**TECHNICAL REPORT**

**Direct effects of COVID19 on pregnant women, newborns, infants, and children: Focus on transmission in the first year of the pandemic**

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**Executive Summary**

Since the end of 2019, SARS-CoV-2 and its associated disease, COVID-19, has been the dominant health crisis in the world. Despite the increased vulnerability of children to other respiratory infections, it appears that children only account for about 5-15% of infections, although this percentage did increase over the course of the pandemic for a variety of possible reasons, including changes in testing protocols and re-opening of schools and other in-person institutions.

In late 2020, to compliment many of the rapid and scoping reviews which were conducted to understand the most recent knowledge about COVID-19, we undertook a rigorous systematic review on the direct effects of SARS-CoV-2 on pregnant women, newborns, infants, and children. We did not address the indirect effects, such as health service disruptions or school closures. Our review focused specifically on transmission risk from pregnant women to fetuses and newborns, and among pediatric and adolescent populations. We reviewed published literature from 1 November 2019 – 31 December 2021, screened titles and abstracts for relevance, extracted pertinent information on the studies and their findings, and categorized them based on their objectives, sample sizes, and outcomes. We also assessed the quality of studies, although those data are not included here.

The overall rate of vertical transmission is not known but appears to be quite low at 1-4% of deliveries, although this may even be an overestimate as it is difficult to rule out immediate postpartum transmission in cases of infection. The risk may be elevated if the woman is symptomatic at the time of delivery, and may possibly be related to viral load. While there has been evidence of virus in breastmilk, in most cases it has been only transiently positive, and only among lactating women with active symptoms.

It is clear from the evidence that children can transmit the virus to each other. The risk of adult to child transmission seems to be low, and is related to community transmission levels. Children are not the highest age risk category for disease severity or deaths compared to older population groups; they tend to have milder symptoms, however, children may experience more gastrointestinal disturbances as compared to adults who are infected with SARS-CoV-2.

Adolescent patterns of disease transmission and susceptibility seem to mirror adults, and high rates of transmission may be related to adolescent behavior, as compared to younger children who may have been more sheltered or more likely to spend time outdoors.

From the few papers focused on transmission is school, there appears to be low child-child transmission. However, there is a lack of good data on school transmission because of poor documentation on what mitigation and testing strategies were introduced and poor standardization of collected data in schools (especially early in the pandemic, data were much more likely to come from hospital and clinic records, and the preponderance of studies in our review were single-site case studies or series, and a very limited number from schools, daycares, and overnight camps).

Evidence in the first year was not conclusive around risk of preterm birth or stillbirth with COVID19 infection during pregnancy, although more recent studies have confirmed the increased risk of stillbirth among women infected in pregnancy. Although it appears there is slight increased risk of preterm birth among women with COVID-19 as compared to uninfected women, there may be physician bias with more likelihood to admit pregnant women or perform Caesarean sections.

This review provides strong evidence from the first year of the pandemic around perinatal and pediatric transmission risk, but as the pandemic changes, new risks (such as emergent variants) and new interventions (such as vaccines) will shift the transmission landscape and risk will need to be continually reassessed. This review should be complementary to other efforts ongoing within Unicef (especially related to schools), as well as reviews being led by Innocenti, WHO, and the living systematic review being done by University of Birmingham.

**Introduction**

Since the end of 2019, SARS-CoV-2 and its associated disease, COVID-19, has been the dominant health crisis in the world. There have been over 160 million cases, and over 3 million deaths[[1]](#footnote-1). According to the World Health Organization, which collects sex and age disaggregated data via a Case Reporting Form, by mid-2021, there had been 10,675,304 cases of COVID19 from ages 0-19[[2]](#footnote-2). While the pandemic began in a few countries, it spread quickly and became a global phenomenon within months. Among 25.72 million total cases from low and middle income countries in the first 18 months of the pandemic, 2.77 million (10.8 per cent) were in children and adolescents under age 20 years[[3]](#footnote-3).

Despite the explosion of research on COVID-19 since the beginning of the pandemic, the impact of infection on pregnant women, newborns, and children is not well understood. As the population with the highest mortality from SARS-CoV-2 is those over 65 years old[[4]](#footnote-4), the focus understandably has been on adult populations. However, pregnancy and pediatrics are vulnerable time periods and require special attention. In previous epidemics from SARS and MERS, children were similarly found to be less vulnerable than other population groups; but concern was warranted: pregnant women are generally more susceptible to flu than non-pregnant women and children often have more severe outcomes from acute respiratory illnesses than adults.

As the pandemic has continued, a more nuanced picture of the effect of SARS-CoV-2 infection on pregnant women, newborns and children has emerged. Originally, it was thought that children and pregnant women were not as negatively impacted by SARS-CoV-2 infection than older adults. Conflicting evidence has since emerged about the impact of the virus on pregnancy outcomes, on the rate of transmission among various age groups including children, the patterns revealed by test type and timing, and the potential impacts both of virus variants and vaccines. As policies are made around prioritization of medical treatment and vaccine administration, and how and when to open schools, daycares, and other institutions, it is essential to gain a balanced understanding of the risks of viral transmission among pregnant women, newborns, and children.

The COVID-19 pandemic has impacted both mortality and morbidity[[5]](#footnote-5), through direct and indirect pathways, and has had varying effects on different populations. This review focuses on the direct effects of COVID-19 on a specific population in the first year of the pandemic. It is already clear that the pandemic had an effect on health care service delivery, and there is both modeled and observed data on the impact of service disruption on mortality and morbidity of pregnant women, newborns, and children[[6]](#footnote-6)-[[7]](#footnote-7); however, these impacts fall outside of the scope of this review.

This systematic review seeks to understand the state of the research on COVID-19 transmission on pregnant women, newborns, and children through the end of 2020. Given the rapidly-changing nature of evidence, new information is added almost daily, and new concerns arise. Specifically, in 2021, the emergence of new viral variants have introduced new complexities into our understanding of viral spread and effective mitigation and treatment measures. Early evidence indicates that many emerging variants may be more highly transmissible among children. 2021 also saw the introduction of multiple new vaccines, rolled out at unprecedented scale, which is likely to have impact on susceptibility, transmissibility, disease severity, and mortality risk, as well as the behavior of individuals and communities. The data presented from this review are current as of 14 December 2020, although we have noted some new areas of concern since completion of the search.

The type of research conducted over the course of the pandemic has also changed, and the topics of interest and locations of studies and how these have shifted over time are findings in themselves. Early in the pandemic, many COVID19 cases were reported to have occurred in high-income countries. However, the true number of cases in low and middle income countries may have been underestimated due to unavailability of testing, and fewer funds available for research and surveillance[[8]](#footnote-8). Geographic regions have different age structures and susceptibilities, but those most at risk of severe impact from the pandemic are not necessarily the most likely to be researched. Further, testing challenges greatly impacted the type of research conducted and results available. Limited testing capacity, especially early in the pandemic, led many governments to prioritize testing only among symptomatic cases, or among even those with most severe illness. Thus, those with no or mild symptoms (including children and adolescents) may be less likely to be captured. Advances in testing technology itself, and the sensitivity and sensitivity of various methods, also continues to impact the timing and accuracy of disease detection[[9]](#footnote-9).

COVID-19 is a novel pandemic with new evidence being generated almost daily. Many agencies are concurrently and urgently working hard to control the pandemic and understand effects; this review is one such effort, among many.

**Methodology**

The data included in this report are from multiple sources, but primarily from a systematic review conducted on published data from 1 November 2019 through 14 December 2020. The systematic review focused on *direct* effects of COVID19 on pregnant women, children, and adolescents.

Systematic reviews take longer than rapid and scoping reviews, and more steps are required in the extraction and analysis phases. They utilize a rigorous methodologic process and are the gold standard for evidence synthesis. Systematic reviews provide a full picture of types of studies that have been published and the range of the quality of evidence. Data extracted from each article included are assessed for quality, with documentation of the type of methodology used in the study and potential biases. Systematic reviews can give a more balanced picture than selective reporting, show evidence gaps in the research, and can help develop clearer evidence-based guidelines and policies.

