	1 symptomatic woman (fever, cough, sore throat), patchy chest radiograph, testing positive for COVID-19	case report	1 mother baby dyad	Fever, coughing, odynophagia, sore throat, headache, diarrhoea, rhinorhea, 2 days before admission
Hsu AL 2020	USA	1 pregnant woman, mild symtoms	case report	1 mother baby dyad	myalgia 2 days prior to hospitalisation, no fever throughout hospitalisation

Hu X 2020	China	6 preterm infants born to COVID-19 positive mothers	retrospective cohort study	6 preterm infants, 6 mothers	In the 6 mothers, COVID-19 experienced 9, 10, 20, 13, 2, 2 days before delivery. All mild except one termed uncompli-cated. Fever in 3/6, cough in 2/6.
Khan MA 2020	Pakistan	66 pregnant women testing COVID-19 positive, most asymptomatic	cohort study	66 women; 67 infants (1 twin)	Most of the 66 SARS-CoV-2-positive women were asymptomatic. One woman was admitted with respiratory failure.
Kulkarni R 2020	India	pregnant woman, admiited with fever and body ache, in active labor	case report	1 mother baby dyad	Fever and myalgia one day prior to admission in active labour.
Liu W 2020	China	Neonates born to women with: 1. confirmed COVID-19 (symptoms and positive RT-PCR), 2. suspected COVID-19 (symptoms with negative RT-PCR but chest CT pneumonia) and 3. control cases (with or without symptoms, confirmed as influenza)	retrospective analysis of cases	1. 15 neonates from COVID-positive women; 2. 17 neonates from suspected COVID women; 3. 16 neonates from control group	fever (10/15, 67%) and cough (6/15, 40%) among mothers with COVID-19 diagnosis.

Luo Q 2020	China	23 pregnant women, 14 with confirmed COVID-19, 9 with suspected COVID-19 (chest-CT pneumonia but negative PCR and serology).	cohort study breast feeding	23 women, 23 babies	fever (71%) and cough, 8/14 confirmed COVID-19 cases asymptomatic
Lv Y 2020	China	1 pregnant woman, fever and cough, SARS-CoV-2 PCR positive	case report	1 mother baby dyad	recurrent fever and cough over 2 weeks prior to admission
Maraschini A 2020	Italy	146 pregnant women with confirmed COVID-19, 142 confirmed by RT-PCR, 4 confirmed by chest X-ray; 99 no COVID pneumonia, 47 with COVID pneumonia	cohort study	146 women, 143 singleton babies, 3 twins; 2 stillbirths, 147 live births	41/146 (28.1%) of the COVID-19-positive women asymptomatic. 70/146 had fever, 68 had cough, 52 fatigue. Onset of clinical symptoms occurred in 9.5% of the cases on the day of delivery, and in 90.5% before it, the median value being 8 days (range 1-52 days).

Marin Gabriel MA 2020	Spain	Pregnant women, third trimester, RT-PCR or serology OCVID-19 positive: 222 RT-PCR positive; 19 RT-PCR negative but serology positive at delivery.	multi-centre study, retrospective chart review plus 1 month follow-up	242 mothers, 248 babies	Symptoms: Cough (33%); fever (30%). Odynophagia (2%) and chest pain (<2%%) were uncommon. 7 ppts required ICU. One mother who died due to a massive thromboembolic event.
Masmejan S 2020	Switzerland	13 pregnant women, positive RT-PCR or positive serology (IgG) for SARS-CoV-2. 11 mild symptoms or asymptomatic, 2 critical fever, severe symptoms	retrospective case series	13 women, 13 babies	5 asymptomatic, 6 mild, 1 severe and 1 critical.
Mohakud NK 2020	India	Symptomatic pregnant woman, taking treatment for hypothyroidism, at 32+ weeks tested positive for SARS-CoV-2.	case report	1 mother baby dyad	Presented with four-day history of low-grade fever, malaise, and breathing difficulty.

Moreno SC 2020	USA	Symptomatic pregnant women diagnosed positive for COVID-19 via PCR in the third trimester and all neonates with complete COVID-19 testing and delivery data.	retrospective observational study	19 women, 21 neonates (including two sets of dichorionic diamniotic twins)	Women included in the study if symptomatic and with positive PCR for SARS-CoV-2. Cough 19/19; fever 7/19; shortness of breath 5/19.
Nayak AH 2020	India	Pregnant women attending for obstetric care.	cohort study	977 pregnant women: 141 with positive SARS-CoV-2 test; 836 with negative test.131 neonates tested.	97% of the women were asymptomatic or had mild symptoms like fever or cough not requiring any oxygen therapy. (unclear if 97% of all women in the study, or of all positive-testing women).

Ogamba I 2020	USA	pregnant women 18 years or older with a diagnosis of COVID-19 (testing was performed on admission to the labor & delivery unit, outpatient setting, and/or inpatient hospitalization)	retrospective cohort study	40 women, 25 deliveries within the time frame of the study; 23 neonates	30/40 SARS-CoV-2-positive women reported <= one symptom due to COVID-19; 10/40 were asymptomatic. Symptoms included loss of smell & taste, nausea, vomiting, body aches, chills, headache, fever, dry cough, shortness of breath, abdominal pain, difficulty breathing, chest pain.
Olivini N 2020	Italy	5 women who tested positive after screening due to close contact with an infected maternity services HCW, and their newborns.	retrospective case series	5 mother and infant dyads	3/5 women reported symptoms: 1 low grade fever, 2 anosmia, 1 dysgeusia, 1 musculoskeletal pain. Onset of symptoms occurred at day 1, 5 and 19 after childbirth.

Oncel MY 2020	Turkey	125 pregnant women and their newborns, tested if symptomatic or had had close contact with family members with COVID-19.	cohort study	125 pregnant women; NP swabs available for 120 newborns (not possible for 5 [asymptomatic] newborns)	85/125 SARS-CoV-2 positive women had at least one COVID-19 symptom. (40/125 had had close contact.) 8 were admitted to ICU for mechanical ventilation, 6/these 8 died.
Palalioglu RM 2020	Turkey	Woman aged 42 years, 37 weeks prregnant, with diet-regulated gestational diabetes mellitus, tested SARS-CoV-2 positive, asymptomatic. Admitted two weeks later & C-section performed due to to prelabour rupture of membrane.	case report	1 mother and newborn dyad	asymptomatic
Parsa Y 2020	Iran	41-yr-old pregnant woman with signs and symptoms of acute respiratory illness presented with labor pain and vaginal leak at 37 weeks gestation, tested positive for COVID-19 using RT-PCR, emergency C-section	case report	1 mother & newborn dyad	presented with signs and symptoms of acute respiratory illness including shortness of breath and cough.

