Incidence of SARS-CoV-2 vertical transmission: a meta-analysis

The likelihood of newborns acquiring severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from infected mothers has raised concerns among families and clinicians worldwide. Published case reports and case series have individually reported wide variability in rate of vertical transmission. We therefore aimed to determine a more precise risk of vertical transmission, either intrauterine or during delivery, by pooling evidence from current studies.

We conducted a systematic review according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (CRD42020183500). We searched PubMed, Medline, Embase and China National Knowledge Infrastructure using search terms neonate, pregnancy, COVID-19, 2019-nCoV, SARS-CoV-2 and similar variants until 23 May 2020. Studies reporting mothers who tested positive for SARS-CoV-2 by reverse transcriptase PCR (RT-PCR) and whose newborns were tested by RT-PCR were included. We reviewed 335 full-text articles: 32 studies fulfilled inclusion criteria, 15 overlapping studies were excluded (online supplementary figure 1). An early-onset neonatal infection was defined as newborns with a positive RT-PCR test within the first 2 days of life, and determined by the primary author to not have acquired the infection postnatally. We extracted proportions of newborns with early-onset COVID-19 infection and performed a meta-analysis under a random effects model using the
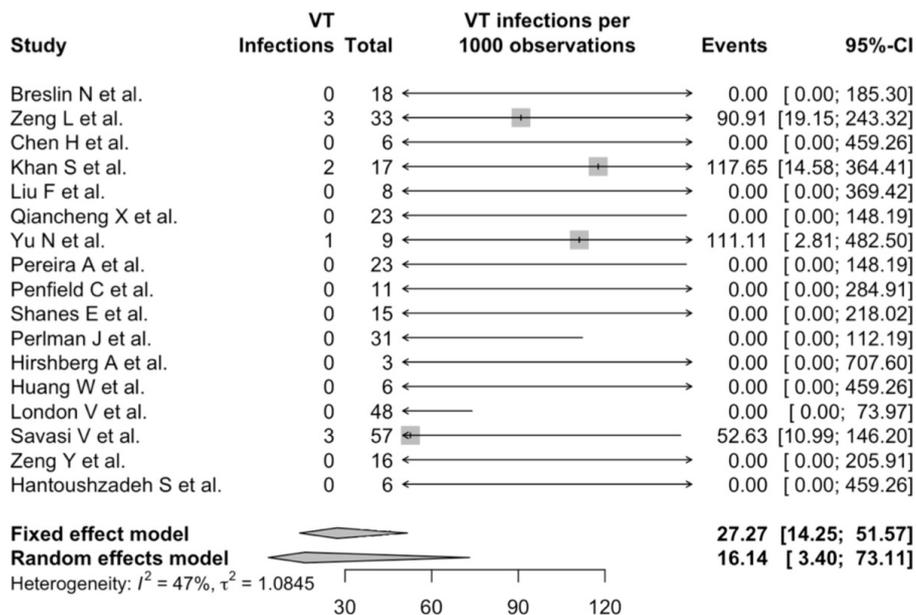
Figure 1 Pooled incidence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vertical transmission (VT).

generalised linear mixed model using R (https://www.r-project.org).[1]

Seventeen studies (two studies in Chinese language) were included, with mean quality assessment score of 5.29 (range: 4–7) based on the Newcastle-Ottawa Scale. Four hundred and two COVID-19-positive mothers delivered 405 newborns, of which 330 newborns underwent early RT-PCR tests. Nine of 330 newborns tested positive for SARS-CoV-2. The average pooled incidence of vertical transmission was 16 per 1000 newborns (95%CI 3.40 to 73.11, figure 1) Therefore, current evidence shows that the risk of vertical transmission of SARS-CoV-2 is low.

One of the nine newborns had elevated IgM antibodies and was symptomatic at birth which suggested intrauterine infection. This is supported by reports of SARS-CoV-2 in amniotic fluid and fetal side of the placenta.[2 3] On the placenta, the expression of ACE2 acts as the receptor for cell entry of SARS-CoV-2.[4] Additionally, vertical transmission can occur during vaginal delivery through contact with virus present in mother's stool.[5]

We hypothesise a few reasons for the low rates of early-onset neonatal COVID-19 infections. First, ACE2 expression in the placenta is low.[4] Second, our meta-analysis is based on published reports and under-reporting is possible in this pandemic situation. Newborns and their mothers may not undergo RT-PCR tests due to resource limitations or if mothers were asymptomatic. Hence, the overall incidence could be higher than what we estimated.

Although our result is reassuring, continued vigilance is needed as COVID-19 infection can potentially cause serious complications in the newborn. The newborn requires continued clinical monitoring and most importantly, be protected from risks of horizontal transmission. As the majority of included articles were of moderate-quality rating, our results could be confounded by the quality of literature. Future studies from larger and diverse populations are required to provide more accurate estimation of the incidence of early-onset neonatal COVID-19 infection.

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