This review was designed to be complementary to multiple other ongoing efforts: the University of Birmingham Living Systematic Review on Maternal COVID[[10]](#footnote-10); the Unicef Innocenti Scoping Review: working paper on pediatric COVID[[11]](#footnote-11); the Johns Hopkins/CDC Humanitarian Center Repository on COVID and nutrition[[12]](#footnote-12); and the International Pediatric Association COVID briefs[[13]](#footnote-13). Our team liaised with various agencies collecting and analysing COVID-19 data, including the Max Planck Institute Database[[14]](#footnote-14) and the World Health Organization’s Maternal Newborn Child and Adolescent Health COVID-19 working group.

The systematic review focused on direct effects of COVID-19 on pregnant women, children, and adolescents and the transmission risks of the virus in these populations. The search strategies (Appendix A) were developed for Medline in collaboration with the Department of Reproductive Health and Research at WHO to standardize extraction questions between maternal, perinatal, and pediatric COVID19 research questions.

Papers were uploaded in Covidence software[[15]](#footnote-15), and duplicates were excluded. Each article was screened first based on title and abstract. Inclusion criteria are as follows: (1) Does the source contain data on humans (not cells, not animals)? (2) Does the source contain data relevant to the COVID19 pandemic? (3) Does the source address direct effects of COVID-19 (not indirect effects)? (4) Does the source contain data relevant to pregnant women, postpartum women, fetus, newborns, children, or adolescents? (5) Does the source contain primary data or a meta-review of primary data? Articles must have been marked YES for each question to meet inclusion for full text review.

The original scope of the review was intended to include everything relevant to perinatal and pediatric COVID and articles published between 1 November 2019 and 30 June 2020 were identified using the primary search strategy. The search was designed to be comprehensive, with stratification by sub-categories. Papers were first screened by title and abstract and then identified as relevant for various categories (not mutually exclusive): transmission, clinical progression, co-morbidities, laboratory and testing, treatment, general population epidemiology, and social determinants. Those marked as transmission were included in the full text review for this analysis, and divided into vertical or pediatric transmission. To manage the large number of new publications on COVID19 and reduce overlap with similar reviews being conducted by partner organizations, the search strategy was adjusted for papers published after 30 June 2020. Only papers related to transmission were identified in the search. Papers were uploaded into Covidence and followed the same protocol for title and abstract screening. Those meeting the inclusion criteria were eligible for full text review, and similarly divided into vertical or pediatric transmission. Upon full text review, articles found to not meet the inclusion criteria were excluded and the reasons recorded. Included articles were assessed for quality, but for expediency, those assessments were not incorporated into the analyses presented here.

Other important sources of data include an assembled review of caseload data from 42 countries (note: definitions vary; there is no public global database with age disaggregated data) and periodic reviews of news sources, including MMRWs and WHO epidemiologic alerts, with potentially “game changing” information about perinatal or pediatric transmission that are more recent than the review. It is worth noting that data included in many of these data sources come primarily from higher income countries (and pandemic situation varies widely among countries), studies are of varying quality (especially from the beginning of the pandemic where even poor quality data was considered better than no data), some data are modelled, with varying accuracy of inputs, and many preprints, news stories, and press releases have not necessarily been peer-reviewed. Finally, there is a heavy reliance on case studies and series, rather than population-based surveillance or active reporting. This is likely due to the fact that early evidence of a new phenomenon is generally reported through case studies; however, larger-scale studies and more routine monitoring will be needed as the pandemic continues.

**Description of dataset**

**Figure 1. Flow chart of included papers**



The main reasons for exclusion of papers were a wrong study design (not primary data) or the wrong patient population (no pregnant women, newborns, or children). Other reasons for exclusion were an assessment of indirect effects of COVID-19 only or a duplicate study.

**Findings**

*Countries and types of studies*

Countries

Almost all the included studies were conducted in high income countries. Because of the first identification of the disease in Asia, 58 (almost 40%) of the papers focus on China. There were only 7 papers from low income countries: Bangladesh, Kenya, Peru, India (2), Thailand, and Venezuela. There were only 2 papers from Brazil, and notably zero from South Africa, despite the high prevalence of disease and high risk of mutations and variants.

**Figure 2. Description of database - Countries**

**Figure 3. Description of database - Study types**

Study types

Over half of the included studies are case reports and clinical case reviews, focusing on a single patient or dyad (Maternal-newborn) or a retrospective record review, generally from one hospital or health facility. Especially at the beginning of the pandemic, these studies were likely the easiest to set up and collect data from quickly, and provided a brief snapshot into the clinical situation for pregnant women, newborns, and children. However, even many months into the pandemic, there are very few population-based or surveillance data studies, limiting our ability to understand transmission patterns within and among populations. There is an urgent need for more population level surveillance data, especially in low-and-middle income countries[[16]](#footnote-16). Further, there is a need to standardize data collection across sites. A review of COVID-19 studies related to acute SARS-CoV-2 infection in children and adolescents included 32 studies, but a meta-analysis could not be performed due to massive heterogeneity [[17]](#footnote-17).

It is also worth noting that the database includes many more papers on vertical transmission than pediatric transmission, there are very few papers directly studying transmission in school settings, and almost no papers related to adolescent transmission. Further, the range of data related to pediatric transmission is very broad encompassing many distinct and overlapping age categories

**Vertical transmission**

Viral transmission from mothers to their fetuses or newborns can happen at various stages: in utero, intrapartum, the immediate postpartum period, or via breastmilk. The risk of vertical transmission of SARS-CoV-2 has been a concern from the beginning of the pandemic. Several infectious diseases, such as HIV, zika and other coronaviruses, have had high risk of transmission from infected pregnant women to their newborns, with severe illness among infants[[18]](#footnote-18),[[19]](#footnote-19). However, from early in the COVID-19 pandemic, it has appeared that risk of transmission and severe illness have been lower in newborns and young infants than in adults.

Our review identified 67 studies including primary data related to vertical transmission of SARS-CoV-2, published between 1 November 2019 and 30 June 2020. Most studies in the review were of a single maternal-newborn dyad, with very few studies including a cohort. Papers included assessments of maternal and newborn swaps, vaginal fluid, amniotic fluid test, cord blood, placental tissue, and maternal and neonatal blood. One of the most important markers of potential transmission is identification of SARS-CoV-2 virus in vaginal swabs; however, identification of the virus in vaginal fluid of SARS-CoV-2 infected women appears to be relatively uncommon[[20]](#footnote-20),[[21]](#footnote-21),[[22]](#footnote-22),[[23]](#footnote-23).

The overall rate of vertical transmission is unknown, but appears low, likely between 1-4%[[24]](#footnote-24). There is a possible higher risk of transmission with cesarean vs vaginal delivery, and a slightly elevated risk if maternal infection was more recent (within one week prior to delivery) or is symptomatic at the time of delivery.

*Adverse pregnancy outcomes*

* 1. There appears to be a slightly higher risk of preterm birth among pregnant women with SARS-CoV-2 infection compared to those without infection[[25]](#footnote-25). It is worth noting that these data come primarily from the US and the UK, countries with higher prevalence and survival rates of preterm infants than lower-income countries, and the impact of the pandemic on preterm infants in settings with weaker registries and poorer tracking of gestational age is more difficult to ascertain. Although clinically it appears that SARS-CoV-2 increases the risk of preterm birth, it is likely that environmental factors, such as decreased pollution from reduced travel and industry and behavioral modifications such as mandated stay-at-home orders and closures of schools and businesses have contributed to decreases in the overall percentages of preterm birth in some settings[[26]](#footnote-26). A CDC study found that preterm birth was higher among women with confirmed SARS-CoV-2 infection as compared to the general population, and that women who were symptomatic during pregnancy were more likely to experience preterm birth than those with asymptomatic infection[[27]](#footnote-27). More research is needed to understand the clinical vs environmental impact of COVID-19 on preterm birth.