Pereira A 2020	Spain	22 pregnant woman with SARS-CoV-2 (11 symptomatic), median age 34 years, median gestational ag 38+5 weeks.	case series	22 mother and newborn dyads	6/22 mild symptoms, 5/22 pneumonia, 10/22 no symptoms
Pessoa FS 2020	Brazil	34 year old woman 33+ weeks pregnant, RT-PCR positive, admitted with flu-like symptoms including fever, dry cough & fatigue from talking; chest computed tomography showed attenuations with ground glass opacification and bilateral consolidations.	case report	1 mother and newborn dyad.	admitted with flu-like symptoms including fever, dry cough & fatigue; symptom onset 7 days prior to admission, progressed to dyspnoea
Pissarra S 2020	Portugal	10 SARS-CoV-2 positive pregnant women (7 were symptomatic) giving birth at the hospital.	case series	10 mother and newborn dyads.	7/10 symptomatic; 1 mother admitted to ICU; days from beginning of symptoms to delivery ranged from 0-15. No details of symptoms or severity

Popofsky S 2020	USA	Women with positive SARS-CoV-2 PCR and their newborns, born at one of 3 hospitals in New York State.	observational longitudinal cohort	160 newborns	59 mothers (36.9%) were symptomatic during perinatal hospitalization, with fever (>37.7°C), cough, shortness of breath, or a combination of these. 25 mothers (15.6%) had been symptomatic before the perinatal admission but were no longer symptomatic during hospitalization. 76 (48%) were never symptomatic. Mean day of symptoms: 14
Pulinx B 2020	Belgium	30 year old woman 22 weeks pregnant with dichorionic diamniotic twins, recently diagnosed with gestational diabetes mellitus, tested positive for SARS-CoV-2 by RT-PCR.	case report	1 mother & two twin neonates	Presented to ED at 22w with rhinitis and fever (39.2 °C)

Rebello CM 2020	China	32-year-old woman pregnant at 34 weeks, with gestational diabetes; symptoms of anosmia, ageusia, runny nose, dry cough, headache, myalgia, no fever, diagnosed with SARS-CoV-2.	case report	1 mother and infant dyad	Symptoms of anosmia, ageusia, runny nose, dry cough, headache and myalgia—without fever (10 days before delivery); diagnosed with COVID-19 eight days before delivery
Rivera-Hernandez P 2020	USA	38-year-old pregnant woman (32/33 weeks) with obesity, poorly controlled type 2 diabetes, asthma and 3-day history of dyspnea and malaise, admitted to ICU.	case report	1 mother and infant dyad	Presented at 33w pregnant, 3-day history of malaise and dyspnoea; ICU admission and ventilation; delivery on day 4 of admission
Rubio Lorente AM 2020	Spain	2 pregnant women, 1: 20w pregnant, fever and cough, positive SARS-CoV-2 PCR test, negative serology. 2: 12w pregnant, delayed abortion, low fever, serology positive, PCR-negative for SARS-CoV-2	analysis of amniotic fluid of 2 cases	2 women	Case 1, symptomatic; Case 2, fever 2 weeks before, resolved prior to amniocentesis

Sajjan GR 2020	India	21yr old primigravida at 32weeks gestational age, diagnosed with PPROM	case report	1 mother and infant dyad	asymptomatic of respiratory disease
Schwartz DA 2020	Iran	19 neonates testing positive for SARS-CoV-2	cohort study	19 neonates	predelivery symptoms: 10 respiratory symptoms (2 severe), 4 asymptomatic, 5 no information reported.
Shende P 2020	India	1 woman, asymptomatic, 8 weeks pregnant, tested positive for SARS-CoV-2 by PCR. Fetal demise at 13 weeks led to dilation and curettage termination procedure.	case report	1 mother and first trimester fetus	asymptomatic
Singh MV 2020	India	1 asymptomatic pregnant woman with positive SARS-CoV-2 test, and her neonate	case report	1 mother and infant dyad	asymptomatic
Sisman J 2020	USA	1 pregnant woman with obesity and diabetes mellitus and late latent syphilis, and her infant.	case report	1 mother and infant dyad	3 days pre-delivery admitted with fever and diarrhoea (admitted due to possible preterm labour)

Smithgall MC 2020	USA	3rd trimester placentas from 51 SARS-CoV-2-positive and 25 SARS-CoV-2-negative women	cohort study (placentas)	76 pregnant women	26/51 SARS-CoV-2-positive women were asymptomatic. Cough (61.5%), fever (53.8%), myalgia (26.9%), sore throat (11.5%) and fatigue (11.5%) were common symptoms in the 25 symptomatic women. 4 had severe disease.
Stonoga E 2020	Brazil	Woman at 27 weeks' gestation wtih COVID-19 symptoms: dyspnea, dry cough, high temperature (38.5°C), anosmia, nausea, vomiting, and diarrhea had developed 2 days before hospitalization.	case report	1 mother and fetus dyad	Dyspnea, dry cough, high temperature (38.5°C), anosmia, nausea, vomiting, and diarrhea had developed 2 days before hospitalization.

Tang F 2020	China	Neonates born during the pandemic period 2nd February - 31st March 2020 in Wuhan, whose mother was confirmed with COVID-19 in the 3rd trimester, or with +ve SARS-CoV-2-IgM and SARS-CoV-2-IgG and/or +ve RT-PCR for SARS-CoV-2 within 14 days after birth. All included neonates had excluded diagnoses of adenovirus, enterovirus, influenza A, influenza B, parainfluenza, chlamydophila pneumonia and mycoplasma pneumonia.	observational cohort	20 mother & neonate dyads	Unclear. However, the mothers of two neonates who tested positive for RT-PCR at 1–2 days after birth were also tested positive and exhibited typical symptoms such as fever and cough just one day before delivery

Tang J 2020	China	Two mothers with symptomatic COVID-19 in the second trimester and their neonates	case report (2 cases)	2 mother & neonate dyads	Case 1: fever & respiratory symptoms 13 weeks prior to delivery, symptoms resolved; admission to hospital 13 weeks later with premature rupture of membranes, no respiratory symptoms, but serum antibodies positive for SARS-CoV-2. Case 2: mild respiratory symptoms predelivery.
Vendola N 2020	Italy	2 pregnant women with positive IGG on peripherical blood test.	case report (2 cases)	2 mother and neonate dyads	Both cases asymptomatic
Vinuela MC 2020	Spain	Systematic screening in asymptomatic women admitted for spontaneous delivery: first 100 consecutive participants; 9 tested positive for SARS-CoV-2 by PCR; 13 (including 7 of the PCR-positive women) had antibodies to SARS-CoV-2.	observational study, asymptomatic screening	100 asymptomatic pregnant woman & their neonates	all asymptomatic

Vivanti AJ 2020	France	Pregnant woman admitted at 35+ weeks with COVID-19-like symptoms and subsequently tested and treated accordingly.	case report	1 mother & infant dyad	fever (38.6 °C) and severe cough
Von Kohorn I 2020	USA	Pregnant woman 34 weeks with vaginal bleeding and cramping, found to have thrombocy-topenia, transaminitis, and hyperuricemia; infant delivered by C-section at 34 weeks (due to hemolysis, elevated liver enzymes, low platelet syndrome, suspicion for systemic COVID-19, and history of prior cesarean section)	case report	1 mother & infant dyad	Presented with cough, vaginal bleeding. Diagnosed as COVID-19 + 14h prior to delivery.