Early studies anticipated increase in miscarriage due to SARS-CoV-2 infection[[28]](#footnote-28), but no conclusive evidence has been found of increased risk. There is, however, a potential increase in underreporting due to underutilization of medical services. Despite early studies indicating a possible increase in hospital-based stillbirth rates[[29]](#footnote-29), data on stillbirth are too limited to be conclusive, but preliminary data suggest that there are no direct clinical impacts[[30]](#footnote-30), but rather indirect (including environmental) impacts affecting prevalence[[31]](#footnote-31).

*In-utero and immediate postpartum transmission*

* 1. It is difficult to identify the exact timing of viral transmission and therefore to identify if transmission was in-utero, intrapartum, or immediate postpartum. In most cases, the newborn is kept in close proximity to the mother (or health workers) immediately after childbirth and thus has exposure to droplets or fluids from the infected mother (or asymptomatic health workers)[[32]](#footnote-32); therefore it is difficult to rule out immediate postpartum transmission. Nonetheless, it appears that in utero transmission is rare. Using the most recent WHO definition at the time of the analysis, there has been only one definite confirmed case of in utero transmission, although more are suspected[[33]](#footnote-33).
	2. There does not appear to be increased risk to the newborn of rooming in or being kept in skin to skin position with a parent (who is infected or of unknown SARS-CoV-2 status), if appropriate mitigation measures are taken[[34]](#footnote-34). Thus, WHO continues to recommend that evidence-based essential newborn care be offered or provided in every case where it is feasible[[35]](#footnote-35). A recent modeling study demonstrated that the increased mortality due to lack of skin-to-skin and breastfeeding would likely be larger than newborn deaths due to COVID-19, and from a population standpoint, early essential newborn practices should be continued and encouraged[[36]](#footnote-36).
	3. *Transmission via breastmilk*
	4. While there has been evidence of virus in breastmilk, in most cases it has been only transiently positive, and only among lactating women with active symptoms. Even in the few cases where breastmilk has been tested and found to contain virus, transmission via breastmilk was unable to be confirmed, as there may have been other routes of transmission[[37]](#footnote-37). WHO continues to promote breastfeeding for infants born to SARS-CoV-2 infected mothers so long as they are medically stable and able to adhere to infection control mitigation measures.

*Neonatal outcomes*

* 1. It appears that there are very few severe outcomes in newborns who were infected with SARS-CoV-2[[38]](#footnote-38). Among infants testing positive, all had either no or mild symptoms, and only rarely required hospital admission due to COVID-19 symptoms. Preterm infants had a higher likelihood of readmission, but this may be partially attributable to other co-morbidities.

**Table 1. Studies on vertical transmission with sample size > 20 pregnant women or dyads (in descending order of sample size)**

|  |  |  |  |
| --- | --- | --- | --- |
| **Author** | **Title** | **Country** | **Sample size and findings** |
| Salvatore C | Neonatal Management and Outcomes during the COVID-19 pandemic: an observational cohort study | USA (New York) | N = 1481 deliveries; N=116 (8%) mothers tested positive; N = 120 neonates, with 106 referred to outpatient clinic for follow-up. Study describes clinical characteristics and outcomes for mothers and babies, with focus on clinical management and treatment efforts. |
| McDevitt, K | Outcome of universal screening of neonates for COVID-19 from asymptomatic mothers | United Kingdom | N=481 infants were delivered and 418 were screened with maternal consent. Nine (2.2%) infants born to asymptomatic mothers screened positive for SARS-CoV-2 all within the first 24 h, three within the first three hours. Only one infant was symptomatic requiring oxygen for two hours and high flow humidified nasal cannula for 22 hours. |
| Knight, M | Characteristics and outcomes of pregnant women admitted to hospital with confirmed SARS-CoV-2 infection in UK: national population based cohort study | United Kingdom | N=427 pregnant women admitted with confirmed SARS-CoV-2 (median gestational age= 34 weeks). 5 neonates died (three were stillborn and two died in the neonatal period; Three deaths were unrelated to SARS-CoV-2 infection and were due to obstetric conditions unrelated to SARS-CoV-2 infection and/or pre-existing fetal conditions; for two stillbirths, whether SARS-CoV-2 contributed to the death was unclear.). Twelve (5%) infants of women admitted to hospital with infection tested positive for SARS-CoV-2 RNA, six of them within the first 12 hours after birth. No viral analyses were performed on umbilical cord blood, placenta, or vaginal secretions. The six infants who developed later infection were born by pre-labour caesarean (n=4) and vaginal birth (n=2). Only one of the infants with an early positive test for SARS-CoV-2 RNA was admitted to a neonatal unit, compared with five infants with a later positive test.  |
| Khoury, R | Characteristics and Outcomes of 241 Births to Women With Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection at Five New York City Medical Centers | United States | N=241 pregnant women with confirmed SARS-CoV-2 (RT-PCR test). On admission, 148 were asymptomatic, 102 remained asymptomatic; 93 were symptomatic. There were 245 live births to 241 women, including six sets of twins, and there were two stillbirths (one stillbirth had sever growth restriction and HELLP syndrome; the family of the other declined all testing/autopsy). Of the 245 liveborn infants, nearly all tested negative for SARS-CoV-2 infection immediately after birth (97.5%). |
| Yan, J | Coronavirus disease 2019 in pregnant women: a report based on 116 cases | China | N=116; assessments of amniotic fluid, cord blood, and neonatal pharyngeal swab samples at birth to ascertain the possibility of vertical transmission. Results indicated that SARS-CoV-2 was negative in all of the above biological samples, suggesting that no intrauterine fetal infection occurred because of SARS-CoV-2 infection during the third trimester of pregnancy when the time interval from clinical manifestation to delivery was up to 38 days.  |
| Cheng B | Clinical Characteristics of Pregnant Women with Coronavirus Disease 2019 in Wuhan, China | China | N=111 (n=31 pregnant, n=80 non pregnant). Among the 31 pregnant women, 17 live births were recorded, and all showed results negative for postnatal COVID-19 detection at the first testing, and 2 became positive thereafter, indicating that vertical transmission is **rare**. Seventeen live births had a median 1-minute Apgar score of 9 and a median 5-minute Apgar score of 10. One live birth had a 1-minute Apgar score of 7 and a 5-minute Apgar score of 9. All of live births had negative results of immediately postnatal COVID-19 detection. Two had positive results for COVID-19 2 days after birth mainly due to the contact transmission. Pregnant patients had a lower level of severity of COVID-19 together with an enhanced inflammatory response and cell immunity when compared with nonpregnant patients.  |
| Lamouroux A | Evidence for and against vertical transmissionfor severe acute respiratory syndromecoronavirus 2 | France  | N=71 pregnant women, 10 amniotic fluid samples and in 5 placental samples; all results returned negative. SARS-CoV-2 all returned negative in 12 cases from RT-PCR of cord blood that was tested; Onenewborn delivered by cesarean delivery who had no contact with her mother had a positive RT-PCR result in a pharyngeal swab collected 36 hours after birth. In a single series of 33 neonates delivered by mothers with symptoms of COVID-19, 3 neonates (9%) with symptoms of COVID-19 tested positive for SARS-CoV-2 in an RT-PCR of anal and nasopharyngeal swabs; one child had elevated IgM and IgG antibody levels 2 hours after birth. Nasopharyngeal swabs tested negative on RT-PCR on 5 occasions, and both IgM and IgG antibody levels decreased on day 14 of life and throughout the duration of the assay.; study describes potential serologic evidence of vertical transmission in 2 of 6 infants from mothers with SARS-CoV-2 infection |
| Pereira, A | Clinical course of coronavirus disease-2019 in pregnancy | Spain | N=60 pregnant women were diagnosed with SARS-CoV-2. During the study period, 18 of the women (78%) delivered vaginally. All newborns tested negative for SARS-CoV-2 and none of them were infected during breastfeeding. No SARS-CoV-2 was detected in placental tissue. |
| Liu, P | The immunologic status of newborns born to SARS-CoV-2–infected mothers in Wuhan, China | China | N=51; From January 20 to March 3, 2020, 71 newborns born to pregnant women with SARS-CoV-2 were admitted to the neonatal intensive care unit isolation ward of Zhongnan Hospital. 20 cases were excluded (less than 35 wks gestational age, incomplete lab data, or suspected congenital malformations). None of the 51 newborns showed fever or respiratory distress during hospitalization. One (1.96%) infant with an extremely elevated IL-6 concentration developed necrotizing enterocolitis in the third week after birth, the other 50 infants did not show abnormal symptoms through the end of the follow-up period. |
| Gabriel, M | Multicentre Spanish study found no incidences of viral transmission in infants born to mothers with COVID-19 | Spain | N=42 neonates born to pregnant women with SARS-CoV-2 with RT-PCR tests: nasopharyngeal swab samples in 37 cases (88.1%) and oropharyngeal swab samples in 36 cases (85.7%). All tests on the infants came back negative, with no evidence of any vertical transmission from mother to child. |
| Schwartz, D | An Analysis of 38 Pregnant Women With COVID-19, Their Newborn Infants, and Maternal-Fetal Transmissionof SARS-CoV-2 | China | N=38 pregnant women with SARS-CoV-2, who delivered 39 neonates. All women had tested positive for COVID via RT-PCR. There were no confirmed cases of intrauterine transmission of SARS-CoV-2 from mothers with COVID-19 to their fetuses. All neonatal specimens tested, including placentas, were negative by RT-PCR for SARS-CoV-2. |
| Penfield, C | Detection of severe acute respiratory syndrome coronavirus 2 in placental and fetal membrane samples | United States | N=32 women pregnant women with SARS-CoV-2, categorized as mild, severe or critical. 11 had placental or membrane swabs performed. 3 tested positive, all women who had severe to critical COVID at time of delivery. No infants tested positive for SARS-CoV-2 on day 1 of life to day 5 of life. No newborns demonstrated symptoms of COVID.  |
| Wu, Y | Neonatal outcome in 29 pregnant women with COVID-19: A retrospective study in Wuhan, China | China | N= 29 women with confirmed or clinical diagnosed SARS-CoV-2 infection, 5 neonates were diagnosed with a SARS-CoV-2 infection (2 confirmed and 3 suspected). None of these 5 neonates had contact with infected patients, except for their mothers during delivery, which suggests vertical or intrapartum transmission. When the neonates were born through cesarean, they stayed unprotected in the operating room for about 30 minutes for observation before they were transferred to isolated neonatal wards. The increased occurrence of necrotizing enterocolitis among neonates born to SARS-CoV-2-infected women warrants further investigation. |
| Patane, L | Vertical transmission of coronavirus disease 2019: severe acute respiratory syndrome coronavirus 2 RNA on the fetal side of the placenta in pregnancieswith coronavirus disease 2019 - positive mothers and neonates at birth | Italy | N=22 pregnant women who tested positive for SARS-CoV-2. 2 neonates tested positive via nasopharyngeal PCR test. Both had 9/10 Apgar scores and no observes respiratory distress. Both neonates were discharged after observation. No deaths observed. At time of publication, this was the first report on cases with positive PCR results for SARS-CoV-2 in the mother, neonate, and the placental tissues. Researchers used RNA ISH assays to visualize the virus in tissue from placenta.  |