Vouga M 2020	International	Women with symptoms for COVID-19 included in the study. The study was conducted from 24th March to 26th July 2020.	cohort study	1,033 pregnant women tested for SARS-CoV-2: 926 tested positive, 107 tested negative. Data available for 384 newborns tested at birth.	Symptoms included fever, anosmia, cough, sore throat, dyspnoea, myalgia, fatigue, headache, nausea. Symptom frequency reported in the cohort, symptom severity not reported. Some asymptomatic
Woodworth KR 2020	USA	4,442 women with known pregnancy outcomes with laboratory-confirmed SARS-CoV-2 infection reported during 29th March to 14th October 2020. 4,495 live births.	longitudinal surveillance	4,442 women with laboratory confirmed SARS-CoV-2, who had 4,495 live births. Molecular testing results available for 610 infants.	Symptom status was known for 2,691 (60.6%) women (including women with symptom reported on COVID-19 form), 376 (14.0%) of whom were reported to be asymptomatic. Symptoms and severity not reported

Yang R 2020	China	All pregnant women with singleton live birth recorded by the system between 13th January and 18th March 2020.	cohort study.	11,078 live singleton birth mother & infant dyads: 65 pregnant women tested positive for SARS-CoV-2; 38 /58 newborns of positive testing mothers were tested for SARS-CoV-2 after birth.	Those with fever and cough or having abnormal computed tomography (CT) scan were tested for SARS-CoV-2. Severity of symptoms not reported.
Zaigham M 2020	Sweden	Case report of a pregnant woman admitted with COVID-19 symptoms & then diagnosis; and subsequent investigations in the neonate.	case report	1 mother + neonate dyad	34w pregnant. Fever, dry cough, abdominal pain. Treated in postpartum ward (no ICU)
Zhang L 2020	China	18 patients with COVID-19 during late pregnancy, none critically ill.	case series (18 cases). Epidemiological characteristics, clinical manifestations, laboratory tests, chest CT and pregnancy outcomes reported.	18	35-41w pregnant, Most pregnant women had fever, cough, sore throat, fatigue, chest tightness or shortness of breath, diarrhea, and runny nose; Clinical typing: 1 case ”mild”, 16 cases ”ordinary”, 1 case ”severe”

Zhang P 2020	USA	364 consecutive women attending to give birth including 74 positive and 290 negative for SARS-CoV-2 by NP swab PCR.	case series (placenta analysis). Placental pathology and clinical characteristics reported.	364 pregnant women, 74 testing positive for SARS-CoV-2	Not reported
Zheng T 2020	China	Two pregnant women, admitted due to symptoms suggestive of Covid-19. (The only reported Covid-19 cases among pregnant women in this city during 20 January 2020, to 9 April 2020)	case report (2 cases). Laboratory, imaging & SARS-CoV-2 nucleic acid tests were performed on the 2 women with COVID-19 and their newborns	2 x mother + neonate dyads	1 woman: 36w pregnant, fever and asthenia at admission, CT showed bilateral lung infection, classified as "severe COVID-19"; 2nd woman: 39w, admitted due to abnormal chest CT; no fever or cough, CT showed bilateral lung infection,

Table 1b. Characteristics of included primary studies (continued)

Study	**Mode of delivery (if reported)**	**Sample sources: mother**	**Sample sources: neonate /infant**	**Potential vertical transmission (samples PCR-positive n/d for SARs-CoV-2 RNA unless otherwise stated)**	**Other results**

Alamar I 2020	Urgent C-section due to bleeding	tested for SARS-CoV-2 using qRT-PCR of a NPl swab	NP swab qRT-PCR for SARS-CoV-2 was positive at 24 and 48 HOL; placental tissue biopsy using RNA in situ hybridisation	1/1	The infant's NP qRT-PCR remained positive on DOL 7. She remained asymptomatic during the daily follow-up period. Placenta ISH for SARS-CoV-2 RNA revealed a strong signal in the villous syncytiotrophoblast; but no signal in villous stromal cells, Hofbauer cells, or villous endothelium
Anand P 2020	Elective C-section delivery: 9/69; emergency C-section: 17/69. Remainder vaginal.	NP RT-PCR	NP/OPl RT-PCR, tested within 24h	7/65; no deaths	2 maternal deaths attributed to COVID; All COVID+ neonates remained asymptomatic to last follow-up at day 29
Ayed A 2020	17/41: emergency C-section; remainder vaginal	SARS-CoV-2 infection, as confirmed by RT-PCR of NP swab (Cobas 6800 Systems, Roche/(Taq Path, Thermo-Fisher Scientific. Patients who had equivocal or negative testing results were excluded.	NP swab, RT-PCR	0/41 tested positive within 24h; 2/41 neonates tested positive on day 5; no deaths	Assessed cases between 15 March and 31 May 2020; follow-up to 15 June 2020. At follow-up 98.8% of women had been discharged, median hospital stay 15 days.

Bachani S 2020	Spontaneous labour: 42; Induced labour: 15; Elective C-section: 9; Emergency C-section: 17	NP specimen; qRT-PCR (LabGun COVID-19 RT-PCR kit, India)	NP specimen; qRT-PCR (LabGun COVID-19 RT-PCR kit, India)	5/56 neonates positive; 2 tested positive withim 24h; 2 tested positive on day 4; 1 tested positive on day 14 no deaths	
Bandyopadhyay T 2020	Vaginal	pharyngeal swab, RT-PCR	NP swab, RT-PCR; qualitative IgG serum antibody test positive; qualitative IgM serum antibody test negative	1/1	On day 2 and day 3 after birth infant tested negative with NP swab RT-PCR. Mother asymptomatic after admission; tested negative 2 days before birth.
Barbero P 2020	C-section: 11/23; remainder vaginal	pharyngeal swab, RT-PCR or radiological findings in chest X-ray highly suggested COVID-19 if 2 consecutive negative PCR tests	NP swab, RT-PCR	0/23 babies of women with active infection	no suggestive symptoms in neonates on clinical follow-up; 1 baby tested positive on day 8 - not vertical transmission
Birindwa EK 2020	C-section	NP swab, RT-PCR	NP swab, RT-PCR	1/1, baby tested positive at birth, on day 3; died on day 5 of sepsis	inflamed placenta
Bordbar A 2020	C-section	NP swab, RT-PCR	NP swab, RT-PCR, day 2, chest Xray	1/1; RT-PCR test on day 2, no symptoms; no symptoms at follow-up on day 14	
Chaudhary S 2020	3/14 vaginal, 11/14 C-section	NP swab, RT-PCR	NP swab, RT-PCR	0/14 All infants negative by RT-PCR	

Cojocaru L 2020	8/31 C-section; 23/31 vaginal	Not clearly stated. Imply NP swab, RT-PCR?	OP and NP swab at 24h and 48h, RT-PCR	0/31 (all neonates tested negative)	Project on bonding and transmission. Maternal bonding was defined by events such as rooming-in, skin to skin contact (STSC), and breastfeeding. None of the neonates who bonded with their mothers tested positive for SARS-CoV-2 during hospitalization

Demirjian A 2020	C-section	Respiratory samples (day 6) and sputum (day 8), RT-PCR	NP swab, at birth and day 3, stool and blood samples day 3	1/1; RT-PCRnegative at birth, RT-PCR respiratory sample positive on day 3, stool and blood samples negative	Baby no symptoms up to day 5, then developed fever (38.0°C), coryza, and mild tachypnea lasting 2 days. No respiratory support required. No symptoms at discharge on day 18. Mother on ventilation for 17 days. Discharged at 31 days. Genomic viral sequencing of SARS-CoV-2 virus isolated from samples from the mother's and the neonate's respiratory tract secretions. Genetic sequences were identical across the entire genome apart from a single-nucleotide difference between the baby and mother's genomes.

Farsi Z 2020	Emergency C-section	PCR, test type and sample not specified	PCR, test type and sample not specified	1/3; baby1: PCR negative (day 3), ; baby2: PCR neg day 3, PCR + day 6, 23, PCR neg day 30, healthy at 37 day follow-up; baby3: PCR neg day 3,6	Baby1: died from respiratory and gastroin-testinal bleeding; Baby2: healthy at follow-up; baby3:died day 16 of abdominal distension and enterocolitis

Fenizia B 2020	25/31 vaginal; 6/31 C-section	NP swab, RT-PCR; placenta and umbilical cord biopsy, umbilical cord blood; amniotic fluid from C-section where possible, vaginal swab before delivery and maternal blood sample; breast milk on day 5 from breastfeeding mothers	NP swab, RT=PCR	2/31, all babies healthy	virus detected in 2/31 maternal plasma samples (both characterized by a severe clinical outcome). Detected the presence of SARS-CoV-2 in vaginal swab, placental tissue and cord plasma from 1 mother (severe outcome). Detected SARS-CoV-2 in placental tissue from subject 1 mother. Detected SARS-CoV-2 in one milk specimen only (severe clinical outcome). 0/6 amniotic fluids & 0/12 umbilical cords tested positive. Placentae from SARS-CoV-2 infected patients display a generalized immune activation profile compared to the uninfected

Ferraiolo A 2020	elective C-section	NP RT-PCR; placental biopsy and placental swab	NP swab, RT-PCR, 0h and 24h	0/1, healthy, discharged at 21 days	Placental swabs COVID-19 positive, some placental inflammation on biopsy
Gale C 2020	not reported	not specified	NP swab? - not specified for all	17 babies born to mothers with confirmed infection within 7 days before or after birth. Only 2 babies considered vertical transmission due to positive NP swab	Over the study period, estimated 118 347 livebirths,66 positive cases, giving a neonatal incidence of SARS-CoV-2 infection of 5·6 (95% CI 4·3–7·1) per 10 000 livebirths.
Gao W 2020	emergency C-section	pharyngeal swab , PCR; positive serum IgM and IgG antibody (colloidal gold method) were weak positive and strong positive	pharyngeal swab, PCR	0/1; day 4 PCR test negative	
Gao X 2020	2 vaginal, 12 C-section section	OP or NP swabs; RT-PCR positive; tested positive by the IgM-IgG combined antibody test for SARS-CoV-2; breast milk - immunoassay	nasal or OP swab	0/14	all breast milk samples negative for viral RNA, 3 breast milk samples positive for SARS-CoV-2 antibodies
Grimminck K 2020	vaginal, induced labour	OP, RT-PCR; vaginal sample, urinary catheter sample, placenta	OP swab, RT-PCR	0/1 - no vertical transmission,	none of the samples taken from vagina, placenta, catheter or baby were positive

He Z 2020	not reported	not reported	Amniotic fluid, umbilical cord blood, faeces, urine, blood, throat swab samples; qRT-PCR	0/22	None of the samples taken from newborns tested positive for SARS-CoV-2. 3 newborns had elevated IgM Ab in umbilical cord and fetal blood; 12/22 had IgG positive for SARS-CoV-2; no deaths; 17/22 had hyperbilirubinaemia; report potential kidney damage in newborns

Hinojosa-Velasco A 2020	emergency C-section	NP and OP swabs, RT-PCR; milk and stool sample	NP and OP swabs, during delivery, RT-PCR; stool sample	1/1	Neonate considered to have a severe case of COVID-19 based on severity of symptoms, placed on oxygen. day 4 RT-PCR analyses of the mother's milk and stool samples, and stool samples from baby, were positive for SARS-CoV-2 RNA. 13 days after delivery, the infant's NP and OP swabs and stool samples were negativem, maternal samples remained positive.

Hsu AL 2020	vaginal	placenta, RT-PCR and histology with immunohisto-chemical staining	not stated; RT-PCR	0/1, SARS-CoV-2 RT-PCR test negative at 24h for baby (sample source not stated)	IHC using SARS-CoV-2 nucleocapsid-specific monoclonal antibody demonstrated SARS-CoV-2 antigens throughout the placenta, under the umbilical cord, and at the central and peripheral placenta disc in chorionic villi endothelial cells, and rarely in CK7-expressing trophoblasts.
Hu X 2020	5 C- section; 1 vaginal	Not specified. OP sample? maternal COVID-19 was based on the positive result of SARS-CoV-2 nucleic acid testing or serologic tests according to the WHO guideline. Amniotic fluid and umbilical cord blood at delivery, and mothers' expressed breast milk also tested for SARS-CoV-2	throat and anal swabs, blood sample; gastric aspiration before feeding, urine and stool samples,	0/6; all samples of amniotic fluid, cord blood and breast milk negative. All infant samples negative	

Khan MA 2020	20 spontaneous vaginal delivery; 7 elective C-section; 40 emergency C-section (numbers as reported in paper)	Not reported	NP swab, PCR	0/67	
Kulkarni R 2020	vaginal delivery, ventouse	NP swab	NP aspirate, cord stump, and placenta at birth, RT-PCR	1/1; baby tested SARS-CoV-2 positive on all samples at 12h, tested positive on swab at day 5, 10, negative day 14. Serology negative on day 11, but positive on day 21. Mother: tested PCR negative on admission and on day 5, serology negative on day 2, but serology positive on day 10	baby admiited with fever, suspected sepsis. SARS-CoV-2 PCR-negative on day 14, discharged on day 21.
Liu W 2020	42 C-section; 6 vaginal (no differences between the 3 groups of women)	NP swab, CT scan	amniotic fluid, placental swab, gastric lavage fluid at birth; neonatal serum,throat swab, and feces; RT-PCR	0/48. None of the neonates had SARS-CoV-2 positive RT-PCR in any of the samples tested	Samples from amniotic fluid, placental swab, gastric lavage fluid at birth; neonatal serum,throat swab, and feces were all RT-PCR negative for SARS-CoV-2 RT-PCR

Luo Q 2020	C-section: 17; vaginal: 6	Throat swabs, breast milk and blood, qRT-PCR; serum and breast milk, ELISA for IgG and IgM	throat swabs at delivery, serum at 1 month	0/23, all throat swabs negative, all antibody tests at 1 month negative (8 infants)	none of the women required ventilation. All breast milk samples negative for viral RNA; IgM antibody present in milk in 4 confirmed cases, IgG antibody negative in all samples
Lv Y 2020	C-section	not stated, PCR test	Amniotic fluid, umbilical cord blood, placenta, and neonatal gastric fluid, pharyngeal and anal swab	0/1; all samples tested negative	SARS-COV-2 nucleic acid test results were negative in 4 times pharyngeal swabs, but also the anal swab, amniotic fluid, umbilical cord blood, placenta, and neonatal gastric fluid were negative