**Pediatric transmission**

Transmission of SARS-CoV-2 can affect children in multiple ways. Children of various age groups can be affected, from infants through adolescence. Children may transmit the virus to each other, in daycare, school or community settings. Children may pass the virus to adult family members, teachers, or other caregivers, and they may become infected through exposure to an infected adult.

Although reporting categories by age has not been consistent, the percentage of cases in children under 20 years old has generally been found to be between 5-15% of cases with some notable outliers in either direction (not higher than 25%)[[39]](#footnote-39). Although higher percentages of pediatric cases have been reported in low income countries, but this may be due to differences in testing policies between countries and larger overall youth populations or demographic structures. Countries with larger youth populations are underrepresented in the data; the first study on pediatric COVID-19 in Africa was published only at the end of 2020, is from a higher-income city, and uses hospital records, rather than population data[[40]](#footnote-40). Global data are not readily available in age-disaggregated or comparable formats, so the exact impact on children is still not completely known.

*Table 2. COVID-19 cases in children and adolescents under age 20 years (Max Planck data, as of July 2021)*

|  |  |  |  |
| --- | --- | --- | --- |
| **Age group (years)** | **Total** | **High/Upper Middle-Income****Country**  | **Low/Lower Middle- Income** **Country** |
| **<5 years** | 400,492 (14.5%) | 260,390 | 140,102 |
| **5-9 years** | 479,026 (17.3%) | 294,646 | 184,380 |
| **10-19 years** | 1,886,825 (68.2%) | 1,243,100  | 643,725 |
| **Total <20 years** | 2,766,343 | 1,798,136 | 968,207 |

There appears to have been an increase in pediatric and adolescent infections over the course of the epidemic, raising concerns about the growing role of children in the transmission of the virus. However, the identification of more children and adolescents with SARS-CoV-2 infection may be due to increased testing of asymptomatic and mildly symptomatic carriers. Due to the impact on older populations, early in pandemic where testing availability was much more limited, most screening was among older age populations or among those with more severe symptoms). There are also external and environmental causes, such as opening of schools and colleges, workplaces, and social gatherings, which may increase exposure and opportunities for transmission.

*Transmission among infants and young children*

Early data show that transmission risk of younger children (0-9 years) is lower than for older children (10-18 years). There is biologic plausibility for this difference (related to ACE2 protein expression and immune responses to virus); however the difference in infection risk between younger and older children/adolescents may also be related to “risk-taking” behaviors (e.g., participating in social gatherings, not wearing masks, etc) and more opportunities for exposure among older children and adolescents.

*School settings*

Our review identified only 10 studies with the primary objective of studying transmission in school settings using primary data. The studies included a wide range of sample sizes (12 children – 13,000 children) and included a wide mix of settings: preschool, primary school, and high school. The studies also had huge variation in format in terms of timing of closing/opening, mask or shield wearing policies and adherence, indoor/outdoor setting, class size, and number of contact hours.

Overall, schools are settings of low child-child transmission and outbreaks were rare. Where outbreaks occurred, there was strong association with regional COVID-19 incidence, suggesting community transmission. Further, two of the studied outbreaks were linked to unmasking due to heatwaves and crowded classrooms.

The type of testing impacts the identification of asymptomatic cases in school settings. Outbreaks in schools have been difficult to identify and many have likely occurred without detection because many children may be asymptomatic and routine testing has been poor. Although teachers are considered a priority vaccination category in many places, and vaccines may soon be available for younger age groups, routine testing will continue to be important for monitoring potential asymptomatic spread, especially in places with high prevalence of variants.

Examples of school transmission from studies included in the systematic review

* Comprehensive surveillance study in Singapore found no evidence of disease transmission in school, including after symptomatic student contact tracing following a known exposure
* Review of all outbreaks in Ireland determined no transmission found in schools (cases linked to family clusters)
* German school case review estimated index cases were in school 2 days/week, and calculated 1 secondary case per every 25 infectious school days
* British summer school study determined outbreaks were rare, but saw strong association with regional COVID incidence, suggesting community transmission
* Australian study found low secondary transmission in schools during first wave
* One secondary school outbreak (Israel) was potentially linked to a heatwave prior, allowing children to unmask, as well as crowded classrooms and high number of contact hours (6h/day plus 2-4 extracurricular)

*Day care settings*

Our review identified only 3 studies with the primary objective of studying transmission in day care settings using primary data. One study tracked cases from daycare to household settings (US); however no routine testing was performed. Another was a case report (South Korea) tracking the contacts of an infected 4 year old from a day care; none of the 190 close contacts tested positive. One study examined child-child transmission across a large geographic area (Germany), but aggregated day care and various levels of schools. Overall, transmission was found to be very low.