Maraschini A 2020	Vaginal: 98; Elective C-section: 12; Emergency C-section (maternal or foetal indication): 25; Emergency C-section (COVID-19): 11	NP swab, RT-PCR	not stated, RT-PCR	9/149; 9 infants tested positive for SARS-CoV-2, testing either at birth or up to 9 days after. Of 5 newborns with positive test within 24h, 4 were delivered vaginally, 1 by pre-labor C-section; none developed serious illness	On hospital admission, 28.1% of the women were asymptomatic. The onset of clinical symptoms occurred in 9.5% of the cases on the day of delivery, and in 90.5% before it, the median value being 8 days. 11 women received ventilation, no ECMO, no deaths. Two stillbirths at 30 and 35 weeks pregnancy. 23 infants admitted to NICU, 18 premature, no deaths
Marin Gabriel MA 2020	Vaginal: 179; C-section: 63	NP and/or OP swab, RT-PCR or blood-serology	NP and/or OP swab, RT-PCR	RT-PCR on 230 infants, 11/230 positive (test at 18h). 2 additional cases at second test (48h)	222/248 babies did not need respiratory support, no deaths. No cases of pneumonia or pneumotho-rax. No additional cases at 1 month follow-up, 40% breast-fed exclusively at follow-up
Masmejan S 2020	Vaginal: 9; forceps: 2; C-section: 2	NP swab, placental swab. RT-PCR	NP swab, cord blood	0/13; all samples (cord blood, placenta, neonate NP swab) negative	1 critical case amongst the women, requiring ventilation. no deaths; placental sample negative

Mohakud NK 2020	C-section	Not reported	Tracheal aspirate swab after 12 hours of life	1/1	Woman developed breathing difficulty, decreased fetal movements, edema, and visual disturbance and was admitted to hospital & diagnosed with HELLP syndrome with hypothy-roidism and moderate COVID-19 pneumonia. Neonate chest X-ray normal; neonate required ventilation at birth, subsequently experienced a seizure but recovered & was discharged healthy.

Moreno SC 2020	12 spontaneous vaginal; 7 C-section	NP swab	NP swab within first 24 hours of life.	0/21	All 19 women presented with cough. Abnormal radiologic chest X-ray findings in 13/19 women. 8/19 births were premature deliveries. Among the neonates, no invasive mechanical ventilation was required. No neonatal sepsis or neonatal mortality was observed.
Nayak AH 2020	481 vaginal (66/141 SARS-CoV-2 positive mothers); 443 C-section (67/141 SARS-CoV-2 positive mothers); 10 instrumental (1/141 SARS-CoV-2 positive mothers)	Not reported directly but refer to the standard test as NP mucosal swab tested by RT-PCR.	Swab within first 24 hours of life	3/131	Of 131 neonates tested, 3 tested positive on first swab within 24 hours of birth; all tested negative on day 5. No significant effect of COVID infection on maternal and foetal outcome in pregnancy was observed. Among positive testing women, chest X-ray was performed:

Ogamba I 2020	17/25 vaginal; 8/25 C-section	NP or nasal swab	NP or nasal swab	0/20	10/40 asymptomatic; among symptomatic women symptoms included: loss of smell and taste, nausea, vomiting, body aches, chills, headache, fever, dry cough, shortness of breath, abdominal pain, difficulty breathing, and chest pain. Two women received convalescent plasma; four received supplemental oxygen due to respiratory distress. None required intubation or ICU admission. Two patients had spontaneous second trimester fetal loss.

Olivini N 2020	2 vaginal, 3 elective C-section	rhino-pharyngeal swabs	rhino-pharyngeal and rectal swabs	0/1 neonate tested within 24h; 5/5 tested positive, at day 2, 16, 12, 6 and 4	Neonates were asymptomatic or paucisymptomatic, no fever or respiratory symptoms. Three women reported symptoms: 1 low grade fever, 2 anosmia, 1 dysgeusia, 1 musculoskeletal pain. Onset of symptoms occurred at day 1, 5 and 19 after childbirth. Single samples of breastmilk from each of two of the SARS-CoV-2 positive mothers tested negative by RT-PCR.

Oncel MY 2020	89 C-section, 36 other (mode not reported)	Not reported	NP/ pharyngeal; later, deep tracheal aspirates	4/120; no NP sample tested positive within 24h; 1 positive on day 2, 2 positive on day 4; 1 deep tracheal aspirate tested positive on day 1	Additional COVID-19 tests done in some (rationale not recorded): placenta tissue (n: 5), amnion fluid (n: 4), deep tracheal aspirate (n: 9), serum (n: 3), stool (n: 2), and breast milk (n: 6), which were all negative for SARS-CoV-2 except only one positive deep tracheal aspirate. 8/125 mothers were admitted to ICU for mechanical ventilation; 6 died.

Palalioglu RM 2020	C-section	NP swab	NP swab	0/1	CT performed after C-section showed ground glass opacities in both lungs of the mother despite no COVID-19 symptoms. Baby was admitted to the ICU after developing feeding intolerance and vomiting 6 h after being breastfed, later discharged healthy. Also amniotic fluid, cord blood and placenta, postoperative breast milk were negative by RT-PCR.

Parsa Y 2020	C-section	NP swab	Not reported	1/1 24 hours after delivery	The mother of the positive test neonate was aged 41 years, with opium addiction, with signs and symptoms of acute respiratory illness presenting with labor pain & vaginal leak at 37 weeks of gestation. CT-scan revealed ground-glass opacities. The RT-PCR results of the amniotic fluid and neonate (less than 24 hours after birth) were positive for COVID-19. The newborn suffered vomiting during the first 24 hours after birth, due to opium withdrawal syndrome. She was admitted to the neonatal intensive care unit (NICU) and received supportive care without need for respiratory support.

Pereira A 2020	4 C-section, 18 vaginal (4 of which instrumental)	Not reported.	Naspharyngeal swab taken within first two hours of life.	0/22	Two born preterm needed admission to the NICU. During follow-up period, there were no major complications, and no neonates were infected during breastfeeding.
Pessoa FS 2020	C-section	Not reported	Swab, sample source not reported; sample was taken at 6 hours of life.	1/1	
Pissarra S 2020	6 vaginal, 4 C-section (obstetrical indication)	NP swab or OP swab	NP swab and bronchial secretions	0/10	All newborns remained symptom free and tested negative for SARS CoV2 at birth and at 48 h of life.
Popofsky S 2020	122 vaginal; 38 C-section	NP swab	NP swab	1/ 160 newborns (positive test was on day of life 5, after a negative test at birth)	Mother of infant testing positive was symptomatic at the time of birth and had close contact with the newborn whilst symptomatic.