*Overnight camps*

Our review identified only 2 studies with the primary objective of studying transmission in overnight camps using primary data, with both papers from the US. In one, COVID spread efficiently among children (6-19) and staff at an overnight camp in the state of Georgia despite camp claims of following recommended safety practices. In the other, no secondary transmission was identified at four overnight camps in the state of Maine. The study reported diligent use of multiple mitigation measures. In both studies, the safety procedures were measured retrospectively, rather than prospectively at the time of case transmission.

*Family clusters and community settings*

Our review identified 42 studies focusing on family cluster, and 20 focusing on community settings, with the primary objective of studying transmission using primary data. Despite poor age disaggregation, most studies of children 0-9 show reduced likelihood of infection as compared to adults (less likely to be an infected contact in contact tracing and case cluster studies). In most studies, it was difficult to identify if transmission was in household or community, as members of household units may have exposure at various community events or interactions, even with safety precautions in place, and timing of exposure or transmission was unknown.

Overall, there were very few studies on adolescents, especially outside of schools; however, most indicate similar infection rates for adolescents and adults.

*Child-Adult transmission*

Transmission risk between adults and children has conflicting evidence whether same risk or lower risk of infection among children. A number of studies show lower susceptibility to infection only among younger children, but similar rates of infection risk between older children, adolescents, and adults. As measured by PCR (nasopharyngeal swabs), infected children age 5-18 had the same viral load as adults, but lower amounts of virus for children under 5 years[[41]](#footnote-41). However, most of these data are from intra-household studies and contact tracing of known positive cases, which may undercount asymptomatic spread, especially among children. Where contact tracing has been done, children were far less likely to be identified as the index case for adult cases. There have been documented cases of transmission from infected children to their adult close contacts (daycare-acquired cases; contact tracing from hospital studies). When routine screening of children was performed, more cases were identified with more possible transmission than with contact tracing of known cases alone. Overall, child-adult transmission outside of household settings is minimal compared to adult transmission, although this is likely compounded by lockdowns and other closures.

**Beyond transmission**

Although the review focused on transmission, there are important other aspects to consider with regards to pregnant women, children, and adolescents and COVID-19. Much of the research early in the pandemic focused on transmission, but outcomes for those infected, and long term consequences of exposure and infection will become more important in the future. This is an overview of some of the additional areas that warrant attention and, although the search strategy of the systematic review captured studies in each of these areas, analysis has not yet been conducted, and findings are drawn from other data sources.

*Children with underlying medical conditions*

Disease severity appears to be worse in children with underlying medical conditions, however most data come from high income countries and focus on chronic illnesses (such as cancer, obesity, and immunosuppressive illnesses). There are few papers on infection risk among children with COVID19 and illnesses common in low income countries, such as malaria and diarrhea. More data are clearly needed on the disease progression patterns, and by age, of children with common illnesses. Even into the second year of the pandemic, there had not yet been good analysis yet related to transmission risk and nutritional status or syntheses of data related to transmission risk of individuals (including children) living with HIV.

In data from high income countries, it appears that congenital cardiac disease is a severe risk factor for infants less than 1 year with SARS-CoV-2 infection. [[42]](#footnote-42) However, despite early concerns about the impact of a respiratory virus on children with breathing difficulties, Asthma was not found to be more prevalent among children with severe vs mild symptoms of COVID[[43]](#footnote-43).

It is also worth noting that children with medical conditions (who may be identified as “high risk”) may self-select for lower exposure risk (“shielding”) and, in some settings, may be able to get accommodations more easily in order to keep exposure lower.

*Disease progression*

There are many studies documenting disease progression among individuals who are infected with SARS-CoV-2 and present for care. However, due to the nature of hospital-based records and potential bias of self-selection, it is difficult to generalize about overall patterns in every age group.

In a published review of 77 studies, pregnant women with COVID were less likely to have symptoms than non-pregnant women with COVID, but were slightly more likely to need intensive care. This may include treatment bias, as pregnant women may be more likely to be admitted for monitoring. Noted risk factors for advanced disease in pregnant women include pre-existing medical conditions and obesity[[44]](#footnote-44), which are known as risk factors for more severe outcomes of COVID within the general population.

Similarly, neonates born to mothers with COVID were more likely to be preterm and require intensive care, but again there may be a possible treatment bias due to interest in additional monitoring for these infants[[45]](#footnote-45).

Among children infected with SARS-CoV-2, the signs and symptoms appear to be mostly similar between children and adults with children generally having less frequency of symptoms. There are some notable exceptions, as children have been found to be slightly more likely to present with gastrointestinal symptoms, diarrhea, and nausea/vomiting, compared to adults.

Clinical progression appears to be milder in children than adults with fewer patients needing ventilation or intensive care. Children with COVID also had a lower risk of pneumonia and lower likelihood of irregular radiology than adults with COVID[[46]](#footnote-46).

In examinations of case fatality ratio, mortality was much lower among younger age groups (as of the end of 2020: age 0-4 = 0.22% and age 5-19 =0.08%, compared to adults). There are consistent increases in mortality risk with age, with case fatalities over age 60 = 6-27%.

One alarming sequelae of COVID-19 among children is the risk of Multi-Inflammatory Syndrome in Children (MIS-C) and inflammatory response. In cities with high prevalence ratios of COVID cases, a small but greatly-increased number of children presented with Kawasaki-like syndrome as a result of an uncontrolled inflammatory response after SARS-CoV-2 infection. Although there is still little known about MIS-C, it appears that the risk is slightly higher among male children, and there is no evidence yet of increased risk of MIS-C with the introduction of new SARS-CoV-2 variants.

It is worth noting that different countries have different diagnostic criteria for MIS-C (including the USA and UK) and that these cases may not be well-monitored in low and middle income countries. The World Health Organization has begun a study of MIS-C and Severe Covid-19 (in children) in 5 low and middle income countries (as of January 2021), and more information about this risk may be forthcoming[[47]](#footnote-47).

*Equity issues*

It is clear that the pandemic has had a disproportionate impact on marginalized individuals and communities, and especially ethnic and racial minority groups. In data from the USA, Black and Hispanic children were found to have significantly higher rates of COVID, even after adjusting for age and median household income[[48]](#footnote-48). Among those infected, there are significant racial disparities in severity of illness among children, although this is likely due to children in minority groups more likely to have underlying conditions and have unequal access to medical care.

Many pediatric studies, including those from school and daycare settings with aggregated data, do not report on race or ethnicity, and few papers from outside of USA and UK address race or ethnicity, despite every country having ethnic groups with historical and current inequities. Even where disease acquisition is highly inequitable, disease progression is closely linked to access to care; where care is universal, mortality rates are more similar[[49]](#footnote-49).

Although there are some slight indications that male children are more likely to have inflammatory disease as a result of SARS-CoV-2, in general, there does not appear to be clear association with sex of child and severity of disease.

***Research implications***

*Evidence gaps*

From early in the pandemic, it appeared that the severity of disease and higher rates of mortality were occurring in the elderly population. Many of the first reports were case studies or reports of infected cases at a single health center, mainly comprising adults and elderly patients. Cases among children and adolescents were not identified as easily, as many cases were asymptomatic and required routine or universal testing to find. Because of the focus on the elderly population, there were few studies from schools and among youth. Further, as the need for data was urgent, many early studies came from hospital-based records, which are often already designed for aggregation and analysis. Few schools or day care centers are set up to collect consent and data from students and parents, and standardized tools may not have been available. Thus, despite the impact of the pandemic on schools, day care settings, and other community institutions, there are still few systematic, prospective studies on school transmission.

In a global health crisis, standardization is helpful for comparing prevalence rates and trends. Across studies, there is no standard age disaggregation. Further, in cases of school and community transmission, there is no standard for the frequency of asymptomatic testing and in many cases, data from various types of tests (with potentially different sensitivities, specificities, and error rates) were combined. It is difficult with a respiratory virus to identify exact duration of exposure, but details around contact hours in schools and other institutions were often not defined in transmission studies.