Pulinx B 2020	Vaginal	NP swab	placental and amniotic fluid	2/2 (placental and amniotic fluid)	Both fetuses died prepartum. Placental histological examinations showed chronic intervillositis and extensive intervillous fibrin depositions with ischemic necrosis of the surrounding villi. Viral localization in the placental syncytiotrophoblast cells was confirmed by immunohistochemistry. These findings support the possibility of vertical transmission of SARS-CoV-2 infection. No other cause of fetal demise was identified.
Rebello CM 2020	Vaginal	NP swab	umbilical cord blood and skin swabs	1/1 (cord blood and neonate skin swabs)	

Rivera-Hernandez P 2020	C-section	NP swab	NP swab	1/1	Airborne precautions were maintained throughout perinatal care and delivery; no postdelivery contact of infant with mother or father; paternal SARS-CoV-2 testing was negative. Chest radiography in infant showed mild ground glass appearance and increased pulmonary vascularity bilaterally, consistent with respiratory distress syndrome. Infant was transferred to the neonatal intensive care unit.
Rubio Lorente AM 2020	n/a	serology and NP swab; amniocentesis	amniotic fluid	0/2; Amniotic fluid negative for SARS-CoV-2 by RT-PCR for both cases	

Sajjan GR 2020	C-section	not reported	not reported	1/1 (infant positive for Covid IgG)	Infant Covid Ig G positive, following which mother's Covid IgM and IgG and RT PCR was sent, reported as RT PCR and IgG positive which indicates that the lower limb gangrene is due to in utero transmission of SARS-CoV-2 infection. At 15 days baby is stable.
Schwartz DA 2020	11 births by C-section; 5 vaginal; 3 mode of delivery not reported	Not reported	Neonatal NP, endotracheal or OP swabs	19/19 (these neonates were selected on positivity). 5/19 mothers tested negative despite neonate testing positive.	3 infants were discharged but then readmitted later due to signs of possible COVID-19 clinical symptoms. One of the included 19 neonates was one of triplets, the other two neonates died of respiratory distress.

Shende P 2020	Termination at 13 weeks	Throat swab	Products of conception after dilation and curettage procedure: serum, placenta, amniotic fluid	1/1 in amniotic fluid, also in placental cell supernatant	Products of conception negative for IgM; To determine if SARS-CoV-2 has infected placental cells we carried out immunofluorescence using monoclonal antibodies against the spike protein S1 and S2 on placental sections. Both, S1 and S2 proteins were diffusely localized mainly in the cytoplasm of syncytiotrophoblasts and some cytotrophoblasts cells. Some villus stromal cells were also positive for both the proteins. In some syncytiotrophoblasts, S2 was also found as aggregates. These results indicate that the viremia persisted in the placenta six weeks after the mother was tested positive.

Singh MV 2020	C-section	NP swab	NP swab	1/1	C-section performed at 38 weeks due to positive SARS-CoV-2 test. Neonate healthy. NP swab turned negative on day 10 of life.
Sisman J 2020	vaginal	NP swab	NP swab	1/1	Premature rupture of membranes so labour induced. Hyperbilirubinemia in the infant developed and was treated. Infant's NP swab was positive by RT-PCR for SARS-CoV-2 at 24 and 48 hours of life. Developed fever & respiratory distress at day 2, resolved by day 5. Chest radiograph normal. Discharged as healthy at day 21.

Smithgall MC 2020	51/76 vaginal; 25/76 C-section	placentas	NR	0/51	No adverse perinatal outcomes; no specific histo-morphologic changes in placentas; no evidence of direct viral involvement identified by ISH and IHC. Evidence of maternal–fetal vascular malperfusion was identified: SARS-CoV-2 positive women's placentas significantly more likely to show villous agglutination & subchorionic thrombi than SARS-CoV-2-negative women's placentas. 26/51 SARS-CoV-2-positive women were asymptomatic; 32 had cough, 27 had fever, 14 had myalgia, 6 had sore throat, 6 had fatigue. 4 suffered severe disease.

Stonoga E 2020	C-section	NP swab tested by RT-PCR	amniotic fluid (before amniotic membranes ruptured), umbilical cord blood, placental membranes, and cotyledon fragments	0/1	fetus died; multifocal chronic histiocytic intervillositis in the placenta, potentially relevant to cause of death of the fetus, but other causes not excluded.
Tang F 2020	5 vaginal, 15 C-section	Unclear	Throat swabs, serum, amniotic fluid, umbilical blood (and radiology)	3/20	No neonate had a fever. Radiological examination showed that 10 neonates, eight neonates, and two neonates were diagnosed with pneumonia, increased lung markings, and no abnormality in the lungs, respectively. The samples of amniotic fluid and umbilical cord blood of all neonates were tested negative for SARS-CoV-2

Tang J 2020	1 vaginal birth, 1 birth by C-section	Throat swabs (negative by PCR), 2/2 were positive for serum IgM, 1/2 positive for IgG antibodies	RNA test was negative in throat swabs taken immediately after birth, on the 3rd and the 7th day. Serum IgM antibody to SARS-COV-2 was negative and IgG was positive on the 7th day after birth.	0/2 by PCR; 2/2 positive by IgG, 1/2 positive by IgM.	The two women did not develop serious complications; outcomes in the neonates were good.
Vendola N 2020	1 vaginal, 1 C-section	NP swab tested by RT-PCR and serum IgG antibody testing	NP swab tested by RC-PCR; also IgG testing in umbilical cord blood and peripheral blood soon after delivery.	0/2 for SARS-CoV-2 RNA in throat swabs; 2/2 for IgG in neonatal serum	
Vinuela MC 2020	94 vaginal, 6 C-section	NP swab	Unclear	0/100	The Ct determination (RT-PCR test) of the 9 positive patients ranged from 36 to 41 cycles, median of 40. No fetal transmission was observed and maternal and neonatal prognosis was excellent.

Vivanti AJ 2020	C-section	Blood, NP swab, vaginal swab, amniotic fluid during C-section.	NP and rectal swabs at 1 hour and repeated at 3 and 18 days postnatal age. Cerebrospinal fluid sample at 3 days.	1/1	Mother admitted at 35+2 weeks of gestation with fever (38.6 °C), severe cough, abundant expectoration for 2 days before hospitalisation. Neonatal blood culture was negative for bacteria or fungi. All neonatal swab samples tested positive by PCR. CSF sample negative. Placenta histology some positive Ab staining for SARS-CoV-2

Von Kohorn I 2020	C-section	NP swab	Cord blood was collected immediately after C-section delivery. NP swabs at 24 hours and 49 hours of life. Infant blood and urine collected over first 7 days of life.	1/1 (several consecutive samples tested, some were positive by PCR with variable Ct values)	Mother had a cough for 1 week prior to NP swab and test. 34 weeks gestation, mother had vaginal bleeding and cramping, was found to have thrombocy-topenia, transaminitis, and hyperuricemia. Maternal history of gestational diabetes controlled by diet, not hypertensive. Infant asymptomatic with normal laboratory studies but some NP swabs tested positive for SARS-CoV-2 RNA. Placenta histology - no direct evidence of virus
Vouga M 2020	Among 926 SARS-CoV-2 positive women: 469 vaginal, 256 C-section, 6 unknown; among 107 SARS-CoV-2 negative women: 44 vaginal; 22 C-section, 1 unknown.	NP swab for RT-PCR.	NR	11/384	No difference in obstetrical and neonatal outcomes were observed between positive- and negative-testing women.