Overall, there are insufficient surveillance systems, especially in low and middle income countries, and even fewer systems that are able to collect and analyze data quickly. The importance of real-time data in a changing pandemic is paramount. There are many fewer studies from low-income countries, especially those with large populations and high likelihood of having variants.

*Emerging areas of concern*

As we are now in the second year of the COVID-19 pandemic, new questions have emerged. Although transmission data will continue to be important, especially as variants with different characteristics arise, much of the information needed for governments and health systems to reduce virus exposure and mitigate transmission risk while maintaining services is already known. However, longitudinal research is urgently needed to understand the longer term impacts of the virus and ways to combat it as greater numbers of people survive and live with the disease, develop and maintain antibodies to the virus, and become vaccinated against primary or secondary infection.

There is a need for better pediatric data, especially standardized age-disaggregated data globally. Further, pediatric and adolescent cohorts should be established and followed. These studies could help explore the implications of immunity, co-morbidities, disease severity, and treatment response. As children may be exposed multiple times, the needs for mitigation measures and vaccinations may change, but some sub-populations may still be more vulnerable to infection or severe disease than others. More studies are needed with routine surveillance and population data, including asymptomatic random testing which can identify those children who are not obviously ill but may be spreading virus.

There is a need for more and continuing antibody and immunity research. It is still unclear how long natural immunity may last, and why this duration differs greatly among individuals. It is not known if pregnant women, infants or children have shorter or longer immunity, and why they may or may not mount as robust a defense or maintain higher or lower antibody titer levels. There is new evidence that protective antibodies can be transferred through the placenta, and the newborn may receive more of them if the mother is infected with SARS-CoV-2 earlier in her pregnancy[[50]](#footnote-50). There is also new evidence indicating that newborns can acquire protective antibodies if the mother is vaccinated during pregnancy[[51]](#footnote-51). Observational studies going forward should include pregnant women and their newborns and should consider the inclusion of participants who may have asymptomatic disease.

As vaccines become more available and a larger part of the population obtains acquired immunity, special attention is needed to the effects of the vaccine on pregnant women and fetuses. There is an urgent need to include pregnant women and children in vaccine trials in order to understand the potential risks of vaccines[[52]](#footnote-52). Vaccines are now available in many countries for children above age 5, but children continue to be low priority for vaccination in many settings. Vaccine trials are also beginning to include infants and younger children, but results are not anticipated for at least another year[[53]](#footnote-53). Although early evidence indicates the vaccine is safe, rigorous research is needed to confirm, and further information may be useful, for example if there are optimal times during the pregnancy (gestational age) at which the vaccine would provide the most protection with the least risk, or optimal ages of infants and children to receive the first vaccine or subsequent doses.

Further, as vaccine coverage spreads, more documentation is needed of school testing and vaccine policies. Almost every school in the world has been affected by COVID-19, either directly or indirectly, and the reopening schedules, contexts, and policies are different in every locality. Understanding the situation in each, including indoor/outdoor, school size, teacher susceptibility and vaccination coverage, and mitigation measures, will help identify the most effective policies that can be replicated and adapted in various contexts. Schools should document their reopening policies, vaccination requirements, testing policies, and mitigation strategies, in as standard a way as possible, including confirmation by external observers. Policies about response planning and reporting of positive cases, to families as well as local health authorities, should be developed and shared. Examples of successful school and country case studies should be developed and shared, with details about specific contextual factors, such that other localities can learn from previous experiences.

Studies on the emerging variants have focused on transmissibility more than severity. It is still unknown how the new variants, or reinfection with different variants, might affect immunity (either from previous infection or vaccination), or disease severity. As new variants are identified and circulate, it will be crucial to understand the impact on the specific populations of pregnant women, newborns, and children.

The pandemic has had a vastly inequitable impact on vulnerable populations both between and within countries. Although a lot of research has disaggregated the mortality impacts of COVID-19 in adults[[54]](#footnote-54), fewer studies on pregnant women, newborns, and children have provided data disaggregated by race, wealth or sex. There is further need for research on COVID19 and indigenous populations, who have been disproportionately affected throughout the world[[55]](#footnote-55)

The COVID-19 pandemic has highlighted the need for stronger health information systems. Health systems with more robust and “real time” data are better able to forecast need (e.g. for testing, treatment, and critical care) and should be able to better adjust services as capacity or demand changes Countries and regions with stronger data systems have been better able to understand the impact of the epidemic on various parts of the population. This information can help prioritize groups for vaccinations, and where vaccine roll out has been slow, can help design mitigation strategies that protect the most vulnerable. Countries must be supported to be able to report on age and sex specific information, both for monitoring COVID-19 and to prepare for future pandemics.

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**Appendices**

Appendix A: Search strategies

*Direct effects perinatal and pediatric COVID review - Medline search strategy*

 ((((("Coronavirus"[MeSH Terms] OR (("severe acute respiratory syndrome coronavirus 2"[Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2"[All Fields]) OR "2019 ncov"[All Fields])) OR ((((((("covid 19"[All Fields] OR "covid 2019"[All Fields]) OR "severe acute respiratory syndrome coronavirus 2"[Supplementary Concept]) OR "severe acute respiratory syndrome coronavirus 2"[All Fields]) OR "2019 ncov"[All Fields]) OR "sars cov 2"[All Fields]) OR "2019ncov"[All Fields]) OR (("wuhan"[All Fields] AND ("Coronavirus"[MeSH Terms] OR "Coronavirus"[All Fields]))))) OR "SARS-CoV2"[All Fields]) OR (("Coronavirus"[MeSH Terms] OR "Coronavirus"[All Fields]) OR "coronaviruses"[All Fields])) AND ((((( (((((((“pregnancy”[All Fields] OR “pregnant”[All Fields] OR "birth"[All Fields] OR "birthed"[All Fields]) OR "birthing"[All Fields]) OR "Parturition"[MeSH Terms] OR "Parturition"[All Fields]) OR "intrapartum"[All Fields]) OR "births"[All Fields])) OR (((("obstetric"[All Fields] OR "obstetrically"[All Fields]) OR "obstetrics"[MeSH Terms]) OR "obstetrics"[All Fields]) OR "obstetrical"[All Fields])) OR ((("postpartum period"[MeSH Terms] OR ("postpartum"[All Fields] AND "period"[All Fields])) OR "postpartum period"[All Fields]) OR "postpartum"[All Fields])) OR ("postnatal"[All Fields] OR "postnatally"[All Fields] OR "post-natal"[All Fields] OR “post-natally”[All Fields])) OR (("perinatal"[All Fields] OR "perinatally"[All Fields])) OR “newborn”[All Fields] OR “newborns”[All Fields] OR “new-born”[All Fields] OR “newly-born”[All Fields] OR "neonatal"[All Fields] OR "neonate"[All Fields] OR "neonatal"[All Fields] OR "stillbirth"[All Fields] OR "stillbirths"[All Fields] OR "stillborn"[All Fields] OR "stillborn infant"[All Fields] OR "stillborn infants"[All Fields]) OR ("birth outcome"[All Fields] OR "birth outcomes"[All Fields]) OR ("reproductive loss"[All Fields] OR "pregnancy loss"[All Fields] OR "fetal death"[All Fields] OR "fetal demise" OR “foetal death”[All Fields] Or “foetal demise”[All Fields]) OR ("amniotic" OR "placenta"[All Fields] OR "placental"[All Fields] OR "breastmilk"[All Fields] OR "breastfeed"[All Fields] OR "breastfeeding"[All Fields] OR "lactate"[All Fields] OR "lactating"[All Fields] OR “vertical transmission”[All Fields] OR “mother-to-child transmission”[All Fields] OR “MTCT”[All Fields] OR ("infant"[All Fields] OR "infants"[All Fields] OR "infancy"[All Fields] OR "young children"[All Fields]) OR ("pediatric"[All Fields] OR "pediatrics"[All Fields] OR “paediatric”[All Fields] OR “paediatrics”[All Fields] OR "child"[All Fields] OR "children"[All Fields] OR "youth"[All Fields] OR "adolescent"[All Fields] OR "teenage"[All Fields] ) ))) AND (2015:2020[pdat])) AND (("2019/11/01"[Date - Publication] : "2020/06/30"[Date - Publication]))