Woodworth KR 2020	2,589 vaginal, 1,331 C-section. Among 3,920 women testing positive for SARS-CoV-2: 2,589 vaginal, 1,331 C-section.	NR	NR	16/610	% positivity was 4.3% (14 of 328) among infants born to women with documentation of infection identified [?]14 days before delivery and 0% (0 of 84) among those born to women with documentation of infection identified >14 days before delivery. Other perinatal outcomes also reported.
Yang R 2020	5006/11,078 vaginal, 6,072 C-section (Among 65 SARS-CoV-2 positive women, 13 vaginal, 52 C-section)	Pharyngeal swab	Unclear, probably pharyngeal swab as for mother.	0/38	65/11,078 mothers tested positive during pregnancy. OR for perinatal conditions & SARS-CoV-2 positivity also reported.

Zaigham M 2020	C-section	NP throat swab	NP swab 48 hours after delivery	1/1	virological, pathological & genetic investigations indicate intrauterine SARS-CoV-2 transmission via I) maternal viremia in a seemingly mildly symptomatic patient, II) high viral load in placenta with massive perivillous fibrin deposition, acute intervillositis in areas with strong positivity for SARS-CoV-2 & chorangiosis in the areas less affected by infection and inflammation III) intrauterine fetal distress with pathological cardiotocography & acidemia in validated umbilical cord blood gases and IV) mild neonatal COVID-19. Whole genome sequencing of isolates from the mother & placenta revealed a single variant of the virus.
Zhang L 2020	1 vaginal, 17 C-section	throat swab	Neonates: sample source NR, possibly NP as for mothers.	0/18	5/18 neonates diagnosed with bacterial pneuomonia, successfully treated.

Zhang P 2020	137/364 vaginal, 227/364 C-section; among SARS-CoV-2 positive women 54/74 vaginal, 20/74 C-section.	NPl swab	Placental tissue (tested for SARS-CoV-2 using automated in situ hybridization using a specific COVID-19 probe)	2/53 by in situ hybridization in placenta (53 placental samples from PCR positive mothers. Among 10 placental samples from PCR negative mothers, 0/10 SARS-CoV-2 positive by in situ hybridization).	No histopathological features within the placentas specific to maternal SARS-CoV-2 infection were found. Clinical diagnoses of preeclampsia and category 2 fetal heart monitoring negatively associated with positive maternal NP PCR.
Zheng T 2020	C-section (both)	throat swab	neonates' throat swab, anal swab, urine, and blood; sample timing unclear	0/2	

Table 2. Included reviews.

Study	**Fulfils systematic review methods; Risk of bias (RoB) tool used**
Akhtar H 2020	Yes. RoB: Newcastle Ottawa Scale
Al Qahtani MA 2020	No, narrative review
Amaral W 2020	Yes. RoB: GRADE
Bellos I 2020	Yes RoB: Quality appraisal by domains, tool not stated
Bwire GM 2020	Unclear RoB: No quality assessment justified as "most of the extracted studies were case rep
Caparros-Gonzalez RA 2020	No, narrative review
Cavalcante de Melo 2020	Yes. RoB: Newcastle Ottawa Scale
Centeno-Tablante E 2020	Yes. RoB: Newcastle Ottawa Scale. Stated to be a "living review"
Chi J 2020	Yes. RoB: methodological quality of case reports and case series described by Murad et al.
Della Gatta AN 2020	Yes. RoB: methodological quality of case reports and case series described by Murad et al.
Deniz M 2020	No, no risk of bias assessment
Dhir SK 2020	Yes. RoB: Newcastle Ottawa Scale
Di Toro F 2020	Yes. RoB: Joanna Briggs Institute (JBI) manual
Diriba K 2020	Yes. RoB: Joanna Briggs Institute (JBI) manual
Dube R 2020	No, no risk of bias assessment
El-Wahab EWA 2020	No, narrative review
Figueiro-Filho EA 2020	No, No RoB assessment
Gao Y 2020	Yes. RoB: Institute of Health Economics (IHE) case series methodological quality evaluation
Goh XL 2020	Unclear. RoB: Newcastle Ottawa Scale but paper is a Letter without full data
Han Y 2020	No, No RoB assessment
Hessami K 2020	No, No RoB assessment
Huntley BJF 2020	Yes. RoB: methodological quality of case reports and case series described by Murad et al.

Juan J 2020	Yes. RoB: Joanna Briggs Institute (JBI) manual
Khalil A 2020	Yes RoB: Newcastle-Ottawa Scale
Kotlyar AM 2020	Yes. RoB: Newcastle-Ottawa Scale
Mahyuddin AP 2020	No, narrative review
Novoa RH 2020	Yes. RoB: Newcastle Ottawa Scale
Pettirosso E 2020	No. No RoB assessment
Raschetti R 2020	Yes. RoB: Mayo Evidence-Based Practice Centre tool
Rodrigues C 2020	No, No RoB assessment
Romeo G 2020	No, No RoB assessment
Salem D 2020	No, narrative review
Sampieri CL 2020	Yes. RoB: GRADE.
Sheth S 2020	No, narrative review
Shrestha R 2020	No, No RoB assessment
Thomas P 2020	Yes. RoB: Case control and cohort studies: from the CLARITY group at McMaster Universi
Tripella G 2020	Yes. RoB: Joanna Briggs Institute (JBI) manual
Turan O 2020	Yes RoB: NIH assessment tools.
Walker KF 2020	No. No RoB assessment
Yoon SH 2020	No, No RoB assessment

Table 3. Quality assessment of included primary studies.

Study	**Description of methods and sufficient detail to replicate**	**Sample sources clear**	**An**
Anand P 2020	Yes	Yes	Yes
Ayed A 2020	Yes	Yes	Yes
Bachani S 2020	Yes	Yes	Yes
Barbero P 2020	Yes	Yes	Yes
Chaudhary S 2020	Yes	Unclear	Yes
Cojocaru L 2020	Yes	Yes	Yes
Fenizia B 2020	Yes	Yes	Yes
Gale C 2020	Yes	Yes	Unc
Gao X 2020	Unclear	Yes	Yes
He Z 2020	Yes	Yes	Yes
Hu X 2020	Yes	Yes	Yes
Khan MA 2020	Yes	Unclear	Yes
Liu W 2020	Yes	Yes	Yes
Luo Q 2020	Yes	Yes	Yes
Maraschini A 2020	Unclear	Yes	Yes
Marin Gabriel MA 2020	Yes	Yes	Yes
Masmejan S 2020	Yes	Yes	Yes
Moreno SC 2020	Yes	Yes	Yes
Nayak AH 2020	Yes	Unclear	Yes
Ogamba I 2020	Yes	Yes	Yes
Olivini N 2020	Unclear	Yes	Yes
Oncel MY 2020	Yes	Yes	Yes
Pereira A 2020	Yes	Unclear	Yes
Pissarra S 2020	Yes	Yes	Yes
Popofsky S 2020	Yes	Yes	Yes
Smithgall MC 2020	Yes	Yes	Yes
Schwartz DA 2020	Unclear	Yes	Yes
Tang F 2020	Yes	Unclear	Yes
Vinuela MC 2020	Yes	Unclear	Yes

Vouga M 2020	Yes	Yes	Yes
Woodworth KR 2020	Unclear	No	Unc
Yang R 2020	Yes	Yes	Yes
Zhang L 2020	Yes	Yes	Yes
Zhang P 2020	Unclear	Yes	Yes

Table 4. Main findings of included cohort and case series studies.