*Direct effects perinatal and pediatric COVID review - Medline search strategy TRANSMISSION ONLY*

 ((((("Coronavirus"[MeSH Terms] OR (("severe acute respiratory syndrome coronavirus 2"[Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2"[All Fields]) OR "2019 ncov"[All Fields])) OR ((((((("covid 19"[All Fields] OR "covid 2019"[All Fields]) OR "severe acute respiratory syndrome coronavirus 2"[Supplementary Concept]) OR "severe acute respiratory syndrome coronavirus 2"[All Fields]) OR "2019 ncov"[All Fields]) OR "sars cov 2"[All Fields]) OR "2019ncov"[All Fields]) OR (("wuhan"[All Fields] AND ("Coronavirus"[MeSH Terms] OR "Coronavirus"[All Fields]))))) OR "SARS-CoV2"[All Fields]) OR (("Coronavirus"[MeSH Terms] OR "Coronavirus"[All Fields]) OR "coronaviruses"[All Fields])) AND ((((( (((((((“pregnancy”[All Fields] OR “pregnant”[All Fields] OR "birth"[All Fields] OR "birthed"[All Fields]) OR "birthing"[All Fields]) OR "Parturition"[MeSH Terms] OR "Parturition"[All Fields]) OR "intrapartum"[All Fields]) OR "births"[All Fields])) OR (((("obstetric"[All Fields] OR "obstetrically"[All Fields]) OR "obstetrics"[MeSH Terms]) OR "obstetrics"[All Fields]) OR "obstetrical"[All Fields])) OR ((("postpartum period"[MeSH Terms] OR ("postpartum"[All Fields] AND "period"[All Fields])) OR "postpartum period"[All Fields]) OR "postpartum"[All Fields])) OR ("postnatal"[All Fields] OR "postnatally"[All Fields] OR "post-natal"[All Fields] OR “post-natally”[All Fields])) OR (("perinatal"[All Fields] OR "perinatally"[All Fields])) OR “newborn”[All Fields] OR “newborns”[All Fields] OR “new-born”[All Fields] OR “newly-born”[All Fields] OR "neonatal"[All Fields] OR "neonate"[All Fields] OR "neonatal"[All Fields] OR "stillbirth"[All Fields] OR "stillbirths"[All Fields] OR "stillborn"[All Fields] OR "stillborn infant"[All Fields] OR "stillborn infants"[All Fields]) OR ("birth outcome"[All Fields] OR "birth outcomes"[All Fields]) OR ("reproductive loss"[All Fields] OR "pregnancy loss"[All Fields] OR "fetal death"[All Fields] OR "fetal demise" OR “foetal death”[All Fields] Or “foetal demise”[All Fields]) OR ("amniotic" OR "placenta"[All Fields] OR "placental"[All Fields] OR "breastmilk"[All Fields] OR "breastfeed"[All Fields] OR "breastfeeding"[All Fields] OR "lactate"[All Fields] OR "lactating"[All Fields] OR “vertical transmission”[All Fields] OR “mother-to-child transmission”[All Fields] OR “MTCT”[All Fields] OR ("infant"[All Fields] OR "infants"[All Fields] OR "infancy"[All Fields] OR "young children"[All Fields]) OR ("pediatric"[All Fields] OR "pediatrics"[All Fields] OR “paediatric”[All Fields] OR “paediatrics”[All Fields] OR "child"[All Fields] OR "children"[All Fields] OR "youth"[All Fields] OR "adolescent"[All Fields] OR "teenage"[All Fields] ) ))) AND (“transmission” OR “transmissible” OR “transmit”) AND (2015:2020[pdat])) AND (("2020/08/01"[Date - Publication] : "2020/08/31"[Date - Publication]))