Study	**Ppts (n)**	**No. of women diagnosed with COVID-19***	**No. of births**	**No.of positive neonates /no. of neonates tested from women with COVID-19 diagnosis)**	**No. of positive neonates (RT-PCR) at birth (testing positive within 24h of birth)**	**Total number of neonates from women with COVID-19 diagnosis**	**% neonates positive for SARs-CoV-2 RNA**	**Clinica outcomes for neonat testing positive**
Ayed A 2020	185	185	41	2/41	0	41	0.0%	1 asymptomatic 1 developed tachypnoea required humidified high flow nasal cannula for 5 days. No deaths
Barbero P 2020	91	91	23	0/23	0	23	0.0%	n/a
Chaudhary S 2020	26	26	14	0/14	0	14	0.0%	n/a
Cojocaru L 2020	1989	86	34; 31 tested	0/31	0	31	0.0%	n/a
Gao X 2020	14	14	14	0/14	0	14	0.0%	n/a
He Z 2020	22	22	22	0/22	0	22	0.0%	n/a

Hu X 2020	6	6	6	0/6	0	6	0.0%	n/a
Khan MA 2020	66	66	67	0/67	0	67	0.0%	n/a
Liu W 2020	48	15	48	0/15	0	15	0.0%	n/a
Luo Q 2020	23	14	23	0/14	0	14	0.0%	n/a
Masmejan S 2020 (n=13)	13	13	13	0/13	0	13	0.0%	n/a
Moreno SC 2020	19	19	21	0/21	0	21	0.0%	n/a
Ogamba I 2020	40	40	25; 20 tested	0/20	0	20	0.0%	n/a
Olivini N 2020	5	5	5	4/5	0	5	0.0%	Two of the positive neonate devel-oped symp-toms possibly related to SARS -CoV-2, no serious illness, no deaths.
Pereira A 2020	22	22	22	0/22	0	22	0.0%	n/a
Pissarra S 2020	10	10	10	0/10	0	10	0.0%	n/a

Popofsky S 2020	160	160	160	1/160	0	160	0.0%	In the cohort, among the 15 symptomatic neonate 4 had fever, 1 had respiratory distress 4 had feeding intolerance, 1 had rhinorrhea and 7 had hypothermia. Only one tested positive for SARS-CoV-2
Vinuela MC 2020	100	15	100	0/15	0	15	0.0%	n/a
Yang R 2020	11078	65	11078; 38 neonates from 65 positive women tested	0/38	0	38	0.0%	n/a
Zhang L 2020	18	18	18	0/18	0	18	0.0%	n/a

Oncel MY 2020	125	125	125; 120 tested	4/120	1	120	0.8%	1 asymptomatic 3 required mechanical ventilation or nasal CPAP; however unclear whether these requirements were due to either SARS-CoV-2 infection or premat
Nayak AH 2020	977	141	134; 131 tested	3/131	3	131	2.3%	no evidence of transmission of COVID-19 infectio

Woodworth KR 2020	4442	4442	4495; 610 tested	16*/610 (*timing of test not reported)	16	610	2.6%	8 of the infants with positive test results were born preterm (26–35 weeks); all were admitted to a neonata ICU (NICU) without indications reported. Among the 8 term infants with positive test results, one was admitted to a NICU for feve and receipt of supplemental oxygen, one had no infor mation on NICU admission, and the remaining six were no admitted to a NICU.

Vouga M 2020	1033	926	820; 384 tested	11/384	11	384	2.9%	obstetri and neonata outcom did not differ betwee positive and negativ patient compar positive women with se materna outcom to posit women with no mild adverse outcom showed significa increase risk of preterm birth a neonata admissi to the intensiv care un
Maraschini A 2020	146	146	149	9/149	5	149	3.4%	3 admit ted to NICU, none de veloped serious illness

Bachani S 2020	348	57	56	5/56	2	56	3.6%	4 asymptomatic 1 symptomatic and received respiratory support for 48 hours. No deaths
Marin Gabriel MA 2020	185	242	248; 230 tested	11/230	11	230	4.8%	none presented with pneumonia or any other clinical feature compatible with SARS-CoV-2 infection
Fenizia B 2020	31	31	31	2/31	2	31	6.5%	all asymptomatic and healthy
Anand P 2020	69	69	65	7/65	7	65	10.8%	6/7 asymptomatic 1 received respiratory support (CPAP) for 48 h indication: prematurity. No deaths

Gale C 2020	66 (66 neonates selected based on positivity)	17	66	2/17	2	17	11.8%	all asymp-tomatic and healthy
Tang F 2020	20 (20 neonates selected based on positivity)	20	20	3/20	3	20	15.0%	Infectio in infan pre-sumed based on presenc of IgM. Symp-toms not reporte
Schwartz DA 2020	19 (19 neonates selected based on positivity)	9	19	2/9	2	9	22.2%	17/19 neonate showed symp-toms, includ-ing respira-tory distress Selecte series o cases. 2 deaths.

*based on testing and/or clinical criteria.

Table 5. Findings of studies reporting placental analysis.

Study ID	**Study design (n)**	**Vertical transmission**	**Pl**
Alamar I 2020	Case report (n=1)	1/1	NR
Birindwa EK 2020	Case report (n=1)	1/1	NR
Fenizia B 2020	Cohort (n=31)	2/31	Po
Ferraiolo A 2020	Case report (n=1)	0/1	Pla
Grimminck K 2020	Case report (n=1)	0/1	Pla
Kulkarni R 2020	Case report (n=1)	1/1	Pla
Hsu AL 2020	Case report (n=1)	0/1	NR
Liu W 2020	Retrospective case analysis (n=48)	0/48	Pla
Lv Y 2020	Case report (n=1)	0/1	Pla
Masmejan S 2020	Retrospective case series (n=13)	0/13	Pla
Ogamba I 2020	Retrospective cohort (n=25)	0/20	NR
Oncel MY 2020	Cohort (n=125)	4/120	Pla
Palalioglu RM 2020	Case report (n=1)	0/1	Pla
Pulinx B 2020	Case report (n=1 mother, 2 neonates)	2/2 (placental and amniotic fluid)	Pla

Rebello CM 2020	Case report (n=1)	1/1	Un
Shende P 2020	Case report (n=1)	1/1 in amniotic fluid, also in placental cell supernatant	pla
Sisman J 2020	Case report (n=1)	1/1	NR
Smithgall MC 2020	Cohort (n=76 placentas)	0/51	NR
Stonoga E 2020	Case report (n=1)	0/1	Pla
Tang J 2020	Case report (n=2)	0/2	NR
Vivanti AJ 2020	Case report (n=1)	1/1	pla
Von Kohorn I 2020	Case report (n=1)	1/1	
Zaigham M 2020	Case report (n=1)	1/1	NR
Zhang P 2020	Case series (n= 364 placenta samples)	2/53	NR
Zheng T 2020	Case report (n=2)	0/2	

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