Appendix B: List of included studies from systematic review

***Vertical transmission***

|  |  |  |
| --- | --- | --- |
| **First Author** | **Year** | **Title** |
| Alzamora | 2020 | Severe COVID-19 during Pregnancy and Possible Vertical Transmission |
| Bahadur  | 2020 |  Adverse outcomes in SAR-CoV-2 (COVID-19) and SARS virus related pregnancies with probable vertical transmission |
| Chen H | 2020 | Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records |
| Fan C | 2020 | Perinatal Transmission of 2019 Coronavirus Disease–Associated Severe Acute Respiratory Syndrome Coronavirus 2: Should We Worry? |
| Hu X | 2020 | Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Vertical Transmission in Neonates Born to Mothers with Coronavirus Disease 2019 (COVID-19) Pneumonia |
| Khan S | 2020 | Impact of COVID-19 infection on pregnancy outcomes and the risk of maternal-to-neonatal intrapartum transmission of COVID-19 during natural birth |
| Lamouroux A  | 2020 | Evidence for and against vertical transmission for severe acute respiratory syndrome coronavirus 2 |
| Li Y | 2020 |  Lack of Vertical Transmission of Severe Acute Respiratory Syndrome Coronavirus 2, China |
| Liu W | 2020 | Clinical characteristics of 19 neonates born to mothers with COVID-19 |
| Lu D | 2020 | Asymptomatic COVID‐19 infection in late pregnancy indicated no vertical transmission |
| Masmejan S | 2020 | Vertical transmission and materno-fetal outcomes in 13 patients with coronavirus disease 2019 |
| Musa A | 2020 | SARS-CoV-2 is not present in the vaginal fluid of pregnant women with COVID-19 |
| Peng Z | 2020 | Unlikely SARS-CoV-2 vertical transmission from mother to child: A case report |
| Pulinx B | 2020 | Vertical transmission of SARS-CoV-2 infection and preterm birth |
| Salvatore C | 2020 | Neonatal management and outcomes during the COVID-19 pandemic: an observation cohort study |
| Tang J | 2020 | No evidence for vertical transmission of SARS-CoV-2 in two neonates with mothers infected in the second trimester |
| Vivanti A | 2020 | Transplacental transmission of SARS-CoV-2 infection |
| Wu Y | 2020 | Coronavirus disease 2019 among pregnant Chinese women: case series data on the safety of vaginal birth and breastfeeding |
| Xiong X | 2020 | Vaginal delivery report of a healthy neonate born to a convalescent mother with COVID‐19 |
| Zeng H | 2020 | Antibodies in Infants Born to Mothers With COVID-19 Pneumonia |
| Chen Y | 2020 | Infants Born to Mothers with a New Coronavirus (COVID-19) |
| Cheng B | 2020 | Clinical Characteristics of Pregnant Women with Coronavirus Disease 2019 in Wuhan, China |
| Han M | 2020 | Sequential Analysis of Viral Load in aNeonate and Her Mother Infected WithSevere Acute Respiratory SyndromeCoronavirus2 |
| Lang, G | 2020 | Can SARS-CoV-2-infected women breastfeed after viral clearance? |
| Jing, L | 2020 | Analysis of vaginal delivery outcomes among pregnant women in Wuhan, China during the COVID‐19 pandemic |
| Liu, P | 2020 | The immunologic status of newborns born to SARS-CoV-2–infected mothers in Wuhan, China |
| Peng, J | 2020 | A Case Report of a pregnant woman infected with Coronavirus disease 2019 pneumonia |
| Sun, M | 2020 | Evidence of mother-to-newborn infection with COVID-19 |
| Tam, P | 2020 | Detectable Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in Human Breast Milk of a Mildly Symptomatic Patient With Coronavirus Disease 2019 (COVID-19) |
| Wang, S | 2020 | A Case Report of Neonatal 2019 Coronavirus Disease in China |
| Wang, X | 2020 | A Case of 2019 Novel Coronavirus in a Pregnant Woman With Preterm Delivery |
| Wu, Y | 2020 | Neonatal outcome in 29 pregnant women with COVID-19: A retrospective study in Wuhan, China |
| Gabriel, MAM | 2020 | Negative Transmission of SARS-CoV-2 to Hand-Expressed Colostrum from SARS-CoV-2–Positive Mothers |
| Gabriel, MAM | 2020 | Multicentre Spanish study found no incidences of viral transmission in infants born to mothers with COVID-19 |
| Filimonovic, D | 2020 | Intrauterine transfusion in COVID-19 positive mother vertical transmission risk assessment |
| Garcia-Manau, P | 2020 | Fetal Transient Skin Edema in Two Pregnant Women With Coronavirus Disease2019 (COVID-19) |
| Alberca RW | 2020 | Pregnancy, Viral Infection, and COVID-19 |
| Capobianco G | 2020 | COVID-19 in pregnant women: A systematic review and meta-analysis |
| Slayton-Milam, S | 2020 | Induction of Labor in an Intubated Patient With Coronavirus Disease 2019 (COVID-19) |
| Pereira, A | 2020 | Clinical course of coronavirus disease-2019 in pregnancy |
| Polónia, R | 2020 | Vaginal delivery in a woman infected with SARS-CoV-2 – The first case reported in Portugal |
| Yan, J | 2020 | Coronavirus disease 2019 in pregnant women: a report based on 116 cases |
| Yu, N | 2020 | No SARS-CoV-2 detected in amniotic fluid in mid-pregnancy |
| De Socio, GV | 2020 | Delivery in Asymptomatic Italian Woman with SARS-CoV-2 Infection |
| Forero DePena, DA | 2020 | The first pregnant woman with COVID-19 in Venezuela: Pre-symptomatic transmission |
| Gordon, M | 2020 | Rapid systematic review of neonatal COVID-19 including a case of presumed vertical transmission |
| Grimminck, K | 2020 | No evidence of vertical transmission of SARS- CoV -2 after induction of labour in an immune- suppressed SARS- CoV-2- positive patient |
| Huntley, B | 2020 | Rates of Maternal and Perinatal Mortality andVertical Transmission in PregnanciesComplicated by Severe Acute RespiratorySyndrome Coronavirus 2(SARS-Co-V-2) Infection |
| Iqbal, SN | 2020 | An Uncomplicated Delivery in a Patient with Covid-19 in the United States |
| Khoury, R | 2020 | Characteristics and Outcomes of 241 Births toWomen With Severe Acute RespiratorySyndrome Coronavirus 2 (SARS-CoV-2)Infection at Five New York CityMedical Centers |
| Kirtsman, M | 2020 | Probable congenital SARS-CoV-2 infectionin a neonate born to a woman with activeSARS-CoV-2 infection |
| Knight, M | 2020 | Characteristics and outcomes of pregnant women admitted to hospital with confirmed SARS-CoV-2 infection in UK: national population based cohort study |
| Lackey, K | 2020 | SARS-CoV-2 and human milk: what is the evidence |
| Lowe, B | 2020 | COVID-19 vaginal delivery – A case report |
| Matar, R | 2020 | Clinical Presentation and Outcomes of Pregnant WomenWith Coronavirus Disease 2019: A Systematic Review andMeta-analysis |
| Melo, GC | 2020 | COVID-19 infection in pregnant women,preterm delivery, birth weight, and verticaltransmission: a systematic review andmeta-analysis |
| Patane, L | 2020 | Vertical transmission of coronavirus disease 2019:severe acute respiratory syndrome coronavirus 2RNA on the fetal side of the placenta in pregnancieswith coronavirus disease 2019 - positive mothers and neonates at birth |
| Penfield, C | 2020 | Detection of severe acute respiratory syndrome coronavirus 2 in placental and fetal membrane samples |
| Schwartz, D | 2020 | Infections in Pregnancy With COVID-19 and OtherRespiratory RNA Virus Diseases Are Rarely, If Ever,Transmitted to the Fetus |
| Schwartz, D (March) | 2020 | An Analysis of 38 Pregnant Women With COVID-19,Their Newborn Infants, and Maternal-Fetal Transmissionof SARS-CoV-2 |
| Yu, N (May) | 2020 | Clinical features and obstetric and neonatal outcomes of pregnant patients with COVID-19 in Wuhan, China: a retrospective, single-centre, descriptive study |
| Zheng, T | 2020 | Coronavirus disease 2019 (COVID-19) in pregnancy: 2 case reports on maternal and neonatal outcomes in Yichang city, Hubei Province, China |
| Cheruiyot, I | 2020 | Is there evidence of intra-uterine verticaltransmission potential of COVID-19 infection insamples tested by quantitative RT-PCR? |
| Rubin., E | 2020 | Detection of COVID-19 in a Vulvar Lesion |
| Walker, KF | 2020 | Maternal transmission of SARS-COV-2 to theneonate, and possible routes for suchtransmission: a systematic review and criticalanalysis |
| Richtmann, R | 2020 | Fetal deaths in pregnancies with SARS-CoV-2 infection in Brazil:A case series |
| LaCourse, S | 2020 | Low Prevalence of Severe AcuteRespiratory Syndrome Coronavirus2 Among Pregnant and PostpartumPatients With Universal Screening inSeattle, Washington |

***Pediatric transmission***

|  |  |  |
| --- | --- | --- |
| **First Author** | **Year** | **Title** |
| Goldstein E | 2020 | On the effect of age on the transmission of SARS-CoV-2 in households, schools and the community |
| Zhen-Dong Y | 2020 | Clinical and transmission dynamics characteristics of 406 children with coronavirus disease 2019 in China: A review |
| Davies N | 2020 | Age-dependent effects in the transmission and control of COVID-19 epidemics |
| Cao Q | 2020 | SARS-CoV-2 infection in children: Transmission dynamics and clinical characteristics |
| Le HT | 2020 | The first infant case of COVID-19 acquired from a secondary transmission in Vietnam |
| Li Q | 2020 | Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus–Infected Pneumonia |
| Gudbjarsson | 2020 | Spread of SARS-CoV-2 in the Icelandic Population |
| Danis K | 2020 | Cluster of Coronavirus Disease 2019 (COVID-19) in the French Alps, February 2020 |
| Jung J | 2020 | Investigation of a nosocomial outbreak of coronavirus disease 2019 in a pediatric ward in South Korea: successful control by early detection and extensive contact tracing with testing |
| Han Y | 2020 | The transmission and diagnosis of 2019 novel coronavirus infection disease (COVID‐19): A Chinese perspective |
| Cook K | 2020 | Horizontal transmission of severe acute respiratory syndrome coronavirus 2 to a premature infant: multiple organ injury and association with markers of inflammation |
| Posfay-Barbe | 2020 | COVID-19 in Children and the Dynamics of Infection in Families |
| Qian G | 2020 | COVID-19 Transmission Within a Family Cluster by Presymptomatic Carriers in China |
| Wongsawat J | 2020 | Risk of novel coronavirus 2019 transmission from children to caregivers: A case series |
| Yousaf AR | 2020 | A Prospective Cohort Study in Non-hospitalized HouseholdContacts With Severe Acute Respiratory Syndrome Coronavirus 2 Infection: Symptom Profiles and Symptom Change Over Time |
| Yung CF (October) | 2020 | Household Transmission of Severe Acute Respiratory Syndrome Coronavirus 2 from Adults to Children |
| Li P | 2020 | Transmission of COVID-19 in the terminal stages of the incubation period: A familial cluster |
| Li W | 2020 | Characteristics of Household Transmission of COVID-19 |
| Wang Z | 2020 | Household transmission of SARS-CoV-2 |
| Jing QL | 2020 | Household secondary attack rate of COVID-19 and associated determinants |
| Nassih H | 2020 | Absence of Evidence of Transmission of Coronavirus Disease 2019 from a Young Child to Mother Despite Prolonged Contact |
| Wolf G | 2020 | Household transmission of SARS-CoV-2 |
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